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ABSTRACTS

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Schälbasis Joint Session mit der European Association of Neurosurgical Societies (EANS)/*Skull base Joint session with European Association of Neurosurgical Societies (EANS)*

V001

Unterschiede des intraoperativen Samplings während Meningeom-Operationen bezüglich der ZNS-Invasion - Ergebnisse einer Umfrage im Namen der EANS Schädelbasis-Sektion.

Differences in intraoperative sampling during meningioma surgery regarding CNS invasion – results of a survey on behalf of the EANS skull base section.

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Objective

Invasive growth of meningiomas into CNS tissue is rare but of prognostic significance. While it has entered the WHO classification as a stand-alone criterion for atypia, its real prognostic impact is controversial. Retrospective analyses, on which the current evidence is based, show conflicting results. Discordant findings might be explained by different intraoperative sampling methodologies that lead to heterogenous histopathological diagnostic yield.

Methods

To assess the currently applied sampling methods in the light of the novel prognostic impact of CNS invasion, an anonymous survey was designed and distributed via the EANS website and E-Mail newsletter. The survey was open from June 5th 2022 until July 15th 2022.

Results

Overall, 155 responses were submitted, and after exclusion of 13 incomplete responses, 142 (91.6%) datasets were used for further statistical analysis. Only 47.2% of the participants" institutions utilize a standardized sampling method during meningioma surgery, and 54.9% regularly attempt a complete sampling of the area of contact between the meningioma surface and adjacent CNS tissue. The majority did not change their sampling practice since the WHO classification of 2016 (77.5%). More participants agreed with the statement that CNS invasion could be detected intraoperatively (82.4%) compared to detection by preoperative MR-imaging (58.5%). Intraoperative suspicion of CNS invasion changes the sampling for half of the participants (49.3%). An additional sampling of suspicious areas of interest is done in 53.5%. Dural attachment and adjacent bone are more readily sampled separately if tumor invasion is suspected (72.5% and 74.6%, respectively), compared to meningioma tissue with signs of CNS invasion (59.9%).

Conclusion

Current intraoperative sampling methods during meningioma resection vary among neurosurgical departments. In light of the integration of CNS invasion into the WHO classification, insufficient awareness of the need for a structured and complete sampling to optimize the diagnostic yield of CNS invasion exists. A standardized sampling recommendation is needed.

Schälbasis Joint Session mit der European Association of Neurosurgical Societies (EANS)/*Skull base Joint session with European Association of Neurosurgical Societies (EANS)*

V002

Die endoskopische endonasale Resektionstechnik von Clivuschordomen
Endoscopic endonasal resection technique of clival chordomas

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Objective

To demonstrate the surgical technique for endoscopic endonasal resection of skullbase chordomas (video session).

Methods

3 patients with interesting skullbase chordomas will be presented focussing on the surgical technique.

Results

1. A 36-year-old female with a history of deep venous thrombosis 6 months ago which required anticoagulation (Marcumar) presented with sudden headache and third nerve palsy. CT scan showed a haemorrhage into a clival lesion. While waiting for MR imaging she developed a hemiparesis and a complete cavernous sinus syndrome. An emergency endonasal transclival resection was performed and a gross total resection achieved. Hemiparesis and cavernous sinus syndrome resolved soon after surgery.
2. A 2.5-year-old boy presented with bilateral abducens paly. Although very young, an endonasal gross total resection was possible. Abducens palsy improved only on one side.
3. A 42-years-old female presented just with headache. CT and MR imaging showed a giant chordoma involving clivus and craniovertebral junction. A 2-staged resection was performed. At first the endoscopic endonasal approach was choosen. One day later, a dorsal approach with resection of the residual tumor and craniovertebral fusion was performed. She made an uneventful recovery. MR imaging showed a near total tumor removal.

Conclusion

The endoscopic endonasal transclival approach is the procedure of choice for most chordomas because they are midline lesions arising from the clivus. All nerves are displaced laterally which reduces the risks of neurological deficits.

Therapie neurovaskulärer Erkrankungen I/*Therapy of neurovascular diseases I*

V003

Rolle der Mikroskop-integrierten ICG-Angiographie im Vergleich zur nicht Mikroskop-integrierten ICG-Angiographie in der Aneurysmachirurgie

Evaluation of the role of microscope-integrated ICG angiography in comparison to conventional ICG angiography in aneurysm surgery

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Objective

Indocyanin-green angiography (ICG-A) is a frequently used tool in aneurysm surgery. A new technique is the integration of the fluorescence as a green overlay into the microscopic image. Recently, it has been claimed that the use of this microscope-integrated ICG-A may better support the work-flow, since the surgeon has not to look onto a separate video screen while providing the same information as the conventional ICG-A. The aim of the study was to evaluate if this assumption of superiority holds true.

Methods

The video recordings of 20 patients (15 female, 5 male) undergoing aneurysm clipping were re-evaluated. The only inclusion criteria was that the microscope-integrated ICG-A as well as the conventional ICG-A were available in full length Using a 3-level Likert scale, two raters compared four decisive criteria for good operability in the two video sequences: illumination of the operation field, visibility of large, medium-sized and small vessels, influence of heartbeat-associated pulsations, and quality of green overlay. A 3-point Likert scale was used for comparison. In addition, angiographic proof of aneurysm occlusion (yes, no) was assessed.

Results

Complete aneurysm occlusion could be confirmed by both methods. Overall, 2.1 parameters were assessed as good for the microscope-ICG-A and 2.5 parameters for the conventional one. The microscope-integrated sequence was more often rated as good for illumination of the surgical field (1.8 times more often). However, pulsations were noticeable in the microscope-integrated ICG angiography in 12/20 patients (60%); in 8/12 patients, the pulsations disturbed the interpretation of the image. Irrespective of the pulsations, the green overlay was moderate (n=7) or poor (n=10) in 17/20 patients (85%). In additional six patients, the conventional ICG-A delineated small vessels, while medium-sized and large vessels can be visualized by both techniques.

Conclusion

For fundamental information (occlusion of the aneurysm, normal flow in large vessels), both techniques could be used. However, more subtle changes such as perforator occlusion or flow reduction might remain unnoticed, if conventional ICG-A is substituted by microscope-integrated ICG-A, outweighing the benefit of a less hindered workflow for the surgeon.

Therapie neurovaskulärer Erkrankungen I/*Therapy of neurovascular diseases I*

V005

Natürlicher Verlauf von zerebralen und spinalen kavernösen Malformationen: Eine vollständige Zehn-Jahres-Nachbeobachtungsstudie

Natural Course of Cerebral and Spinal Cavernous Malformations: A Complete Ten-Year Follow-Up Study

A. Santos[1], H. Gull[2], L. Rauschenbach[2], A. Olbrich[2], T. F. Dinger[3], M. D. Oppong[3], C. Rieß[2], B. Chen[2], A. Lenkeit[2], R. Jabbarli[2], K. Wrede[2], U. Sure[2], P. Dammann[2]

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Objective

Investigate the natural course of cavernous malformations (CM) of the central nervous system (CNS) over a 10-year period, with special emphasis on the risk of first and recurrent bleeding.

Methods

Our institutional database was screened for patients with intracerebral or intramedullary CM admitted between 2003 and 2021. Patients with complete magnetic resonance imaging (MRI) dataset and clinical baseline characteristics were included. Patients who underwent surgical CM removal and patients without completed 10-year follow-up were excluded. Kaplan–Meier and Cox regression analyses were performed to determine the cumulative 10-year risk for hemorrhage.

Results

91 CM patients were included. Cox regression analysis adjusted for age and sex identified bleeding at diagnosis (HR, 2.41 [95% CI, 1.05-5.54], P=0.039) and CM localization to the spine (ISCM) (HR, 4.2 [95% CI, 1.40-12.57], P=0.010) as predictors for (re)hemorrhage during follow-up. Both risk factors remained independent predictors through multivariate cox regression analysis (aHR, 2.31 [95% CI, 1.00-5.35], *P*=0.049), and (aHR, 3.91 [95% CI, 1.29–11.78], *P*=0.016) respectively. The cumulative 10-year risk of bleeding was 29.7% (95% CI, 20.8%-40.3%) for the whole cohort, 38.8% (95% CI, 25.6%-53.8%) for patients with bleeding at diagnosis and 66.7% (95% CI, 24.1%-94%) for ISCM

Conclusion

During an untreated 10-year follow-up, the probability of hemorrhage increased over time, especially in cases with bleeding at presentation and spinal cord localization. The intensity of such increase may decline throughout time but remains considerably high. These findings may indicate a rather aggressive course in patients with ISCM and may endorse early surgical treatment.

Therapie neurovaskulärer Erkrankungen I/*Therapy of neurovascular diseases I*

V006

Zerebrale Kavernöse Malformation: Stellt eine DVA einen Risikofaktor für die chirurgische Behandlung dar?
Cerebral Cavernous Malformation: Does a Developmental Venous Anomaly represent a risk factor for surgery?

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Objective

Goal of this study was to analyze the impact of Developmental Venous Anomaly (DVA) on the clinical course and outcome after surgical removal of Cerebral Cavernous Malformation (CCM) lesions. In our institution, the surgical policy is to systematically spare DVAs during CCM resection.

Methods

Medical records of patients with CCM referred to our institution from 2003 to 2020 were analyzed. Adult patients with sporadic CCM, complete magnetic resonance imaging dataset, clinical data and ≥ 1 follow up investigation after surgical resection were included. Patients with associated DVA were highlighted. Multiple factors regarding functional outcome were scanned by using univariate and multivariable regression with $p < 0.05$. Preoperative and postoperative neurological function was assessed using the modified Rankin Scale (mRS)

Results

154 patients were included in this study; 54 of 154 presented associated DVA (CCM + DVA).The mean age in the CCM+DVA group was 38.5 ± 14.8 years, and 35 individuals (64.8%) were female, while the group without associated DVA (CCM-DVA) had a mean age of 38.5 ± 14.0 years and 59 female individuals (59%). In the CCM + DVA group, 30 lesions (55.6%) were located supratentorial, while 12 (22.2%) were located in the brainstem and 12 (22.2%) in the cerebellum. The group without associated DVA showed 60 lesions (60%) supratentorial, 23 (23%) in the brainstem and 20 (20%) in the cerebellum. The mean preoperative mRS in the CCM + DVA group was 1.7 (± 0.9), in the CCM – DVA group 2.0 (± 0.8), while the mean mRS within 3 – 6 months after surgical resection of the CCM lesion was 1.28 (± 1.0) in the CCM + DVA group, and 1.3 (± 0.9) in the CCM – DVA group. At last follow-up investigation (median last follow-up: 24 months after surgical resection), the mRS was 0.65 (± 0.89) in the CCM + DVA group, and 0.9 (± 0.9) in the CCM – DVA group. Mann-Whitney U and Chi-square tests identified significant differences in the lesion localization between the two groups ($p = 0.001$), as well as significant differences in the neurological status preoperatively ($p = 0.046$) and at last follow-up ($p = 0.049$) for the benefit of the CCM + DVA group.

Conclusion

Patients with CCM and associated DVA did not show a worse neurological performance after surgery compared to patients with CCM but without associated DVA. DVA does not represent an additional risk in the surgical resection of CCM if intentionally spared during surgery.

Therapie neurovaskulärer Erkrankungen I/*Therapy of neurovascular diseases I*

V007

Ergebnisse nach präoperativer transarterieller Embolisation und Resektion von zerebralen Arteriovenösen Malformationen in einem großem Neurovaskulären Zentrum.

Preoperative Transarterial Embolization followed by Microsurgical Resection of Cerebral Arteriovenous Malformations: Outcome Analysis of a High-Volume Neurovascular Center.

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Objective

The role of preoperative embolization of AVM prior to surgery is still under debate. In this study we evaluated the outcome and results of a large series of patients with cerebral arteriovenous malformations (AVM) who underwent preoperative transarterial embolisation followed by microsurgical resection in a high-volume neurovascular center using the supplemented Spetzler-Martin Grade.

Methods

We retrospectively analysed 131 AVM surgeries on 119 patients in a time period from 2014 to 2021. All patients harboured AVMs and were treated with combined embolization following resection in each case. The data were collected from paediatric and adult patients including all treated ruptured and unruptured AVMs between 2014 and 2021. Patient"s age ranged from 4 to 87 years. Spetzler-Martin grades (SM), supplemented Spetzler-Martin grades (sSM) as well as neurological outcome using the mRS score prior to surgery and upon discharge were measured and compared to a recent metaanalysis on the outcome of AVM surgery.

Results

In the examined period we treated 65 unruptured (54.6%) and 54 ruptured (45.4%) AVMs. Preoperative transarterial embolization in multiple sessions was performed prior to microsurgical resection in every single case independent from AVM grade. Neurological deterioration of mRS scores were observed in 21 patients (17.6%). Mortality rate was 1.7 %. There was deterioration in SM Grades I-V in 3.3%, 8.1%, 25%, 26.3% and 33.3% respectively. Using the sSM grading score neurological deterioration was 9%, 21%,27%, 55%, 50%, 40% gradually from sSM grade 4-9. The observed data were significantly better in higher sSM scores compared to the multicenter cohort of 1009 surgical patients published by Kim et al. (Validation of the Supplemented Spetzler-Martin Grading System for Brain Arteriovenous Malformations in a Multicenter Cohort of 1009 Surgical Patients, Neurosurgery 76(1), 2015).

Conclusion

Preoperative transarterial embolization followed by microsurgical resection seems to be beneficial in regard to neurological outcome especially in high risk patients.

Therapie neurovaskulärer Erkrankungen I/*Therapy of neurovascular diseases I*

V008

Präoperative Embolisation und operative Behandlung zerebraler AV Malformationen (Spetzler Martin III-V) - Ergebnis bei 245 Patienten

Preoperative Embolization and Surgical Treatment of Spetzler Martin Grade III-V Brain AVMs – Results from 245 Patients

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Objective

Our study aimed to evaluate the efficacy, outcomes and safety of preoperative embolization for Spetzler Martin grade III-V brain arteriovenous malformations (bAVMs).

Methods

The clinical and imaging records of all patients treated with endovascular embolization before surgical resection between January 1992 and December 2021 were reviewed. The senior author participated in the endovascular treatment of all patients. The endovascular treatment occurred in three institutions, and 58 neurosurgeons performed the operations. Patient demographic data, imaging characteristics including aneurysms, number of embolization procedures and which material was used, complications resulting in a new permanent deficit after either embolization or surgery, and mRS were recorded.

Results

We identified 245 patients; 57.6% were male, 158 (64.4%) were unruptured, and the average age at first embolization was 36.2±15.4. Regarding angiographic appearance, 60% were SM III, 33.5% SM IV, and 6.5% were SM V. In 72.8% of cases, no aneurysms were seen. An average of 5.71±5.52 embolizations were performed, and in 69.5% of cases, >80% of the AVM vasculature was excluded from the circulation. The clinical outcome was as follows:

mRS	0-2 (%)	3 (%)	4-5 (%)	6
pre, N=245	221 (90.2)	11 (4.5)	13 (5.3)	0
post embolization	212 (86.5)	14 (5.7)	19 (7.8)	0
post surgery	200 (81.6)	21 (8.6)	15 (6.1)	9 (3.7)

An average of 1.1±0.3 surgical procedures was performed. Angiographic imaging following surgery was available in 227 patients. Post-surgery complete excision of the AVM was seen in 187 (82.4%), and residual nidus was seen in 40 patients (17.6%). The mean length of follow-up was 99.1±95.6 months.

Conclusion

Large brain AVMs involving eloquent brain regions remain a therapeutic challenge. Preoperative embolization can achieve significant devascularization, and combined embolization and surgery result in high rates of cure for SM grade III-IV bAVMs. The associated morbidity and mortality, however, are not negligible.

SAB Behandlung/*SAH treatment*

V009

Korrelation von Perfusionsdefiziten in der CT-Perfusion mit Abweichungen des zerebralen Perfusionsdruckes vom individuell errechneten optimalen zerebralen Perfusionsdruck bei Patienten mit aneurysmatischen Subarachnoidalblutung

Correlation of perfusion deficits on CT perfusion with deviations of actual cerebral perfusion pressure from individually calculated optimal cerebral perfusion pressure in patients with aneurysmal subarachnoid hemorrhage

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Objective

Preservation of an optimal cerebral perfusion is a crucial part of acute management in patients with aneurysmal subarachnoid hemorrhage (aSAH). A few studies indicated possible benefits of maintaining a cerebral perfusion pressure (CPP) near the calculated optimal CPP (CPPopt), representing an individually optimal condition at which cerebral autoregulation functions at its best. The of this study was to investigate, whether "suboptimal" perfusion with actual CPP deviating from CPPopt correlates with perfusion deficits detected by CT-perfusion (CTP).

Methods

Consecutive patients with aSAH and with available parameters for CPPopt-calculation, who simultaneously received CTP during the acute phase after the bleeding, were enrolled in the study. Pressure reactivity index (PRx) was calculated as the correlation coefficient between ICP and MAP in a four-hour time window. By plotting PRx versus CPP, CPP correlating the lowest PRx value, was identified as CPPopt. The CTP-parameters were measured, and perfusion deficits were documented.

Results

In 86 out of 324 patients the inclusion criteria were met, which were included in the analysis. Mean age was 54±11 years, 65% of whom were female. Median WFNS grade was 4, and all patients had high Fisher grade of ≥ 3. Perfusion deficits were detected in 47% (40/86) of all patients. In 43% of analyzed patients, CPP was lower than CPPopt, which correlated with more often detected perfusion deficits ($r=0.23$, $p=0.03$). Perfusion deficits were found in 62% of patients with CPP<CPPopt compared to 34% in patients without deviation or CPP>CPPopt (OR 3, $p=0.01$).

Conclusion

A deviation of actual CPP from individually calculated CPPopt with CPP<CPPopt correlated with a higher incidence of perfusion deficits detected on CTP. Although the study was not powered to demonstrate causality, these findings support the hypothesis, that a deviation of CPP from CPPopt may indicate possibly suboptimal cerebral perfusion, and trigger further diagnostic and therapeutic measures.

SAB Behandlung/*SAH treatment*

V010

Dekompressive Kraniektomie in Patienten mit aneurysmaler Subarachnoidalblutung - Vergeblicher Versuch oder Lebensretter?

Decompressive craniectomy in patients with aneurysmal subarachnoid hemorrhage – Futile attempt or live saver?

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Objective

Decompressive craniectomy (DC) is an established treatment option for intracranial refractory hypertension in patients with traumatic brain injury or stroke. However, the clinical benefits of DC in patients with aneurysmal subarachnoid hemorrhage (aSAH) are highly controversial.

Methods

We retrospectively reviewed our department"s records for patients with an aSAH between 2010 and 2021. Patients with complete medical records and a minimum follow-up of 6 months who were treated with DC were included in this analysis. By using the Hunt&Hess grading, initial severity of aSAH was grouped into mild (°1-3), and severe (°4-5). In addition to patient demographics, we evaluated initial aneurysm treatment modality as well as the timing, and the reason for DC. Outcomes were evaluated using the modified Rankin scale, separated in favorable outcome (0-3), unfavorable outcome (4-5), and deceased (6).

Results

Between 2010 and 2021, 548 patients were treated for aSAH in our department. Hereof, 68 underwent DC and were included in this analysis. The majority received microsurgical clipping as primary aneurysm treatment modality (59%, n=40) while 41% (n=28) received endovascular aneurysm embolization. On average, DC was performed on day 4 (±3) after aSAH. Among the included patients, 25 (37%) presented with a mild, and 43 (63%) with a severe aSAH. Most patients required DC because of generalized brain edema (52%, n=35), 26% (n=18) had delayed cerebral infarction, and 22% (n=15) intracerebral hemorrhage (ICH). Favorable outcome was observed in 30 patients (44%), while 23 (34%) patients showed unfavorable outcome, and 15 patients (22%) died during hospitalization. Although not statistically significant, we observed the highest rates of unfavorable outcome or death if DC was performed for ICH (67%), while patients with generalized brain edema showed the highest rates of favorable outcomes (51%). Initial severity of aSAH did not appear to have a significant influence on outcomes (p=0.800), while patients with favorable outcome were younger (49 years ±10) than patients who died or had unfavorable clinical outcome (55 years ±11, p=0.024).

Conclusion

While DC in aSAH patients is associated with high rates of morbidity and mortality, a significant number of patients achieved favorable clinical outcome. In contrast to age, initial severity of aSAH did not appear to significantly influence the outcome after DC. The highest rates of favorable outcomes were observed if DC was performed for generalized brain edema.

SAB Behandlung/*SAH treatment*

V011

Therapie und Behandlungsergebnis von Patienten mit einer spontanen Subarachnoidalblutung – erste Ergebnisse der prospektiven Registerstudie

Therapy and outcome of treatment in patients with spontaneous subarachnoid hemorrhage – first results of prospective register study

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Objective

Up to 70% of all patients develop cerebral vasospasm within 14 days after aneurysmal SAB. Nimodipine is given to prevent vasospasm and subsequent DCI. Studies have shown no difference between oral and intravenous administration with regard to the outcome or new infarctions. We have performed the detailed outcome evaluation.

Methods

A total of 51 patients have been included in our prospective, bicentric, non-randomized registry study and followed up after three months.The characteristics of patients according to demographic data, therapy, neurological improvement and outcome score (National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), Montreal Cognitive Assessment Test (Moca), Glasgow Outcome Score (GOS), Reha-Phase) were analyzed and correlated with the application method of nimodipine.

Results

The WFNS score and mWFNS score were 1 in 52.9% of the patients, the HH score was between 1 and 3 in 76.5% Median of the Moca tests was 10.5 on admission and the average NIHSS was 8.4. The most common type of treatment was coiling (62.7%). 60.8% of the patients developed a vasospasm, 51% initially received nimodipine intravenously. Patients receiving nimodipine only intravenously had an average NIHSS of 10.5 at admission and 6.6 at discharge. Patients receiving nimodipine orally had NIHSS of 3 at admission and 0.7 at discharge. 3.9% initially received nimodipine intraarterially. The mean NIHSS on admission was 16 and on discharge 24.5. In 71.4% of the patients, the therapy was switched to intravenous nimodipine. A switch to intraarterial therapy was necessary in 10.2% of patients (NIHSS at admission 18.4, NIHSS at discharge 14.8). Most patients had GOS of five (39.2%) at discharge. The most common mRS value was 1 (35.3%), followed by five (21.6%). The NIHSS at discharge averaged 5.7. In the MOCA test, the patients had median score of 21. 54.9% of patients were discharged from a regular ward and 23.5% of patients need a B rehabilitation phase. Mortality achieved 7.8%. In the follow-up after three most patients had GOS 5 (57.4%) and mRS 1 (46.8%), the NIHSS averaged 2.98 and in the Moca median was 23 points.

Conclusion

Most patients benefit from the therapy and achieve a good clinical outcome measured by Moca, NIHSS and GOS. Most of the patients are discharged form a normal ward. Intravenous our intra-arterial application of nimodipine might be an option as the escalation therapy in severe vasospasm and DCI which can result in a good clinical outcome.

SAB Behandlung/*SAH treatment*

V012

Vorhersage der Shunt-Abhängigkeit nach aneurysmatischer Subarachnoidalblutung anhand ventrikulärer Messungen.

Predicting shunt dependency after aneurysmal subarachnoid hemorrhage with ventricular measurements.

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Objective

Chronic hydrocephalus requiring shunt placement is a common complication of aneurysmal subarachnoid hemorrhage (SAH). Different risk factors and prediction scores for post-SAH shunt dependency have been evaluated so far. We analyzed the value of ventricle measurements for prediction of shunt dependency in SAH patients.

Methods

Eligible SAH cases treated between 01/2003 and 06/2016 were included. Initial computed tomography scans were reviewed to measure ventricle indices (bifrontal, bicaudate, Evans", ventricular, Huckman"s, and third ventricle ratio). Previously introduced CHESS and SDASH scores for shunt dependency were calculated. Receiver operating characteristic analyses were performed for diagnostic accuracy of the ventricle indices and to identify the clinically relevant cutoffs.

Results

Shunt placement followed in 221 (36.5%) of 606 patients. In univariate analyses, all ventricular indices were associated with shunting (all: $p<0.0001$). The area under the curve (AUC) ranged between 0.622 and 0.662. In multivariate analyses, only Huckman"s index was associated with shunt dependency (cut-off at ³6.0cm, $p<0.0001$) independent of the CHESS score as baseline prediction model. A combined score (0-10 points) containing the CHESS score components (0-8 points) and Huckman"s index (+2 points), showed better diagnostic accuracy (AUC=0.751) than the CHESS (AUC=0.713) and SDASH (AUC=0.693) scores, and the highest overall model quality (0.71 vs. 0.65 and 0.67) respectively.

Conclusion

Ventricle measurements are feasible for early prediction of shunt dependency after SAH. The combined prediction model containing the CHESS score and Huckman"s index showed remarkable diagnostic accuracy regarding identification of SAH individuals requiring shunt placement. External validation of the presented combined CHESS-Huckman-score is mandatory.

SAB Behandlung/*SAH treatment*

V013

Der Einfluss der Liquordrainage auf die Schwere der frühen Hirnschädigung in den ersten Tagen nach Aneurysmaruptur bei einer aneurysmatischen Subarachnoidalblutung

Impact of cerebrospinal fluid drainage in the first days after aneurysm rupture on the severity of early brain injury following aneurysmal subarachnoid hemorrhage

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Objective

Progressive brain edema with refractory intracranial hypertension (ICP) requiring decompressive hemicraniectomy (DHC) represents a severe early brain injury (EBI) after aneurysmal subarachnoid hemorrhage (aSAH). The EBI-pathophysiology is multifactorial, whereby the intracranial blood burden belongs to the contributors to EBI after aSAH. The aim of this study was to evaluate whether a more pronounced cerebrospinal fluid (CSF) drainage promoting a faster blood clearance has an impact on cerebral perfusion pressure (CPP) and EBI-severity after aSAH.

Methods

A retrospective analysis of consecutive aSAH-patients admitted to the Department of Neurosurgery Göttingen, from 2012 to 2020 was performed. EBI-grading was conducted considering the intracranial blood burden, persistent loss of consciousness, and the SEBES (Subarachnoid Hemorrhage Early Brain Edema Score) score on day 3 after ictus. The drained CSF and vital signs such as ICP and CPP were documented on a daily base.

Results

In 90 out of 324 consecutive aSAH patients (28%) an ICP monitoring was performed were included in this study. The mean age was 54.2 ± 11.9 years (range 28-80). DHC was performed in 26% (23/90) of the included patients. Mean CSF drainage within the first 3 days after ictus was 168.5 ± 78.5 ml. A higher CSF drainage within 72 h after ictus correlated with a less severe EBI and consequently less frequent need for DHC (r=-0.2949, p=0.004) and with a higher mean CPP on day 3 after ictus (r=0.2351, p=0.02).

Conclusion

A more pronounced CSF drainage in the first 3 days after aneurysm rupture was associated with higher CPP and a less severe course of EBI requiring less frequently a DHC, which supports the hypothesis that an early and pronounced CSF drainage may facilitate blood clearance and positively influence the course of EBI.

SAB Behandlung/*SAH treatment*

V014

Funktionelles Outcome nach VP Shunt Anlage im Zeitraum von zerebralen Vasospasmen bei Hydrozephalus nach Subarachnoidalblutung

Safety and functional outcome of ventriculoperitoneal shunt placement for hydrocephalus after subarachnoid hemorrhage within the period of possible delayed cerebral ischemia

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Objective

Shunt-dependent hydrocephalus (HC) is a common sequela following subarachnoid hemorrhage (SAH). However, there is still poor evidence as to the optimal timing of ventriculoperitoneal shunt (VPS) placement, particularly in the context of early complications such as delayed cerebral ischemia (DCI). The purpose of this study was to compare the impact of early (<21 days after SAH) versus late VPS placement (≥21 days after SAH) on functional clinical outcome.

Methods

Data from 92 patients with VPS placement after SAH enrolled in our institutional database between 2011-2021 were analyzed retrospectively. We compared 2 groups, early VPS placement (<21 days after SAH) vs. late VPS placement (≥21 days after SAH) in terms of demographics, SAH grading, radiological parameters, externalized cerebrospinal fluid diversions, DCI, VPS variables and functional outcome.

Results

62 patients with early and 30 patients with late VPS implantation were identified. Baseline variables, such as modified Rankin Scale (mRS: p=0.3), WFNS, GCS and Fisher grade were not significantly different between both groups. Postoperative mRS (p=0.002), Glasgow Outcome Scale (GOS: p=0.002) and extended Glasgow Outcome Scale (GOS-E: p=0.0028) showed significantly better functional results in patients with early cerebrospinal fluid diversion. The rate of DCI did not differ significantly between both groups (p=0.45). There was no difference in the rate of VPS placement associated complications (p=0.38) or overall mortality (p=0.35).

Conclusion

Early shunt implantation, within the first 21 days after SAH and during the time of possible DCI, might not be harmful in patients developing HC after SAH.

Neurophysiologie, IOM und Bildgebung I Motor mapping, Konnektivität und Netzwerke/*Neurophysiology, IOM & imaging Motor mapping, connectivity and networks*

V015

Kartierung des supplementär-motorischen Areals mittels repetitiver navigierter transkranieller Magnetstimulation

Mapping of the supplementary motor area using repetitive navigated transcranial magnetic stimulation

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Objective

The supplementary motor area (SMA) plays an important role in both motor and language function yet may be inadvertently damaged due to growth of a lesion or surgical procedures. Recently, a protocol to map the SMA using repetitive navigated transcranial magnetic stimulation (rnTMS) has been proposed. The aim of this study was to validate and extend this protocol for both hemispheres and lower extremities.

Methods

To this purpose, the SMA regions of both hemispheres were mapped based on a finger tapping task performance of 30 healthy subjects (35.97±15.11, range 21-67 years; 14 females) using rnTMS at 20 Hz (120% resting motor threshold (RMT)). Points with induced errors were marked on the corresponding MRI and a SMA hotspot was identified. For this hotspot, a bimanual finger tapping task and the Nine-Hole Peg Test (NHPT) were performed additionally. Further, the lower extremity was mapped using a toe tapping task at 20 Hz (140% RMT).

Results

In 24 out of 30 healthy subjects SMA mapping of the upper extremity was successful (13 bi-hemispherically, 11 uni-hemispherically). Mean finger tapping scores were significantly reduced during stimulation (25.70 taps) compared to baseline (30.48; $p<0.01$). Bimanual finger tapping led to a significant increase in taps during stimulation (28.43 taps) compared to unimanual tapping ($p<0.01$). Compared to baseline, a significant increase in completion time for the NHPT could be observed during stimulation (baseline: 13.6s, stimulation: 16.4s; $p<0.01$). For the lower extremity, replicable errors could be induced in 28 out of 30 subjects in at least one hemisphere.

Conclusion

The present study validated and extended an rnTMS-based protocol to map upper and lower extremity motor function over the SMA. Hence, this protocol could further be used to acquire a better understanding of the functional SMA organization and potentially help to improve preoperative planning for patients with lesions within this region.

Neurophysiologie, IOM und Bildgebung I Motor mapping, Konnektivität und Netzwerke/*Neurophysiology, IOM & imaging Motor mapping, connectivity and networks*

V016

nTMS-basierte neurophysiologische Analyse der motorischen Erregbarkeit anhand von 888 motorisch-eloquenten Hirntumoren

nTMS-based neurophysiological analysis of motor excitability based on 888 motor-eloquent brain tumors

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Objective

Navigated transcranial magnetic stimulation (nTMS) has been established as a routine preoperative assessment of motor-eloquent tumors near the motor cortex and the corticospinal tract. Here we analyse the relationship between various tumour variables and nTMS derived neurophysiological data in a large cohort of patients.

Methods

We retrospectively analysed the prospectively collected cohort of patients with motor-eloquent brain tumors who underwent resection in our department during the last 11 years (2011-2022). All patients received a preoperative nTMS motor mapping with bihemispheric determination of the resting motor threshold (RMT), which is representative for the excitability of the motor system. In addition to histopathologic diagnosis and WHO grading, we also included presence of edema, recurrency, contrast agent enhancement, number of tumors (for metastases) and IDH/MGMT status (for gliomas).

Results

We included 888 patients (mean age: 54.1 years; 482 women), of whom 482 had right hemispheric tumors (54.3%) and 189 (21.3%) suffered from recurrence. Glioma (503; 56.6%), metastases (208; 23.4%), vascular malformations (69; 7.8%) and meningiomas (43; 4.8%) were the most common entities. More patients with malignant tumors (glioma WHO III°/IV° or metastases) had pathologic interhemispheric excitability (bihemispheric RMT ratio <90% or >110%) compared to benign lesions (62.6% vs. 43.6%) (p = .001). Subgroup analysis of glioma patients revealed that a balanced interhemispheric excitability (bihemispheric RMT ratio 90%-110%) was detected more frequently in WHO grade I°/II° glioma (49.2% vs. 37.6%) (p =.060), in patients with IDH mutation (49.0% vs. 34.7%) (p = .006) and with MGMT promoter methylation (45.8% vs. 34.5%) (p = .044).

Conclusion

Malignant tumors (gliomas and metastases) impaired the excitability of the motor system significantly more than benign lesions. This effect was even more pronounced in IDH wild-type and MGMT nonmethylated gliomas, suggesting a relevant correlation and potentially diagnostic utility of genetic tumour profiles and TMS-derived excitability measures. Innovative multivariate analyses (such as AI-based methods) should be applied to match neurophysiological clusters of motor excitability and biological tumour profiles.

Neurophysiologie, IOM und Bildgebung I Motor mapping, Konnektivität und Netzwerke/*Neurophysiology, IOM & imaging Motor mapping, connectivity and networks*

V017

Der Effekt von unterschiedlichen klinischen und anatomischen Faktoren auf die kortikale Erregbarkeit gemessen mit transkranieller Magnetstimulation (TMS)

The effect of distinct clinical and anatomical factors on cortical excitability measured with transcranial magnetic stimulation (TMS)

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Objective

Preoperative assessment of motor and language function using navigated transcranial magnetic stimulation (nTMS) is becoming increasingly popular in neurosurgical practice. The resting motor threshold (RMT) is a measure of the cortical excitability and has been identified as predictor for the postoperative motor outcome. Thus, a reliable assessment of the RMT is crucial to integrate nTMS results into preoperative planning. Nonetheless the RMT presents a wide inter-individual variation can potentially impact the accurate assessment of the RMT. The aim of the present study was to examine the effect of multiple clinical and anatomical factors on variability of the RMT in neurosurgical patients.

Methods

653 patients (288 females, mean age 53 ± 15.65, range 19-85 years) were investigated preoperatively using nTMS due to brain tumors affecting the motor cortex and/or the corticospinal tract. The analysed factors were: gender (male, female), age, volume of the peritumoral edema, volume of the tumor, side of the tumor (right/ left hemisphere), skull to cortex distance, histology (glioblastoma, astrocytoma grade 3, other glioma, metastasis, other), tumor recurrence (yes, no), motor deficit of upper extremity (yes, no) and intake of antiepileptic medication (yes, no). A linear mixed model was used to analyse the effect of these factors on the RMT in a between-subjects design.

Results

There was considerable variation in the RMT across subjects (mean 35.39 ± 8.59, range 15-86% of maximum stimulator output). Higher skull to cortex distances as well as presence of a preoperative motor deficit were associated with a higher RMT values ($p<0.01$). Further, patients with a higher preoperative edema volume tended to present with lower RMTs ($p=0.079$). The remaining analysed factors showed no significant effect on the RMT.

Conclusion

Our results align with previous studies showing an effect of the peritumoral edema, skull to cortex distance and motor deficit on the RMT. Conversely, we could not establish a significant relationship between tumor size, intake of antiepileptic medication or histology with RMT as expected by the literature. These results are strengthened by the large sample size of the present study.

Neurophysiologie, IOM und Bildgebung I Motor mapping, Konnektivität und Netzwerke/*Neurophysiology, IOM & imaging Motor mapping, connectivity and networks*

V019

Unterschiedliche Veränderungen präoperativer Fraktionsanisotrope bei Patienten mit Gliomen, Metastasen sowie extra-axialen Tumoren

Distinct alterations of preoperative fractional anisotropy in patients with glioma, metastases, and extra-axial tumors

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Objective

White matter integrity measured by fractional anisotropy (FA) has proven itself as a marker of neurological function and prognostication. However, it remains unclear, how FA is altered by different types of damage, namely compression, edema, or infiltration. We therefore analyzed the relation of corticospinal tract (CST) affection with FA in dependence of the lesion type.

Methods

42 consecutive patients undergoing craniotomy for microsurgical resection of intracranial tumors were retrospectively analyzed (mean age: 59 ± 2 years; female gender: 45%). We applied our tractography workflow to reconstruct the CST in the affected hemisphere and recorded mean FA, streamline count and paresis according to the Janda scale. Tract affection was recorded as 'unaffected', 'dislocated', 'compressed', or 'infiltrated'.

Results

27 patients suffered from glioma, 9 patients from metastases, and 6 patients from extra-axial tumors. Mean FA in the CST of the affected hemisphere was 0.39 ± 0.01. 10 patients suffered from preoperative paresis. In multivariate regression analysis, tract affection was the only predictor of FA decline ($p = 0.022$), while patient age ($p = 0.632$), patient sex ($p = 0.934$), and type of tumor ($p = 0.195$) were not. In group analysis of all glioma patients, FA correlated significantly with tract affection ($p = 0.028$), but not with paresis ($p = 0.116$). For patients with metastases, FA correlated significantly with paresis ($p = 0.027$), but not with tract affection ($p = 0.981$). Group analysis of extra-axial tumors showed no significant correlation of FA with paresis ($p = 0.512$) or tract affection ($p = 0.470$). Importantly, none of the above tests yielded significant results for streamline count of the CST in the affected hemisphere.

Conclusion

FA appears as a useful marker for assessment of functional tract integrity in patients with intra-axial tumors, especially metastases. In evaluation of glioma, FA could be a biomarker of tumor progression along white matter tracts. White matter damage is distinct between different tumor entities. The biological relevance of streamline count remains doubtful.

Neurophysiologie, IOM und Bildgebung I Motor mapping, Konnektivität und Netzwerke/*Neurophysiology, IOM & imaging Motor mapping, connectivity and networks*

V020

Eine erhöhte funktionelle Konnektivität zwischen einem Glioblastom und seiner Umgebung beeinträchtigt die Small-World-Netzwerke des Gehirns.

Increased functional connectivity between glioblastoma and its surrounding disrupts small-world networks of the brain.

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Objective

Small-world networks can be used to describe the physiological connectivity of the brain. Glioblastoma multiforme uses neuronal mechanisms for brain invasion by sending tumor cells to interact with its surrounding and built pathologic networks. Resting-state functional connectivity (FC) analyses can help to study the architecture and complexity of the functional connectome and its vulnerability to tumor-related changes. Here, we applied graph theory to describe the tumor"s connectedness to its peritumoral surrounding as well as its local and global impact on small world networks of the brain.

Methods

54 treatment-naîve glioblastoma patients (mean age: 64±11 years) were included and underwent resting-state fMRI. Tumor lesions were segmented, and different peritumoral distances were created by dilating the tumor mask by 10, 20 and 40mm and subtracting the tumor area. While controlling for tumor volume, tumor to peritumoral (TP10mm, TP20mm, TP40mm) FC was determined and differences were analyzed. The tumor"s impact on a network of whole-brain regions of interest was analyzed by applying graph theory, investigating the association between tumor FC and the whole-brain network"s local and global (inter)connectedness.

Results

The tumor was most highly connected to its directly surrounding peritumoral area TP10mm, and, although still high, TP FC decreased significantly from 10mm to 40mm distance from the tumor (MTP10mm=.69, MTP20mm=.62, MTP40mm=.55, all p<.01). More importantly, functionally higher connected tumors disrupted the small-world network properties of the brain, reducing the whole-brain network"s local efficiency (LE) and clustering coefficient (CC) (rLE-TP20mm=-.336, p=.015; rLE-TP40mm=-.411, p=.003; rCC-TP20mm=-.323, p=.019; rCC-TP40mm=-.387, p=.005), indicating a lower whole-brain"s local integration and interconnectedness in patients with a high coupling of the tumor and its neighborhood.

Conclusion

Resting-state fMRI suggested that glioblastomas are highly functionally connected to their peritumoral surrounding. The disruption of the physiological small-world network properties of the brain indicates disruptions of the functional connectome that go far beyond tumor borders. Investigating tumor-related FC and network dynamics may aid in the identification of tumor infiltration, particularly with regard to neurosurgical resection, and in this way may help to improve functional and oncological outcome.

Behandlung des pädiatrischen Hydrozephalus Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Treatment Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V021

Hypophysenhypertrophie als Langzeitfolge der Implantatione eines ventrikulo-peritonealen Shunts und hoher Liquordrainage: die Läsion erkennen und nicht mit einer Neoplasie verwechseln.

Pituitary hypertrophia as a long-term sequelae of ventriculo-peritoneal shunt insertion and high CSF drainage: Recognize the condition and do not mistake for adenoma.

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Objective

Childhood hydrocephalus patients treated by ventriculo-peritoneal (v.-p.) shunting are sometimes referred years later for evaluation of suspicious pituitary enlargement. We found this radiological finding not to be accompanied by any other clinical, biochemical or imaging signs supporting the diagnosis of pituitary neoplasia, which leads us to believe that this may be a diagnostic pitfall. Since pituitary size depends on cerebrospinal fluid (CSF) pressure, we suppose this phenomenon to be caused by shunt overdrainage. Therefore, we studied pituitary size and morphology in shunted hydrocephalus patients with radiological signs of CSF overdrainage.

Methods

Retrospective exploratory study of pituitary size and morphology in 15 shunted patients with non-tumoral hydrocephalus (8 female, 7 male patients, age at shunt insertion was about 0 years, except for two patients, who received their shunt at age of 8 and 21 years) and 7 shunted hydrocephalus patients due to childhood brain tumor (6 female, 1 male, age at shunt insertion 9,3 years) compared to a published population mean. In five patients from the tumor hydrocephalus group also pre- and postsurgical comparisons could be performed.

Results

All but one patient had a nonadjustable valve implanted. Indirect signs of pituitary adenoma such as a deviation of the pituitary stalk or enlargement of bony sella were absent in all patients. Pituitary mid-sagittal size and pituitary volume were significantly higher in both hydrocephalus groups, as compared to the population mean (mid-sagittal size $t = 5.91$; $p < 0.001$; pituitary volume, $t = 3.03$; $p = 0.006$). In those patients available for pre- and postoperative comparison, there was also a significant increase in pituitary size and volume postoperatively (mean preoperative midsagittal height 2.54 ± 1.0 mm vs. 6.6 ± 0.7mm p.o.; mean pre-operative pituitary volume 120.5± 69.2mm^3 vs. 368.9 ± 57.9mm^3 p.o.).

Conclusion

Our results confirmed a significant increase in pituitary size and volume, mimicking pituitary pathology, after v.-p. shunt insertion. This phenomenon can be explained by the Monro-Kellie doctrine, stating the sum of brain, CSF and intracranial blood volumes to be always constant. Depletion of CSF - as caused by v.p. shunting – leads to compensatory intracranial hyperemia, especially in the venous system with the consequence of engorged venous sinuses, most likely responsible for enlargement of the pituitary gland.

Behandlung des pädiatrischen Hydrozephalus Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Treatment Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V022

Entwicklung des Kopfumfangs bei hydrocephalen Kindern - macht das Ventil einen Unterschied? Differentialdruck- versus Gravitationsventile

Development of Head Circumference during Infancy with Hydrocephalus: Differential Pressure Controlled Valve versus Gravity-Assisted Valve

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Objective

Head circumference is occasionally reduced in children with hydrocephalus treated with a CSF drainage during infancy, thus developing microcephalus. It is believed to be due to overdrainage and has been shown for children treated with differential pressure valves. The use of gravity-assisted valves is known to significantly reduce the rate of overdrainage in shunted patients. If the use of gravity-assisted valves may protect infants from microcephalic development is not yet investigated to the best of our knowledge.

Methods

This retrospective study involved all children from our hospital who were diagnosed with hydrocephalus and treated with a CSF shunt within the first 6 months of life from 1 January 1990 to 31 December 2011. The development of the head circumference while growing up at least six years was documented as well as the etiology of the hydrocephalus and the valve type used. Patient"s gender, weight and height, shunt revision rate, the extent of brain matter defect, and the severity of disability were also collected.

Results

Sixty-two children were eligible for the study. Thirty-four children were treated with differential pressure valves, and twenty-eight children with gravity-assisted valves. The comparison of head circumferences between shunt treated patients and the normal population showed significantly smaller heads only in boys regardless of the used valve type. Head circumference was mainly influenced by weight and height as well as by the amount of brain matter defects and the severity of disability. The smaller and slimmer the children and the worse brain damage and disability was the smaller were their heads. In this cohort boys were more severely affected neurologically and in general development compared with girls. The shunt revision rate did not have any significant impact on the development of head circumference in shunted children.

Conclusion

The development of the head circumference in hydrocephalic children is influenced by the general and neurological development of the entire child and not by the use of a certain valve type. Developmentally and growth retarded children experience smaller heads than their less affected counterparts.

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V023

Programmierbare vs. fixierte Gravitationsventile bei pädiatrischen Patienten mit Hydrozephalus: Eine 16 Jahre retrospektive monozentrische Vergleichsstudie zwischen proSA® und SA®

Programmable vs. fixed gravitational valves in pediatric patients with hydrocephalus: A 16 years retrospective single-center comparative study between proSA® and SA®

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Objective

In pediatric hydrocephalus treatment, programmable gravitational valves offer greater flexibility to manage overdrainage during children"s growth. However, it remains unclear whether these advanced devices feature better outcomes and survival rates than their precursors. To assess pediatric patients" benefit from the programmability of the gravitational valve, i.e., proSA® vs. ShuntAssistent® (SA®).

Methods

In this retrospective single-center study, the clinical records and imaging of pediatric patients with hydrocephalus of non-tumoral etiology, fitted with fixed (SA®) or adjustable (proSA®) gravitational valves between January 2006 and January 2022 were analyzed. Valves explanted starting from mid 2017 were sent to the manufacturer"s laboratory for a biomechanical analysis.

Results

374 gravitational valves (240 SA® and 134 proSA®) were inserted in 226 patients (n=123 males). 118 SA® (49.2%) and 64 proSA® (47.8%) were explanted during a follow-up of 84.8±44.0 months. Valve survival rate at 1 and 5 years with SA® was 86.3% and 62.5% compared to 89.6% and 61.9% with proSA®, while the mean survival time was 54.3±2.7 and 57.7±3.1 months, respectively. Overdrainage alone accounted for significantly more SA® revisions (39.8% vs. 3.1%, $p<0.001$), while dysfunctions of the adjustment system were the first cause of valve replacement in the proSA® cohort (45.3%). The biomechanical analysis performed on 31 SA® and 41 proSA® showed deposits on the valve"s internal surface in 90.3% and 97.6% of the cases.

Conclusion

Both valves showed on long terms almost similar results and survival rates. The programmability may be beneficial in regard to better control of symptoms but with higher revision rate due to dysfunction. The presence of internal deposits might affect the adjustment system representing the major limitation of these sophisticated devices and should be addressed by the manufacturer for future improvements.

Behandlung des pädiatrischen Hydrozephalus Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Treatment Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V024

Häufigkeit und Zeitpunkt von Ventil-Obstruktionen von proGAV und proGAV 2.0 Ventilen implantiert bei Kindern < 3 Jahren mit Hydrocephalus

Frequency and time of shunt valve occlusion of proGAV and proGAV 2.0 valves implanted in hydrocephalic children below 3y of age with hydrocepahlus

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Objective

The standard therapy for pediatric hydrocephalus (HC) is the placement of a shunt system. After introduction of the Miethke proGAV 2.0 valve it was felt that early valve obstruction due to deposits in the valve increased in infants compared to the previous model. The following retrospective institutional analysis compares two cohorts with proGAV (K1) and proGAV2.0 (K2).

Methods

Retrospectively, children who underwent initial implantation at age <3Y in 2012-2014 with proGAV (K1) or 2018-2020 with proGAV2.0 (K2) were included. The minimum follow-up was 1 year. All causes of shunt revision were recorded. Explanted valves were usually investigated at the manufacturer.

Results

K1 consisted of 54, K2 of 48 children. 50/54 children (93%) in K1 received a proGAV, and 41/48 (85%) in K2 a proGAV 2.0. Posthemorragic HC, myelomeningocele, and other congenital malformations were the most common causes of HC in the 2 cohorts, accounting for 26% and 24%, 34% and 24%, and 20% and 21%, respectively. Children's age at implantation and valve setting were not different between groups. 52% of children in K1 and 45% in K2 experienced shunt revision during FU. Both groups had an infection rate of 6% and 7%, respectively. In K2 valve blockages were the only cause of revision, whereas catheter problems were also causes of revision in K1. The interval until the first revision was 516 days in K1 and 210 days in K2. Accordingly, 48% of the revisions in K1 and 84% in K2 took place in the first year of life. Valve obstruction was the cause of revision in 11/26 cases (42%) in K1 and in 16/19 cases (84%) in K2.

Conclusion

Given the good comparability of the cohorts with regard to boundary conditions, a twice as high rate of valve dysfunctions due to deposits in the valve was found in K2 (proGAV2.0) compared to K1 (proGAV). Revisions furthermore were earlier in K2 and took place in 84% of cases in the first year of life, on average after 210 days. There appears to be a structural problem with the new valve type with a tendency for earlier and increased valve dysfunction due to deposits. If multicenter studies with higher case numbers confirm this institutional analysis, the use of the current proGAV 2.0 in first shunt implantations in infancy might not be recommendable.

Gliom Imaging I/*Glioma Imaging I*

V025

Diffusions- und Kontrastmittelverstärkte- Magnetresonanztomographie zur Darstellung der APLN-vermittelten Gefäßfunktion beim murinen GBM

Diffusion- and Contrast Enhanced- Magnetic Resonance Imaging to monitor APLN-controlled vascular function in murine GBM

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Objective

Glioblastoma (GBM) expansion is accompanied by aberrant tumor vascularization. We previously demonstrated that the peptide hormone Apelin (APLN) controls GBM neo-vascularization and that its antagonist Apelin-F13A improved efficiency and reduced side effects of established antiangiogenic therapy. Here, we investigated the impact of APLN on vascular stability and function and established MR-imaging protocols to monitor GBM vascularization.

Methods

To measure vascular tightness, we orthotopically implanted murine or patient-derived GBM cells into mouse brains and analyzed the stabilization of the tumor vasculature by the investment of mural cells by immunofluorescence. We characterized vascular functionality by intravenously injecting Evans blue (EB) dye or fluorescently labelled dextran. Pathological endothelia partially lose their cell-cell contacts showing increased leakage of EB bound albumin. Crossing of solutes through the blood-tumor barrier by endothelial transcytosis was followed by fluorescent dextran. Finally, T2-, diffusion-weighted MRI (DWI) and dynamic contrast enhanced (DCE) MRI was used to follow tumor growth and vascular function.

Results

We found that EB extravasation is significantly increased by 3-fold in APLN-KO tumors compared to wildtype (WT). Dextran uptake by CD31+ endothelia was quantified and increased from 200 µm2 area-covered per high magnification field (HMF) in WT to 3500 µm2 per HMF in APLN-KO. Intracerebral infusion of Apelin-F13A into WT mice enhanced vascular pericyte coverage by 50%, decreased EB extravasation from 25 µg/ml in controls to 8 µg/ml in treated tumors significantly and reversed the APLN-dependent vasogenic edema recorded by the comparison of T2w-MRI to post mortem H&E tumor volumes. For DCE-MRI, T1w 3D FLASH images were acquired every second over a time course of 360s during and after injection of Gd-based MR contrast agent. While in DWI no difference could be observed depending on the presence of APLN, the DCE protocol demonstrated a delayed wash-out of the contrast agent in APLN-KO compared to APLN-WT GBM.

Conclusion

We show that loss-of-APLN in murine GBM leads to increased vascular leakage and that the application of Apelin-F13A can alleviate the GBM-associated vasogenic edema. Utilizing different MRI protocols on APLN-deficient tumors, we found that DCE-MR imaging over a specified time-course is suited to image tumor areas of leaky vasculature in GBM.

Gliom Imaging I/*Glioma Imaging I*

V026

Elastische Fusion von intraoperativen Ultraschal und preoperativen MRT zur Navigationverbesserung in der Gehirntumor Chirugie

Elastic image fusion of intraoperative ultrasound and preoperative MRI for improving navigation accuracy in brain tumor surgery

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Objective

In brain surgery, neuronavgation based on preoperative MRI is limited by various physical and operational factors, such as surgery-induced brain shift.Using navigated intraoperative ultrasound (iUS) imaging and 3D iUS image reconstruction may help improve neuronavigation. However,the registration of MRI and US scans can lead to spatial inconsistencies between the two modalities.This study aims to evaluate the clinical integration of navigated iUS imaging and its potential to improve the accuracy of resection during brain tumor surgery by comparing the performance of rigid and elastic MRI-iUS image fusion algorithms during retrospective evaluation.

Methods

N=50 patients with brain tumors were prospectively enrolled in this trial.The neuronavigation system (BrainLabAG) used in the study allowed for the reconstruction and integration of 3D iUS imaging,which was acquired multiple times throughout the surgery using a tracked ultrasound probe (BKMedical).Protoypes of automatic rigid and elastic MRI-iUS image fusion algorithms (BrainLabElements) were retrospectiveley applied to improve co-registration accuracy between the MRI and iUS data.To evaluate the image co-registration accuracy, anatomical landmarks were defined in the MRI and iUS scans and used to measure Euclidean distances between each landmark pair.

Results

Improvements in the image quality over the course of the study indicated that skills in US handling are essential.Contrast behavior and tumor structure influence the visibility of the tumor in the US.Artifacts caused by hemostatic agents challenge the US image quality and the fluid-filled resection cavity requires experience in probe handling.In terms of image fusion,significant mismatches of the iUS and MRI data were reported.Representative pairs of preoperative MRI and iUS data aquired before resection are shown in Fig.1. For scans aquired before resection,rigid fusion using a novel co-registration algorithm may enhance the registration accuracy with mean target registration errors for two representative patients of 6.5/8.9mm and 3.7/3.4mm before and after registration update,respectively.For iUS scans aquired after resection,rigid fusion is inherently limited due to non-linear brain-shifts.Therefore,elastic image fusion has been applied to provide deformable MR-iUS image co-registration, Fig.2

Conclusion

Navigated iUS imaging can be integrated into clinical routine and the use of MRI-iUS co-registration for updating navigation is a promising tool to compensate brainshift.

Abb. 1

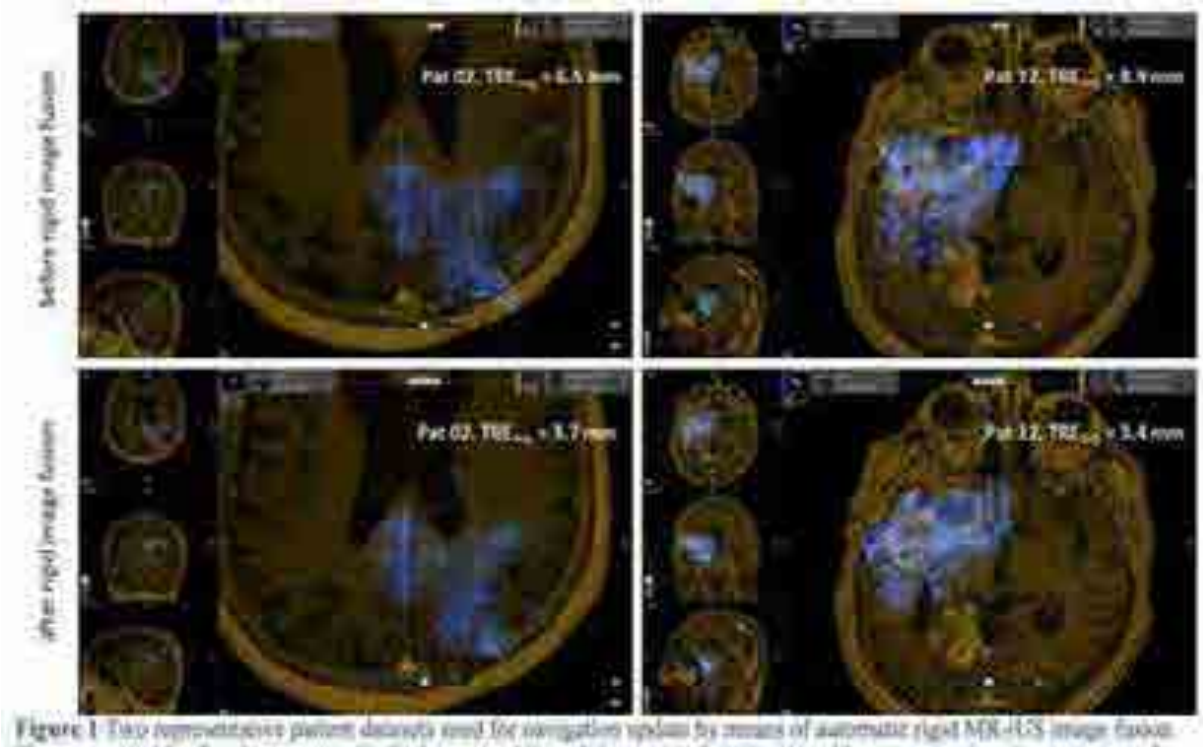

Figure 1 Two representative patient datasets used for navigation update by means of automatic rigid MR-US image fusion. The anatomical landmarks retrospectively determined in each image set show improved image co-registration accuracy of intra-cranial structures with mean target registration errors (TRE_avg) of 6.5 / 8.9 mm and 3.7 / 3.4 mm before and after registration update, respectively.

Abb. 2

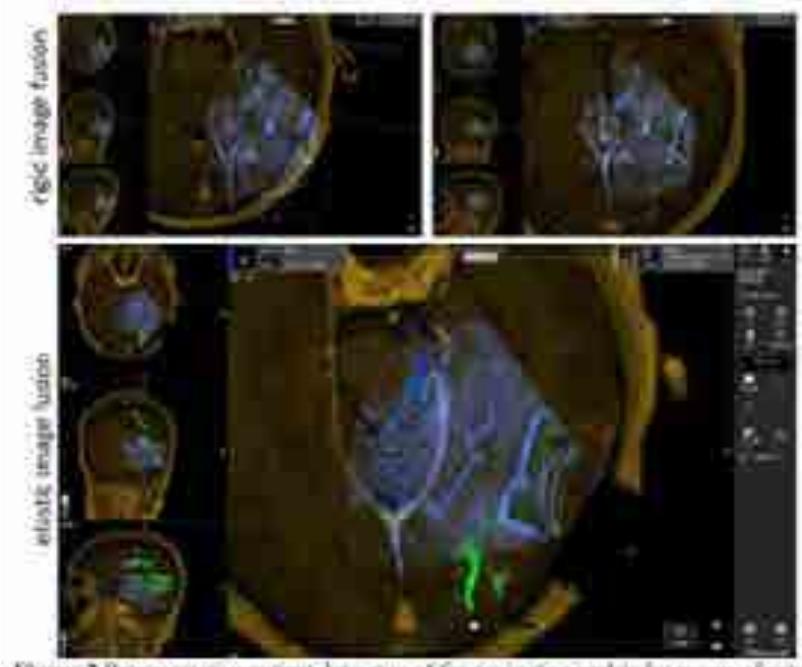

Figure 2 Representative patient dataset used for navigation update by means of automatic rigid (top row) and elastic (bottom row) MR-US image fusion. Initial rigid alignment of MRI and iUS data acquired after resection is required to support elastic image fusion resulting in a 3D deformation vector field (visualized by arrows showing greatest magnitudes in voxels beneath the resection cavity).

Gliom Imaging I/*Glioma Imaging I*

V027

Local and global effects of F-18-fluorethyltyrosin (FET) positive brain tumors on language associated B(lood)O(xygen)L(level)D(ependent) signal

Local and global effects of F-18-fluorethyltyrosin (FET) positive brain tumors on language associated B(lood)O(xygen)L(level)D(ependent) signal

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Objective

FET PET is capable to non-invasively define the extend of gliomas. It is still unclear if FET-positive brain cortex still carries functionality, or if FET-positivity affects neural plasticity of adjacent functions. Therefore, we investigated the effect of FET-positive cortical brain tissue on language associated BOLD signal.

Methods

27 patients (aged 42±yy years) with 15 FET-positive and 12 FET-negative gliomas located in the language critical brain areas were included. Patients underwent presurgical language fMRI by performing a covert verb generation task. fMRI data analysis was done using S(tatistical) P(arametric) M(apping)12 including R(egion) O(f) I(nterest) analysis. Up to 6 spherical ROIs (diameter 10 mm) were defined: (1) located in an overlap area of fMRI signal and FET positivity (only in the FET-positive group), (2) and (3) located in the fMRI signal adjacent to the tumor (not overlapping with the FET signal in the FET-positive group), and reference ROIs in the anterior cingulate cortex (4), in the occipital cortex (5) and in a tumor-contralateral language associated area (6). ROI-dependent percent signal change was calculated and compared between groups and ROI locations using parametric t-tests for independent dependent samples. Additionally, percent signal changes correlated with tumor grade.

Results

Patients with FET-negative tumors showed significantly higher fMRI signal in tumor adjacent ROIs, as well as in the anterior cingulate and the contralateral language area compared to patients with FET-positive tumors ($p<.001$). Both groups showed significantly lower signal in tumor-adjacent ROIs compared to control ROIs ($p<.001$). In the FET-positive group there was no statistical difference between fMRI signal in ROI(1) with overlapping PET/fMRI-signal and ROIs adjacent to PET-signal (ROI2-3). There was no group difference according to tumor grade but there was a significant negative correlation of fMRI signal strength and WHO-grade in the ROI(1) ($p=.009$; $r=-.499$) and reference ROI(5) ($p=.048$; $r=-.391$) and ROI(6) ($p=.-513$, $r=.007$).

Conclusion

These preliminary results indicate that FET-positivity in brain tumors may influence fMRI signal on a global but not a local level independently of tumor grade.

Gliom Imaging I/*Glioma Imaging I*

V028

Der prognostische Wert präoperativer [18F]-FET-PET nach mikrochirurgischer Resektion diffuser niedriggradiger Gliome

The prognostic impact of preoperative [18F]-FET-PET after resection of diffuse lower grade gliomas

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Objective

Amino acid PET with [18F]-fluoroethylthyrosine ([18F]-FET-PET) is frequently used for prognostication and response assessment in treatment of malignant gliomas. For diffuse low grade gliomas (DLGG) or indeterminate grade gliomas, [18F]-FET-PET can inform delineation of metabolically active tumor components and can help guide decisions on surgical strategy. This study sheds light on the prognostic value of [18F]-FET-PET for therapy-naive patients with DLGG.

Methods

Retrospectively, all therapy-naive patients with preoperative [18F]-FET-PET before microsurgical resection 2012-2021 and diagnosed with a WHO grade II (WHO CNS 2016) tumor were included in the analysis. [18F]FET-PET/CT or PET/MRI were quantitatively analyzed. In cases in which dynamic imaging was available, late uptake kinetics were graded as increasing vs. indifferent/decreasing. Imaging measures were correlated with progression-free survival (PFS).

Results

Out of 115 patients, 28 (24%) patients were diagnosed with an oligodendroglioma and 87 patients (76%) with astrocytoma. Tumors of 64 patients (74%) were IDH-mutated and 23 tumors (26%) were of IDH-Wiltdype. 33 patients (32%) did not show significantly elevated tracer uptake. TBRmax values are significantly higher in oligodendrogliomas compared to IDH-mutated astrocytomas ($p<0.001$). IDH status does not affect static uptake parameters of astrocytomas. Increasing late kinetics are associated with longer PFS compared to indifferent/declining kinetics ($p=0.015$). In the subgroup of IDH-mutated astrocytomas without adjuvant treatment, patients with a TBRmax >1.9 showed significantly longer PFS compared to patients with lower TBRmax ($p<0.001$).

Conclusion

Besides being helpful for surgical tumor sampling by depicting tumor heterogeneity, preoperative [18F]-FET-PET is of prognostic importance. Prospective studies need to demonstrate whether [18F]-FET-PET can be used as decision support to vote for or against adjuvant therapies after microsurgical resection.

Gliom Imaging I/*Glioma Imaging I*

V029

Produktion und Evaluation von PET-Tracern über die SuFEx 18F-Fluorination von nanomolaren Precursormengen für die Bildgebung von Hirntumoren

Production and Evaluation of PET-tracers via SuFEx 18F-fluorination of nanomolar precursor amounts for Brain Tumor Imaging

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Objective

Early detection and treatment of malignant brain tumors can significantly improve survival time and life quality of affected patients. While positron emission tomography (PET) with O-(2-[18F]fluoroethyl)tyrosin ([18F]FET) offers improved diagnostic accuracy in comparison to other imaging methods, there is still a need for PET-tracers with greater tumor-specificity. Higher protein incorporation rate as well as higher affinity for the amino acid transporter LAT1 could provide probes with superior image quality compared to [18F]FET. Recently, a protocol for radiolabeling via ultrafast 18F/19F isotopic exchange on aryl fluorosulfates ("SuFEx click radiolabeling") has been described. Although promising, the original procedure proved to be rather inefficient.

Methods

In vitro studies were conducted with MCF-7, PC-3 and U87 MG human tumor cell lines. In vivo µPET studies were carried out in healthy rats with/without benserazide pre-treatment (n=3 each), in mice bearing subcutaneous MCF-7 or PC-3 tumor xenografts (n=10), and in rats bearing orthotopic U87 MG tumor xenografts (n=14). Tracer accumulation was quantified by SUVmax, SUVmean and tumor-to-brain ratios (TBrR).

Results

Careful optimization of the reaction parameters allowed us to develop a robust method for SuFEx radiolabeling which omits any azeotropic drying, external base and, in most cases, HPLC purification. The protocol enables efficient 18F-fluorination of low nanomolar amounts of aryl fluorosulfates in highly diluted solution (micromolar concentrations). Uptake of 3-L-[18F]FPhe in MCF-7 and PC-3 cells was significantly higher than with [18F]FET. In benserazide-treated healthy rats, brain uptake after 42–120 min was significantly higher for 3-D-[18F]FPhe vs. 3-L-[18F]FPhe. [18F]FET showed significantly higher uptake into subcutaneous MCF-7 tumors (52–60 min p.i), while early uptake into orthotopic U87 MG tumors was significantly higher for 3-L-[18F]FPhe (SUVmax: 3-L-[18F]FPhe, 107.6±11.3; 3-D-[18F]FPhe, 86.0±4.3; [18F]FET, 90.2±7.7).

Conclusion

The results show that 3-L- and 3-D-[18F]FPhe enable high quality visualization of tumor tissues with certain advantages over [18F]FET, making them promising candidates for further preclinical and clinical evaluations.

Gliom Imaging I/*Glioma Imaging I*

V030

Peritumorale Glutamat- und Glutamin-Detektion in diffusen Gliomen mittels 7T MRSI
Peritumoral glutamate and glutamine detection in diffuse gliomas using 7T MRSI

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Objective

The worse patient prognosis (Wen et al 2008) of diffuse gliomas originates predominately from their infiltrative growth into surrounding brain parenchyma making tumor resection challenging. Recent research highlighted the role of glutamate (Glu) and the related amino-acid glutamine (Gln) in glioma progression and infiltration (Yao et al 2014, Venkataramani et al 2019). We have developed a 7T MRSI technique able to deliver high-resolution Glu/Gln maps in gliomas, finding Glu heterogeneity within gliomas (Hangel et al 2020).

We hypothesised that 7T MRSI could detect peritumoral changes in Glu that differ from Gln and the MRS standard tCho.

Methods

This study retrospectively evaluated 7T MRSI data of a cohort of 36 glioma patients (3.4 mm nominal resolution, 15 min scan, spectral fitting by LCmodel). We evaluated the resulting metabolite ratios in a tumour segmentation (TU) based on clinical 3T MRI, a normal-appearing white matter (NAWM) control ROI and a peritumoral region (PT, 2cm of brain around the tumour). From PT, GM-voxels were subtracted as the inclusion of higher-Glu GM would skew a comparison to NAWM.

We assessed the differences in the median ratios of Glu/tNAA, Gln/tNAA, tCho/tNAA, Glu/tCr, and Gln/tCr between the ROIs of TU, PT, and NAWM using paired two-sided t-tests.

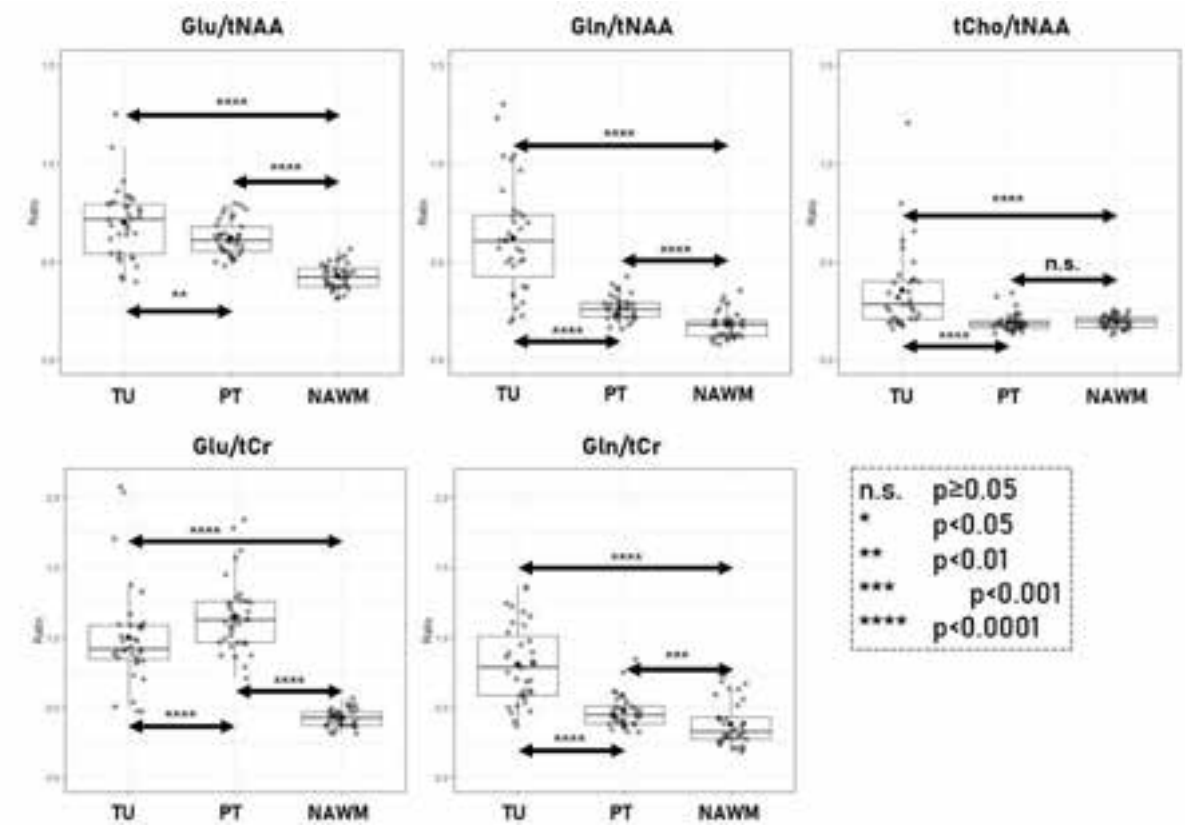
Results

The cohort consisted of 8 WHO grade 2, 9 grade 3, and 19 grade 4 gliomas, and respectively of 6 cases of oligodendroglioma, IDH-mutant and 1p/19q-codeleted; 14 astrocytoma, IDH-mutant; and 16 glioblastoma, IDH-wildtype. For Glu/tNAA, Gln/tNAA, Glu/tCr, and Gln/tCr, all differences were statistically significant (most so for Glu/tCr PT vs NAWM), while for tCho/tNAA only the differences of TU to PT and TU to NAWM were significant, as displayed in Figure 1.

Conclusion

For the first time, we demonstrated significant increases of imaged peritumoral Glu and Gln ratios derived from 7T MRSI compared to NAWM in diffuse gliomas. Consequently, Glu/Gln distributions could offer new insights into the detection of infiltration/progression in diffuse gliomas.

Abb. 1


Glu/tNAA
Gln/tNAA
tCho/tNAA
Glu/tCr
Gln/tCr
TU
PT
NAWM
n.s.
n.s. p≥0.05
* p<0.05
** p<0.01
*** p<0.001
**** p<0.0001

Neuroanatomie und Lehrkonzepte/*Neurosurgical anatomy and teaching concepts*

V031

Arteria vertebralis und paramedianer subokzipitaler Zugang: Orientierungspunkte zur Vermeidung von Verletzungen

Vertebral artery and Paramedian Suboccipital approach: Landmarks to avoid injury

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Objective

Although various landmarks have been defined to identify the V3 segment of the vertebral artery (V3-VA) during diverse approaches to the craniovertebral junction, these landmarks are not routinely exposed during a paramedian suboccipital (PMSO) approach.

Our objective is to present the first system of anatomic and topographic landmarks to identify the V3-VA during the PMSO approach.

Methods

The study was divided in 2 stages. The first was a retrospective analysis of the angiotomography (ATC) of 50 patients, and also 9 formalized heads were dissected. The V3-VA was delimited with 2 vertical lines (line A and line B). A line between the inion and the tip of the mastoid process was then traced (X line); this line was divided in 3 thirds. Then, a correlation between V3-VA and that middle third was sought (Fig 1 A).

The distance between the inion and the superior and inferior edge of V3-VA was measured, to determine its location in the longitudinal plane. With the purpose of capturing the 90% of the cases, those measures were defined as cut points: the 5 percentile for the Upper Cut Point (UCP) and the 95 percentile for Lower Cut Point (LCP). Within the previously mentioned lines the risk area of the vertebral artery (RAsV3-VA) and the risk point of the vertebral artery (RPsV3-VA) were defined (Fig1).

The second stage was prospective, where the previous measurements were carried out by using neuronavigation in 10 patients (20 sides) operated with the PMSO approach in order to confirm the presence of the V3 segment in the RAsV3-VA and RPsV3-VA (Fig 2).

Results

In the first stage, the V3 segment was found in the middle third of the X line in 96,6% of the cases. The distance between the inion and the UCP (percentile 5) was 20 mm and to the LCP (percentile 95) was 40 mm. In the range between the UCP and the LCP, in the middle third of the inion-mastoid line (RAsV3-VA), we found 90% of the V3-VA.

The measurements taken during the second stage revealed that the artery was in the middle third of the X line in 97 % of the cases. 85% of the patients presented the total of the V3s-VA on the RAsV3-VA and in the 85% there was a direct relationship with the V3 segment and the RPV3s-VA (Fig 2 D).

Conclusion

We propose a system of simple implementation in the OR to delimit the risk area of the V3-VA during the PMSO approach. We believe that these landmarks provide a fast, reliable and useful tool that could decrease the risk of lesion of the V3-VA during this approach.

Abb. 1

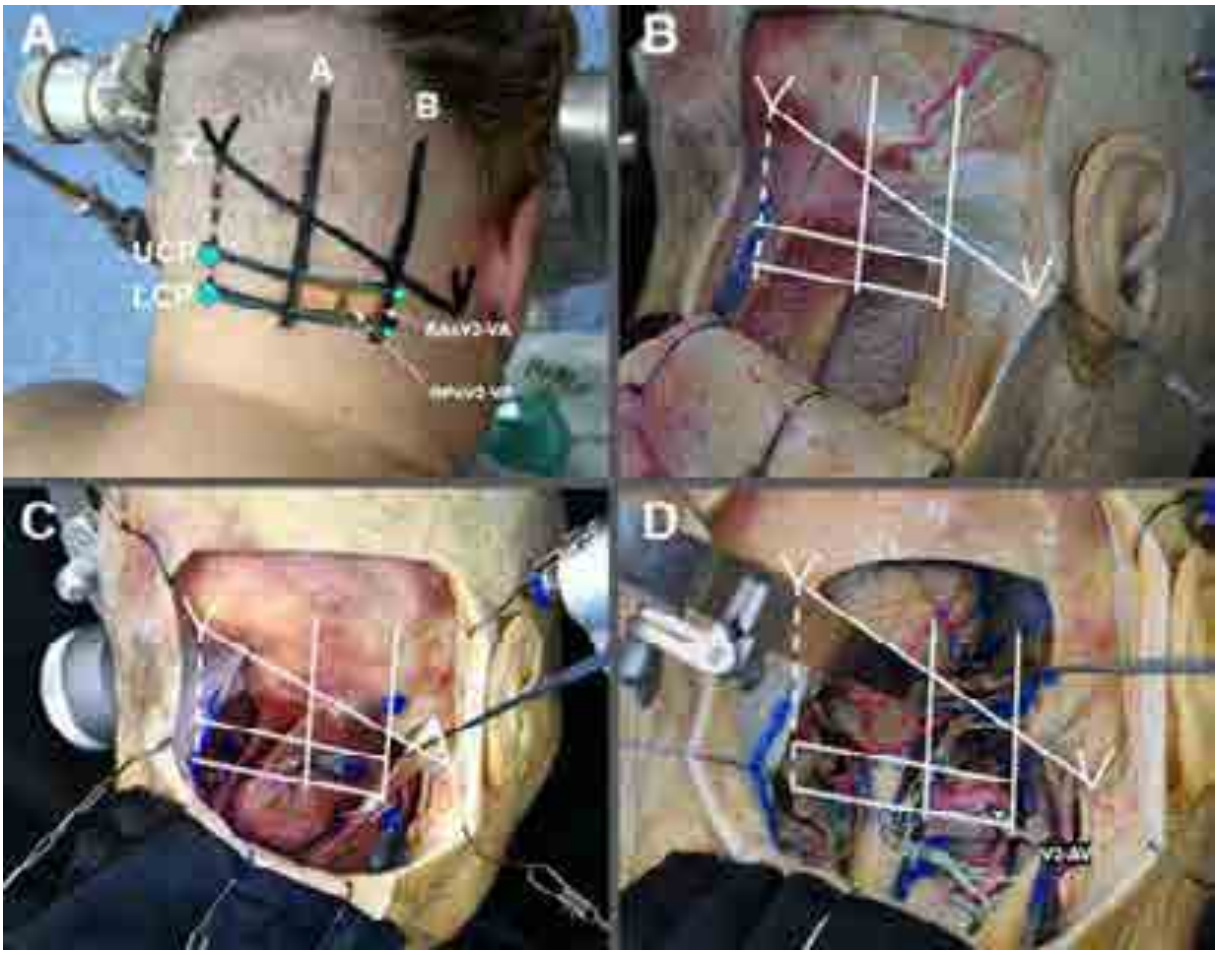
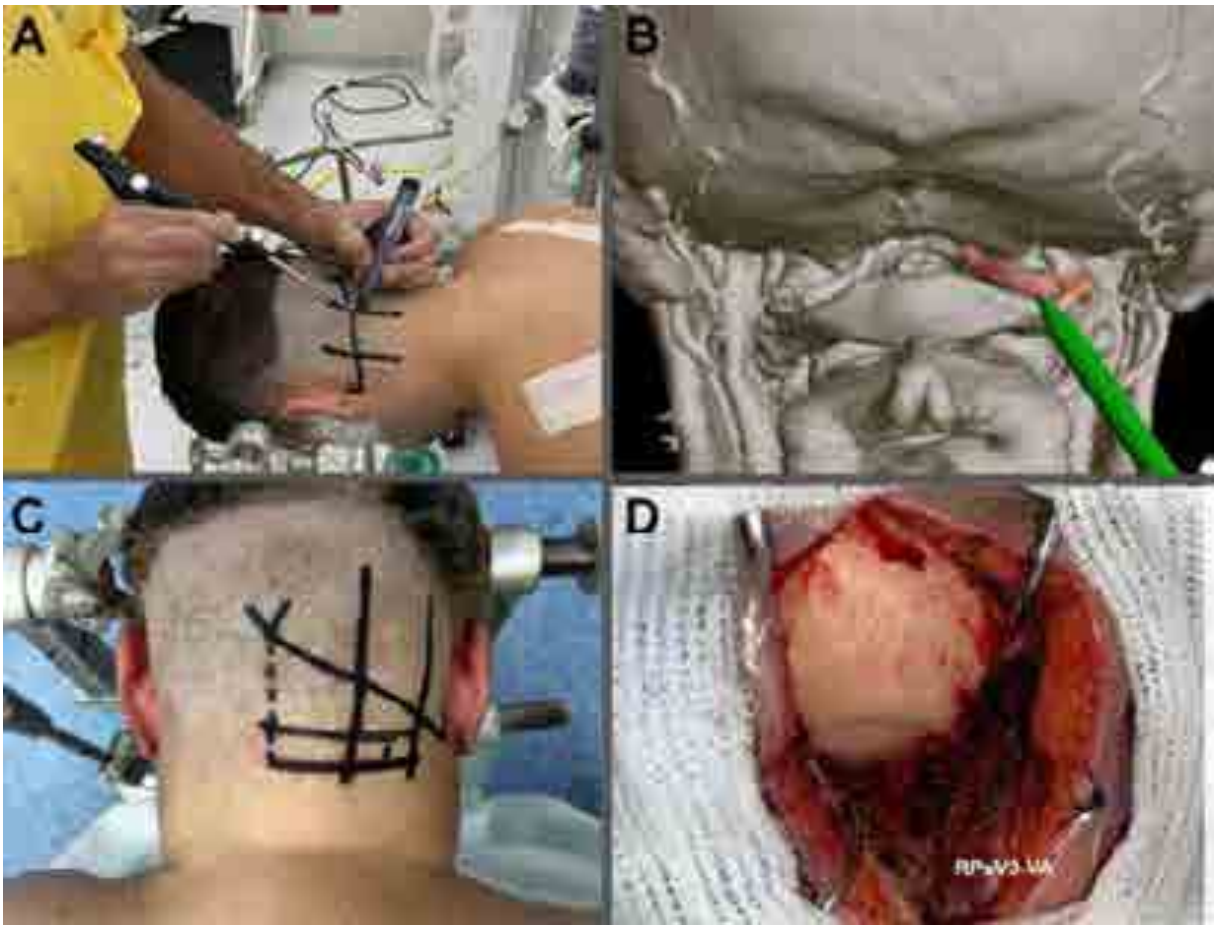


Abb. 2



Neuroanatomie und Lehrkonzepte/*Neurosurgical anatomy and teaching concepts*

V032

Immersive 3D-Anatomie der postero- und antero-lateralen Zugänge zum Kranio-zervikalen Übergang
The immersive 3D-anatomy of postero- and anterolateral approaches to cranio-cervical junction

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Objective

The cranio-cervical junction is a highly complex anatomical region. With modern technology it has become possible to create photorealistic 3D anatomical models that may be viewed in immersive 3D settings. Allowing a comprehensive understanding of the complexity of this region this may improve education of residents and pre-operative planning.

Methods

We dissected 2 cadaver latex injected cadaver heads. Anatomical layered dissections as well as surgical approaches (far lateral and anterolateral) were realized with an up-to date surgical microscope. Every step of the dissection was 3D scanned using photogrammetry technology allowing the extraction of 3D data from 2D photographs.

Results

In total, 29 3D photorealistic models were created presenting posterior and anterolateral neck anatomy (n=17) and posterior and anterolateral surgical approaches (n=12) to the cranio-cervical junction. The models allow observation of the spatial relations of each anatomical structure of interest in augmented and virtual reality settings.

Conclusion

Photorealistic 3D scanning technology is a promising tool to present complex anatomy in a more comprehensive way. These 3D models can be used for education, training and preoperative planning.

Abb. 1


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Abb. 2


Please scan the QR code to see the
3D model in AR. No special App needed.

Neuroanatomie und Lehrkonzepte/*Neurosurgical anatomy and teaching concepts*

V033

Nutzen der gemischten Realität bei der präoperativen Planung von intrakraniellen und Schädelbasistumoren
Mixed reality utility in the preoperative planning for intracranial and skull base tumors

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Objective

Extended reality had a tremendous development over the past decades, but its effective use in the medical field is still being adopted and evaluated. It must be discerned between true virtual reality (VR), augmented reality (AR) and mixed reality (MR). The aims pursued in the use of each respective technology is different. While augmented reality tools are used like image-guided tools in the OR, aiming to reduce the surgeon"s guesswork, VR and MR tools which are mostly head mounted systems focus on enhanced complex 3-D visualization of neurosurgical anatomy with interactive elements. In the current study we systematically investigate the utility of an MR system for the surgical planning and its value for the decision-making progress in approach selection.

Methods

We have integrated the MR viewer (Brainlab, Munich) system using the Magic Leap headset (Magic Leap, USA) in our preoperative planning routine for intracranial and skull base tumors. Patient´s imaging including MRI and CT are transferred to a navigation workstation and elaborated using the Brainlab Elements software (Brainlab, USA). In 20 patients a Three-dimensional (3D) model of the anatomy is generated using automatic and/or manual segmentation of the tumor and surrounding structures. Once the plan is created the information can be moved from the computer screen to a mixed reality environment wearing the headset. The analysis for approach planning is performed with 2 senior neurosurgeons and 2 residents. This allows the team to walk around and inside the 3D model assessing the preoperative plan from all angles with discussing the pros and cons.

Results

The systematic use of MR in this study has significantly enhanced the critical discussion for approach selection among seniors. At the same time residents could benefit considerably from this enriched multidimensional exchange. The benefits will be demonstrated systematically in three exemplary cases of intraaxial, skull base and posterior fossa tumors. All these cases have been studied with preoperative navigation planning followed by MR visualization. The correlating real surgery and the surgical results will also be demonstrated

Conclusion

Based on our preliminary experience the use of of an MR system is valuable to improve the discussion on decision-making for surgical approaches within the neurosurgical team and to enhance the education of residents.

Neuroanatomie und Lehrkonzepte/*Neurosurgical anatomy and teaching concepts*

V034

Vor- und Nachteile von Simulationsverfahren in der neurochirurgischen Ausbildung: Virtuelle Realität versus Phantom

Virtual vs. Phantom: Benefits and drawbacks of simulation training in neurosurgery

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Objective

To overcome the growing obstacle of training the next generation of neurosurgeons despite declining case numbers, neurosurgical simulators are regarded as highly desirable training tools. While physical simulators provide the freedom of focused, hands-on training in a more controlled environment, recent advancements in software-based simulations allow unlimited immersive training and teaching possibilities. This study aims to compare the benefits and drawbacks of both, physical and software-based simulation methods, as effective training tools for the microsurgical management of middle cerebral artery aneurysms.

Methods

In cooperation with the local Department of Graphics and Simulation, a virtual clipping tool was developed based on MRI and CT imaging datasets, using the Unity game engine and the XR Interaction Toolkit (Fig. 1). Concurrently, the same datasets were used to reconstruct and 3D-print models of the skull, brain and cerebral arteries. Based on neurosurgical expertise and rheological measurements, a phantom model with life-like tactile properties of the brain, meninges and cerebral arteries was deleveloped, allowing the practical simulation of the clipping procedure using a neurosurgical microscope and real microsurgical instruments was developed (Fig. 2). A group of 10 medical students tested both simulation techniques and assessed the simulations in respect to their atomical correctness, realism, and general usability, scored on a 5-point Likert scale. Additionally, each participant's performance was assessed based on the objective standardized assessment criteria for aneurysm clipping skills (OSAACS) (E Belykh et al., 2017)

Results

All participants deemed the VR-based simulation as highly desirable for visualization and planning of the surgical procedure. The phantom model was rated superior by all participants in accuracy and handling of instruments. Both simulation methods were perceived superior to conventional training methods.

Conclusion

Both simulation models constitute a major improvement of neurosurgical education. However, these methods should not be regarded as mutually exclusive but rather complimentary training tools with emphasis on different aspects of microsurgical procedures.

Abb. 1

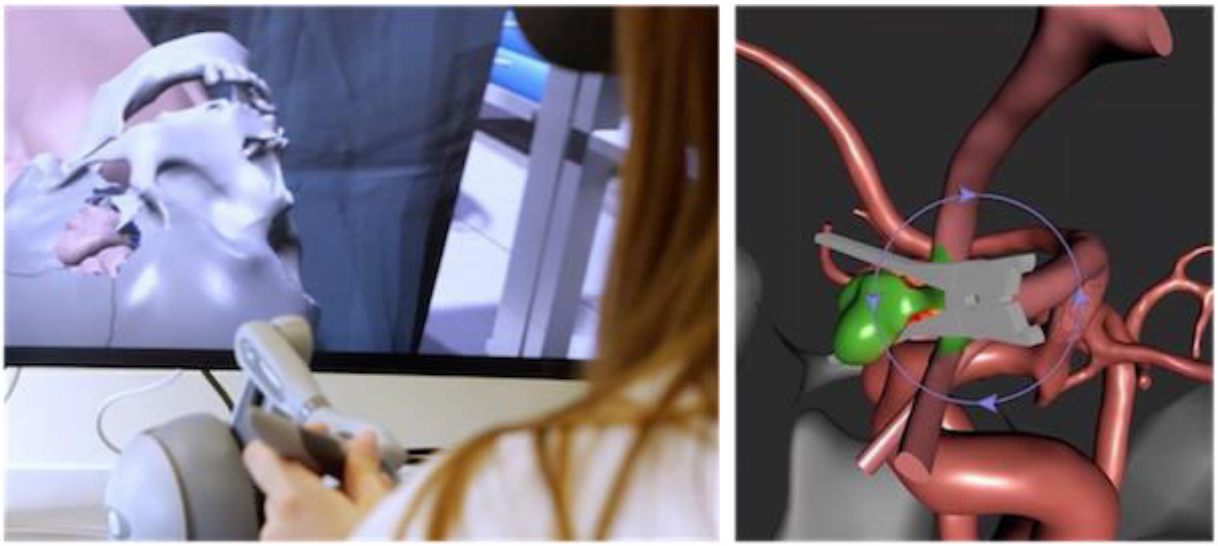

Fig. 1: Immersive Virtual Reality Clipping Simulation using the Oculus Quest 2 headset and a haptic feedback device (Touch Haptic Device - 3D Systems)

Abb. 2

Fig. 2: High-fidelity phantom for cerebral aneurysm clipping with life-like tactile properties of the sylvian fissure, meninges and cerebral arteries.

Neuroanatomie und Lehrkonzepte/*Neurosurgical anatomy and teaching concepts*

V035

Neurochirurgische Lehre neugedacht – innovative Lösungsmöglichkeiten mittels mixed reality während der COVID-19 Pandemie

Transforming Education Reality – Innovation in neurosurgical teaching using mixed reality under COVID-19 conditions

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Objective

The COVID-19 pandemic led to more limited exposure to surgical subspecialties such as neurosurgery, consequently leading to restricted medical insight into the specialty. Mixed Reality (XR)-Simulation can be used to deliver a highly immersive experience through head-mounted displays and has become one of the most promising teaching tools in medical education. We aimed to identify whether an XR neurosurgical simulation module within an undergraduate neurosurgical workshop setting could improve the satisfaction of medical students.

Methods

The quasi-experimental study was conducted from January 2019 to June 2022. The 1-day Workshop for medical students is undertaken yearly. It is divided into two parts. First, the medical students are trained in the basics of systematic neurosurgical/neurological examinations and learn about the most common neurosurgical diseases. Then, in the second part, exercises with neurosurgical instruments, endoscopes, and microscopes are carried out on various simulation models in our Skills Lab. Unlike the conventional group, participants in the intervention group could additionally virtually interact with 3D models using XR devices (augmented and/or virtual reality) and plan the surgical intervention. The students evaluated the teaching experience through a Likert-scale questionnaire using the standardized, anonymous online tool EVALuna (1 for the best and 100 for the worst evaluation).

Results

The satisfaction score for CG and XRG were 88,27±13,3 and 93,2±7,4, respectively. The Welch's t-test concluded that the difference between groups was statistically significant [T-Welch (192,16) =3,5; p=5,86-4] with moderate effect size (Hedges" g=0,46), thus demonstrating that the utilization of XR-Simulation is associated with greater satisfaction.

Conclusion

The workshop with XR achieved the highest rating despite limited patient interaction during the COVID-19 pandemic. In addition, the feedback from the medical students indicates an increased acceptance of this new teaching format and encourages the adoption of disruptive technology into medical school curricula.

Cerebrale Metastasen/*Cerebral metastases*

V036

Natrium Fluoreszein und YELLOW 560 nm Filter für die Resektion cerebraler Metastasen: Einfluss auf Resktionsgüte und Outcome

Sodium Fluorescein and YELLOW 560 nm filter for resection of cerebral metastases: Impact on resection quality and outcome

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Objective

Maximal surgical resection of cerebral metastases (CM) improves progression–free and overall survival. Recently, fluorescein sodium in combination with the YELLOW 560 nm filter (Carl Zeiss Meditec, Germany) (FY) has been introduced as a safe and feasible method to visualize residual tumor tissue during CM resection. We hypothesized that the use FY may positively influence the volumetric extent of resection and the overall survival in patients who undergo surgical resection of CM.

Methods

From a prospective CM registry (METRESECT), a cohort of 539 patients (median age 62.8 years) was selected from which high quality preoperative magnetic resonance imaging (MRI) was available for volumetric analysis. Resection was performed without FY support in 297 (54.7%; group A) and with FI support in 246 (45.3%; group B) patients. Gender, age, presurgical Karnofsky Performance Index (KPI), metastasis status and timing, primary cancer etiology and adjuvant treatment modalities were well balanced between the groups. Volumetric analysis was performed using Brainlab iPlan cranial software by quantifying pre- and postoperative tumor volume, based on the gadolinium-enhanced T1 sequences.

Results

The preoperative volume of group A was moderately larger compared to group B (p=0.073). The postoperative tumor volume and the volume difference was significantly smaller in group B (p=0.01, p=0.028). Accordingly, the quantitative extent of resection was significantly larger in group B (p=0.003). Of group B, significantly more complete resections were achieved compared to group A (p=0.024). Surgical mortality and morbidity were not significantly different between the groups (p=0.154 and 0.283, resp.). Overall survival was significantly longer for group B (p=0.0001, log rank testing). Multivariate Cox regression modelling revealed age, presurgical KPI, metastases status and FY-guided resection as independent prognostic factors for survival.

Conclusion

FY-guided resection of CM results in improved extent of resection and prolonged overall survival.

Cerebrale Metastasen/*Cerebral metastases*

V037

Modifizierter Frailty Index (mFI) als Prädiktor des Überlebens und funktionellen Outcomes bei älteren Patienten nach Hirnmetastasenoperationen

Modified Frailty Index (mFI) as a survival and functional outcome predictor in older patients undergoing surgery for brain metastases

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Objective

Surgical decision making in older patients with brain metastases (BM) is challenging. Frailty and comorbidities are often thought to limit therapeutic options as well as functional and survival outcomes.

Methods

139 consecutive patients undergoing surgery 2017-2021 for BM were analyzed retrospectively. Cut-off for age was ≥60 yrs. in accordance with the graded prognostic assessment (GPA) index. Frailty was investigated using the mFI index, a compound measure assessing comorbidities and the patients" functional health status.

Results

Median age was 69.0 (IQR: 63.0-74.5) yrs. 55.4% had multiple metastases. We recorded 9.4% major (CTCAE III-V) surgical and 10.1% medical complications. 7.9% of patients had major new focal neurological deficits ≥30 days. Median overall survival (mOS) was 7.8 (IQR: 5.0-10.6) months. Frailer patients lived shorter (mOS for "least-frail"/mFI 0: 13.6 [IQR: 8.6-18.6], "moderately frail"/mFI 1-2: 9.0 [IQR: 4.9-13.0] and "frailest"/mFI ≥3: 2.7 [IQR: 0.9-4.5] months; p<0.001). Multivariate analysis with all parameters correlating significantly with mOS in the univariate analysis (mFI, higher preop. KPS, younger age [<69 yrs.], female sex) revealed a higher preop. KPS to be the only independent significant survival predictor (70 vs. 80-100%; HR 2.1, p<0.001). Frailer patients had poorer functional outcomes (patients w/ postop. KPS ≤70 vs. 80-100%; mFI 0: 9/36 [25.0%], mFI 1-2: 20/65 [30.8%], mFI ≥3: 25/38 [65.8%]; p<0.001). Multivariate analysis with all parameters correlating significantly with better functional outcome in the univariate analysis (mFI, higher preop. KPS, younger age, female sex and single metastasis) showed that a higher preop. KPS was the strongest prognostic parameter (RR 17.2, p<0.001). The mFI was not an independent outcome predictor. In a ROC analysis the preoperative KPS proved a much better predictor of functional outcome than the mFI (AUC 92 vs. 71%; sensitivity/specificity optimum 80 vs. 2, resp.). mFI was not a predictor of complications (p=NS).

Conclusion

The mFI proved a strong survival and functional outcome predictor in older patients. However, this effect was no longer seen in multivariate analyses when the KPS was included as a covariate. This may suggest that surgical outcomes depend on the patients" presurgical functional health status rather than comorbidities. The presence of comorbidities (if well treated) should therefore not deter from BM surgery in older patients.

Cerebrale Metastasen/*Cerebral metastases*

V038

Einzelne Hirnmetastasen - Prognostische Faktoren und Einfluss der chirurgischen Resektion auf das Gesamtüberleben

Single Brain Metastases – Prognostic factors and impact of surgical resection on overall survival

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[2]Klinikum rechts der Isar, Technische Universität München, Anästhesiologie, München, Deutschland
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Objective

Brain metastases (BM) represent the most frequent intracranial tumors, with the majority of the patients having single BM. They are divided into two subgroups: singular BMs, with simultaneous extracranial metastases and solitary BMs, without other metastases in the organism. In contrast to the surgical treatment of gliomas, where maximal cytoreduction has been established as a decisive prognostic marker, the influence of resection and residual tumor burden(RTB) in the treatment of singular and solitary BMs is still debated.The aim of this study was to determine the impact of resection and RTB on overall survival (OS) in patients with single BM.

Methods

Patients with surgery for single BM between 04/2007–01/2020 were retrospectively included. RTB was segmented using early postoperative MRI (72h). Survival analyses were performed using Kaplan-Meier estimates for univariate analysis and Cox regression proportional hazards model for multivariate analysis.

Results

340 patients were included, with a median age of 64 years (IQR 54-71). 119 patients (35%) had a solitary BM, 221 patients (65%) a singular BM. Complete resection (RTB=0) was achieved in 247 cases (73%), median preoperative tumor burden was 11.2 cm3 (5-25cm^3) and postoperative tumor burden 0cm3 (0-0.2cm^3). Median OS of the patients with a singular BM was 13 months(4-33 months) and solitary BM 20 months (5-92 months); p=0.062. Multivariate analysis revealed singular BM as an independent risk factor for poorer OS: HR 1.655 (1.156-2.370), p=0.006 for singular vs. solitary BM. When complete cytoreduction was achieved, patients with solitary BM had higher survival rates compared to patients with singular BM (21 vs. 12 months, p=0.027). Furthermore, patients receiving postoperative radiotherapy (RT) had a significantly longer OS compared to patients without postoperative RT (18 months vs. 5 months, p<0.001) with favorable OS especially in patients receiving stereotactic radiosurgery compared to no RT, whole brain radiation therapy and hypofractionated Stereotactic Radiotherapy(OS 15 months (3-42 months); p<0.001).

Conclusion

When complete intracranial tumor resection (RTB=0) is achieved, patients with solitary BM have a favorable outcome compared to patients with singular BM. In a multivariate Cox regression analysis, singular BM (compared to solitary BM) was confirmed as an independent risk factor. Furthermore, the positive impact of postoperative RT on OS was confirmed, especially in patients with single BM.

Cerebrale Metastasen/*Cerebral metastases*

V039

Stellenwert der stereotaktisch geführten Probenentnahme bei Patienten mit Hirnmetastasen
The Value of Stereotactic Biopsy of Primary and Recurrent Brain Metastases in the Era of Precision Medicine

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Objective

Brain metastases (BM) represent the most frequent intracranial tumors with increasing incidence. Many primary tumors are currently treated in protocols that incorporate targeted therapies either upfront or for progressive metastatic disease. Hence, molecular markers are gaining increasing importance in the diagnostic framework of BM. In cases with diagnostic uncertainty, both in newly diagnosed or recurrent BM, stereotactic biopsy serves as an alternative to microsurgical resection whenever resection is not deemed to be safe or feasible. This retrospective study aimed to analyze both diagnostic yield and safety of an image-guided frame based stereotactic biopsy technique (STX).

Methods

Our institutional neurosurgical data base was searched for suspected brain metastases between January 2016 and March 2021. Of these, only patients with STX were included. Clinical parameters, procedural complications, and tissue histology and concomitant molecular signature were assessed.

Results

Overall, 467 patients were identified including 234 (50%) with STX. Median age at biopsy was 64 years (range 29 – 87 years). MRI was used for frame-based trajectory planning in every case with PET-guidance in 38 cases (16%). Serial tumor probes provided a definite diagnosis in 230 procedures (98%). In 4 cases (1.7%), the pathological tissue did not allow a definitive neuropathological diagnosis. 24 cases had to be excluded due to non-metastatic histology, leaving 206 cases for further analyses. 114 patients (49%) exhibited newly diagnosed BM, while 46 patients (20%) displayed progressive BM. Pseudoprogression was seen in 46 patients, a median of 12 months after prior therapy. Metastatic tissue was found most frequently from lung cancer (40%), followed by breast cancer (9%), and malignant melanoma (7%). Other entities included gastrointestinal cancer, squamous cell cancer, renal cell carcinoma, and thyroid cancer. Molecular genetic analyses were successful in 137 out of 144 analyzed cases (95%). Relevant peri-procedural complications were observed in 5 cases (2.4%), which were all transient.

Conclusion

In patients with BM, frame-based stereotactic biopsy constitutes a safe procedure with a high diagnostic yield. Importantly, this extended to discerning pseudoprogression from tumor relapse after prior therapy. Thus, comprehensive molecular characterization based on minimal-invasive stereotactic biopsies lays the foundation for precision medicine approaches in the treatment of primary and recurrent BM.

Cerebrale Metastasen/*Cerebral metastases*

V040

Stellenwert der chirurgischen Resektion bei Patienten mit multiplen Hirnmetastasen
Impact of surgery on survival in patients with multiple brain metastases

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Objective

Surgical resection of brain metastases (BM) alleviates symptoms and can improve patients´ survival. However, the benefit of resection in multiple BM is controversial due to patients´ limited life expectancy. Therefore, we investigated the impact of resection of multiple BM on patients´ survival.

Methods

We reviewed clinical data from 544 patients (216 female, 328 male) who underwent surgery for BM in our hospital between 2010 and 2022. Overall survival (OS) was estimated using the Kaplan-Meier estimator. In addition, follow-up data, adjuvant treatment and tumor recurrence data were collected.

Results

We identified 280 patients (51.5%) with one and 264 patients (48.5%) with two or more BM. Bronchial carcinoma represented the most common primary tumor entity (n= 185, 88 one and 97 multiple BM), followed by melanoma (n= 109, 44 one and 65 multiple BM), breast cancer (n= 54, 31 one and 23 multiple BM), gastro-intestinal tumor (n= 64, 39 one and 25 multiple BM) and lastly cancer of unknown primary (CUP) (n= 29, 11 one and 18 multiple BM). We then compared the survival between patients with a single with those with multiple BM. The median OS of all patients with one BM was with 11.6 months significantly longer than those with two or more BM (7.3 months, p< 0.001, 95% CI one vs. multiple BM: 8.6-14.5 vs. 6.2-8.4 months, respectively). Notably, 29.3% of patients with one BM and 16.5% with multiple BM lived longer than 24 months after resection (long-term survivor, p= 0.001). Regarding primary tumor histology, patients with breast cancer with a single BM had a significant longer OS with 19.7 compared to patients with multiple BM (5.0 months, p= 0.031). Remarkably, 33.3% of all long-term survivors with breast cancer had multiple BM. Patients with a single BM originating from other cancers showed a superior but yet not significant OS in comparison with their counterparts with multiple BM after resection. This included: gastro-intestinal cancer 12.2 vs. 6.5 months (p= 0.160), melanoma 11.6 vs. 7.3 months (p= 0.236) and CUP 3.0 vs. 2.7 months (p= 0.258). The long-term survivor rate of patients with resected multiple BM varied between 20.6% in melanoma and 7.4% in patients with CUP.

Conclusion

Despite limited prognosis in patients with multiple BM, surgical resection should be considered as an effective treatment option. Our study shows that a substantial subset of patients with multiple BM who underwent resection survive longer than 24 months after resection.

Cerebrale Metastasen/*Cerebral metastases*

V041

Chirurgische Resektion von Hirnmetastasen und postoperatives Outcome – spielt der Zeitpunkt der Krebsdiagnose eine prognostische Rolle?

Time of cancer diagnosis in surgically treated brain metastases and postoperative outcome – Does is matter prognostically?

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Objective

For many decades, brain metastases (BM) were associated with a poor outcome. With significant improvement of systemic treatment in various cancers, survival and life quality have improved over the past years. An increasing number of patients is treated surgically for brain metastases. Based on the diagnostic-specific graded prognostic assessment score (ds-GPA), the prognosis for several entities can be estimated. Limited data exists regarding the prognosis in patients with diagnosed BM and cancer history, and patients, who were diagnosed with cancer based on the histology after resection of the metastasis.

Methods

This retrospective study included 635/795 patients (79.9%) with BM and neurosurgical treatment in the authors department between 01/2007 and 12/2020, whose time of death was known. Patients were allocated to the group with BM and known cancer diagnosis or to the group with BM without cancer history. Time of survival of both groups was compared using Kaplan-Meier curve. Special attention was paid to patients with NSCLC as most frequent diagnosis in the presented cohort.

Results

In 260 patients (40.9%) cancer was already diagnosed at the time of surgery for BM in 375 patients (59.1%) cancer has not been diagnosed so far. Significantly more patients with BM as first manifestation of cancer were admitted to the hospital being symptomatic ($p < 0.05$). Further, in this group multiple intracerebral metastases were diagnosed more often compared to patients with a history of cancer ($p < 0.05$). Patients with diagnosed cancer had a significantly longer median survival time of 36.4 months (95%-CI 29.2-443.6) compared to patients, who have not been diagnosed prior to the surgical procedure (median survival time of 20.7 months; 95%-CI 15.7-25.7). The same observation was made in patients with NSCLC. In this cohort, patients, who had already been diagnosed with NCSLC had a median survival time of 44.1 months (95%-CI 29.4-58.9) compared to patients with NCSLC diagnosis based on the histological results of the BM with 14.6 months (95%-CI 11.0-18.1).

Conclusion

Patients, who develop BM and have already been treated for the primary neoplasm have a better prognosis regarding survival time in comparison with patients, who are diagnosed with cancer based on the histology of brain metastases. The results might have an additional prognostic value in cancer treatment especially regarding surgical therapy.

Cerebrale Metastasen/*Cerebral metastases*

J-SPNC004

Management von Lungenmetastasen: Eine terziäre Krankenhauserfahrung während fünf Jahren
Management of lung metastasis: A terciary hospital experience during five years

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Objective

In adults cerebral metastasis are the most common intracranial tumours and with the increase in global survival their incidence is rising. Lung tumours are the most common origin of brains metastasis, and, in our experience, this is true for men but also for women. Taking into consideration their growing part in our everyday case load, it is important to know our results with an emphasis in patient selection, surgical approach and overall outcome.

Methods

Histopathological, radiological, surgical and physical examination findings of all consecutive patients with confirmed brain metastasis with a primary lung tumour were retrospectively reviewed

Results

Between 2015 and 2020 we treated 162 patients with brain metastasis, 79 of which with confirmed brain metastasis with origin in primary lung tumours. By far the most common histological type was adenocarcinoma (82%). The craniotomy with GTR intent was our preferred approach in 92% of the cases and over 90% of patients had a Karnofski Performance Status >70 at presentation. We managed a very high rate of GTR when that was our objective and our complication rate 16%, most commonly surgical site infection and de novo postoperative transitory deficits. Our mortality rate was 6%, most of them related with medical complications.

Conclusion

The review of our case load allows us to better know the characteristics of our population and to sharpen our criteria for surgery. Our complication rate and outcomes, both in relation with the degree of resection and with the functional status, will serve as grounding in which to further improve the care of our patients

Cerebrale Metastasen/*Cerebral metastases*

V042

Einfluss von perioperativem Dexamethason auf das outcome von Patienten mit neurochirurgisch resezierten Hirnmetastasen

Impact of perioperative Dexamethasone dosage in the context of neurosurgical brain metastasis resection

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Objective

Patients with symptomatic brain metastases that are subjected to brain metastasis resection regularly receive perioperative dexamethasone. We sought to evaluate whether dosage and duration of perioperative dexamethasone in context of neurosurgical brain metastasis resection associates with clinical outcome.

Methods

We retrospectively collected data on perioperative dexamethasone treatment dose and duration in brain metastasis patients in the context of neurosurgical metastasis removal at three hospital sites of the Charité from 2010-2022. Cut-off values for cumulative perioperative dexamethasone dose as a continuous predictor variable for survival were evaluated and determined using maximally selected rank statistics. Patients were dichotomized based on determined cut-offs (< 40 mg vs ≥ 40 mg for pre-operative dexamethasone, < 180 mg vs ≥ 180 mg for post-operative dexamethasone, < 281 mg vs ≥ 281 mg for pre- and post-operative). Patient record data included baseline characteristics such as demographic, radiological, histopathological data and treatment-related features. Based on the cut-off values for dexamethasone downstream statistical analyses included Kaplan-Meier analyses, propensity score matching and Cox proportional hazards regression for overall survival as a main endpoint with adjustment for potential confounding factors including age, gender, Karnofsky performance index and presence of extracranial metastasis.

Results

A total of 539 patients were included. Median time of follow-up were 58,97 months (IQR: 31.97;89.17). 38 patients did not receive dexamethasone at all; median dexamethasone dose was 80 mg for the pre-operative period, 96 mg for the postoperative period and 190 mg for the total pre- and postoperative period. Patients with higher total dexamethasone (≥281 mg) showed significant worse overall survival (8.43 months; 95% CI: 5.6 – 10.9) as compared to patients with lower dexamethasone total dosage (

Conclusion

Patients with resected brain metastases receiving higher cumulative pre- and postoperative dexamethasone exposure show worse overall survival. Strict dosage, down taper or methods reducing corticosteroid dependency should be regularly evaluated in clinical practice in patients with brain metastases.

Abb. 1

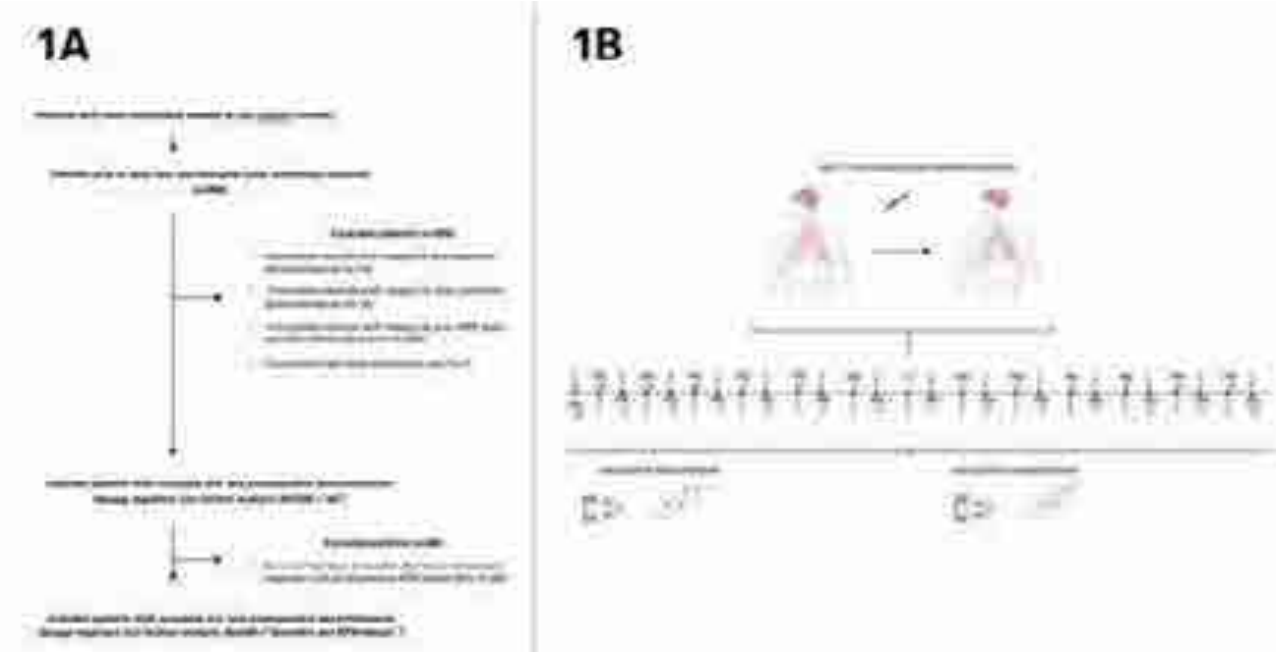
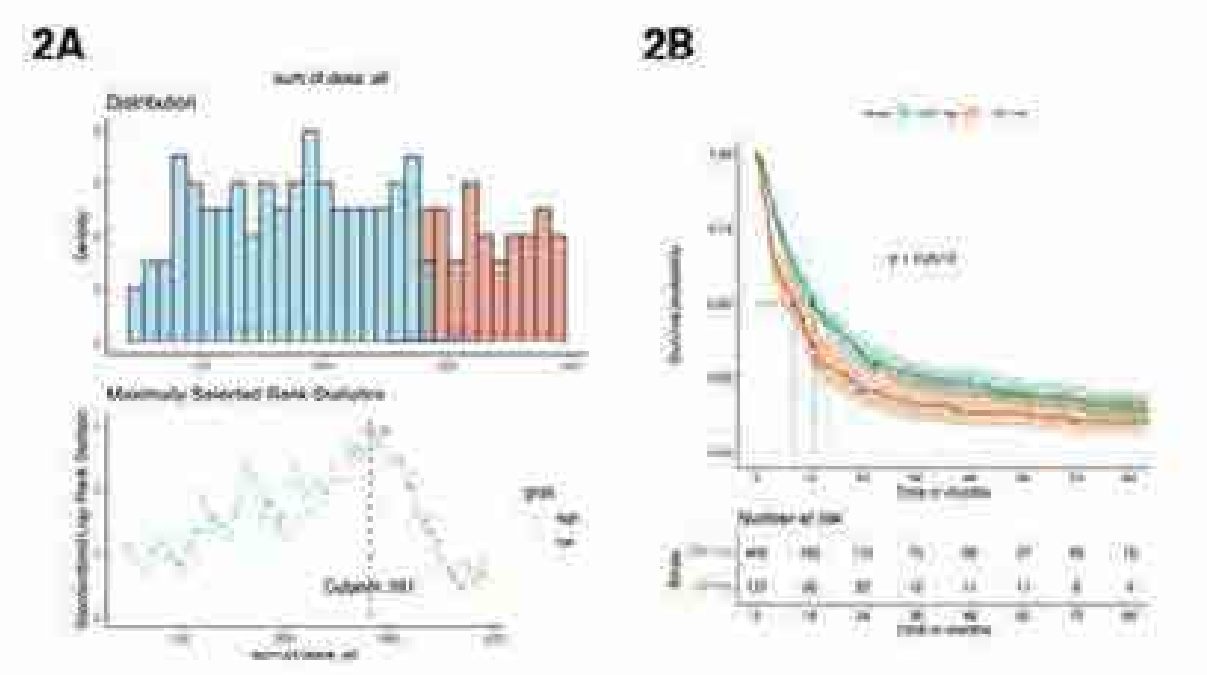

1A
1B

Abb. 2


2A
Distribution
Maximally Selected Rank Statistics
2B

Cerebrale Metastasen/*Cerebral metastases*

V043

Verzicht einer routinemäßigen ITS – Überwachung in selektierten Patienten nach intrakraniellen onkologischen Eingriffen

Safety of Step-Down non-ICU Care Following Elective Intracranial Oncological Surgery

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Objective

The standard of care following elective intracranial oncological surgery is postoperative monitoring in an intensive care unit (ICU). However, previous research has shown that this may not be necessary for selected low-risk patients, potentially leading to benefits such as increased patient satisfaction, more availability of critical care resources, and economic benefits. The aim of this study was to evaluate the safety and feasibility of a standardized selection algorithm to identify low-risk patients suitable for postoperative non-ICU step-down care in a German tertiary university hospital.

Methods

All patients scheduled for elective intracranial oncological surgery between August to December 2022 were screened for inclusion in our newly implemented step-down care protocol based on the criteria listed in Figure 1. The non-ICU approach consisted of four hours of postoperative monitoring in a post-anesthesia care unit, followed by transfer to the general ward if vital signs and neurologic status were stable. No additional monitoring beyond routine nursing care was conducted thereafter.

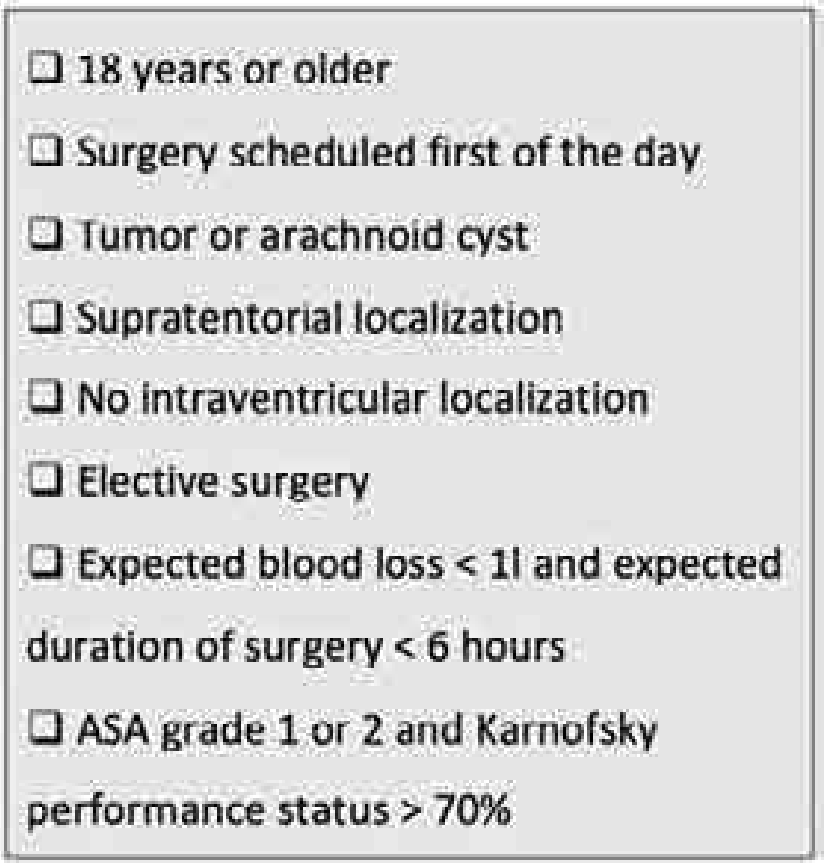
Results

We screened a total of 187 patients; of those, 68 (36.4%) fulfilled the criteria for the proposed non-ICU approach. The main reasons for exclusion were infratentorial location (35.3%), estimated duration of surgery > 6 hours (19.3%), and American Society of Anesthesiologists (ASA) risk classification score > 2 (14.3%). Of the included patients, 55/68 (80.9%) were transferred to the general ward after uneventful postoperative monitoring, while 13/68 (19.1%) were transferred to the ICU due to unexpected neurological deficits (3/13; 23.1%), postoperative seizures (1/13; 7.7%), postoperative diabetes insipidus (1/13; 7.7%), duration of surgery > 6 hours (2/13; 15.4%), or unexpected intra- and perioperative events (6/13; 42.6%). None of these patients required further intensive care interventions other than close neurologic monitoring. Following admission to the general ward, none of the 68 patients required subsequent ICU treatment.

Conclusion

Our data suggest that a low-risk subset of patients undergoing intracranial surgery can be safely managed without routine postoperative ICU-monitoring within the framework of the German health care system. Further studies in a multicenter setting are needed to improve appropriate patient selection.

Abb. 1


❑ 18 years or older
❑ Surgery scheduled first of the day
❑ Tumor or arachnoid cyst
❑ Supratentorial localization
❑ No intraventricular localization
❑ Elective surgery
❑ Expected blood loss < 1l and expected duration of surgery < 6 hours
❑ ASA grade 1 or 2 and Karnofsky performance status > 70%

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

V044

Mikrochirurgisches Clipping als Behandlungsmethode für intial rupturierte mit dem Woven EndoBridge (WEB) device versorgte Aneurysmen: eine monozentirsche Fallserie

Microsurgical clipping as a retreatment strategy for previously ruptured aneurysms treated with the Woven EndoBridge (WEB) device: a mono-institutional case series

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Objective

Since its approval by the U.S. Food and Drug Administration (FDA) in 2018 the flow disruptor Woven EndoBridge (WEB) device has become increasingly popular for the endovascular treatment of unruptured and ruptured cerebral aneurysms. However, the occlusion rates seem rather low, and the retreatment rates rather high compared to other treatment methods. For initially ruptured aneurysms a retreatment rate of 13 % has been reported. A variety of retreatment strategies has been proposed; however, there is a paucity of data concerning microsurgical clipping of WEB pretreated aneurysms, especially previously ruptured ones. Thus, we present a single-center series of five ruptured aneurysms treated with the WEB device and retreated with microsurgical clipping.

Methods

A retrospective study including all patients presenting with a ruptured aneurysm undergoing WEB treatment at our institution between 2019 – 2021 was performed. Subsequently, all patients with a remnant or a recurrence of the target aneurysm who underwent retreatment with microsurgical clipping were identified.

Results

Overall, five patients with a ruptured aneurysm treated with WEB and retreated with microsurgical clipping were included. Besides one basilar apex aneurysm, all aneurysms were located at the anterior communicating artery (AcomA) complex. All aneurysms were wide-necked with a mean dome-to-neck ratio of 1.5. Median time between WEB treatment and retreatment was 19 months (range: 8 – 37). Clipping was feasible and safe in all aneurysms and complete occlusion was achieved in 4 of 5 aneurysms.

Conclusion

Microsurgical clipping for initially ruptured WEB-treated aneurysms is a feasible, safe, and effective treatment method in well-selected patients.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

V045

Prädiktiver Wert des intraoperativen Neuromonitorings beim Clipping nicht-rupturierter intrakranieller Aneurysmen

Predictive value of intraoperative neuromonitoring during clipping of unruptured intracranial aneurysms.

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Objective

Ischemic complications after aneurysm clipping are a source of immense postoperative neurological morbidity. Intraoperative neuromonitoring (IOM) of motor and somatosensory evoked potentials is a well-established approach for reducing morbidity. The aim of this study was to determine the predictive validity of IOM for postoperative functional outcome and its perceived added value for intraoperative real-time feedback of functional impairment in the surgical treatment of unruptured intracranial aneurysms (UIAs).

Methods

This study prospectively included patients scheduled for elective microsurgical clipping of UIAs between 02/2019 – 02/2021. Transcranial motor evoked potentials (tcMEP) were used in all cases, a significant decline was defined as a loss of at least 50% in amplitude strength or a 50% increase in latency. Clinical data were analyzed and correlated to postoperative deficits. A surgeon"s questionnaire, assessing the subjective perceived value while using IOM during clipping and the impact of IOM on the surgical outcome, was conceived.

Results

47 patients were included, median age at surgery 57 years (range 26 – 76). IOM was successful in all cases. In 87.2%, IOM modalities were stable throughout surgery, although 1 patient (2.4%) of these demonstrated a permanent postoperative neurological deficit. All patients with an intraoperatively reversible decline of tcMEPs (12.7%) showed no surgery-related deficit, regardless of the duration of the decline, ranging from 0.5 – 40.0 minutes (mean: 13.8 min). Temporary clipping (TC) was performed in 12 cases (25.5%). A decline in amplitude was seen in 4 of these patients (8.5%). After removal of the clip, all amplitudes returned to baseline. IOM provided the surgeon with a higher sense of subjective security for the clipping procedure in 30 of 47 cases (63.8 %).

Conclusion

IOM remains invaluable during elective microsurgical clipping, particularly during TC of MCA and AcomA aneurysms. It alerts the surgeon of impending ischemic injury and offers a way of maximizing the time frame for TC. Furthermore, it has highly increased surgeons" subjective feeling of security during the procedure.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

V046

Zerebrale Ischämie nach temporärer arterieller Okklusion bei MCA Aneurysmen und deren Berechenbarkeit in präoperativen Bedingungen

Cerebral ischemia after temporary artery occlusion in MCA aneurysms and its predictability in pre-surgical conditions

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Objective

Temporary artery occlusion (TAO) of the middle cerebral artery in microsurgical clipping is a widely used technique. In the past safety has been attested in different situations. However, there is no established safe time frame for temporary clipping in MCA aneurysms. The relationship between TAO and ischemic changes on imaging within 48 hours after surgery in relation to the length of its appliance remains unclear. We aimed to investigate the safety and safe time frame of TAO strategies and scores for predictability of postoperative ischemia in MCA aneurysms.

Methods

All cases of surgically treated MCA aneurysms from January 2010 to December 2020 were retrospectively analyzed. Demographic, clinical data and detailed information regarding the surgery and TAO (i.e. length, multiplicity, side, presence of postoperative cerebral ischemia) were retrospectively collected.

Results

In total, 245 patients were analyzed, 91 (37.1%) were treated for ruptured and 154 (62.9%) for unruptured MCA aneurysms. Cerebral ischemia occurred in 62 (27.2.%) patients. TAO was performed in 133 (54.3%) cases, intermittent TAO in 30 (22.6%) of these. Ischemia occurred in 38 (28.6%) with TAO and 24 (21.4%) w/o TAO. Ischemia occurred in 12 (40%) cases of intermittent TAO compared to 26 (25.2%) without. Elective cases had ischemic changes after surgery in 29 (18.8%) cases vs. 33 (36.3%) in ruptured aneurysms. Both subarachnoid hemorrhage ($p < 0.001$) and aneurysm size ($p = 0.012$) increased the odds for postoperative cerebral ischemia.

Intermittent TAO was safe until a certain threshold was reached. Leaving the clip in place for longer than eight minutes ($p = 0.025$) increased risk for ischemia by 5% each minute. The critical threshold in SAH patients was even lower at five minutes ($p = 0.033$) with a risk increase 9.4-fold.

TAO in itself posed no risk for postoperative ischemic changes.

PHASES score proved prediction capability ($p = 0.026$), with 12.2% higher risk for ischemia with every point-increase after a threshold of 7 points. With SAH present at admission, the threshold was lowered to 6 and the overall odds for ischemia 3.2 times higher.

Conclusion

Prolonged TAO seems to increase the odds for postoperative ischemia on imaging. The eight-minute brink should not be crossed, in SAH even five minutes marked the critical barrier. Ischemic risk can be assessed using the PHASES score in the preoperative setting.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

V047

Sicherheit und Wirksamkeit von Nicardipin-freisetzenden Pellets bei Patienten mit aneurysmatischer Subarachnoidalblutung, nach Aneurysma-Clipping

A Safety and Efficacy Study of Nicardipin releasing Pellets in Aneurysmal Subarachnoid Haemorrhage Patients Undergoing Aneurysm Clipping

L. Wessels[1], S. Wolf[1], N. Hecht[2], T. Adage[3], J. Breitenbach[3], C. Thomé[4], J. Kerschbaumer[4], M. Bendszus[5], M. Gmeiner[6], A. Gruber[6], D. Mielke[7], V. Rohde[7], M. Wostrack[8], J. Gempt[8], G. Bavinzski[9], D. Hirschmann[9], P. Vajkoczy[2]

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Objective

Cerebral vasospasm (aVS) is one of the most relevant causes of secondary injury in aneurysmal subarachnoid hemorrhage (aSAH). The only approved treatment is the prophylactic oral application of nimodipine which shows limited effectiveness. To overcome this lack of treatment options, NicaPlant was developed. Previous studies have already demonstrated safety and initial pharmacological effects and feasibility, as well as identified the optimal dose; this study aims to investigate the efficacy and safety of the selected dose of NicaPlant pellets.

Methods

We performed a multicentre, randomized, controlled, single-blinded study. 40 Patients with WFNS grade 3 and 4 aSAH undergoing surgical repair of their ruptured aneurysm were randomized (1:1) to receive 10 Nicardipin pellets (total 40mg) plus standard of care or standard of care alone. The implants were administered following clip ligation of the ruptured aneurysm in proximity to all the exposed cerebral blood vessels. The primary endpoint was the incidence of moderate to severe aVS. The primary safety endpoint was the occurrence of adverse events.

Results

In the implant group, 20% of patients presented moderate or severe aVS, compared to 58% of patients in the control group (p=0.02). Including mild vasospasm, 75% of all patients in the control group developed vasospasm compared to 30% in the implant group (p=0.01). Endovascular rescue therapy was performed in 10% of the patients in the implant group compared to 58% in the control group (p=0.002). 32% of the patients in the control group developed new cerebral infarction, compared to 10% in the implant group (p=0.13). 20% of the control group experienced life-threatening treatment-emergent adverse events compared with none in the active group; 45% of the control group, compared with 19% of the active group, experienced SAEs.

Conclusion

We could demonstrate the safety and efficacy of NicaPlant® implants in preventing cerebral vasospasm in patients with aSAH WFNS grades 3 and 4.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

V048

Postoperative Risikostratifizierung und Lernkurvenanalyse direkter EC-IC Bypass-Operationen bei erwachsenen Patienten mit Moyamoya-Angiopathie – 10 Jahre Erfahrung in einem Single-Center

Perioperative risk stratification and learning curve analysis of direct EC-IC bypass surgery in adult patients with Moyamoya angiopathy - 10 years of experience in a single center

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[1]Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Deutschland
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[3]Universitätskinderspital Zürich, Moyamoya Center, Zürich, Schweiz

Objective

Direct extracranial-intracranial (EC-IC) bypasses for revascularization of affected vascular territories represent the gold standard in the treatment of adult patients with moyamoya angiopathy (MMA). Although direct vascular anastomosis is considered a well-standardized procedure, little data is available on the surgical risk profile and surgical learning curve. We report our 10 years single-center experience.

Methods

All direct EC-IC bypass operations on adult MMA patients were evaluated retrospectively and perioperative complications were graded according to Clavien-Dindo. The Cumulative Sum Method (CUSUM) was used for process analysis to describe the learning curve of the surgeons.

Results

From 11/2012 to 11/2022, 161 direct EC-IC bypasses for MCA revascularization were performed in 102 adult MMA patients. Relevant complications (Clavien Dindo grade ≥3) occurred in n = 8 (5.0%), severe complications (Clavien-Dindo grade ≥3b) in n = 7 bypasses (4.3%). Overall, temporary hyperperfusion was the most frequent complication with 7.5%, followed by wound healing disorders with and without need for surgical revision in 10 cases (6.2%). Perioperative hemorrhage was seen after 2 (1.2%), ischemia after 4 (2.5%) bypasses. Bypass-patency after 1 year was seen in 159 of 161 bypasses (98.8%). The surgical learning curve at target incision-suture time (IST) of 120min +-25% was crossed continuously by a newly trained surgeon from the 84th direct EC-IC bypass operation. There was no statistical correlation between IST and the occurrence of complications.

Conclusion

The specific risk profile of direct EC-IC bypasses should be known for risk stratification of a planned bypass surgery, for informing patients and to possibly avoid complications by creating awareness for them. The number of surgeries required to progress through the learning curve and a high numbers of bypass patency show the need for treatment in highly specialized revascularization centers.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

J-SBNC017

Schlaganfallsterblichkeit in den letzten 10 Jahren in Brasilien
Stroke mortality in the last 10 years in Brazil

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Objective

To analyze the mortality picture of hemorrhagic or ischemic stroke in Brazil.

Methods

An observational, cross-sectional, descriptive study was carried out by means of a survey of epidemiological data obtained from the SUS Hospital Morbidity Session (SIH/SUS), at the Computer Department of the Brazilian Unified Health System (DATASUS), using the variables federation unit, sex, age group, and education in the content deaths by residence in Brazil. Data were collected from January 2012 to December 2022. The sample presents patients classified in the ICD-10 as "Non-specific hemorrhagic or ischemic stroke" - I64. The information obtained from the SIM was organized in tables using Microsoft Excel for statistical analysis of the values found according to each variable. The analysis relied on a simple comparison of the results, highlighting those of greatest value to form the epidemiological profile of patients affected by hemorrhagic or ischemic stroke in Brazil.

Results

Brazil accounted for 345,984 of deaths in the period from January 2012 to December 2022, with the highest prevalence represented by the Southeast region with 38.14%, followed by the Northeast region with 34.15%. In terms of age, 80 years and over corresponded to the highest mortality rate (42.25%). Moreover, males had a slight prevalence, with 50.86% of the cases, while females accounted for 49.11%. In addition, regarding education, patients classified with 12 years or more of schooling have 2.26% of the total number of deaths, in contrast to those with no education (27.39%).

Conclusion

The southeast region led the national pattern, and also had the most men affected by stroke. It also showed that the aging of the population is a risk factor for cerebrovascular diseases, and that education reflects directly on the death rates of patients.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

J-SBNC018

Mikrochirurgisches Clipping und endovaskuläre Embolisation bei intrakraniellen Aneurysmen: ein Vergleich der Ausgaben in Brasilien

Microsurgical Clipping and Endovascular Embolization for intracranial aneurysms: a comparison of expenditure in Brazil

V. Emanuelle Cunha Santos[1], J. Pedro Fernandes Gonçalves[2], F. Augusto Travi Squizzato[2], I. Paixão Vasconcelos[3], F. Adélia Almeida Custódio Pires de Jesus[4], L. Lemos Pinto Castanheira[1], V. Luiz Sant'ana Junior[1], B. Franco[4], L. Piason de Freitas Martins[1]

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[4]Universidade Salvador (UNIFACS), Salvador, Brasilien

Objective

Currently, the conventional treatment for intracranial aneurysm is microsurgical clipping and/or endovascular embolization. There are variations in the literature about the best therapeutical strategy. The aim of the study is to compare the mean cost of hospitalizations in Brazilian Public Health System between two different procedures in the period comprehended within 2008 and 2019.

Methods

In this observational ecological research, data were collected on the Informatic Department of the Unified Health System (DATASUS), examining the mean cost of hospitalization of patients that underwent through procedures of microsurgical clipping and embolization from the year of 2008 till 2019, navigating by the topic "Hospital Production" (SIH/SUS) from the item "Health Assistance". Statistical analyses were effectuated by the program Statistical Package for the Social Sciences (SPSS). To compare data, it was performed a U test of Mann-Whitney after the confirmation of normality regression to determine the behavior of our variables in the referred period.

Results

The median average hospitalization expenses by embolization patients was R$15,633.10 (qi: 5,539.86), while by neurosurgical clipping was R$8,420.37 (qi: 1,513.22). It was verified a difference of +85.65% ($p<0.001$) in the median of medium cost of hospitalization within embolization patients compared to the neurosurgical clipping group. In the linear regression, the behavior of the averages of hospitalization costs inside the embolization group exhibited a fall trend (beta= -0.829; $R^2=0.687$; $p<0.001$) and the microsurgical group manifested a high trend (beta= 0.849; $R^2=0.720$; $p<0.001$).

Conclusion

The approach to the aneurysm by microsurgical clipping demonstrated potential to generate savings in hospitalization when compared to embolization to treat the same disorder, although the linear regression showing that there was a downward trend on the average spending in the last 12 years.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

J-SBNC019

Behandlung von intrakraniellen Aneurysmen in Brasilien: ein Vergleich der durchschnittlichen Aufenthaltsdauer
Intracranial aneurysms treatments in Brazil: a comparison of the mean length of stay

V. Emanuelle Cunha Santos[1], J. Pedro Fernandes Gonçalves[2], F. Augusto Travi Squizzato[2], I. Paixão Vasconcelos[3], F. Adélia Almeida Custódio Pires de Jesus[4], L. Lemos Pinto Castanheira[1], V. Luiz Sant'ana Junior[1], B. Franco[1], L. Piason de Freitas Martins[1]

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[2]FAMEB/UFBA, Salvador, Brasilien
[3]DCV-UNEB, Salvador, Brasilien
[4]Universidade Salvador (UNIFACS), Salvador, Brasilien

Objective

Currently, the conventional treatment for intracranial aneurysm is microsurgical clipping and/or endovascular embolization. There are variations in the literature about the best therapeutical strategy. The aim of the study is to compare the mean length of stay between both procedures in Brazilian Public Health System in the period comprehended within 2008 and 2019.

Methods

In this observational ecological research, data were collected on the Informatic Department of the Unified Health System (DATASUS), examining the mean length of stay of patients that underwent through procedures of microsurgical clipping and embolization from the year of 2008 till 2019, navigating by the topic "Hospital Production" (SIH/SUS) from the item "Health Assistance". Statistical analyses were effectuated by the program Statistical Package for the Social Sciences (SPSS). To compare data, it was performed a T test of Student after the confirmation of normality with Kolmogorov-Smirnov tests, as well to perform a linear regression to determine the behavior of our variables in the referred period.

Results

The mean length of stay by embolization patients was 7.54 (Standard Deviation (sd): ±0.22), while by neurosurgical clipping was 16.99 (sd= ±0.2). It was verified a difference of +125.33% ($p<0.001$; Confidence Interval 95% = from 2.0795 to 2.4552) in mortality rate within neurosurgical clipping group compared to the embolization patients. In the linear regression, the behavior of the averages of length of stay inside the embolization group exhibited a high trend (beta= 0.811; $R^2=0.658$; $p=0.001$) and the microsurgical group also manifested a high trend (beta= 0.115; $R^2=0.013$; p=0723).

Conclusion

The mean length of stay for endovascular embolization is smaller than microsurgical clipping to intracranial aneurysms in the last 12 years. On the other hand, there is a high tendency, with statistical significance, in length of stay of embolization patients, as shown by linear regression.

Therapie neurovaskulärer Erkrankungen II/*Therapy of neurovascular diseases II*

V049

Clips, Coils und Stents: das Management der aneurysmatischen Subarachnoidalblutung in Deutschland zwischen 2005 bis 2018

Clips, coils, and stents: the management of aneurysmal subarachnoid hemorrhage in Germany between 2005 to 2018

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Objective

Obliteration techniques for ruptured intracranial aneurysms (rIA) causing aneurysmal subarachnoid hemorrhage (aSAH) have undergone dramatic changes over recent decades. Our study aims to examine management techniques for rIA in Germany between 2005 and 2018 with special emphasis on aneurysm location.

Methods

Data on all patients hospitalized in Germany with the International classification of disease codes (ICD) I60.0 to I60.7, representing rIA, were analyzed according to standardized operation and procedure codes (OPS) for craniotomy, coiling and stenting. Data was provided by the German Federal Statistics Office with ethical approval of local authorities (EA 1/272/20). The presence of systematic time trends was investigated with the prop.trend.test function.

Results

Between 2005 and 2018, 101,105 patients were hospitalized for aSAH, of which 25,300 underwent coiling, 21,403 clipping and 2,702 stenting. The total numbers of coiling increased from 1,340 in 2005 to 1,952 in 2018 ($p<0.001$). Clipping numbers decreased significantly from 1,959 in 2005 to 1,279 in 2018 ($p<0.001$). From 2007 on, coiling was the most frequent intervention in patients with aSAH in Germany. Stenting procedures were first performed in 2008 and increased from 102 in 2008 to 359 in 2018 ($p<0.001$). Only in rIA of the MCA did clipping remain the most frequent mode of treatment throughout the entire study period with only a slight decrease of total clipping numbers from 772 to 581 and an increase in the numbers of coiling from 171 in 2005 to 230 in 2018 (both with $p<0.001$).

Conclusion

This first comprehensive study on rIA management in a national cohort shows that, in Germany, between 2005 and 2018, the total numbers of endovascular procedures, most prominently coiling, have surpassed those of clipping at all locations except at the MCA, where clipping remains the most frequent type of rIA management even today. Our findings suggest that neurosurgical rIA management remains relevant in times of growing availability of endovascular rIA management.

Wirbelsäule und Tumor/*Spine and Tumor*

V050

Gefäßversorgung und klinischer Verlauf nach chirurgischer Resektion spinaler Hämangioblastome: eine multizentrische retrospektive Fallserie

Vascular supply and neurological outcome after surgical treatment of spinal intradural hemangioblastoma: a multicenter retrospective case series

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Objective

Spinal cord hemangioblastoma are rare highly hypervascularized benign neoplasms. Surgical resection remains the treatment of choice, with a significant risk of postoperative neurological deterioration.

Methods

Retrospective multicenter study including five high-volume neurosurgical centers assessing patients surgically treated for spinal hemangioblastoma between 2006 and 2021. Clinical status, surgical data, preoperative angiograms, and embolization were analyzed when available. Follow-up records were reviewed, and logistic regression performed to assess possible risk factors for neurological deterioration.

Results

We included 60 patients in 5 high-volume neurosurgical centers in Germany and Austria. Preoperative angiography was performed in 30% of the cases, ten patients underwent preoperative embolization. The clinical outcome revealed a transient postoperative neurological deterioration in 38.3%, depending on symptom duration and preoperative McCormick grading, but patients recovered in most cases until follow-up. Posterior tumor location and presence of a syrinx favored gross total tumor resection. Preoperative embolization was not associated with postoperative worsening.

Conclusion

Spinal hemangioblastoma patients significantly benefit from early surgical treatment with only transient postoperative deterioration and complete recovery until follow-up. The performance of preoperative angiograms remains subject to center disparities.

Wirbelsäule und Tumor/*Spine and Tumor*

V051

Die Lebensqualität im Langzeitverlauf nach stattgehabter IONM-gestützter mikrochirurgischer Resektion zervikothorakaler intramedullärer Rückenmarkstumore

Quality-of-Life long-term outcomes after IONM-aided microsurgical resection of cervicothoracic intramedullary spinal cord tumors

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Objective

IONM-aided microsurgical resection is the therapy of choice for cervical and thoracic intramedullary spinal cord tumors (IMSCTs). While neurological outcome has been multiply reported, the long-term outcome for quality-of-life (QoL) aspects is still unknown.

Methods

We prospectively assessed 26 patients (m/f: 16/10, median age: 44 years) undergoing cervical/thoracic IMSCT surgery with intraoperative recording of muscular motor and somatosensory evoked potentials, Direct Wave and free-running electromyography. Detailed neurological status, McCormick Score, modified JOA Score (mJOA) as well as QoL with regard to Physical/Mental Compound Short-Form-36 Health Survey Score (SF-36-P/MCS) and Barthel-Index (BI) was assessed pre- and immediately postoperatively as well as at long-term follow-up (mean 28 months, range 24-56 months) and correlated with patients"/tumor characteristics.

Results

62% of the tumors were ependymomas, 15% high-grade gliomas, 12% cavernomas, 8% hemangioblastomas and 3% metastases. 46% of the tumors were located between the C1-C4-level, 23% between the C5-C7-level, 23% between the Th1-Th6-level and 8% below the Th7-level. Gross-total resection was accomplished in 92%. Preoperativeley, motor deficits were present in 35%, sensory disturbances in 73% and gait ataxia in 38% of the patients; median McCormick Score was 1, median mJOA 16, mean SF-36-P-/MCS 46.8/43.4 and median BI 100 in the overall cohort. At last follow-up, 15% of the patients had a persistent deterioration in motor function, 23% in sensory function and 8% in gait function compared to the preoperative status; the overall cohort"s median McCormick Score was 1, median mJOA 15, mean SF-36-P-/MCS 44.8/44.9 and median BI 100 with no significant differences compared to the preoperative status for each item. Rates for individual improvement/deterioration in QoL aspects were 54%/46% for SF36-PCS, 58%/42% for SF-36-MCS and 69%/31% for BI. Presence of a postoperative deterioration in motor function with persistence at last follow-up was the only significant risk factor for a worse QoL long-term outcome ($p_{SF36\text{-}MCS}$=0.04, $r_{SF36\text{-}MCS}$=0.41; $p_{SF36\text{-}PCS}$=0.02, $r_{SF36\text{-}PCS}$=0.46; p_{BI}<0.01, r_{BI}=0.54).

Conclusion

QoL aspects improve in more than half of the patients during long-term follow-up after microsurgical resection of cervicothoracic IMSCTs. Persistence of a postoperative deterioration in motor function is a significant predictor for a worse QoL long-term outcome.

Wirbelsäule und Tumor/*Spine and Tumor*

V052

Auswirkung eines reduzierten präoperativen Leistungsstatus bei metastasierter Wirbelsäulenerkrankung auf das chirurgische Ergebnis

Impact of Reduced Preoperative Performance Status in Metastatic Spine Disease on Surgical outcomes

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Objective

Decompressive surgery is an essential component of multimodality treatment for metastatic spine disease to preserve or restore neurologic function, but carries potential risks related to surgical morbidity, perioperative complications, and subsequent delays in adjuvant treatment. The purpose of this study was to evaluate the impact of reduced preoperative performance status on neurologic outcome and adverse perioperative events.

Methods

In this retrospective analysis we screened 738 patients who underwent surgical treatment for spinal metastasis at our spine center between 2012 and 2022. Based on preoperative functional status, as determined by the Karnofski Performance Scale (KPS), patients were divided into a 'limited' (KPS 30% to 60%) or 'good' (KPS 70% to 100%) performance group and compared in terms of neurological outcome, as classified by the Frankel grading system, and perioperative complications.

Results

A total of 466 patients (63.1%) were included. The median follow-up time was 8 (± 13.5) months. Surgical decompression with or without instrumentation was performed in 93.1% of all patients, and 6.9% were treated with instrumentation only. Preoperative performance status was reduced in 60.5% of all patients (KPS 30 to 60). Perioperative complications occurred in 35.4% of all cases, the most common of which were wound-related (12.2%), cardiovascular (10.3%), or nonsurgical infections (8.8%) and did not differ significantly between patients with 'reduced' (36.9%) or 'good' (33.2%) performance status ($p = 0.429$). Perioperative mortality was 1.7% and was associated with 'reduced' performance status in all cases. Postoperative improvement in Frankel score was not significantly different between patients with 'good' (33.3%) or 'reduced' (39.9%) performance status ($p = 0.935$). Preservation or restoration of walking ability (Frankel grades D and E) after surgical decompression was significantly more frequent in patients with 'good' performance status (98.9% versus 89.2% in patients with reduced performance status; $p < 0.001$).

Conclusion

Our results suggest overall favorable surgical outcomes in terms of neurologic function, although functional outcome may depend on preoperative performance status. However, considering the high burden of perioperative complications in up to one third of all cases, the indication for surgery must be made with caution.

Wirbelsäule und Tumor/*Spine and Tumor*

V053

Langzeit biomechanische Veränderung des spinalen alignments, nach Entfernung der intraspinalen tumore
Spinal long-term biomechanical alterations after intraspinal tumor resection

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Objective

Laminectomy and laminoplasty are frequently used for the resection of intraspinal tumors. These approaches affect spinal alignment. We present follow-up data from a large cohort of patients who underwent resection of intramedullary and extramedullary tumors via laminectomy or laminoplasty.

Methods

A single-center retrospective review of 449 patients with intraspinal tumors was performed. Tumor features, approach modalities, and post-operative spinal alignment alterations were analyzed and compared between the two surgical techniques, using available postoperative images.

Results

Long-term imaging data from 359 patients were available. The intramedullary study group (n = 136) comprised mostly ependymomas (43.4%). The extramedullary group (n = 223) included predominantly neurinomas (55.2%). Intramedullary tumors were most commonly located in the cervical and thoracic spine, while extramedullary originated mainly in the thoracic and lumbar spine (p <.001). Altogether, laminectomy was performed in 55.7%, laminoplasty in 17.6%, and hemilaminectomy in 14.5% of cases (p <.001).

Postoperative spinal alignment impairment occurred significantly prevalent after laminoplasty in the intramedullary group (n = 16 (30.2%) out of 53 cervical laminoplasties) and in the extramedullary group (n = 2 (28.6%;) out of 7 cervical laminoplasties) in comparison with laminectomy (n = 9 (12%) out of 75 laminectomies in the intramedullary group, and n = 7 (11.3%) out of 62 laminectomies in the extramedullary group (p = .013)).

Biomechanical alterations were most common in the cervicothoracic region (n = 6 (54.5%) out of 11 in the intramedullary group), in the cervical region (n = 8 (34.8%) out of 23 in the extramedullary group), followed by the thoracolumbar region (n = 2 (33.3%) out of 6 in the intramedullary group) (p = .004). Other approaches (hemilaminectomy, extended fenestration) did not significantly impair the spinal alignment.

Conclusion

Biomechanical spine alterations present a possible long-term complication in patients with intraspinal tumors after laminectomy and laminoplasty. Those changes occur most commonly in the cervicothoracic region after laminoplasty. Long-term imaging should be obtained to identify biomechanical alterations after laminectomy and laminoplasty in patients with intraspinal tumors.

Wirbelsäule und Tumor/*Spine and Tumor*

V054

Die Rolle einer verlängerten Bettruhe nach einer Operation einer spinalen, intraduralen Pathologie

The role of prolonged bed rest in postoperative cerebrospinal fluid leakage following surgery of intradural pathology

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Objective

Postoperative cerebrospinal fluid leakage (CSFL) is a feared complication after spinal surgery of intradural pathologies and may cause impaired wound healing, infections, prolonged hospital stay (LOS), and subsequently higher treatment costs. In this cohort study we aimed to assess whether prolonged bedrest may lower the risk of CSFL.

Methods

We performed a retrospective analysis of all patients that had an intradural pathology and underwent surgery at our department between 2013 and 2021. Patients were stratified into two cohorts. Patients who were mobilized on the first postoperative day and patients who had a prolonged bed rest for three days. The primary endpoint was the incidence of clinically proven CSFL. In addition, further suspected risk factors and patients" characteristics were analyzed.

Results

We found 433 patients (female 224 (51.7%), male 209 (48.3%)) in our data base, with mean age of 48 years (SD: 20). Prolonged bed rest was ordered in 315 cases (72.7%). In seven cases (1.6%) we identified a postoperative CSFL, which had to be treated surgically in six cases. In four (N=4, 3.4%) of the cases no bed rest was ordered, showing no significant difference in comparison to the bed rest cohort (N=3, 1.0%; P=0.091, RR 0.281 95%CI 0.064-1.237). In univariate analysis Laminectomy as approach (N= 4/61, 6.6%; OR 8.632, 95%CI1.883-39.573), expansion duroplasty (N=6/70, 8.6%; OR 33.938, 95%CI 4.019-286.615) and recurrent surgery (N= 5/66, 7.6%; OR 14.959, 95%CI 2.838-78.838) showed significant risk factor for the development of CSFL. In multivariate analysis dura expansion was confirmed as independent risk factor (OR 33.937, 95%CI 4.018-286.615, P=0.001). In addition, patients with CSFL had significant higher rate of meningitis (N=3/7 42.8%, P=0.001). Bed rest was not associated with thrombotic events (N=4/315 0.9%, P=0.666).

Conclusion

Prolonged bed rest did not protect patients from developing CSFL after surgery on intra-dural pathologies. Expansion duroplasty was found to be a risk factor for developing CSFL. Avoiding laminectomy, large voids and minimal invasive approaches play a role in preventing CSFL.

Wirbelsäule und Tumor/*Spine and Tumor*

V055

Ursachen für eine verzögerte operative Therapie von Wirbelsäulenläsionen des Multiplen Myeloms.
Factors contributing to delayed surgery in Multiple Myeloma vertebral column lesions.

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Objective

Vertebral column lesions occur in more than 50% of Multiple Myeloma (MM) patients. Conservative management is the preferred treatment in MM vertebral spine lesions due to the fear of surgical complications especially in case of instrumented spine surgery. However, there are several patients who fail conservative treatment and receive surgery with a certain delay. Data on influencing factors for conservative treatment failure are not yet available. Therefore, the aim of our study is to identify factors that might indicate conservative treatment failure based on a large multicentric collective of MM patients.

Methods

Patients with MM vertebral column lesions were enrolled at three academic centers between 2005-2020. Data was retrospectively assessed regarding epidemiological, clinical, oncological, treatment and outcome data. Univariate and multivariate logistic regression analyses identifying factors at risk for a cross-over from intended conservative treatment to surgical therapy were performed. In cases with imaging follow-up, changes in the sagittal Cobb-angle of index lesions were assessed longitudinally in a group treated with delayed surgery and a matched-pair group of non-surgical patients. Ethical approval (EA4/063/20) was granted.

Results

450 patients were enrolled. Of 308 patients treated surgically, 75 (24%) crossed over from intended conservative management to surgical treatment at a median of 36 (12-300) months. Univariate and multivariate analyses identified a lower grade in the MM International Staging System (ISS 1/2) as significant risk factor for a cross-over to delayed surgery (p=0.007). Age, clinical status, other oncological factors, and SINS were not statistically significant. Longitudinal changes of >10% in the sagittal Cobb-angle revealed increasing deformity from start to preoperative imaging in more patients in the delayed surgery group (13/24, 55%) than from start to follow-up in the non-surgical group (5/20, 25%, p=0.0685).

Conclusion

Uni- and multivariate analyses identified a lower ISS as the only risk factor for a cross-over from intended conservative management to surgical therapy. Interestingly, neither initial SINS nor worsening of SINS over time were determinants of delayed surgery. However, an increase in sagittal Cobb angle seems to be an indicator, which would need to be confirmed based on a larger cohort with continuous imaging follow-up.

Wirbelsäule und Tumor/*Spine and Tumor*

V056

Sicherheit und Wirksamkeit einer minimal-invasiven bildgeführten Hochfrequenzablation in Kombination mit einer perkutanen vertebralen Kyphoplastie-Augmentation bei der Behandlung von Wirbelsäulenmetastasen

Safety and efficacy of minimally invasive image-guided radiofrequency ablation combined with percutaneous vertebral kyphoplasty augmentation in the management of spinal metastases

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Objective

Cure is usually not a realistic expectation of spinal metastases because life expectancy is usually relative. The decision to undergo surgery is complex and controversial. For preoperative evaluation (Tomita Score, Tokuhashi Score, Karnofski performance status) the degree of malignancy and the presence or absence of bone and/or visceral metastases is necessary.

Methods

176 patients with malignant vertebral lesions caused by peripheral metastases underwent radiofrequency ablation (RFA) combined with kyphoplasty (PKP). Pre- and postoperatively the Visual Analogue Scale (VAS) was used to document the patient"s pain. This study analyzed the tumor entity, types of metastases and ESCC in respect to the therapeutic strategies (stereotactic body radiation, mechanical stabilization, RFA combined with PKP). The postoperative outcome (VAS), the risks and side effects of the therapy were illustrated.

Results

All surgical treatments also have a synergistic effect when paired with radiotherapy. The inherent nature of specific primary and metastatic neoplasms determines their biological behavior and dictates which neoplasms grow slowly or rapidly, which are invasive, and which metastasize. This minimally invasive treatment of spinal metastases, RFA combined with balloon PKP can effectively relieve pain, improve patients' ability to engage in daily activities, improve spinal stability, and controlling local tumor progression. From the total patients number of 176, only 2 patients developed tumor recurrence in the same vertebra during 8 Years of this study.

Conclusion

Based on this new algorithm, patients with spinal metastases can achieve a better quality of life through rapid pain relief, fast recovery and minimal interruption of chemotherapy. This algorithm presented here will improve patient-centered treatment of spinal metastases and could become a structured guide for the treatment of spinal metastases considering treatment by RFA in combination with PKP. RFA combined with PKP with inflated balloon appears to be a safe, practical, effective, and reproducible palliative treatment for painful osteolytic spinal metastases.

Wirbelsäule und Tumor/*Spine and Tumor*

V057

Minimal invasive Facettektomie und Fusion für die Resektion von glasuhrförmigen Tumoren in der lumbalen Wirbelsäule

Minimal invasive facetectomy and fusion for resection of dumbbell tumors in the lumbar spine

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Objective

Resection of Eden type 2 and 3 dumbbell tumors in the lumbar can be challenging and facet joint sparing approaches carry the risk of incomplete resections and impaired hemostasis. Additional facetectomy may allow a better exposure; however, it may lead to spinal instability requiring additional fusion. Aim of this study is to compare both methods. Primary outcome was complete resection, secondary outcome measures were postoperative morbidities, tumor progression, and second surgery on follow-up.

Methods

In a cohort study setting, we analyzed all patients with lumbar spinal dumbbell tumors operated on in our department between 2014 and 2021. The facet-sparing and facetectomy approach with minimal-invasive fusion were performed according to individual surgeons" preferences.

Results

Nineteen patients were included into the study, nine of these in the facet-sparing cohort. While only one patient (N=1, 11%) in the facet-sparing group experienced gross total resection (GTR), it was achieved in all cases in the facetectomy group (N=10, $p<0.001$). The relative risk (RR) of incomplete resection in the facet-sparing cohort was 18.70 (CI 95% [1.23-284.047], $p=0.035$) and progression free survival (PFS) was lower in the facet-sparing cohort ($\chi^2(1)=5.273$, $p=0.022$). Except for one case of a transient monoparesis in the facet-sparing cohort, we did not find any relevant postoperative morbidities in both groups. All patients with residual tumor underwent a second resection after a median follow-up time of 42 months (IQR 25-66).

Conclusion

Minimal invasive resection of lumbar dumbbell tumor including facetectomy in combination with an instrumentation appears to be safe and superior to the facet-sparing approach in terms of grade of resection and local tumor control.

Wirbelsäule und Tumor/*Spine and Tumor*

V058

Stabilisierungsoperationen und Implantatversagen bei metastasierter Wirbelsäulenerkrankung, eine Single-Center Outcome Analyse

Stabilization surgery and implant failure in spinal metastatic disease, a single center's outcome analysis

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Objective

Metastatic spinal lesions frequently cause instability of the affected spinal segments and therefore require surgical stabilization. The aim of this retrospective study was to assess the implant failure rate and to investigate potential risk factors for the occurrence of symptomatic implant failure.

Methods

We retrospectively screened the departmental database for patients who received stabilization surgery with or without decompression of neural structures between 2010 – 2020. Preoperative SINS of the afflicted level was calculated in each case. The general condition of the patients was assessed by Karnofsky Performance Score (KPS), the neurological status by Frankel Score. The incidence of implant failure requiring surgical revision was quantified and risk factors as well as technical parameters were analyzed in regression models.

Results

A total of 151 patients were included. Median age at surgery was 65 years. Males were more commonly affected than females (64.9 vs 35.1%). At the time of initial diagnosis of spinal metastases, male patients were on average 66 years and female patients 62 years old. At the time of surgery 81 (53.6%) of the patients were nonsmokers, 38 (25.2%) were active smokers, and 32 (21.2%) were ex-smokers. Lung (25.2%), prostate (17.2%) and breast (13.9) cancer were the dominat primary tumors. Mean preoperative KPS was 60% (20-90%). Mean preoperative SINS was 10 (4-18). Lesions were located in 58 cases (38.4%) in the semirigid, in 42 cases (27.8%) in the mobile spine, in 49 cases (32.5%) in a junctional segment and in 1 case (0.7%) in the rigid spine. In 37 patients (24.5%) stabilization surgery was required as salvage strategy after primary radiotherapy. Posterior instrumentation was performed in 110 (72.8%) patients, ventral approaches in 15 (9.9%) cases, and 360° fixation in 26 (17.2%) cases. Wound healing disorders occurred in 16 (10.5%), symptomatic implant failure in 10 (6.6%) cases. Six patients (40%) with implant failure were previously radiated. However, neither this nor any of the other parameters correlated significantly with the occurrence of implant failure in regression analyses.

Conclusion

The overall rate of failed implants was acceptable in our cohort. So was the rate of wound healing disorders. None of the single parameters investigated predicted implant failure. However, a high proportion of patients required salvage surgery after failed radiotherapy. Further analysis of this subgroup is of great interest.

Highlights der DGNC 2022 – beste Vorträge der Sektionen und Bereichte der Stipendiaten/*Highlights DGNC 2022 – best talks of the sections and reports of the scholarship holders*

Sektion Neuroonkologie

BO-01

Etablierung einer klinisch verwertbaren in vitro Wirkstoffscreening-Plattform zur Identifizierung therapeutischer Angriffspunkte in Primärkulturen zerebraler Metastasen

A clinically compatible in vitro drug-screening platform identifies therapeutic vulnerabilities in primary cultures of brain metastases

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Background

Approximately 20% of cancer patients (including lung, melanoma, breast, renal, and colorectal cancer patients) develop brain metastases (BM). Current systemic therapies often show limited efficacy for brain metastasis treatment and support palliative care only.

Objective

Establishing and characterizing primary cell culture models from BM patients to facilitate personalized preclinical drug screening and for the evaluation of prospective therapeutic strategies.

Methods

In this preclinical study, short-term cultured primary cancer cells from BM patients were molecularly characterized using next-generation sequencing (NGS) and functionally evaluated using high-throughput in vitro drug screening to identify pharmacological treatment sensitivities.

Results

NGS identified matched genetic alterations between BM tissues and corresponding patient derived cultured cancer cells. Employing our in-house high-throughput in vitro drug screening platform, we screened the primary cultures from the BM patients for response to 267 anticancer compounds and integrated the molecular and high-throughput drug screening data sets.

Conclusion

Our preclinical study provides proof-of-concept for combining molecular profiling with in vitro drug screening for improved prediction of therapeutic vulnerabilities in BM patients. Mutant allele frequencies indicated that short-term cultures of cancer cells reflect the existence of distinct subpopulations of cancer cells within BM. This indicates that our short-term cultured primary BM cells are suitable models for recapitulating heterogeneity in the sensitivity of tumor cells to anti-cancer drugs. This approach could advance the use of patient-derived cancer cells in clinical practice and might eventually facilitate decision-making for personalized drug treatment.

Der Vortrag „Establishment of Cell Culture Models from Intracerebral Carcinoma Metastases for Personalized Preclinical Evaluation of Novel Therapeutic Approaches" aus der Sektionstagung Neuroonkologie 2022 wurde für die Jahrestagung der DGNC 2023 um die Ergebnisse des Hochdurchsatztherapiescreenings ergänzt.

Highlights der DGNC 2022 – beste Vorträge der Sektionen und Bereichte der Stipendiaten/*Highlights DGNC 2022 – best talks of the sections and reports of the scholarship holders*

Sektion Neurotrauma und Intensivmedizin

BO-02

Sichtbarmachung der vertikalen Ausbreitung von Spreading Depolarizations und unterschiedlicher regionaler Sauerstoffsättigungsmuster durch photoakustische Bildgebung in der Tiefe des gyrenzephalen Kortex

Visualization of the vertical spread of spreading depolarizations and different regional oxygen saturation patterns by photoacoustic imaging in the depth of the gyrencephalic cortex

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Objective

The objective of this project is the detection of the oxygen saturation and propagation patterns of Spreading Depolarizations (SDs) in the entire depth of the gyrencephalic cortex using photoacoustics.

Methods

The convexity of the brain surface was surgically exposed in seven female swine. Brains were immersed and preconditioned with an elevated K+ concentration (11 mmol/l). SDs were triggered using 1-2 µl of 1 mol/l KCl solution. Changes in local oxygen saturation were registered with a hybrid photoacoustic ultrasonic imaging system that combines a research ultrasound system that uses a center frequency of 7.5MHz and broad acoustic response, with a near-infrared fast tuning optical parametric oscillator laser placed over the exposed cortex in a sagittal view. Additional monitoring by electrocorticography was used to validate the detection of SDs.

A box of 3x3 Regions of interest (ROIs) with a maximum depth of 4mm and inter-ROIs distance of 1,3 mm explored the propagation and local oxygen saturation patterns on the depth plane.

Results

19 SDs were quantified in all experiments in 128 ROIs. A basal local saturation of 62.84 s.d. 6.23% was measured in the cortex. 5 SDs showed not only the known horizontal movement but also a vertical direction through the cortex that has not been seen in vivo before. Those recordings add a dimension of depth to the current understanding of SD movement patterns. The morphology of the waves showed 6 different components formed by hypoxia and hyperoxia. Additionally to the previously described, 13 different hemodynamic patterns in depth were recognized. The most common hemodynamic responses were triphasic, which includes two hyperoxic components and one hypoxic (49.2 %). Mono-, bi-, tetra-, and penta-phasic patterns were also detected. Saturation changes to SDs vary according to brain depth and horizontal localization of the ROIs.

Diffusion gradients seen on the depth of the cortex make the gyrencephalic brain prone to the appearance of heterogeneous SD movement patterns. This adds more complexity to the known movement patterns of the SDs and makes them more unpredictable. Whether SDs that move on deeper layers can be detected using contact electrodes is not known.

Conclusion

The gyrencephalic brain is capable of heterogeneous 3-D SD propagation patterns. The irregularities of the brain cortex may promote the presence of several types of hypoxic responses that may worsen the tissue conditions.

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Sektion Technik und Innovation

BO-03

Neuer Score zur Erfolgsbewertung der endoskopischen dritten Ventrikulostomie bei Hydrocephalus occlusus aufgrund einer Aquäduktstenose – eine retrospektive monozentrale Studie

New score to assess success of endoscopic third ventriculostomy by hydrocephalus occlusus due to aqueduct stenosis: A retrospective monocentral study

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Objective

In occlusive hydrocephalus, a pressure difference between ventricles and basal cisterns is expressed in the form of bulging of third ventricular floor and lamina terminalis. Endoscopic third ventriculocisternostomy (ETV) is the standard treatment in these patients. We tried to assess the success rate of ETV depending on those radiological findings.

Methods

We implemented a simple D-score system retrospectively to assess the state of third ventricular floor (bulging +1, straight 0, retracted -1) as well as lamina terminalis in same manner in the midsagittal CISS MR image. Hence, every patient had a preoperative score from -2 to +2, we compared that score with the direct postoperative MRI and 3 months later and correlated the values with clinical course to decide whether this score is reliable in defining success of ETV.

Results

From 2017-2021, 27 patients were included, who received ETV as a treatment of aqueduct stenosis. Mean age was 29.2 ±24.1 years, 66.7% were females. There was a marked drop in the mean D-score in immediate postoperative MRI grade 2 and 1 (66.7% and 25.9%) to grade 0 and -1 (56% and 24%) and further drop after 3 months in 44.0% and 52.0% of the cases, **p=0.001**. Pediatric and adult patients could be equally assessed using this score.

Conclusio

Using suggested D-Score seems to be reliable in assessment of MR images to define success of ETV correlated with the clinical course in patients with idiopathic aqueduct stenosis. This score should be validated in all other etiologies before widely using it in assessment of MR imaging following ETV.

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Sektion Pädiatrische Neurochirurgie

BO-04

Postnatales Management nach minimal-invasiv fetoskopischem Patch-Verschluss von fetalen Myelomeningocelen (MMC)

Postnatal management after minimally invasive fetoscopic patch closure of fetal myelomeningoceles (MMC)

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Objective

Die MMC gehört zu den häufigsten offenen Neuralrohrdefekten mit Langzeitüberleben. Seit der MOMS-Studie (2011) wird der Vorteil eines pränatalen MMC-Verschlusses diskutiert. Der schwerpunktmäßig am DZFT-Standort Mannheim praktizierte komplett perkutane, minimal-invasiv fetoskopische Patch-Verschluss bietet -bei geringer Invasivität für die Schwangere- eine frühe Neuroprotektion mit vielversprechendem funktionellem Outcome. Das postoperative Management des Patches ist essenziell für einen erfolgreichen Behandlungsabschluss.

Methods

Von 2020-2022 erfolgten 20 minimal-invasiv fetoskopische Patchverschlüsse (25.-30.SSW) in materno-fetaler Vollnarkose. Der Defekt wurde nach Lösung des Rückenmarks und Entfernung pathologischen Gewebes durch Einnaht eines Patches aus Schweine-Dünndarmsubmukosa (Surgisis®) verschlossen. Postnatal erfolgte das stationäre Patchmanagement nach Vorgabe des DZFT ausschließlich mit einem Hydrokolloidpflasterverband (Varihesive®dünn, ConvaTEC). Eine Antibiotikumprophylaxe und strikte Bauch-/Seitlagerung des Kindes erfolgten bis zum vollständigen Defektverschluss. Bei Liquorleck des Patches erfolgte eine Rickhamreservoir-Implantation.

Results

Einmalig wurde ein inkompletter Patchverschluss postnatal neurochirurgisch verschlossen. Die anatomische MMC-Höhe lag bei Th8(n=1), L4(n=10), L5(n=7) und S1(n=2). Der mittlere Durchmesser des Defektes betrug 4cm, der des exponierten Rückenmarks 3,7cm. Frühgeburtlichkeit (<SSW 37) bestand bei 18 Patienten. Davon wurden n=11 spät bis mäßig vorzeitig (SSW 32-36 6/7), n=7 früh (SSW 28-31 6/7) und n=4 sehr früh (<SSW 28) entbunden. In n=9 bestand eine non-/invasive Beatmungspflicht. Eine Antibiotikumprophylaxe in Meningitisdosis wurde nach Liquordichte des Patches reduziert und das Nahtmaterial entfernt. Liquorlecks (n=3) wurden durch Rickhamreservoirpunktion behoben. Bei IVH mit Hydrocephalus (n=2) erfolgte eine Rickhamreservoiranlage (IVH°III-IV, n=1). Die Rate der VP-Shuntimplantation lag bei n=7, die der Ventrikulocisternostomie bei n=1.

Conclusion

Das postoperative Management eines fetoskopischen Patch-Verschlusses einer MMC ist bei Anwendung der speziellen Wundabdeckung, der Lagerungsempfehlungen sowie der Antibiotikumprophylaxe sicher und erfolgreich durchführbar. Die sehr frühe Frühgeburtlichkeit (<28. SSW) bei 20% der Kinder ging in dieser Kohorte

nur in einem Fall mit anhaltenden Komplikationen (posthämorrhagischer Hydrocephalus) einher, bleibt aber Gegenstand der Besorgnis und erfordert eine hochspezialisierte Neonatologie.

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Sektion Vaskuläre Neurochirurgie

BO-05

Umweltbedingte Risikofaktoren bei aneurysmatischer Subarachnoidalblutung (SAH) – globale ultraviolette Strahlung korreliert invers mit der SAH-Inzidenz

Environmental risk factors in aneurysmal subarachnoid hemorrhage (SAH): global Ultraviolet Radiation correlates inversely with SAH incidence

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Objective

Inflammation is involved in development and rupture of intracranial aneurysms. Accordingly, anti-inflammatory counter-regulation could reduce this inflammatory process and decrease incidence of aneurysmal subarachnoid hemorrhage (SAH). Sun exposure, hence ultraviolet (UV) radiation, leads to an anti-inflammatory response by immunosuppression. We therefore studied whether the occurrence of SAH correlates with UV radiation.

Methods

SAH incidences were available from 32 countries based on a recent metaanalysis of 75 studies of our working group. Data for UV radiation quantified by the UV index were obtained from the Tropospheric Emission Monitoring Internet Service (TEMIS), a database provided by the Royal Netherlands Meteorological Institute (KNMI). We included only those countries where we had data on both incidence and UV index. Statistical Spearman correlation analysis of the data was performed with R Studio (R Version 4.1.2; Boston, USA).

Results

In the selected 27 countries the SAH incidence ranged from 1.3 to 27 per 100,000 person-years (p-y) and UV Index ranged from 1.76 to 11.27. The correlation analysis showed a significant negative correlation between crude SAH incidence and UV index (rho = -0.48, p=0.012). The SAH incidence was highest in Japan (13.7 - 27.9 p-y) with an UV index 6.28. The country with the highest UV index 11.27 was Chile with a lower SAH incidence (3.8 – 4.8 p-y); the lowest UV index 1.76 was seen in Iceland with a higher SAH incidence (9.8 p-y).Within Europe, regions with higher UV indices reported slightly lower SAH incidences (Northwest Europe: mean SAH incidence p-y 8.61/ UV index 2.85; Southern and Eastern Europe: mean SAH incidence p-y 7.37 / UV index 4.65) with a significant inverse correlation (rho = -0.68, p= 0.004) and not a significant correlation between non-European countries (rho=-0.43, p= 0.19).

Conclusion

Incidence of SAH correlates inversely with the UV radiation, which is in line with the winter peak in SAH incidence. Although the UV index per se is not a singular factor leading to aneurysm wall rupture, our findings implicate and support the hypothesis that anti-inflammatory effects of a patient's environment such as the sun exposure and thus, UV light exposition and vitamin D synthesis, might modulate tissue properties and prevent intracranial aneurysm rupture. Thus, the preventive intake of vitamin D for patients with intracranial aneurysms should be investigated in further studies.

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Sektion Funktionelle Neurochirurgie

BO-07

Tiefe Hirnstimulation des vorderen Schenkels der inneren Kapsel bei Zwangsneurosen. Wo soll stimuliert werden?

Deep brain stimulation of the anterior limb of the internal capsule for obsessive-compulsive disorder: Where to stimulate?

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Objective

Deep brain stimulation (DBS) can be offered to patients with treatment refractory obsessive-compulsive disorder (OCD) as a last resort therapy. Since the first case in 1999, several possible stimulation targets have emerged, including the nucleus accumbens (Nacc), the anterior limb of the internal capsule (ALIC), the subthalamic nucleus and the bed nucleus of stria terminalis. In recent studies a novel, unified connectomic network has been suggested, which links all these targets with projections to the orbitofrontal cortex. Nevertheless, the most optimal location to stimulate these targets is still controversial. The aim of this study was to analyze the clinical outcome of OCD patients based on the anatomical location of the stimulated area within the ALIC.

Methods

We retrospectively analyzed the clinical outcome of 13 OCD patients who were treated with bilateral Nacc/ALIC DBS at our clinic. Lead localization was reconstructed based on the preoperative MRI and the postoperative CT using Lead-DBS. The electric field profile was calculated based on the stimulation parameters 12 months after the surgery. Clinical improvement of the patients was measured using the Yale-Brown Obsessive-Compulsive Scale (YBOCS) before the surgery and after one year of DBS.

Results

The electric fields generated by the active contacts were more central in the coronal plane within the ALIC on the left side in responders than in non-responders, which were more medial or more lateral. There was no difference between the two groups in the anterior-posterior or dorsal-ventral location of the electric fields.

Conclusion

Stimulation of the central ALIC on the left side seems to be associated with a better clinical outcome in patients with treatment refractory OCD. A correlation between clinical improvement and more dorsal and posterior location of the stimulation fields, as reported in previous studies, could not be shown in our cohort.

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Sektion Periphere Nerven

BO-08

Der Nervus musculocutaneus als Empfänger der Nervenreparatur bei der Wiederherstellung der Bizepsfunktion - eine retrospektive Überprüfung von 146 Brachialplexusoperationen

The musculocutaneus nerve as a recipient of nerve repair in restoration of biceps function – a retrospective review of 146 brachial plexus operations

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Objective

A brachial plexus lesion is a devastating injury often affecting young, male adults after traffic accidents. Therefore, surgical restoration of elbow flexion is critical for establishing antigravity movement of the upper extremity. We analyzed different methods for musculocutaneous reconstruction in regard to outcome.

Methods

We conducted a retrospective analysis of 146 brachial plexus surgeries with musculocutaneous reconstruction performed at our department from 2013 to 2017. Demographic data, surgical method, donor and graft nerve characteristics, body mass index (BMI) as well as functional outcome of biceps muscle based on medical research council (MRC) strength grades before and after surgery were analyzed. Multivariate analysis was performed using SPSS.

Results

Oberlin reconstruction was the procedure performed most often (34.2%, n=50). In case of nerve transfers, we found no significant difference whether reconstruction was performed with or without a nerve graft (e.g. sural nerve) (p=0.277, OR 0.619 CI95% 0.261-1.469). Furthermore, nerve transfer and autologous repair showed no significant differences regarding outcome (p=0.599, OR 0.644 CI95% 0.126-3.307). Multivariate analysis identifies patient age as a strong predictor for outcome, univariate analysis indicates that nerve graft length >15 cm and BMI of > 25 could lead to inferior outcome. When patients with early recovery (n=19) are included into final evaluation after 24 months, the general success rate of reconstructions is 62,7% (52/83).

Conclusion

Reconstruction of musculocutaneous nerve after brachial plexus injury results in a high rate of clinical improvement. Nerve transfer and autologous reconstruction both show similar results. Young age was confirmed as an independent predictor for better clinical outcome. Prospective multicenter studies are needed to further clarify.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V059

Neues Anatomisch-Funktionalles Aphasie-Screening (AFAS) bei Patienten mit links-hemisphäriellen Hirntumoren
New Anatomical Functional Aphasia Screening (AFAS) in patients with left sided brain tumors

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Objective

The Aachener Aphasia Test (AAT) is the most commonly used diagnostic tool for a detailed language analysis for German speaking patients. However, it is very time consuming as well as primarily developed for aphasia therapy of stroke patients and does not account for specific anatomical-functional disruptions of the complex language network relevant in neurosurgery. Here, we describe our preliminary experience with a newly developed language test.

Methods

After reviewing various language tests in the literature, a new Anatomical Functional Aphasia Screening (AFAS) was designed on the basis of the dual stream model of language with various subtests for auditory and visual receptive and expressive tasks for naming, reading, writing, calculating, phonology/phonetics, articulation, semantics, lexicon, syntax, situational comprehension, working memory, figural description, and face recognition.

Results

The AFAS was compared to the AAT in 11 patients (2 female/9 male, age range 21 to 70, mean 49.5 years) with left sided brain tumors (4 low grade, 5 high grade glioma,2 other entities) pre- and postoperatively. Findings were compared to cortical lesions and subcortical language tract interruptions (fasciculi arcuatus, frontooccipitalis inferior, longitudinalis medialis et inferior, uncinatus and frontal aslant tract) using MRI/DTI tractography.All 4 patients with a postoperative AAT language deterioration were also detected with the AFAS. Two patients from the 7 patients without AAT language decline showed a deterioration in the AFAS score. One patient with a temporal high grade glioma and disruption of UF, MLF and ILF showed a loss of figural description, and face recognition. In the other patient sematic impairment was associated with an interruption of IFOF. With a mean test duration of 25 min (range 17 to 36 min) the AFAS was less time consuming than the AAT with a mean of 68 min (range 43 to 97 min).

Conclusion

The AFAS appears to be a promising clinical tool for precise individual assessment of perioperative language deficits in brain tumor patients. It may allow an assignment of certain task deficit combinations to specific cortical lesions and/or white matter tract interruptions.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V060

Einfluss der Item-Komplexität und Wortfrequenz auf die Reliabilität der Sprachkartierungen bei aphasischen Gliompatient:innen

Impact of item complexity and word frequency on language mapping reliability in aphasic glioma patients

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Objective

Localizing language-relevant cortical sites to preserve residual language abilities is a major objective in the neurosurgical treatment of language-eloquent gliomas. However, in this cohort pre-existing language deficits frequently impact the feasibility and reliability of navigated transcranial magnetic stimulation (nTMS) language mapping. This study ascertained whether complexity of items confounds the outcome of language mappings in aphasic glioma patients.

Methods

A post-hoc analysis of patients with moderate and severe expressive aphasia was conducted based on a cohort of 96 glioma patients undergoing object naming-based mapping between 05/2018 and 01/2021. Patient's performance, particularly the impact of item complexity of individual subsets of items each patient could produce reliably, on feasibility and outcome of mappings was investigated. Item complexity analysis comprised age-of-acquisition, word frequency, syllable length, compound words and animacy.

Results

Within 4 severely and 16 moderately aphasic glioma patients (59.6 ± 14.4yrs, 11 male) items with significantly lower age-of-acquisition, higher word frequency as well as lower relative amount of multisyllabic, compound, and non-animate words were used during the stimulation exam (all $p \leq 0.01$). Still, of these complexity-reduced subsets, objects with significantly lower frequency and higher relative amount of three-syllabic compared to monosyllabic words were more error-prone during stimulation (both $p \leq 0.03$) resulting on average in 5.4 ± 3.6 error-prone items potentially increasing the amount of false positive cortical sites in aphasic cohorts.

Conclusion

The present results demonstrate that more complex and less frequent items are more susceptible to errors during stimulation application in expressive aphasic patients. Thus, tailoring tasks and their linguistic complexity to patients' abilities may substantially support the preservation of residual function in aphasic glioma patients by reducing the impact of pre-existing aphasia, thus improving the reliability by reducing false positives during nTMS-based language mapping.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V061

Automatisierte Pipeline zur Modellierung der Auswirkungen von Gliom-Infiltration und deren Nähe zu Netzwerken der weißen Substanz auf die Sprachfunktion

Automated pipeline for modeling the effects of glioma infiltration and proximity to white matter fiber bundles on language function

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Objective

Understanding how alterations in white matter lead to language impairments in glioma patients enables us to better understand individual fiber bundle functions and improves preoperative patient assessments. In this study, we created an automated pipeline to model the relationship between language function and glioma infiltration as well as its relative positioning to major white matter tracts.

Methods

We included 63 right-handed patients (29 female, mean age 53 years) in this study with left-hemispheric language-eloquent gliomas. Patients were preoperatively assessed using the AAT with four subtests: token test, object naming, speech repetition, and speech comprehension. We performed automated tractography with TractSeg to obtain 41 left-hemispheric white matter tracts (Fig. 1). Furthermore, we used an automated pipeline to measure the lesion to tract distance (LTD) and the tumor tract overlap (TTO). Segmentation of tracts was performed with resampling techniques in MRtrix3 to assess the parts of the affected tract.

Results

Analysis using a three-segment model showed a significant TTO increase in aphasic patients in 7 of the 41 tracts. These were the arcuate fasciculus (AF) (all segments), inferior longitudinal fasciculus (ILF) (mid/post), middle longitudinal fasciculus (MLF) (all segments), the inferior fronto-occipital fasciculus (IFOF) (mid/post) the optic radiation (OR) (all segments), striatal-occipital (ST_OCC) (all segments), and thalamic-occipital (T_OCC) (all segments) pathways (Table 1). Using LTD, regression analyses with the speech repetition test showed an association with the AF ($p = .042$) and SLF_III ($p = .049$). The speech comprehension test was associated with the IFOF ($p = .026$) and the ILF ($p = .035$). The object naming test was also associated with the ILF ($p = .035$) and IFOF ($p = .039$). Additionally, distances from the lesion to the striatal and thalamic pathways as well as the optic radiation were found to correlate with speech comprehension (OR, $p < .001$; ST_OCC, $p = .004$; T_OCC, $p = .009$), object naming (OR, $p = .001$; ST_OCC, $p = .005$, T_OCC, $p < .001$), and speech repetition tasks (ST_OCC, $p = .022$).

Conclusion

In this study, we demonstrated significant associations between glioma infiltration and distance to various language-relevant tracts as well as several tracts connecting the occipital cortex using an automated pipeline. This model's validity has relevant potential to enhance future preoperative neurosurgical planning and analyses.

Abb. 1

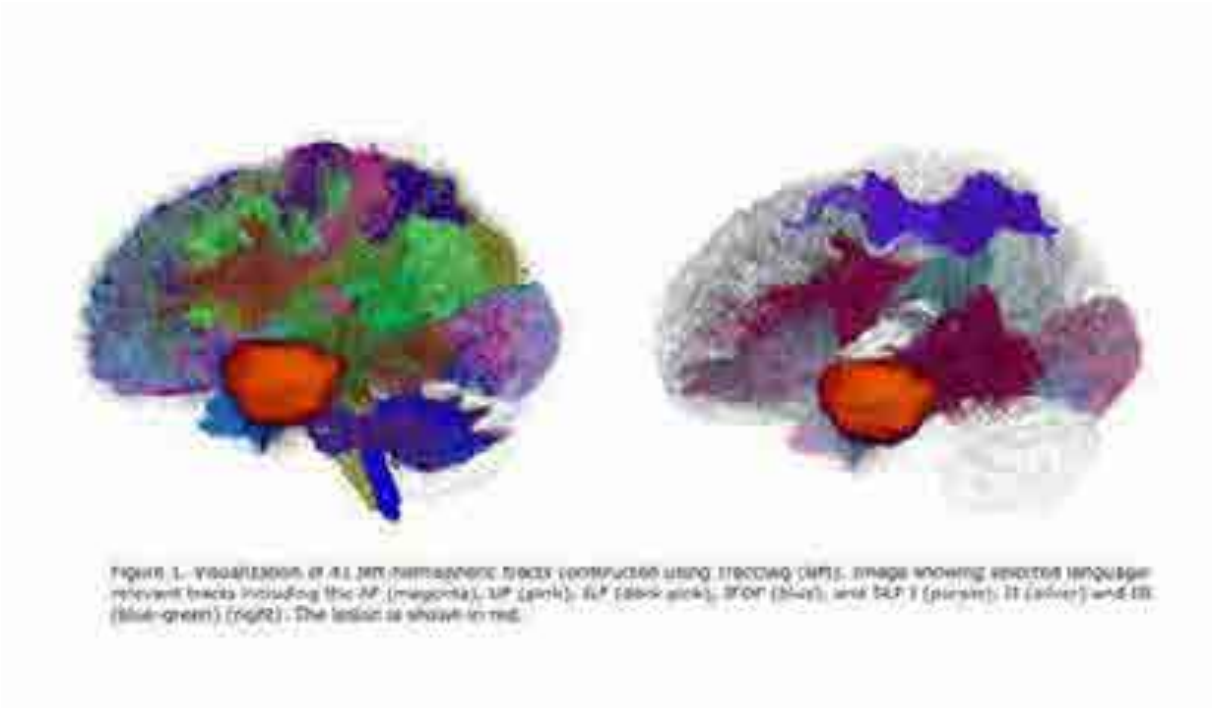

Figure 1. Visualization of 41 left hemispheric tracts constructed using trackvis (left). Image showing selective language relevant tracts including the AF (magenta), UF (pink), ILF (dark pink), IFOF (blue), and SLF I (purple), II (silver) and III (blue-green) (right). The lesion is shown in red.

Abb. 2

Table 1: Fiber bundles and their TTO-AAT associations based on 3-Segment model

Fiber Bundles	Segment 1	Segment 2	Segment 3
	p-values		
AF	0.025*	0.023*	0.011*
ATR	0.107	0.158	0.107
CA	0.288	0.550	0.288
CC	0.135	0.666	0.176
CC_1	0.219	0.219	0.152
CC_2	0.082	0.302	0.084
CC_3	0.139	0.410	0.139
CC_4	0.818	1.000	0.818
CC_5	0.500	0.500	0.500
CC_6	0.053	0.526	0.053
CC_7	0.056	0.165	0.054
CG	0.120	0.120	0.120
CST	0.139	0.172	0.139
FPT	0.306	0.391	0.233
FX	1.000	1.000	1.000
ICP	0.157	1.000	0.157
IFOF	0.057	0.004*	0.019*
ILF	0.030*	0.061	0.026*
MCP	1.000	1.000	1.000
MLF	0.038*	0.036*	0.047*
OR	0.000**	0.000**	0.000**
POPT	0.348	0.348	0.686
SCP	0.200	0.495	0.200
SLF_I	0.090	0.242	0.090
SLF_II	0.550	0.774	0.566
SLF_III	0.180	0.638	0.180
ST_FO	0.104	0.104	0.104
ST_OCC	0.000**	0.000**	0.000**
ST_PAR	0.050	0.058	0.056
ST_POST	0.317	0.200	0.317
ST_PREC	0.609	0.674	0.895
ST_PREF	0.080	0.103	0.085
ST_PREM	0.115	0.201	0.088
STR	0.503	0.249	0.503
T_OCC	0.000**	0.000**	0.000**
T_PAR	0.141	0.059	0.141
T_POSTC	0.951	0.390	0.951
T_PREC	0.711	0.920	0.711
T_PREF	0.077	0.544	0.055
T_PREM	0.135	0.251	0.135
UF	0.440	0.662	0.440

*Significance at a p<.05; **significance at p<.001.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V062

Tractographie der dorsalen und ventralen Sprachnetzwerk-Ströme, informiert durch gebündeltes *sparse sampling* fMRT mit zwei unterschiedlichen Aufgaben

Tractography of the language networks dorsal and ventral streams informed by clustered sparse sampling fMRI of two distinct language tasks

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Objective

Functional MRI (fMRI) can inform not only on eloquent cortex, but also help identify the underlying white matter structures, in combination with diffusion MRI (dMRI). This is of particular importance for mapping language function, due to its complexity and its intra- and interindividual variability. However, scanner acoustic noise introduces bias to the fMRI measurements. Recently, clustered sparse sampling fMRI (css-fMRI) acquisitions have been introduced to deal with this issue. In this study, we assess the feasibility of tractography reconstruction of the language network based on css-fMRI during two distinct language tasks, targeting lexicon retrieval and semantical processes.

Methods

We recruited 18 healthy, right-handed German native speakers to undergo MRI. Overt picture naming (PN) and semantic decision (SD) tasks were conducted under css-fMRI. During the SD task, the volunteer had to identify, from a set of 3 pictures, the one which semantically fitted the sentence presented to the volunteer auditively. Additionally, dMRI was also acquired, with 40 diffusion directions. The fMRI data was processed using SPM12 standard pipeline. The dMRI data was preprocessed, modelled, following fMRI-informed probabilistic tractography reconstruction, using MRtrix. To test clinical feasibility, this protocol has been tested as a pilot trial in a consecutive cohort of 25 patients with supratentorial gliomas.

Results

In our healthy cohort, ubiquitously identified tracts included the arcuate fascicle (PN=90%; SD=95%), inferior fronto occipital fascicle (PN=100%; SD=95%), and inferior longitudinal fascicle (PN=100%; SD=90%). Tracts consistently delineated based on SD were the frontal aslant tract (PN=55%; SD=100%), and the superior longitudinal fascicle (PN=55%; SD=90%). The uncinate fascicle was most consistently delineated using PN (PN=90%; SD=55%). Clinically, the protocol proved feasible in all cases, and was successfully used to inform surgical planning and to guide intraoperative awake mapping and monitoring.

Conclusion

We could identify major tracts of the language network with css-fMRI and a combination of two tasks. These two tasks, PN and SD, target the dorsal and ventral streams of the language network. Their combination might lead to a better depiction of the individual functional anatomy and might be especially useful to identify language-critical structures for the surgery of anatomy corrupting pathologies.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V063

Strukturelle Konnektomanalyse des Sprachnetzwerks bei Gliompatienten
Structural connectome analysis of the language network in glioma patients

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Objective

Left hemispheric gliomas cause damage to white matter (WM) structure and may lead to language dysfunction. The effects of gliomas should be determined individually for better preoperative analysis. Here, we aimed to understand glioma effects on structural connectivity and language function. We used patients" connectomes to identify associations between aphasia and structural network topology using graph theoretical analyses.

Methods

We included 34 patients with left-hemispheric gliomas invading language network (WHO grade II (7), III (8), IV (19), 32 females, mean age=51, SD=12 age range 21-72). Language function was assessed preoperatively using the Aachen aphasia test (AAT). AAT subtests included the token test, naming, repetition, and speech comprehension. To obtain whole brain tractograms, we implemented constrained spherical deconvolution to estimate fiber orientation distributions. Subsequently, we performed anatomically constrained tractography and spherical-deconvolution-informed filtering of tractograms using MRtrix3. Connectome matrices were constructed based on the whole brain tractography and the Desikan-Killiany-Tourville atlas using FastSurfer. Finally, we calculated graph and node network measures such as local and global efficiency, node strength, betweenness centrality (BC), and clustering coefficients. We then correlated these measures with the AAT subtests using Spearman rank correlation analysis.

Results

We found significant correlations between global efficiency and speech repetition (rs(32)=0.37, p=0.04). Nodal measures correlated significantly to AAT subtests in regions of both hemispheres, with a stronger correlation in the left hemisphere. The left inferior temporal gyrus showed the strongest negative correlation between BC and naming (rs(32)=-0.62, p=1.5e-4), and with BC and token test (rs(32)=-0.61, p=1.8e-4). The left paracentral region correlated most strongly with speech repetition and BC (rs(32)=-0.67, p=3.04e-5), and speech comprehension and BC (rs(32)=-0.57, p=5.7e-4).

Conclusion

Network measures allow us to associate language impairments with structural network topology and identify structure-related functional hubs in individual brain networks. We found significant brain-wide correlates of affected network topology in relation to specific language function aspects. These analyses introduce the prospect of novel, integrated preoperative planning and provide more detailed insights into complex language functioning.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V064

Relevante kortikale Sprachverständnisareale bei hochgradigen Gliom-Patient:innen mit rezeptiver Aphasie

Crucial cortical comprehension sites in high-grade glioma patients with receptive aphasia

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Objective

Patients with language-eloquent high-grade gliomas (HGG) typically present with severe language network disruptions and deficits. Whilst the brain's potential to reorganize and compensate functional loss to a certain extent is widely acknowledged, underlying processes remain poorly understood. This study evaluated which cortical hubs of the language network are relevant for comprehension in context of receptive aphasia in HGG patients.

Methods

Patients with language-eloquent HGG underwent left-hemispheric auditory comprehension-based language mapping with navigated transcranial magnetic stimulation. Baseline error rates (BER) prior to stimulation determined the extend of receptive deficits. Correlational analyses between stimulation-induced error rates in highly language-eloquent cortical sites and BER were conducted.

Results

The mean BER of 18 HGG patients (age=53.2±14.2 years, 77.8% male) was 15.3% (range: 0.0%-62.9%). Higher BER correlated with a higher involvement during comprehension, i.e. higher stimulation-induced error rates, of pars opercularis of inferior frontal (opIFG, r=0.62, p=0.008), posterior superior temporal (pSTG, r=0.47, p=0.047) and angular gyrus (AnG, r=0.57, p=0.013) indicating a substantial functional role of these cortical language network hubs in aphasic patients.

Conclusion

The present findings demonstrate that the extent of comprehension difficulties varies considerably in HGG. Poorer language comprehension was associated with the recruitment of opIFG, AnG and pSTG for language comprehension. Thus, these language-relevant cortical sites may become even more crucial for comprehension in patients with language-network infiltrating HGG affecting receptive language skills. These results and subsequent network-based analyses may advance the understanding of neural mechanisms promoting receptive aphasia and of functional adaption in HGG.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V065

Szenariobeschreibung zur standardisierteren intraoperativen Bewertung räumlich-visueller and sprachlicher Fertigkeiten

Scenario description for a more standardised intraoperative monitoring of visuospatial and linguistic skills

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Objective

Picture naming is the most commonly used task for intraoperative language mapping, but it is only conditionally suitable for longer tests during intraoperative monitoring and, due to its simplicity, cannot detect more subtle language deficits such as syntax errors. In contrast, spontaneous speech (e.g. with biographical triggers) is difficult to monitor, which has a negative impact on sensitivity. Here we designed and tested scenario drawings to trigger controllable production of sentences.

Methods

Twelve healthy subjects (6 males; 6 females) between 18-75 years of age were asked to describe black-and-white drawn pictures in two conditions, either in one sentence (A) or as detailed as possible with unlimited sentences (B). The pictures, either black and white (line pictures) or grey-scale colored (fill pictures), were then rated in a Likert scale (1-10) on "familiarity", "recognisability", "describability" and "emotions". All sessions were performed via video-conference. The distinct task conditions were presented in pseudo-randomised order using a custom PsychoPy skript. Groups were compared using Student"s t-test. In addition, the aformentioned scenario pictures were used before and during awake glioma surgery to test the clinical feasibility, especially for the fill version of the pictures.

Results

When comparing line and fill pictures, "recognisability"was betterfor fill pictures ($p=0.01$). There was a trend towards a higher number of produced words and speaking time in both conditions A and B ($p<0.1$). When condition A was presented in the first block of testing, total word count and speaking time were increased compared to second block ($p<0.001$). Vice versa, in condition B, total word count and speaking time were increased when presented in the second testing block ($p<0.001$). The pilot experience from the intraoperative use of the scenario images during awake brain tumour surgery confirms its feasibility and very good acceptance by the patients.

Conclusion

Scenario description might nicely complement the awake surgery material, especially for the monitoring part. The usage of colored (fill) pictures is favourable with regard to recognisability. For unlimited sentence production, there is a positive effect of training on the test performance.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V066

Korrelationen von visuokonstruktiven Defiziten und visuell-räumlichen Gedächtnisstörungen mit Tumorlokalisationen im rechtshemisphärischen ventralen Verarbeitungsstrom

Correlation of deficits in visuoconstructional abilities and visuospatial memory with tumor locations in different parts of the right hemispheric ventral stream

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Objective

Glioblastoma (GB) patients suffer frequently from neurocognitive deficits. This can lead to severe difficulties in daily living activities and social interaction, with negative effects on quality of life and the therapeutic outcome. Visuospatial ability represents an essential neurocognitive domain and the performance in visuospatial tests can predict difficulties in important everyday activities. The aims of this study were to examine the influence of tumor volume and hemispheric lateralisation on the aforementioned neurocognitive functions, and to identify tumor localisations corresponding to respective deficits.

Methods

226 patients (144 males, median age 63 yrs [24-83]) with previously untreated unilateral GB completed a battery of 11 standard neurocognitive tests which included a compex figure test (CFT) consisting of two trials: (i) copying: visuoperceptional and -constructional abilities and (ii) recall after 20-30 minutes: visuospatial memory. The contrast-enhancing (CE) tumor volumes were segmented in the preoperative CE-T1 MRIs to generate volumes of interest. A mass univariate voxel-based lesion symptom mapping (VLSM; Package LESYMAP, BMfast) followed by intersection with a standard brain atlas was performed to map lesion locations corresponding to deficits in CFT performance. Spearman correlations between test scores of the CFT and the tumor volumes were calculated. Differences in CFT performance between patients with right hemispheric (RH) versus left hemispheric tumors were tested using Wilcoxon test.

Results

The VLSM showed a significant correlation of low scores in the CFT copy trial with tumor localisations in the RH middle temporal gyrus, supramarginal gyrus and posterior inferior parts of the superior and inferior longitudinal fascicle. Lesions located in the RH temporal fusiform gyrus, parahippocampal gyrus and the anterior inferior parts of the superior and inferior longitudinal fascicle were correlated with weaker performance in the recall

trial. RH tumor location correlated with copy ($p=0.019$) and recall ($p=0.048$) trial results, tumor volume with copy trial performance ($p<0.0001$).

Conclusion

GB affecting distinct components of the right ventral stream likely cause deficits in visuospatial memory and visuoconstructional abilities. For such patients, specific neurocognitive testing is advisable. The integration of corresponding tasks in the peri- and intraoperative mapping and monitoring should be considered.

Neurophysiologie, IOM und Bildgebung Sprache und visuo-spatielle Funktionen/*Neurophysiology, IOM and Imaging Language and visuospatial function*

V067

Der Einfluss von Hirntumoren und vaskulären Läsionen im okzipitalen Kortex auf die funktionelle Konnektivität im visuellen System

The influence of brain tumors and vascular lesions in the occipital cortex on functional connectivity networks in the visual system

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Objective

Space-occupying brain lesions as brain tumors in the occipital lobe have only been sparsely investigated so far, as this localization is extremely rare with only 1% of cases. It is still unclear how this affects the overall organization of the visual system. We investigated functional connectivity of functional networks associated with higher visual processing between patients with occipital space-occupying lesion in the occipital cortex and healthy controls.

Methods

12 patients with brain tumors, 7 patients with vascular lesions in the occipital cortex and 19 healthy subjects matched for age and sex were included. During functional MRI patients and subjects performed a visual excentricity mapping task. Data analysis was done using CONN toolbox based on Matlab. See-to-ROI connectivities of 23 Regions of Interest (ROIs) implemented in the CONN toolbox which were assigned to the Default Mode, Visual, Salience, Dorsal Attention, and Frontoparietal network were assessed. For each subject, connectivity was calculated using Fischer transformed pairwise correlations. These correlations were first considered separately for each group in one-sample analyses and then compared between the groups.

Results

Intra- and between-network connectivity in the visual system could be shown for patients with brain tumors and vascular lesions in the occipital cortex. Tumor patients and vascular patients show huge significant differences in the intra- and between-network connectivity in the visual system. Further, a significant weaker between-network connectivity in patients than in healthy subjects was observed next to a stronger between-network connectivity in tumor patients than in vascular patients. Compared to vascular patients and healthy controls, tumor patients show significant intra- and between-network connectivity in many components of the default mode network. Patients with brain tumors and vascular lesions differ significantely from healthy controls mostly in weaker intra- and between-network components of the salience network.

Conclusion

The results indicate that in the course of the disease, compensatory countermeasures take place in the brain against a brain tumor or a space-occupying brain lesion with the aim of maintaining the performance level and cognitive processes for as long as possible.

Vestibularisschwannome I Operation und / oder Radiochirurgie/*Vestibular schwannomas I surgery and/vs radiosurgery*

V068

Interdisziplinäres Behandlungs- & Ausbildungs-Konzept bei einer Serie von 1036 Vestibularisschwannomen
Interdisciplinary treatment & teaching concept in a series of 1,036 vestibular schwannomas

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Objective

As conservative options have evolved, there is a shift towards later surgery at more advanced tumor stages. Skull base surgeons need to provide treatment and its training at a high standard, in order to keep sequels as low as possible. This study focusses on interdisciplinary approaches, master and teaching surgery and related clinical outcome.

Methods

From 2005 to 2020, 1,036 tumor resections were performed in 999 patients (53% female, 14% Neurofibromatosis Type 2) under continuous neuro-monitoring, via a middle fossa approach in 350 VS and via the retro-sigmoid approach in 686 VS, by an interdisciplinary oto-neuro-surgical team led by three experienced neurosurgical skull base surgeons and two oto-surgeons. Standardized documentation of auditory and facial functions before and after surgery, of intra- and postoperative sequels and complications was the basis for this analysis. Parameters of analysis were facial nerve function by House-Brackmann-Scale, auditory function by AAO classification, tumor extension with and without brainstem involvement. Tumor sizes and facial outcomes were compared for resections performed by senior and by trainee surgeons.

Results

There were 586 (57%) small T1 to T3A tumors without brainstem involvement, 450 (43%) large T3B to T5 tumors. In 350 MF approaches resection was always carried out complete; in 686 RS approaches, 640 operations (93%) were performed as CR, 7% as PR.Facial and auditory outcome showed significant dependence on pre-surgical function and on tumor sizes. Despite high incidences of NF-2 (14%) and recurrences (9%) referred to supra-regionally, anatomical facial and cochlear nerve preservation rates were high (98.7%/ 63%).Facial outcome was similar in small tumors by both approaches: HB°1-2 by the MF in 96%, by RS in 89% at 1 year. In large tumors, good facial function HB°1-2 were reached at 83% at 1 year. Auditory preservation at classes A and B was achieved in 177 of 273 cases (65%) for T1 and T2 VS by MF approach, and by RS approach in 37 of 123 (42%) in T2-T3a VS and in 39 of 198 (22%) large tumors. Sub-group analysis of 477 operations provided higher HB°1-2 by the trainee-senior team than by the senior surgeons, at similar complication rates.

Conclusion

Tumor size and individual co-morbidity remain the most important risk factors. Thorough interdisciplinary patient counselling supports identification of the individual adequate treatment and belongs to the overall training concept.

Vestibularisschwannome I Operation und / oder Radiochirurgie/*Vestibular schwannomas I surgery and/vs radiosurgery*

V069

Wie lagert man den Patienten? Eine Metaanalyse zur Lagerung bei der Vestibularisschwannomchirurgie über den retrosigmoidalen Zugang

How to position the patient? A meta-analysis of positioning in vestibular schwannoma surgery via the retrosigmoid approach

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Objective

Positioning is a matter of ongoing debate in the surgical treatment of vestibular schwannoma (VS). Main endpoints of this discussion are preservation of facial nerve functioning, extent of resection, and complications. In this meta-analysis, we aim to investigate the impact of semi-sitting or lateral positioning on VS surgery via the retrosigmoid approach.

Methods

We searched for eligible comparative trials on PubMed, Cochrane library, and Web of Science. Positioning groups were compared regarding facial nerve outcome, extent of resection, postoperative hydrocephalus, postoperative CSF leaks, perioperative venous air embolism, and perioperative mortality. Two groups of positions were defined, and the following positions were allocated to those groups: (1) Semi-sitting, and Sitting-position; (2) Lateral position, supine position with extensive head rotation, lateral oblique (=Fukushima/Three-quarter prone), and park-bench position.

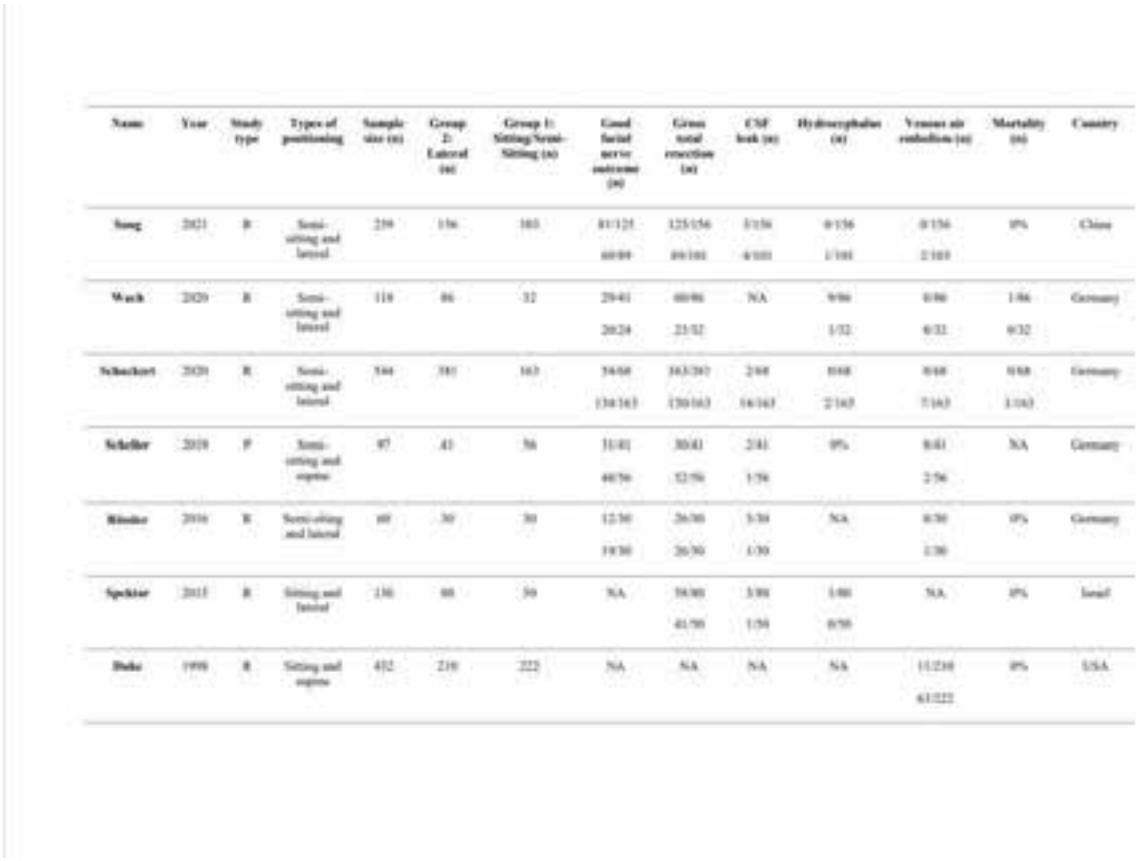
Results

From 374 full-text screenings, 7 studies met the criteria and were included in our meta-analysis comprising 1640 patients. Our results demonstrate a significantly better long-term (≥6 months) outcome of the facial nerve after VS surgery in the semi-sitting positioning (OR: 1.49, 95%CI: 1.03-2.15, $p = 0.03$). Positioning did not influence the extent of resection, rate of postoperative CSF leaks, and the presence of a postoperative hydrocephalus. Overall incidence of venous air embolisms were significantly associated with VS surgery in sitting positioning (OR: 6.77, 95% CI: 3.66-12.54, $p < 0.00001$). Perioperative mortality was equal among both positioning groups.

Conclusion

Semi-sitting positioning seems to be associated with an improved facial nerve outcome after VS surgery via the retrosigmoid approach. Venous air embolisms are significantly more often observed among VS patients who underwent surgery in the sitting position, but the perioperative mortality is equal in both positioning groups. Both positioning groups are a safe procedure. Multicentric prospective randomized trials are needed to evaluate the risk-benefit ratio of each positioning in VS surgery via the retrosigmoid approach.

Abb. 1



Name	Year	Study type	Types of positioning	Sample size (n)	Group 2: Lateral (n)	Group 1: Sitting/Semi-Sitting (n)	Good facial nerve outcome (n)	Gross total resection (n)	CSF leak (n)	Hydrocephalus (n)	Venous air embolism (n)	Mortality (n)	Country
Song	2021	R	Semi-sitting and lateral	259	156	103	81/125 68/89	125/156 89/103	3/156 4/103	0/156 1/103	0/156 2/103	0%	China
Wach	2020	R	Semi-sitting and lateral	118	86	32	29/41 20/24	68/86 23/32	NA	9/86 1/32	0/86 0/32	1/86 0/32	Germany
Schuckert	2020	R	Semi-sitting and lateral	544	381	163	54/68 134/163	163/381 130/163	2/68 14/163	0/68 2/163	0/68 7/163	0/68 1/163	Germany
Schaller	2019	P	Semi-sitting and supine	97	41	56	31/41 46/56	30/41 52/56	2/41 1/56	0%	0/41 2/56	NA	Germany
Rimkus	2016	R	Semi-sitting and lateral	60	30	30	12/30 19/30	26/30 26/30	5/30 1/30	NA	0/30 1/30	0%	Germany
Spektor	2015	R	Sitting and lateral	156	66	90	NA	58/90 41/66	3/90 1/66	1/90 0/66	NA	0%	Israel
Duke	1998	R	Sitting and supine	432	210	222	NA	NA	NA	NA	11/210 63/222	0%	USA

Vestibularisschwannome I Operation und / oder Radiochirurgie/*Vestibular schwannomas I surgery and/vs radiosurgery*

V073

Die Tumorlokalisation beeinflusst das Auftreten von Radionekrosen bei benignen intrakraniellen Tumoren

Tumor location impacts the development of radiation necrosis in benign intracranial tumors.

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Objective

Radiation necrosis (RN) is a possible late sequela of stereotactic radiosurgery (SRS), but despite few accepted risk factors, there is very limited data on the influence of intracranial tumor location. The aim of this study was to assess tumor location in correlation to the development of radiation necrosis for skull-base and non-skull-base tumors.

Methods

All patients treated with radiosurgery for meningioma, vestibular schwannoma and other benign neoplasms between January 2004 and November 2020 were retrospectively evaluated. The clinical, imaging and medication data was gained and largest axial tumor diameter was determined using MRI scans in T1 with gadolinium weighted imaging. The diagnosis of RN was established using imaging parameters. Patients with tumors located at the skull base were compared to patients with tumors in non-skull-base locations.

Results

A total of 205 patients could be included in this study. 157 tumors (76.6%) were located at the SB, while the remaining 48 (23.4%) were distributed over the rest of the cranium. Among SB tumors, the most common were vestibular schwannomas (125 cases) and meningiomas (21 cases). 32 (15.6%) of all patients developed RN after median 10 (IqR 5-12) months during a median follow-up of 24 (IqR 6-62) months. 62 patients (30.2%) had already undergone at least one surgical resection at the time of SRS, while 20.9% of patients had already undergone at least one previous radiosurgical treatment.

In multivariate Cox regression, SB tumors showed a significantly lower risk of radiation necrosis with a Hazard Ratio (HR) of 0.252, $p<0.001$, independently of the applied radiation dose. Furthermore, higher radiation doses had a significant impact on the occurrence of RN (HR 1.372, $p=0.002$).

Conclusion

The risk for development of RN for SB tumors appears to be low, but should never be underestimated. No difference between recurrent tumors and newly diagnosed tumors was found, which may underpin the value of radiosurgical treatment for patients with recurrent SB tumors.

Vestibularisschwannome I Operation und / oder Radiochirurgie/*Vestibular schwannomas I surgery and/vs radiosurgery*

V075

Vestibuläre Nebenwirkungen nach robotisch geführter stereotaktischer Radiochirurgie von Vestibularisschwannomen

Vestibular side effects following robotic guided stereotactic radiosurgery of vestibular schwannoma

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Objective

New-onset of vestibular disorders (VD), such as dizziness and imbalance, are common side effects after stereotactic radiosurgery (SRS) for vestibular schwannomas (VS). Although these symptoms can severely affect the daily life of VS patients, there are limited data available providing prognostic information on the risk of developing VD after SRS.

Methods

We included patients who received Cyberknife® SRS for newly diagnosed unilateral VS between 2012 and 2015. The incidence of vestibular disorders before and after treatment was recorded and correlated with tumor, patient, and treatment characteristics.

Results

We identified 71 patients with a median age of 58 years (range: 21-82) and a median follow-up of 66 months (range: 3-105). Tumor volume before treatment was 1.5 cm3 ± 1.4 (range: 0.1-8.6). A mean marginal dose of 12.9 Gy ± 0.3 (range: 12-14) was administered, and all studied patients remained free of tumor recurrence. Thirty four (48%) of the patients had VD prior to SRS. Of the remaining 37 patients who did not have VD before treatment, 16 (43%) developed new VD (vertigo, n=4; balance disorders, n=8; mixture of VD, n=4). The median time to onset of symptoms was 6 months (range: 2-36). In most patients (n=11, 29%), the new symptoms completely resolved within a median time of 21 months (range: 1-63). In multivariate analysis, neither tumor volume (p=0.7), age (p=0.06), nor radiation dose (p=0.16) were significantly associated with the occurrence of VD.

Conclusion

In this cohort, about half of the patients develop new onset of transient VD after SRS. The incidence of VD after SRS was found to be independent from usual tumor-, patient- and treatment-related factors. Therefore, a detailed analysis of the dose exposure to the structures of the vestibular apparatus is recommended.

Vestibularisschwannome I Operation und / oder Radiochirurgie/*Vestibular schwannomas I surgery and/vs radiosurgery*

Epilepsie/*Epilepsy*

J-SBNC020

Der Einsatz der Insulektomie bei refraktärer Epilepsie
The use of insulectomy for refractory epilepsy

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Objective

Surgical resection of the insula (insulectomy) is a procedure used for brain lesions and for refractory epilepsy. It has a difficult surgical access and the need of a wide anatomical knowledge and preoperative planning. There are two types of surgical approaches of the insular cortex: Transsylvian and Transcortical insulectomies. The importance of insulectomies is linked to their efficacy in providing a remarkable decrease of seizures. The objective is to document the results of a ten patients series submitted to Insulectomies for refractory epilepsies and compare them with the results of other studies reported in the literature, as well as to describe the main nuances of the surgical approaches and their associated risks.

Methods

A new series of ten patients submitted to insulectomy was exposed (Engel classification). The results were compared with a review made from the search in several databases and 35 articles were used. In addition, images and tables were made to illustrate what was discussed.

Results

In the new case series, the preoperative Engel classification was IV for all patients and after a mean two-year follow-up period was II. For six patients a subtotal resection was performed and for the remaining (four) a partial one, most of them leading to temporary complications. Analysis of the data presented reiterates the opinion of several authors that insulectomies - partial or total - are both beneficial and safe for the patients, as long as the broad anatomical knowledge of the insular region, preoperative planning and the use of modern microsurgical techniques are considered as basic principles.

Conclusion

Insulectomies are remarkably safe and effective, although they result in temporary postoperative complications and provide highly satisfactory results in terms of seizure control.

Abb. 1

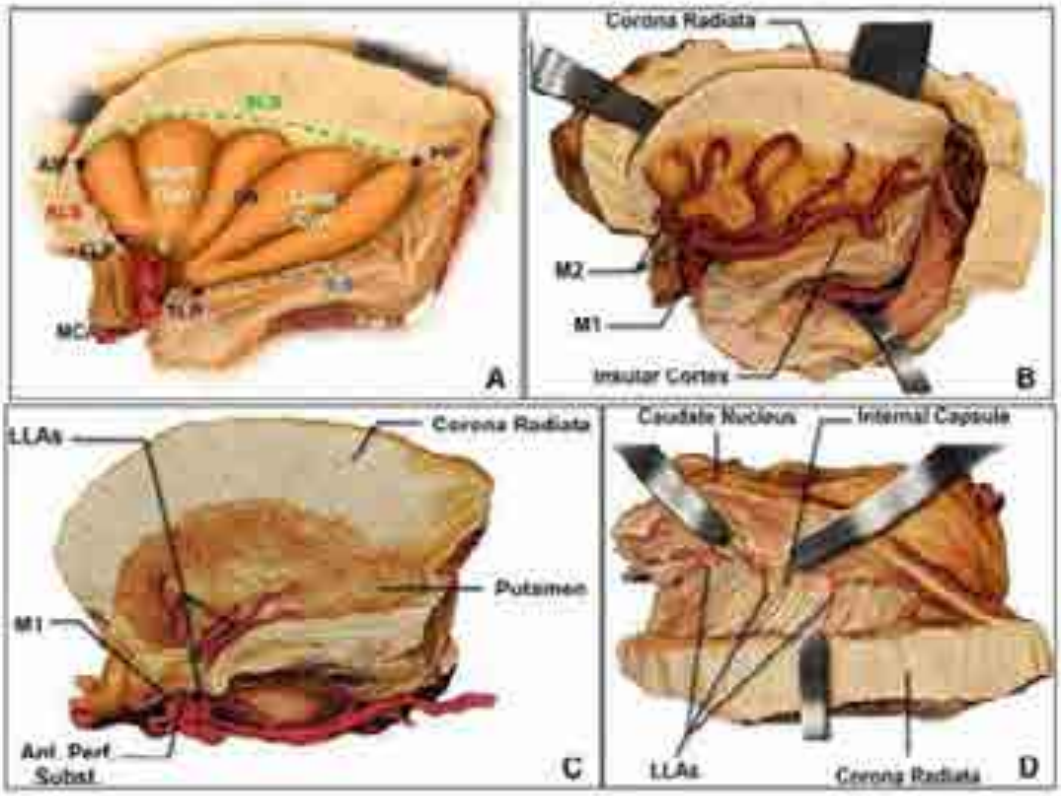

Figure 1: A – Representative illustration of the insular cortex and its main anatomical landmarks: the short and long gyri (separated by the central insular sulcus); the anterior, superior and inferior limiting sulci and, at the anterobasal portion of the insula, the region of the Limen (where the sphenoidal segment of the middle cerebral artery bifurcates into M2). AIP = anterior insular point; ALS = anterior limiting sulcus; cis = central insular sulcus; FLP = frontal Limen point; ILS = inferior Limen sulcus; li = Limen insulae; MCA = middle cerebral artery; PIP = posterior insular point; SLS = superior limiting sulcus; TLP = temporal Limen point. **B** – Illustrative representation of the insular lobe and its adjacents structures, depicting the M1 and M2 branches of the middle cerebral artery (MCA). M1 = M_1 segment of MCA; M2 = M_2 segment of MCA. **C** – Illustration representing a lateral view of LLAs (arising from the sphenoidal segment of the middle cerebral artery) crossing the anterior perforated substance and later the lentiform nucleus, after resection, from medial to lateral, of the following structures: Insular cortex, extreme capsule, claustrum and external capsule. Ant.Perf.Subs. = anterior perforated substance. **D** – Illustration representing a superior view of LLAs crossing the internal capsule, with the caudate nucleus medially and, laterally, the internal capsule, after its resection through the sagittal plane. LLAs = lateral lenticulostriate arteries.

Abb. 2

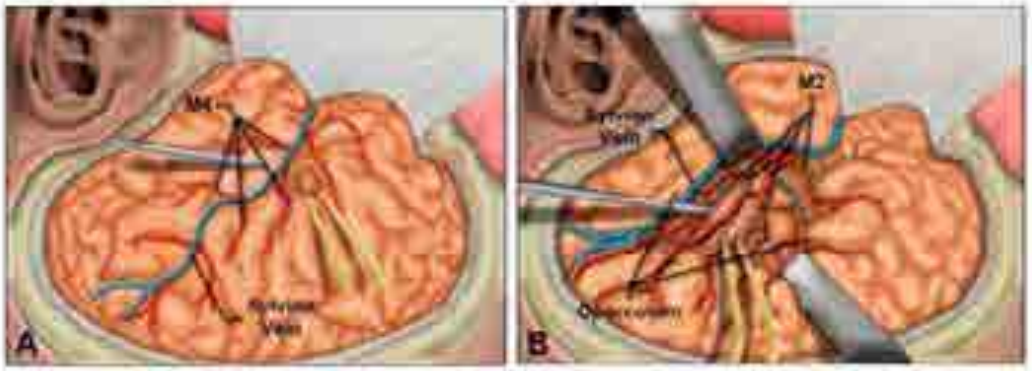

Figure 2: A – Illustration of the Transcortical approach for resection of the insular cortex – by subpial dissection of the operculum between the M4 branches of the middle cerebral artery. **B** – Illustration of the Transsylvian approach for resection of the insular cortex, allowing to observe the divisions of the M2 trunks. M2 = M_2 segment of MCA; M4 = M_4 segment of the MCA.

Epilepsie/*Epilepsy*

V079

Epilepsiechirurgie bei fokaler kortikaler Dysplasie: Positiver Einfluss auf Lebensqualität und epileptologisches Outcome

Epilepsy Surgery for Focal Cortical Dysplasia: Positive Impact on Health-Related Quality of Life and Epileptological Outcome

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Objective

Focal cortical dysplasia (FCD) is one of the most common causes of pharmaco-resistant focal epilepsy. For many patients, epilepsy surgery is the only curative treatment option. The aim is to investigate the impact of epilepsy surgery on the epileptological outcome and the changes in quality of life in relation in a large patient population with confirmed FCD. Moreover, the neuropathological features of FCD will be related to course and outcome.

Methods

Overall 436 operations were retrospectively analyzed in 412 patients (54% male/46% female) with neuropathologically confirmed FCD (FCD I n= 55, FCD IIa n= 168, FCD IIb n= 60, FCD III n=129) who underwent epilepsy surgery during the period 2000-2020 and for whom postoperative follow-up was available. Neuropathological classification was performed according to the ILAE classification (Blümcke et al, 2011). FCD formerly evaluated according to Palmini et al. (2004) were reclassified following re-examination of all specimens. All data regarding pre/postoperative diagnostic findings, the intraoperative and postoperative course, surgical complications, and neurological and epileptological outcome were recorded.To assess the disease-related quality of life in the context of surgical therapy, a subgroup was interviewed separately using the validated questionnaire QOLIE-31 (Cramer et al, 1998). 180 consecutive adult patients operated on during the period 2005-2020 were contacted. Telephone interviews were conducted with n=56 patients (response rate 31.1%). Both, the postoperative current and retrospective pre-operative experienced status were queried and compared.

Results

The last available epileptological outcome (0.25-19 years, median 6.1 years) was Engel 1a in 57%, Engel 1 in 64.3%, and a relevant improvement was experienced by another 25.7% (Engel 2-3). 10% did not benefit from surgery (Engel 4). Surgical complications (n=55, 12.6%) required surgical revision 6.4%. Non-calculated neurological deficits persisted in 15 cases (3.2%). Overall, quality of life was significantly ($p<0.0001$) improved by epilepsy surgery, on average by 30 points (scale 0-100) in QOLIE-31.

Conclusion

This representative analysis corroborates that in the majority of patients with FCD seizure freedom or at least significant improvement of seizure suffering can be achieved in the long term by individualized epilepsy surgery. Overall, patients experience a significant gain in quality of life through epilepsy surgery.

Epilepsie/*Epilepsy*

V080

Etablierung von globalen Prognosefaktoren nach Chirurgie bei Temporallappenepilepsie: Eine multizentrische Analyse von 1010 Fällen

Defining Global Outcomes for Mesial Temporal Lobe Epilepsy Surgery: A Multicenter Analysis of 1010 Cases

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Objective

Benchmarks represent the best possible outcome and help improve future surgical outcomes. However, global thresholds reflecting optimal outcome for mesial temporal lobe (MTL) epilepsy surgery are not available. We aimed to establish standardized outcome benchmarks for MTL surgery.

Methods

A total of 1010 patients from 20 expert centers in 5 continents were analyzed. Patients were categorized into low- and high-risk patients based on known factors affecting worse outcome. The benchmark was defined as the 75th percentile of all centers' scores for a given outcome. Postoperative benchmark outcomes included surgical factors (e.g., complications, surgical site infections, reoperations, mortality) and seizure-free variables (e.g., ILAE outcome, neuropsychology) during follow-up.

Results

Of the 1010 patients, 345 (34.2%) patients formed the low-risk cohort. The proportion of benchmark cases contributing to the final cohort varied between 13.6% and 72.9% across centers. In general, 752 (77.2%) patients underwent anterior temporal lobe resection, and 177 (18.2%) patients underwent selective

amygdalohippocampectomy. A transcortical approach (44.0%) was the most common technique. Morbidity was 17.4% in the low-risk cohort and 23.5% in the high-risk cohort ($p < 0.01$). There was no in-hospital mortality, and 20 (2.0%) patients underwent reoperation. The length of ICU and hospital stay was significantly longer in the high-risk cohort ($p = 0.01$). At one-year follow-up, 617 (72.5%) patients had an ILAE outcome of 0 or 1, while 95 (10.8%) patients were classified as 4 or higher. Based on these results, the following benchmarks for postoperative outcome in low-risk patients are: postoperative complication rate ≤ 19.3%, length of postoperative stay ≤ 8.8 days, new quadrant anopsia ≤ 8.1%, new diplopia ≤ 5.6%, new motor deficit ≤ 3.7%, new language impairment ≤ 3.6%, and at 1-year follow-up: ILAE outcome 1 or 2 ≥ 78.6%, temporal muscle atrophy ≤ 6.7%, deterioration of verbal memory ≤ 33.3%, deterioration of figural memory ≤ 12.5%, and deterioration of attention ≤ 6.3%.

Conclusion

This study presents internationally applicable benchmark cutoffs for clinically relevant outcomes after mesial temporal lobe epilepsy surgery. These benchmark cutoffs can serve as reference values for other centers, patient registries, and for comparing the benefit of future interventions or new surgical techniques (e.g., Laser Interstitial Thermal Therapy).

Epilepsie/*Epilepsy*

V081

'Gliosis only' in pharmacoresistenter Temoprallappenepilepsie
'Hippocampal innate inflammatory gliosis only' in pharmacoresistant temporal lobe epilepsy

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Objective

Drug-resistant mesial-temporal lobe epilepsy is a disease with seizure onset in the hippocampus. A fraction of hippocampi samples reveals a peculiar histological pattern referred to as "gliosis only" with unresolved pathogenesis and enigmatic sequelae. Here, we hypothesize that "gliosis only" represents a particular syndrome defined by distinct clinical and molecular characteristics.

Methods

We curated a multiparameter integration of systematic clinical, neuropsychological as well as neuropathological analysis from a cohort of 627 patients, who underwent hippocampectomy for drug-resistant temporal lobe epilepsy. All patients underwent either classic anterior temporal lobectomy or selective amygdalohippocampectomy. On the basis of their neuropathological exam, patients with hippocampus sclerosis and "gliosis only" were characterized and compared within the whole cohort and within a subset of matched pairs. Integrated transcriptional analysis was performed to address molecular differences between both groups.

Results

"Gliosis only" revealed demographics, clinical and neuropsychological outcomes fundamentally different from hippocampus sclerosis. "Gliosis only" patients had a significantly later seizure onset (16.3 versus 12.2 years, P = 0.005) and worse neuropsychological outcome after surgery compared to patients with hippocampus sclerosis. Epilepsy was less amendable by surgery in "gliosis only" patients, resulting in a significantly worse rate of seizure freedom after surgery in this subgroup (43% versus 68%, P = 0.0001, odds ratio = 2.8, confidence interval 1.7–4.7). This finding remained significant after multivariate and matched-pairs analysis. RNA-sequencing of "gliosis only" patients deciphered a distinct transcriptional program that resembles an innate inflammatory response of reactive astrocytes.

Conclusion

Our data indicate a new temporal lobe epilepsy syndrome for which we suggest the term "Innate inflammatory gliosis only". "Innate inflammatory gliosis only" is characterized by a diffuse gliosis pattern lacking restricted hippocampal focality and is poorly controllable by surgery. Thus, "innate inflammatory gliosis only" patients need to be clearly identified by presurgical examination paradigms of pharmacoresistant temporal lobe epilepsy patients and surgical treatment of this subgroup should be considered with great precaution.

Epilepsie/*Epilepsy*

V082

Neurologische Defizite nach Chirurgie bei Temporallappenepilepsie: Eine Multizentrische Analyse von 1154 Fällen

Neurological deficits after surgery for mesial temporal lobe epilepsy: A multicenter analysis of 1154 cases

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Objective

Surgical resection is still the gold standard in the treatment of pharmacorefractory mesial temporal lobe epilepsy (MTLE) despite new technical approaches. However, reliable worldwide data for the risk of new focal neurological deficits after MTLE surgery are not available. This study aims to provide reliable data on the risk profile against which newer technical processes must be evaluated.

Methods

A total of 1154 patients from 20 expert centers in 5 continents were analyzed. Risk factors for new neurological deficits were calculated using a logistic regression model. Furthermore, Furthermore, the relationship of neurological deterioration to seizure outcome and neuropsychological performance was assessed.

Results

A new focal neurological deficit was detected in 246 of 1154 cases (21.3%). Within these, a quadrantanopia (n=131, 53.3%) and speech impairment (n=40, 16.3%) were the most common deficits. A logistic regression model revealed an older age (p=0.09) and surgery on the dominant hemisphere (p=0.037) as predictors for new neurological deficits. Additionally, selective amygdalohippocampectomy was associated with a higher rate of deficits compared to standard anteromesial temporal lobe resection (p=0.001). Patients with a favorable seizure outcome after 1 year (ILAE outcome scale 1 and 2) showed a new postoperative deficit in 20.6% of cases, while patient with an unfavorable seizure outcome had a deficit in 26.5% (p=0.053). Interestingly, patients with postoperative focal neurological deficits were more likely to present with a deterioration in verbal memory (p=0.009) and attention (p<0.001) at neuropsychological follow-up after 1 year. No difference was detected with in figural memory (p=0.540).

Conclusion

This study provides reliable data on the risk of new focal neurological deficits after surgery for MTLE based on a large international patient population. These results are valuable for comparison with other therapy approaches and can help to better assess and minimize the individual risk profile and to advise patients on this.

Epilepsie/*Epilepsy*

V085

Kavernom-assoziierte Epilepsie: Postoperatives Epilepsieergebnis und Analyse der prädiktiven Faktoren
Cavernoma-related epilepsy: postoperative epilepsy outcome and analysis of the predictive factors

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Objective

Epilepsy is common in patients harboring cavernous malformation (CM), and surgery is reported to be an effective treatment. Small amounts of patients, however, still suffer from seizures after surgery. We analyzed the outcome and predictive factors after cavernoma-related epilepsy (CRE) surgery

Methods

A database was created for all patients with CRE treated surgically from 2003 to 2020 at a university hospital. A chart review, perioperative epilepsy work-up, surgical strategies, postoperative and follow-up notes were analyzed. Postoperative seizure outcome was evaluated according to Engel's classification

Results

Thirty-seven patients (40.5% female; mean age 39.1 ± 14.5 years) were studied. The mean follow-up time was 5.6 ± 3.9 years. Among 37 patients, 32 (86.5%) achieved Engel I at the last follow-up. Engel II was found in 1 (2.7%), Engel III in 1 (2.7%), and Engel IV in 3 (8.1%) cases. Engel Ia was observed in 23 (62.2%) of the patients. None of the patients had a worse seizure outcome after the operation (Engel 4c). Univariate and multivariate analysis showed that short-standing, sporadic, or low-frequent (≤3) seizures were the only variables significantly associated with seizure freedom whereas longstanding, drug-resistant, or high-frequent seizure history were associated with worse seizure outcomes

Conclusion

Surgical treatment results in favorable seizure control in most patients after cavernoma-related epilepsy surgery. Long duration of epilepsy before surgery, high seizure frequency, and drug-resistant epilepsy could have a negative effect on seizure outcome (Engel classification II-IV). Therefore, early surgical resection of the cavernoma after careful presurgical planning is recommended to achieve an optimal result

Pädiatrische Neuro-Onkologie Joint Session mit der er Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Neuro-Oncology Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V086

Der Einfluss des Resektionsausmaßes und des molekularen BRAF-V600E Mutationsstatus auf das postoperative Wachstum pädiatrischer Low-grade Gliome nach Teilresektion

Resection extent and BRAF V600E mutation status determine postoperative tumor growth velocity in pediatric low-grade glioma: results from a single-center cohort analysis

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Objective

Despite excellent long-term overall survival rates, pediatric low-grade gliomas (pLGG) show high variety of clinical behavior regarding progress or senescence post incomplete resection (IR). This study retrospectively analyzes tumor growth velocity (TGV) of pLGG before surgery and after IR to investigate the impact of surgical extent, tumor location and molecular BRAF status on postoperative residual tumor growth behavior.

Methods

Of a total of 172 patients with pLGG receiving surgical treatment, 107 underwent IR (66%). Fifty-three vs 94 patients could be included in the pre- and post-operative cohort, respectively, and were observed over a mean follow-up time of 40.2 vs 60.1 months. Sequential three-dimensional MRI-based tumor volumetry of a total of 407 MRI scans was performed to calculate pre- and postoperative TGV.

Results

Mean preoperative TGV of 0.264 cm^3/month showed significant deceleration of tumor growth to 0.085 cm^3/month, 0.024 cm^3/month and -0.016 cm^3/month after 1st, 2nd, and 3rd IR, respectively ($p < 0.001$). Results remained significant after excluding patients undergoing (neo)adjuvant treatment. Resection extent showed correlation with postoperative reduction of TGV ($R = 0.97$, $p < 0.001$). ROC analysis identified a residual cut-off tumor volume > 2.03 cm^3 associated with a higher risk of progress post IR (sensitivity 78,6%, specificity 76.3%, AUC 0.88). Postoperative TGV of BRAF V600E-mutant LGG was significantly higher than of BRAF wild-type LGG (0.123 cm^3/month vs. 0.016 cm^3/month, $p = 0.047$).

Conclusion

This data suggests that extensive surgical resection may impact pediatric LGG growth kinetics post incomplete resection by inducing a significant deceleration of tumor growth. BRAF-V600E mutation may be a risk factor for higher postoperative TGV.

Pädiatrische Neuro-Onkologie Joint Session mit der er Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/Pediatric Neuro-Oncology Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)

V087

Der supraorbitale Zugang über einen Augenbrauenschnitt in der pädiatrischen Neurochirurgie - Perspektiven und Herausforderungen der frontalen Schlüssellochchirurgie

The supraorbital eyebrow approach in pediatric neurosurgery - perspectives and challenges of frontal keyhole surgery

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Objective

Supraorbital craniotomy via an eyebrow incision provides minimal invasive cosmetically favorable access to both orbital and intracranial pathologies. We describe the indication, surgical technique and clinical course using this surgical approach in a cohort of patients from a single pediatric neurosurgery unit.

Methods

In a retrospective analysis, we identified all surgical cases between January 2013 and April 2022 who underwent the supraorbital craniotomy via an eyebrow incision. Craniotomy was performed using piezosurgery ultrasonic bone incision. An interdisciplinary team of an orbital surgeon and a neurosurgeon performed the orbital surgeries. Clinical and surgical characteristics, perioperative data, possible complications or redo surgeries as well as ophthalmologic status were assessed.

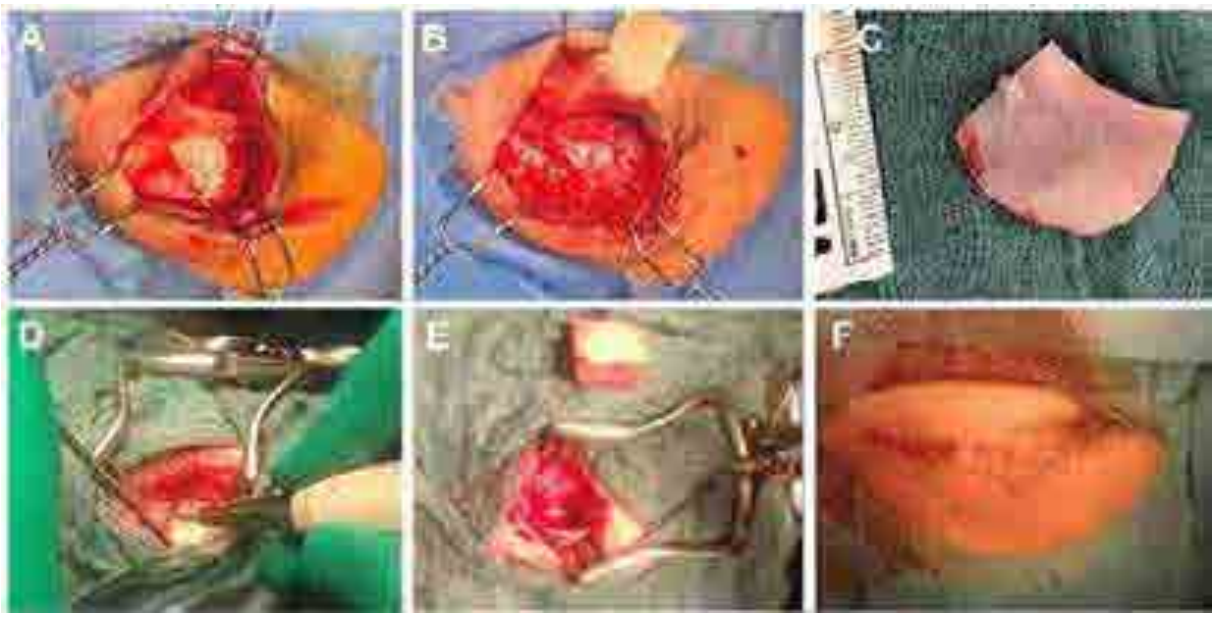
Results

Clinical data of 37 interventions (cases) in 30 patients (age: 8±6.5 yrs.) were analyzed. The supraorbital craniotomy established access to the cranial, lateral and central portions of the orbit (n=11) and ipsilateral fronto-medial portions of the skull base (n=26). Thirty cases suffered from tumor disease with heterogeneous histopathologic diagnoses and in 13 cases, adjuvant therapy was required. In 2 cases (5.4%) the following complications were observed: One infection treated by puncture and antibiotics and one revision surgery was necessary due to loosening of osteosynthesis material. Postoperative visual function was stable compared to preoperative status after all interventions. During a mean follow up time of 26±25.9 months of oncologic cases, complete remission was observed in 13, stable disease in 14, progressive disease in 1 and death in 2 patients.

Conclusion

The supraorbital eyebrow approach is feasible and safe in pediatric neurosurgical cases as a minimal invasive and cosmetic favorable technique and should be considered for intra-orbital as well as ipsilateral intracranial lesions adjacent to the skull base. Interdisciplinary cooperation enables a broader spectrum of surgical options in orbital and complex, fronto-basal, skull base pathologies.

Abb. 1



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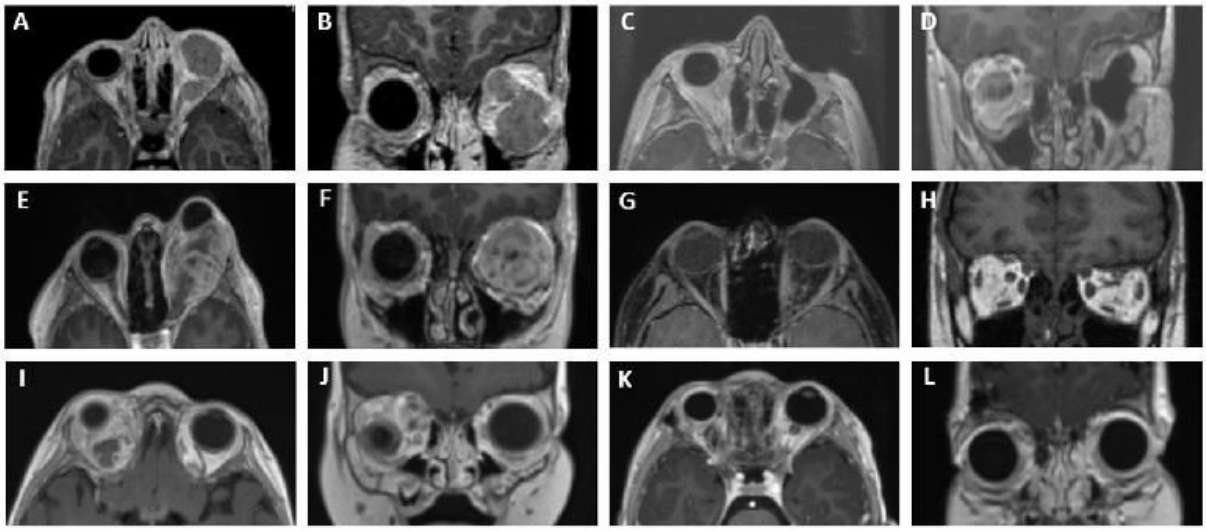

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V088

Genomische Analyse von 390 H3F3A-mutierten diffusen WHO Grad 4 Gliomen

A comprehensive genomic study of 390 H3F3A-mutant diffuse high-grade gliomas, CNS WHO grade 4

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Objective

H3K27-altered diffuse midline glioma (DMG) and H3G34-mutant diffuse hemispheric glioma (DHG) are malignant (CNS WHO grade 4) brain tumors that occur in all age groups. Here, we report comprehensive genomic profiling (CGP) from a large cohort of these tumors from pediatric (

Methods

We identified 390 *H3F3A*-mutant diffuse gliomas (201 females, 189 males) that were characterized in the CGP program at Foundation Medicine between 2013 – 2020. Information from pathology reports, histopathology review, and patient clinical data was assessed.

Results

The cohort comprised 304 (77.9%) H3K27M-mutant DMG (156 females, 148 males) and 86 H3G34-mutant DHG (45 females, 41 males) with a median age of 20 years (1 – 74 years). H3K27M-mutant DMG were found with equal frequency in pediatric and adult patients; 48.6% of the patients were older than 20 years, 31.5% older than 30 years, and 18% older than 40 years at the time of first diagnosis. *FGFR1* hotspot point mutations (N546K; K656E) were exclusively detected in H3K27M-mutant DMG tumors (n = 64/304, 21%; p = 0.0001); these tumors were associated with higher age (median age 32.5 years) occurring more frequently in patients ≥20 years old than pediatric patients (31.7% vs. 11%, p = 0.0001), and were widely distributed across the diencephalon, including the thalamus and adjacent regions. Compared with H3G34-mutant DHG, H3K27M-mutant DMG were enriched for mutations in genes encoding components of the RAS/MAPK pathway including *NF1* (31.0% vs. 8.1%; p = 0.0001) and *PIK3CA/PIK3R1*(27.9% vs. 15.1%; p = 0.016). However, H3G34-mutant DHG were enriched (27.0% vs 9.0%) for targetable alterations of the cell-cycle pathway (*CDK4* and *CDK6* amplification; *CDKN2A/B* deletion) compared to H3K27M-mutant DMG. Potentially targetable *PDGFR* alterations were present in 32% of H3G34-mutant DHG and in 18% of H3K27M-mutant DMG.

Conclusion

In our study H3K27M-mutant DMG were as common in adult patients as pediatric patients. Our analysis presents tumor-specific molecular features of DMG and DHG, identifying disease sub-structure by recurrent co-mutations (such as actionable FGFR1 point mutations which occur in nearly one-third of H3K27M-mutant DMG in young adults) which can inform clinical translational studies, patient diagnosis, and clinical trial design.

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V089

Biopsien von Tumoren des caudalen Hirnstamms bei pädiatrischen Patienten – Eine retrospektive Fallserie
Biopsies of caudal brainstem tumors in pediatric patients - a single center retrospective case series

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Objective

Tumor lesions located in the brainstem comprise up to 10% of all pediatric brain tumors. Thereby, the indication for performing biopsies in patients with diffuse lesions in the brainstem is controversial. Possible risks associated with the technical challenging interventions need to be balanced against clarifying the diagnosis and possible therapeutic options. We reviewed the feasibility, risk profile and diagnostic yield of different biopsy techniques in a pediatric cohort.

Methods

We retrospectively included all patients under 18 years of age that received a biopsy of the caudal brainstem region (pons, medulla oblongata) at our pediatric neurosurgical center from 2009-2022. Depending on the localization of the lesion, patients received either an open, endoscopic, frameless stereotactic (Varioguide) or a frameless robotic assisted (Autoguide) brainstem biopsy (figure 1). The preferentially chosen biopsy technique depended on the time period of intervention and the location and extension of the tumor as illustrated schematically in figure 2.

Results

We identified 27 children. Biopsies were performed using frameless stereotactic (Varioguide) (n=12), robotic assisted (Autoguide) (n=5), endoscopic (n=3) and open biopsy (n=8) technique. Intervention related mortality was not observed. Three patients experienced transient post-surgical neurological deficit. No patient showed intervention related permanent morbidity. Biopsy yielded histopathological diagnosis in all cases. Molecular analysis was feasible in 97% of cases. Most common diagnosis was H3K27M mutated diffuse midline glioma (60%). Low-grade gliomas were identified in 14%. Overall survival was 62.5% after 24 months of follow up.

Conclusion

Our study supports that caudal brainstem biopsies in children are feasible and safe in the presented setting. Sufficient material was acquired at reasonable risk for histopathological diagnosis and molecular pathological profiling. The selection of the surgical technique depended on tumor location and growth pattern. We recommend brainstem tumor biopsies in children to be performed at experienced centers as part of study protocols to confirm diagnosis and to possibly facilitate novel non-surgical therapies.

Abb. 1

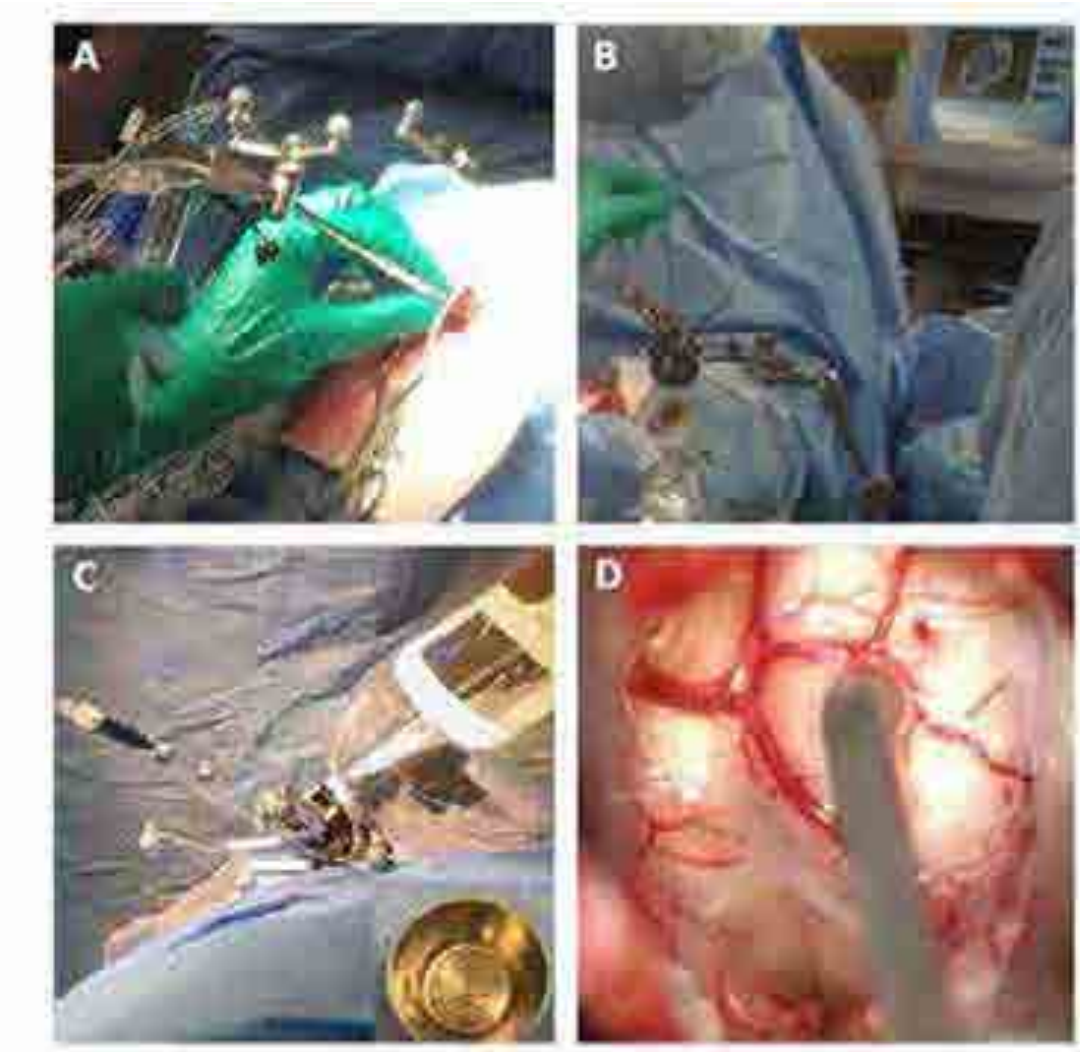

Figure 1. Different biopsy techniques. A: Endoscopic biopsy performed with a Minop endoscope with a 0°-view, B: Varioguide biopsy, C: Autoguide Biopsy, D: Open microsurgical biopsy with intraoperative monitoring.

Abb. 2

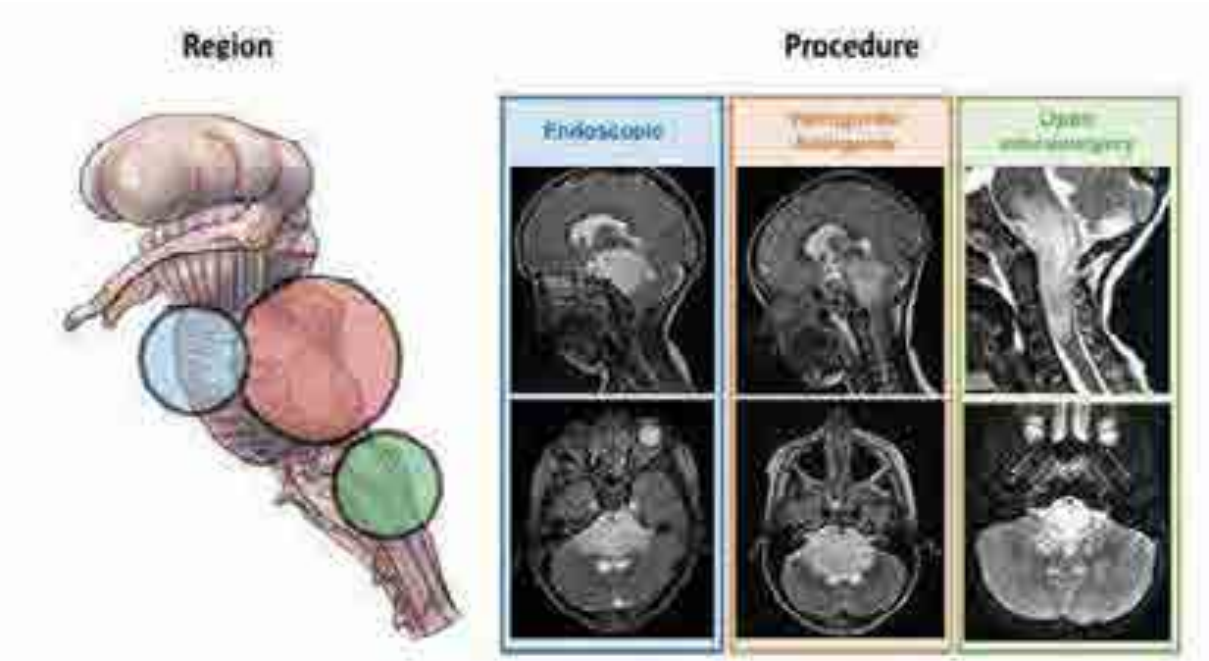

Figure 2. Indication of biopsy technique due to the region of the tumor. Left: Region of the tumor. Right: Corresponding used biopsy technique. Prepontine tumorextension may have been combined with ETV if symptomatic hydrocephalus was present. Stereotactic techniques were used via a suboccipital lateral entrypoint and a transcerebellar trajectory towards the middle cerebellar peduncle. Open microsurgical biopsy were restricted to dorsally located tumors in the medulla oblongata.

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J-SBNPed001

Plexus choroideus papilloma posterior fossa im Kindesalter: Bericht von Fallserien und Überprüfung der Literatur

Posterior fossa choroid plexus papilloma in childhood: report of case series and review of the literature

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Objective

Choroid plexus papillomas (CPP) are rare benign neoplasms. They are exceedingly rare in the posterior fossa in children.

Thus, the aim of the present study is to describe the authors' experience with five cases of choroid plexus papilloma in the posterior fossa, in patients under 18 years of age. A broad narrative review of the current medical literature in English has also been carried out.

Methods

We present a case series of five patients treated in a tertiary care hospital. Additionally, a narrative literature review was carried out.

Results

Patients" agevaried from 4 to 16 years. Gross total resection (GTR) was initially achieved in two patients. All patients showed clinical improvement. Moreover, 27articles were selected for the literature review, all published between 1975 and 2021. This yielded a total of 46 patients overall, whose mean age was 8.18 years.Posterior fossa lesions were located either in the fourth ventricle (64.6%) or the cerebellopontine angle (35.4%). Hydrocephalus was present preoperatively in 71.4% patients and a permanent shunt was required in 28.5% patients. GTR was possible in 59.2%, and 90.1% had clinical improvement

Conclusion

GTR is the gold standard treatment and should be attempted whenever possible, especially because there remains some controversy about the role of adjuvant treatment. Spreading of these tumors has rarely been described (only three cases in the pediatric age group).

Abb. 1

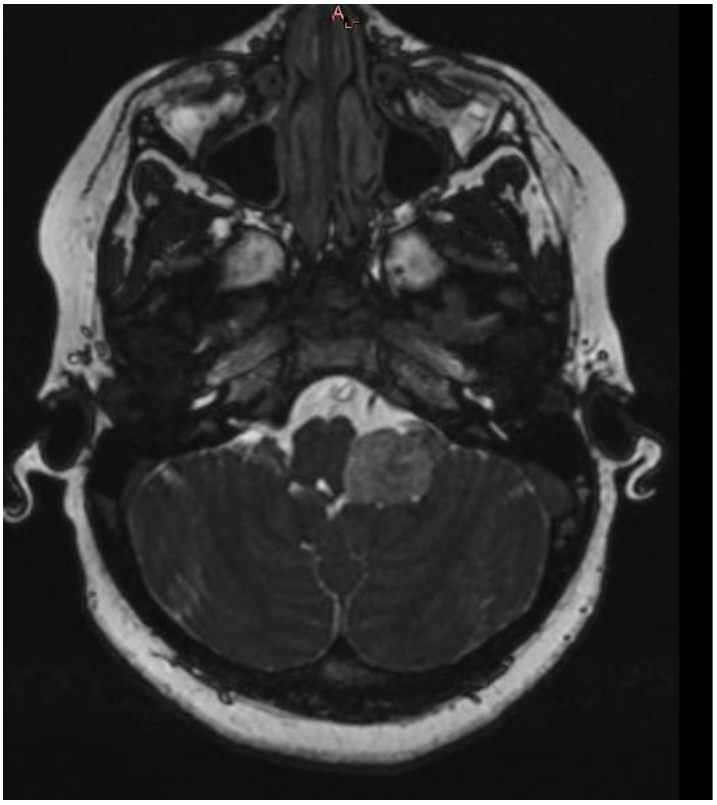

Abb. 2

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V090

Der Nutzen von Natriumfluorescein mit Yellow-560nm-Filter für die Resektion von Tumoren der hinteren Schädelgrube bei Kindern

The use of the sodium fluorescein sodium and YELLOW 560nm filter for the resection of pediatric posterior fossa lesions

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Objective

This study aimed to verify the feasibility, safety, and benefit of using fluorescein sodium (FL) and a yellow 560nm filter in posterior fossa tumors in children.

Methods

All cases of pediatric posterior fossa tumors that have undergone surgery using Fluorescein (2018-2022) have been included and were examined retrospectively. In those cases where resection of the tumor was planned, a blinded neuroradiologist distinguished gross total resection and subtotal resection according to the postoperative MRI findings. The surgical report and medical files were reviewed regarding the intraoperative staining grade and adverse events. The grade of fluorescent staining of the targeted lesion was assessed as described in the surgical reports. The screening was conducted for any reference to the degree of fluorescent staining: "intense," "medium," "slight," and "no staining."

Results

19 cases have been included. In 14 cases, a complete resection was initially intended. In 11 of these cases, a gross total resection could be achieved (78.6%). Staining was described as intense in most cases (58.8%). Except for yellow-colored urine, no side effects obviously related to FL were found throughout the observation period.

Conclusion

In combination with a specific filter, FL is a reliable, safe, and feasible tool in posterior fossa surgery in children.

Schlaganfall/*Stroke*

V091

Intrakranieller Kleinhirninfarkt-Score und Grading-Skala zur Vorhersage der Mortalität und des Outcomes bei Kleinhirninfarkten

Intracranial Cerebellar Stroke Score and Grading Scale for Prediction of Mortality and Outcome in Cerebellar Stroke

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Objective

Several predictors for functional outcome in patients with cerebellar stroke are previously identified, however, there is no standardized clinical grading scale for cerebellar stroke existing. Therefore, the aim of the study was to develop a simple and accurate grading scale for patients with cerebellar stroke to predict mortality and functional outcome.

Methods

This multicentric retrospective study included 531 patients with cerebellar stroke presenting to 5 different neurosurgical and neurological department in Germany between 2008 and 2021. Logistic regression analysis was performed to determine independent predictors for 30 days mortality and unfavorable outcome. By weighting each parameters by its association, intracranial cerebellar stroke (ICS) and ICS-grading scale (ICS-GS) were developed and internally validated by the contingency table analysis.

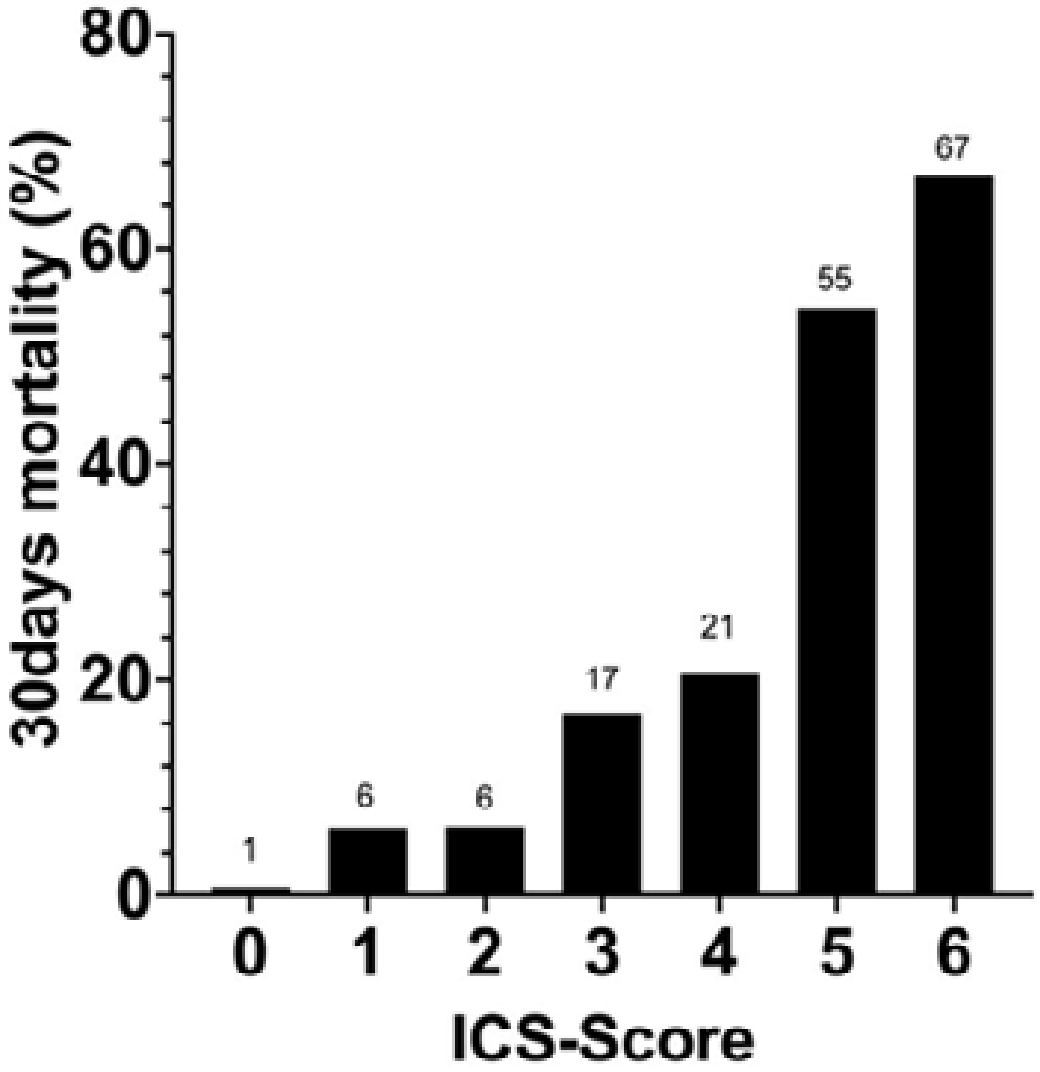
Results

Independent predictors for 30 days mortality were age70y (OR5.2), GCS 3-4 (OR2.6), stroke volume 25cm3 (OR2.7) and brain stem stroke (OR 3.9). By integrating each parameter into ICS-score, age70y and brain stem stroke were assigned with 2 points and GCS 3-4 and stroke volume 25cm3 with 1 point resulting in a score range of 0-6. Patients with 0 point had 1% risk of 30 days mortality, 1-2 points: 6%, 3 points: 17%, 4 points: 21%, 5 points: 55% and 6 points: 67%, respectively. For ICS-GS score, the independent predictor consisted of all components of the ICS score with additional variable of comorbidities. Except GCS 3-4 with 3 points, all other parameters were assigned to 1 point resulting in a score range of 0-7. Patients with 0 point had 1% risk of 30 days unfavorable outcome, 1point: 17%, 2 points 33%, 3 points:40%, 4 points: 50%, 5 points: 80%, 6 points: 77% and 7points: 100%, respectively. 30 days mortality and unfavorable outcome increased steadily with ICS- and ICS-GS score ($p<0.001$).

Conclusion

The ICS- and ICS-GS score is a simple and accurate grading scale for the prediction of 30 days mortality and unfavorable outcome in patients with cerebellar stroke. Further validation is needed to define it as a standardized clinical assessment for the clinical use.

Abb. 1



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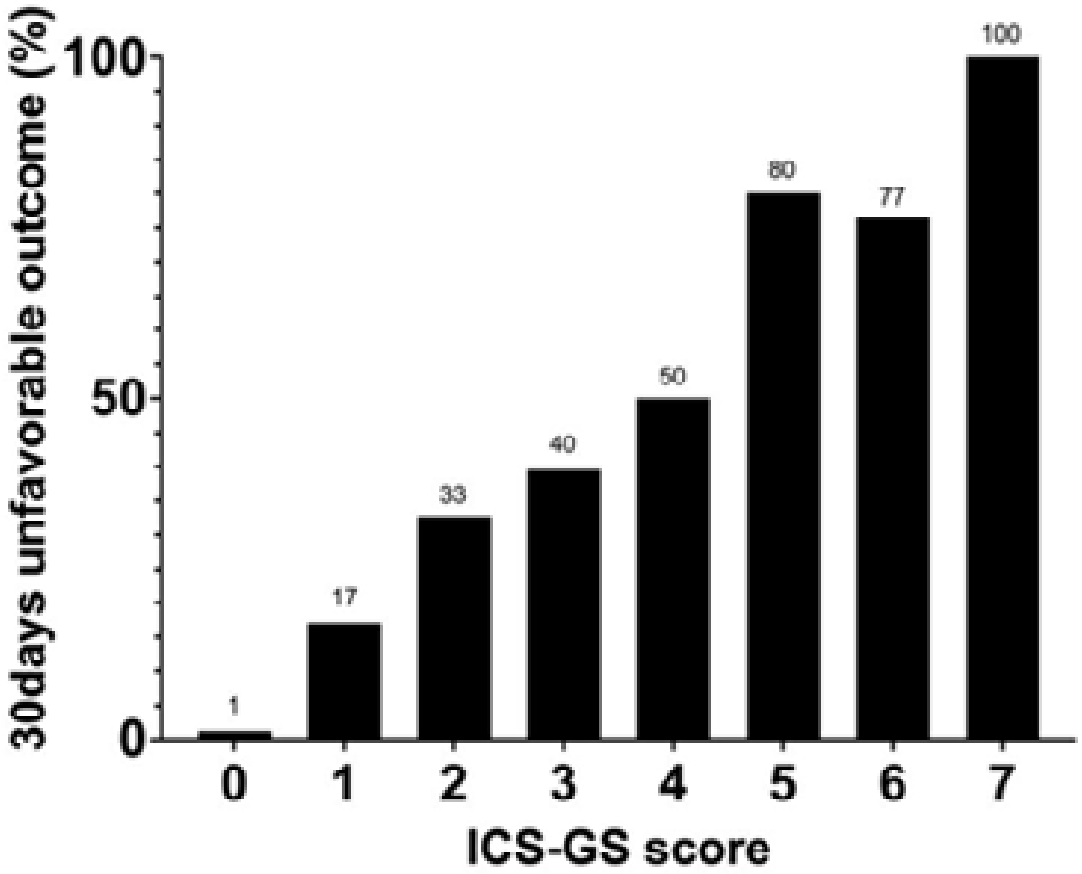
30days unfavorable outcome (%)
100
50
0
1
17
33
40
50
80
77
100
0
1
2
3
4
5
6
7
ICS-GS score

Schlaganfall/*Stroke*

V092

Funktionelles Outcome bei chirurgisch und konservativ behandelten Patienten mit Kleinhirninfarkten
Functional Outcome in Surgically and Conservatively Treated Patients with Cerebellar Stroke

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Objective

According to American-Heart-Association (AHA) guideline, decompressive surgery is indicated in patients with cerebellar stroke and major cerebellar swelling. However, there is no general consensus in making decision on surgery and further, the efficacy of surgery regarding outcomes in patients with cerebellar infarct has not been established. The aim of the study was to determine the functional outcomes in surgically and conservatively treated patients with cerebellar stroke.

Methods

This multicenter study included 531 patients with cerebellar stroke presenting to 5 different neurosurgical/neurological departments throughout Germany between 2008-2021. The primary outcome was the functional outcome evaluated by the modified Rankin Scale at discharge and 1 year follow-up (FU; 0-3:favorable, 4-6:unfavorable). Secondary outcome included mortality at discharge/FU and definition of a cut-off value for surgical indication. Analyses included propensity score matching and predicted probabilities to identify cutoff values for indication of surgical treatment.

Results

In the propensity score-matched groups, 72 patients with surgical and 72 patients with conservative treatment were included. There was no significant different in functional outcome at discharge (50%vs50%; p=1.0; OR1.0) and FU (59.1%vs50.9% ;p=0.4; OR1.4). A cut-off value of 35cm^3 was identified; above the value, surgical treatment was significantly associated with favorable outcome (62.8%vs25%; p=0.02; OR5.1). Regarding neurosurgical approach, suboccipital craniotomy with necrosectomy was significantly associated with favorable outcome compared to sole craniectomy (66.7%vs27.9%; p<0.001;OR5.2).

Conclusion

Surgery was not associated with improved outcome compared to conservative treatment. However, surgery should be considered in infarct volume above 35cm^3 to promote better outcome.

Schlaganfall/*Stroke*

V093

Alte Kontroversen im neuen Licht Chirurgische Vorgehensweise bei raumfordernden Kleinhirninfarkten: Wie?
Old controversies revisited Surgical management of space-occupying cerebellar infarction: how?

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Objective

Space-occupying cerebellar stroke (SOCS) constitutes a neurological emergency. Current evidence supports surgical intervention in patients with SOCS and rapid neurological deterioration, but the surgical technique to be applied is still a matter of debate, as the first reports described resection of ischemic tissue, while in the 1970"s suboccipital decompressive craniectomy (SDC) was introduced as the surgical technique of choice.

Methods

We conducted a retrospective, multi-centric study of patients undergoing surgery for the treatment of SOCS. Patients were stratified according to the type of surgery as (a) SDC; or (b) suboccipital craniotomy with necrosectomy. The primary endpoint was functional outcome at discharge. Secondary endpoints were in-house postoperative complications.

Results

127 patients were included in the analysis: 84 underwent necrosectomy and 43 SDC. Those with necrosectomy had a significantly favorable functional outcome at discharge (modified Rankin Scale 0-3) compared to the SDC group: 66.7% vs. 27.9% (p<.001, OR 5.2, 95% CI 2.3-11.6). No significant differences were observed in postoperative complications, such as hemorrhagic transformation, infection or cerebrospinal fluid fistula.

Conclusion

This is so far the largest series evaluating surgical therapy for SOCS. Necrosectomy appears to achieve better functional outcomes in patients with SOCS than SDC alone. Prospective, randomized studies are needed to corroborate this finding.

Schlaganfall/*Stroke*

V094

Einschlusskriterien in den klinischen Studien zur dekompressiven Kraniektomie (DC) bei malignem Mediainfarkt (mMCAI): eine systematische Literaturrecherche

Inclusion criteria in clinical studies of decompressive craniectomy (DC) for malignant middle cerebral artery infarction (mMCAI): a systematic review of the literature

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Objective

mMCAI is a serious clinical condition with high mortality and morbidity. The introduction of DC as a primary therapy resulted in a significant reduction in the mortality rate shown in many studies. However, the selection of patients to undergo DC varies widely; until now, there has been no consensus. We aimed to summarise and analyse the inclusion criteria in studies of DC for patients with mMCAI and to identify their similarities.

Methods

We searched 7 databases from inception till 31st December 2021. We included randomized controlled studies (RCTs) and non-randomized studies of intervention (NRSIs) if they compared neurological outcomes between patients with mMCAI who underwent DC in addition to medical treatment and patients managed with medical care alone. Two reviewers independently screened full-text publications for eligibility.

Results

We reviewed 30 studies (7 RCTs, 23 NRSIs) published between 1995 and 2020, which included 1680 patients. All studies stated that infarction of at least > 50% of MCA territory was the main inclusion criterion. The mean age of patients was 53 but varied between studies (from 18 to 89); however, most studies (n=25) allowed the inclusion of patients >60 years. The most common clinical inclusion criteria were the National Institutes of Health Stroke Scale (NIHSS)>15, used by 13 studies, and the Glasgow Coma Scale (GCS)≥6, used by 8 studies. Six studies identified different NIHSS cut-offs for inclusion in the right-sided/non-dominant stroke compared to the left-sided/dominant stroke. Six studies specified a midline shift (MLS) of ≥5mm in the inclusion criteria, and another eight used a relatively vague criterion (signs of brain herniation). The stroke duration was an inclusion criterion in 16 studies; it varied from 6h to 96h, with 10 studies limiting the time window to < 48h since the infarct onset. Lastly, 19 studies excluded patients with previous disabilities measured as a modified Rankin Scale (mRS)>1 or patients with signs of brain death (dilated fixed pupils).

Conclusion

Inclusion criteria for patients with mMCAI to undergo DC varied among published studies; however, there were many similarities, namely a large volume of infarction, wide age range without exclusion of older patients, less severe neurological status as assessed with NIHSS or GCS, no previous physical disability, clear midline shift on imaging and the first two days since the onset of stroke. All these factors should be considered when indicating DC in patients with mMCAI.

Schlaganfall/*Stroke*

V095

Erarbeitung zuverlässiger Auswahlkriterien für die dekompressive Hemikraniektomie bei ischämischem Schlaganfall

Elaborating reliable selection criteria for decompressive hemicraniectomy in ischemic stroke

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Objective

Decompressive craniectomy (DHC) has been demonstrated to effectively prevent mortality in patients with progressive brain edema associated with ischemic stroke. Although several factors have been identified contributing to progressive edema no clear selection criteria have been established so far for a reliable and early patient selection for DHC, which is the reason why the indication for DHC is made on an individual basis in clinical practice. The aim of this study was to assess the discrimination power of clinical and radiological parameters for indicating DHC after ischemic stroke.

Methods

A large interdisciplinary database of patients treated with ischemic stroke at our center between 2010 and 2021 was reviewed and patients meeting the inclusion criteria were retrospectively enrolled. Main inclusion criteria were complete data concerning the initial imaging, clinical presentation, stroke treatment (thrombolysis, thrombectomy), and functional outcome at discharge and at 3 months follow-up. ASPECTS was calculated based on the computed tomography (CT) scan as well as on CT-perfusion with volumetric analysis of ischemic core and penumbra. The original EDEMA-score was calculated and modified by adding an age dichotomization. The size of demarcated infarction at end of treatment was semi quantitatively evaluated based on the last CT scan before discharge. The discrimination power of evaluated parameters for identifying patients requiring DHC was assessed performing ROC-analysis.

Results

A total of 534 patients were included, in 153 of whom DHC was performed. A modified EDEMA-score with added age cutoff of 55 years showed a high discrimination power using a cutoff value of 6 points (AUC 0.81, PPV 94%, NPV 83%, OR 72, $p<0.0001$). Patients with smaller infarction at end of treatment had better functional outcome (r=0.3666, $p=0.001$), that in turn correlated with initially higher penumbra volume compared to ischemic core volume (r=-0.3890, $p=0.0006$), and with higher ASPECTS on non-contrast CT scan (r=-0.4980, $p<0.0001$) as well as on CT-perfusion (-0.5009, $p<0.0001$).

Conclusion

A combination of the EDEMA-score adjusted for age, perfusion-based volumetric assessment of ischemic core and penumbra, and CT-perfusion ASPECTS on admission allow a reliable identification of patients with ischemic stroke requiring DHC in course of the disease. These findings may pave the way for establishing a standardized selection criteria for DHC in patients with ischemic stroke and progressive brain edema.

Schlaganfall/*Stroke*

V096

Posttraumatische zerebrale Sinus- und Venenthrombose: retrospektive Evaluation von Risikofaktoren, Management und Komplikationen

Posttraumatic cerebral venous sinus thrombosis: retrospective evaluation of risk factors, management and complications

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Objective

Up to date, there is no clear consensus on the management of posttraumatic cerebral venous sinus thrombosis (CVST). The challenge to establish a guideline in this disease is complicated by various coexisting injuries. This evaluation aims to identify risk factors, management and associated complications of posttraumatic ST.

Methods

A retrospective chart review of 341 traumatic brain injury patients admitted to the neurosurgical clinic from 2020 to 2022 was performed. Of those, 13 were diagnosed with posttraumatic CVST. In these patients, trauma mechanism, associated injuries, location of the CVST as well as treatment and possible complications were evaluated.

Results

Mean age was 48 years (range: 23-84), with mainly male patients (n=8; 61.5%). Trauma mechanisms are illustrated in figure 1. Skull fractures, even though not dislocated were diagnosed in 11 patients (84.5%). Only two patients (15.3%) had CVST of the sagittal superior sinus, while most were diagnosed with CVST of the transverse (n=3, 23.0%), the sigmoid (n=4, 30.6%), or both, transverse and sigmoid sinus (n=4, 30.6%). These CVST were highly associated with skull base fractures p=0.02.

Traumatic intracranial hemorrhage was evident in all patients, requiring surgery in half of the cases (Table 1). Half of all cases were treated with thrombosis prophylaxis only, while the remaining 6 (46.1%) received intravenous heparin being started at day 3 on average (range 1-8), leading to a progressive bleeding with the need for hemicraniectomy in 1 patient (7.6%).

Conclusion

This study addresses the difficulty and inconsistency of the posttraumatic ST treatment. Due to the association with skull base fractures, we advocate performing a CT with contrast agent in a venous phase in these patients.

Abb. 1

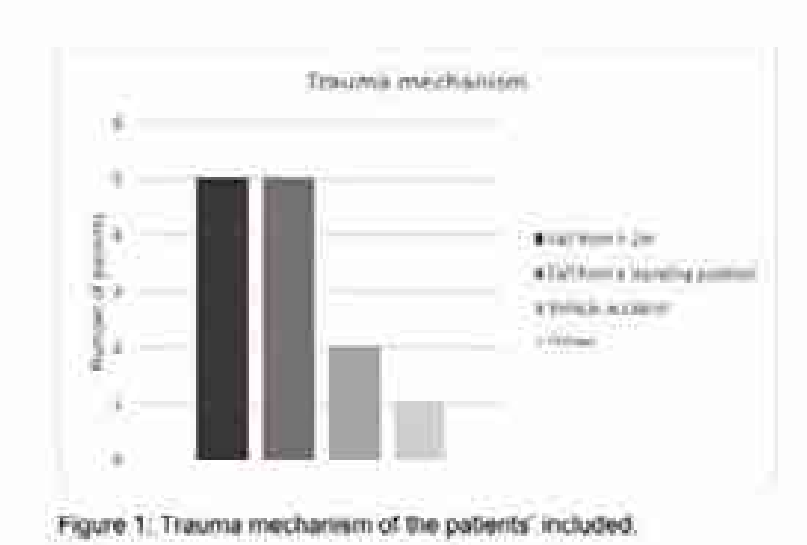

Figure 1: Trauma mechanism of the patients' included.

Abb. 2

Patient	Intracranial bleeding	Surgery
1	SAH, CC	-
2	SAH, aSDH	Hemicraniectomy
3	SAH, aSDH, CC	-
4	aSDH, CC	Hemicraniectomy
5	SAH	EVD
6	SAH	-
7	SAH	Hemicraniectomy
8	SAH, aEDH	EVD
9	SAH	-
10	CC	-
11	CC	-
12	SAH, aSDH	EVD
13	CC	EVD

Table 1: Intracranial bleeding pattern and surgery performed
aSDH – acute subdural hematoma, aEDH – acute epidural hematoma, CC – cerebral contusion, EVD – external ventricular drainage, SAH – subarachnoid hemorrhage

Mikrovaskuläre Dekompression/*Microvascular decompression*

V097

Die Lebensqualität von Patient*innen mit Spasmus hemifacialis steigt nach mikrovaskulärer Dekompression
Microvascular decompression improves quality of life in patients with hemifacial spasm

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Objective

To measure the effect on quality of life in patients with hemifacial spasm before and after microvascular decompression.

Methods

Patients with clinically apparent hemifacial spasm and a suspected neurovascular conflict to the facial nerve on MRI undergoing microvascular decompression were enrolled. The Medical Outcomes Study 36-Item Short Form (SF-36) was administered at the time before surgery, 3 months, and 12 months after surgery. Sociodemographic and clinical data were also collected.

Results

Fifty patients were enrolled. There was a statistically significant lower activity of hemifacial spasm after three and twelve months with a mean residual activity of 17 % (12 months postop, $p < .0001$) comparing to their individual preoperative activity of 100 %. The SF-36 physical component summary (PCS) score remained unaffected while the mental component summary score (MCS) improved postoperatively ($p < .0001$ preop. vs. 3 months postop.; $p = .0153$ preop. vs. 12 months postop.) along its dimensions vitality (VIT), social functioning (SF), and mental health (MH). With respect to the observed clinical outcome after 12 months statistically significant improvement was seen in patients with excellent symptom relieve compared to patients with poor relieve in SF-36 dimensions SF ($p = .0364$), MH ($p = .0088$), PCS ($p = .0471$) and MCS ($p = .0067$).

Conclusion

Patients with hemifacial spasm benefit in a majority of cases from microvascular decompression due to diminishing or even complete resolution of facial spasms. In addition a positive effect is seen on quality of life aspects, especially with regard to mental health and social interaction. Quality of life is increasing more in patients with better resolution of spasm activity showing best results in patients with complete spasm resolution.

Abb. 1

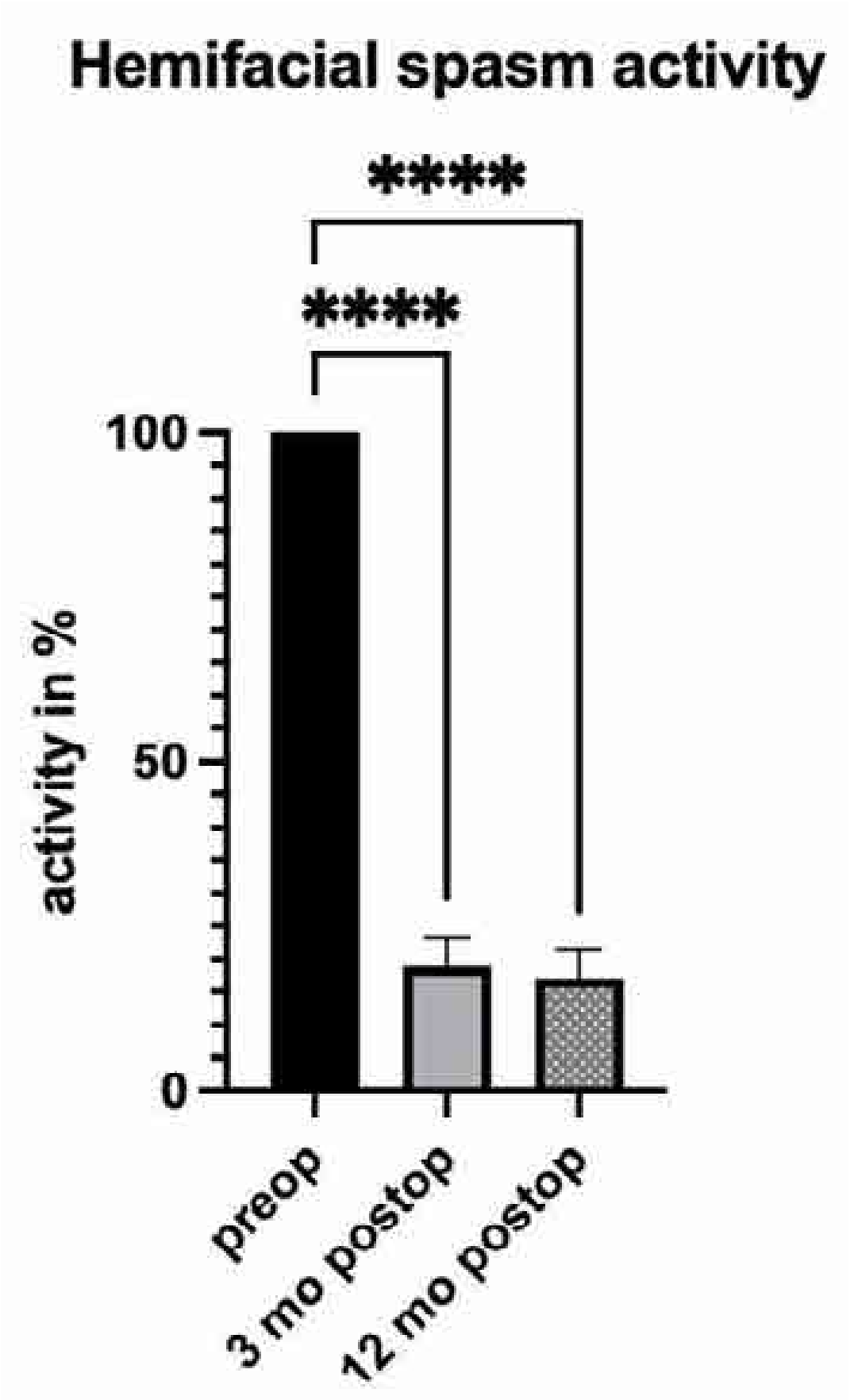
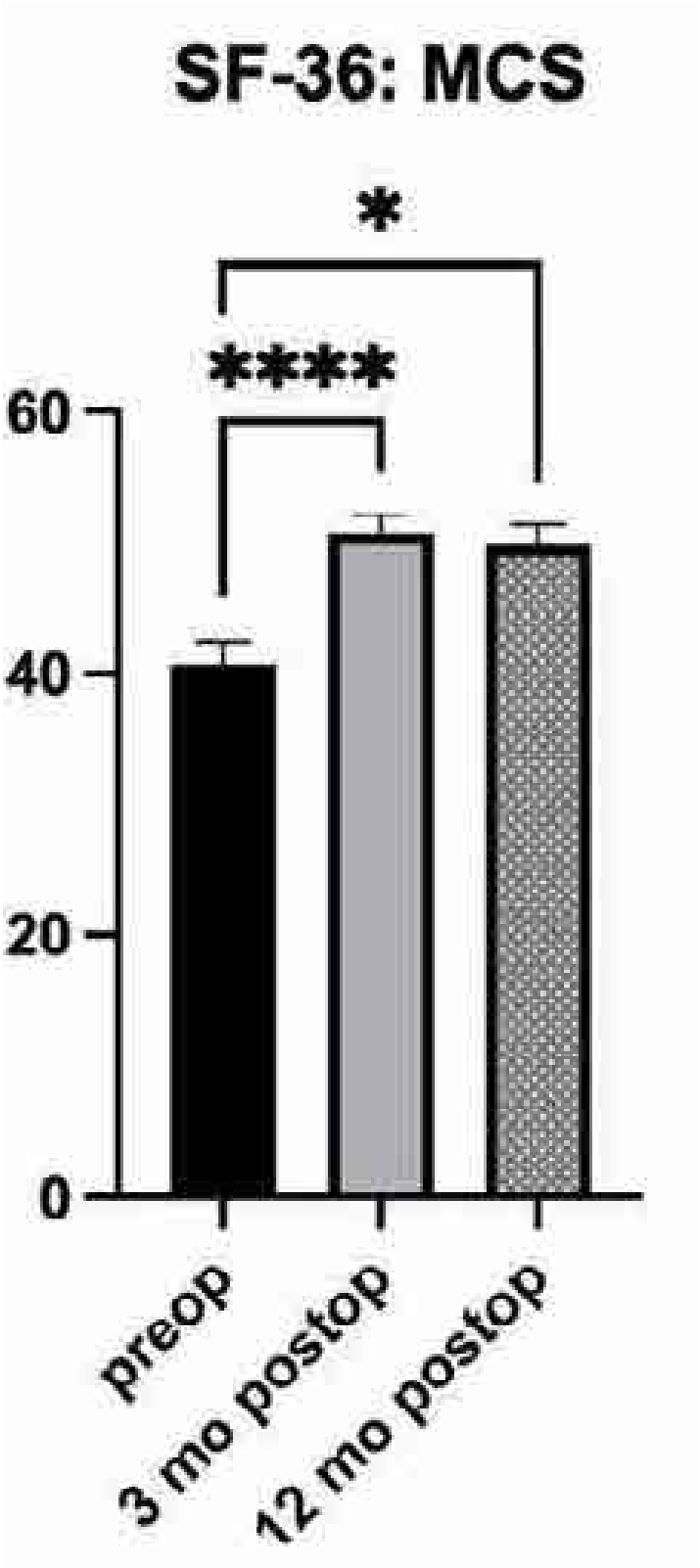

Hemifacial spasm activity
****
****
100
50
0
activity in %
preop
3 mo postop
12 mo postop

Abb. 2



Mikrovaskuläre Dekompression/*Microvascular decompression*

V099

Modifiziertes intraoperatives Monitoring der Lateral spread response bei mikrovaskulärer Dekompression bei Hemispasmus facialis

Modified testing of lateral spread response to guide microvascular decompression for hemifacial spasm

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Objective

The standard for treatment of hemifacial spasm (HFS) is surgical by microvascular decompression (MVD). However, often, more than one vessel conflict exits, which may be more peripheral or proximal to the most obvious conflict. Neurophysiological techniques such as lateral spread response (LSR) are used to predict MVD effectiveness. In our institution, we perform a modified selective LSR testing for two branches of the facial nerve (zygomatic = LSRZ and mandibular= LSRM). The aim of the study was to analyze the benefit of the combined LSR testing to predict postoperative long-term outcome.

Methods

We included all patients who underwent MVD with modified LRS testing in our department between 2015 and 2022. The exact course of the branches of the facial nerve was determined by transcutaneous monopolar stimulation to identify the trajectory of the facial nerve under the skin before the stimulation needles were inserted. Thus, the mandibular and zygomatic branches of the facial nerve were stimulated selectively (LSRZ and LSRM). If LSR was persisting, the surgery was continued to search for a second vessel conflict to achieve loss or at least significant reduction of LSR.

LSRZ and LSRM at the end of the MVD was analyzed and postoperative presence or disappearance of HFS was assessed at discharge, at first follow-up (3 months) and at last follow-up. Statistical analysis was performed calculating sensitivity (Sens), specificity (Spec), positive predictive value (PPV) and negative predictive value (NPV).

Results

In total 31 patients were included. In case, we categorized the combined LSR (LSRM and LSRZ) into two groups (persistent) versus (significant reduction or complete disappearance) at last follow-up, the data accuracy analysis was: Sens 11%, Spec 100%, PPV 100%, NPV 64%.

Conclusion

LSR showed high specificity and moderate NPV. Thus, the absence of LSR at the end of surgery may reassure the surgeon that the patient will not suffer from HFS in the long-term. Consequently, the modified LSRZ and LSRM testing with accurate placement of stimulation electrodes may further improve surgical guidance during MVD for HFS. Larger series are needed to evaluate this concept.

Mikrovaskuläre Dekompression/*Microvascular decompression*

V100

Günstige Prognose der medikamentenrefraktären Trigeminusneuralgie bei Teilnahme an einem multimodalen chirurgischen Therapiekonzept

Favorable prognosis of medically refractory trigeminal neuralgia when enrolled in a multimodal surgical management program: A two-year single center experience

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Objective

Common surgical treatments for trigeminal neuralgia (TN) include microvascular decompression (MVD), radiofrequency ablation (RFA), and subcutaneous trigeminal nerve field stimulation (sTNFS).

Methods

In this observational study, all patients who have been treated with surgical therapy were analyzed for ICHD-3 (3rd edition of the International Classification of Headache Disorders) diagnosis, pre- and postoperative pain intensity, frequency of attacks, complications, and side effects of therapy.

Results

A total of 51 TN patients were treated according to our multimodal surgical management in 2018 and 2019. According to ICHD-3, primary TN was the most common diagnosis in 56.9% of patients. 29.4% (N=15) of all treated patients had received prior surgical therapy, and N=10 of these had MVD. MVD was the significantly most used intervention in classical medically refractory TN, whereas RFA was rarely applied (p=0.001). RFA was significantly more used in MS-associated forms of TN (p=0.001). sTNFS is significantly more prone to complications than RF-TC (p=0.018). The mean VAS was reduced from 8 to 2. N=42 (82,4%) patients reported a reduction of pain attacks of 90% or more. After 8 to 12 weeks, pain medication could be reduced in 36 patients (70,6%). N=3 patients suffered from complications (2 surgical and 1 non-surgical). The mean follow-up duration was 207 days.

Conclusion

MVD secures its place as the first line of therapy in classical medically refractory TN. RFA is a safe method especially in MS associated TN and outweighs sTNFS due to reduced risk of complications.

Mikrovaskuläre Dekompression/*Microvascular decompression*

V101

Partielle sensorische Rhizotomie zur Behandlung der therapierefraktären Trigeminusneuralgie
Partial sensory rhizotomy for therapy-refractory trigeminal neuralgia

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Objective

Partial sensory rhizotomy (PSR) is an "ultima ratio" procedure for patients with therapy-refractory trigeminal neuralgia (TN). The treatment can be offered to patients without a neurovascular conflict or to patients who did not benefit either from previous microvascular decompression (MVD) or from other interventional procedures. The study presents our experience with PSR.

Methods

The prospectively collected database revealed 45 patients treated with PSR between 2004 and 2022. The average age was 59.7 years. Mean history of symptoms was 7.3 years (range:1-30). Besides medical treatment, previous treatment included 22 MVD's, 8 times glycerol injections, 5 thermocoagulations and 2 radiosurgeries. Multiple sclerosis was presumably the cause of TN in 13 patients, another two patients had a history of benign tumor removal and postoperative TN.

Results

A total pain relief was observed in 38 patients immediately after PSR, 4 had a partial pain improvement and 3 observed no difference. An expected, variable hypoesthesia occurred in 41 patients (only related to branches V2 / V3). Surprisingly, 4 patients reported no sensory limitations. In 64.4 % of the cases (29 of 45 patients) 1/3 PSR was done, in 7 2/3 (15.6 %) and 9 received 50% resection of the sensory root (20%).

The mean follow up was 23.9 months (3-100 months), 4 patients were lost to follow-up. 28 patients still had complete, 6 partial pain relief. A total of 6 patients still needed medications, but were satisfied with a lower dose and generally improved or were even pain-free. Five patients, who did benefit from the PSR initially, reported recurrent TN. Three of them received a second PSR after 12-55 months with complete pain relief again.

Conclusion

Early after surgery patient satisfaction regarding pain relief/improvement was 93.3% (42 of 45 patients). During follow-up we observed complete or partial pain relief in 28 of 39 patients (71.8 %) without pain medication. However, the degree of sensitive deficits is not predictable. Because of our convincing results, patients should be informed about PSR as an therapeutic option for refractory TN. We recommend PSR instead of or as an alternative to percutaneous procedures or radiosurgery.

Mikrovaskuläre Dekompression/*Microvascular decompression*

V102

Rezidiv der Trigeminusneuralgie nach mikrovaskulärer Dekompression: Histologie des Teflongranuloms
Recurrence of trigeminal neuralgia after microvascular decompression: the histology of Teflon granuloma

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[2]Medizinische Hochschule Hannover, Institut für Neuropathologie, Hannover, Deutschland

Objective

Teflon granuloma is a possible cause of recurrence in patients with trigeminal neuralgia who underwent successful microvascular decompression (MVD). Its incidence is variable and the pathophysiology and mechanisms for recurrence are not well defined. In this study, we aim to characterize the histological features of Teflon granulomas and to correlate its occurrence with clinical and intraoperative findings.

Methods

Clinical and histological data of patients with recurrent trigeminal neuralgia who underwent posterior fossa re-exploration after previous successful MVD over a 15-year period was collected and analyzed.

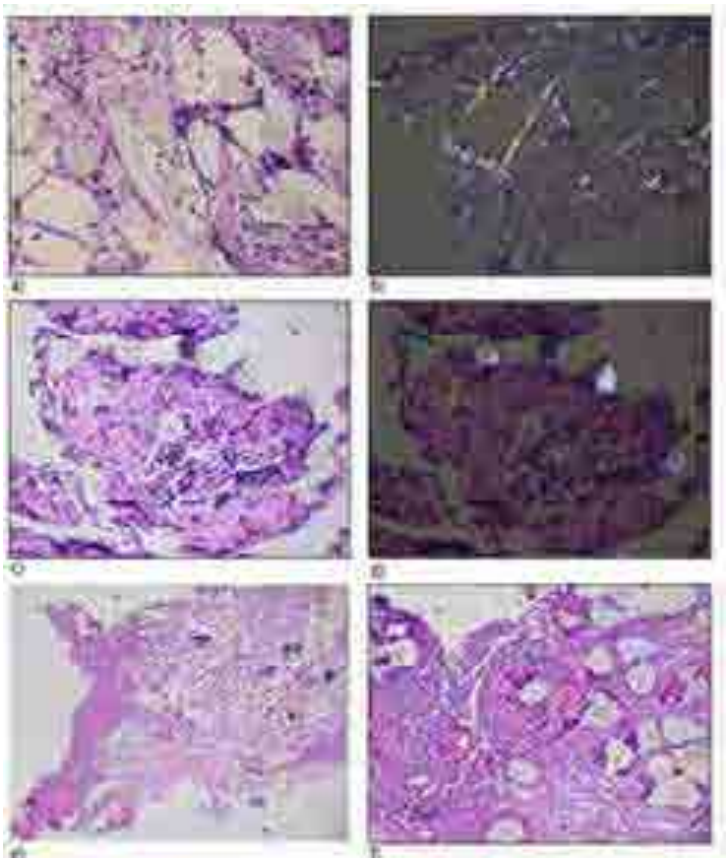
Results

Histopathological specimens were available in a total of 13/41 patients with recurrent trigeminal neuralgia who underwent surgery. In 6 cases the distribution of pain had progressed to an adjacent area, mostly from V2 to V2 and V3. The mean time for recurrence was 30,65 months after the first MVD. Intraoperatively a "piston-effect" was noted clearly in 2/13 cases and calcification of the Teflon felt in 7/13 cases. All samples showed scar tissue and within this scar birefringent Teflon filaments were observed, which were embedded between enlarged and collagenous fibers. The full configuration of foreign body granulomas with Teflon-adherent giant cells and discrete lymphocytic infiltrates was evident in 10/13 cases. Siderophages were found in 4/13 cases. Microcalcifications occurred in 5/13 cases.

Conclusion

The majority of Teflon granulomas were typical foreign body granulomas, corresponding to a scar reaction embedding the Teflon material and an immunological component in the form of giant cells. Clinically, expansion of the distribution of pain during recurrence after a prior successful MVD can be observed. Our data indicates that Teflon is not an inert material when used for MVD and that alternative materials or techniques might be considered.

Abb. 1



Robotik, Präzision und maschinelles Lernen/*Robotics, accuracy & machine learning*

V103

Neues System für die Roboter-gestützte Platzierung von Pedikelschrauben in der Brust- und Lendenwirbelsäule: Erste 234 Schrauben

Novel system for robotic-assisted pedicle screw placement in thoracic and lumbar spine: First 234 screws

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Objective

The aim of this study is to present initial experience with thoracolumbar pedicle screw placement using Brainlab"s Cirq® surgeon-controlled robotic arm (BrainLab, Munich, Germany) and its novel robotic alignment module for various indications.

Methods

All patients who underwent robotic-assisted implantation of pedicle screws in the thoracolumbar spine at our Department were included in the study. Pedicle screw accuracy was assessed using Gertzbein-Robbins scale (GRS).

Results

A team of two surgeons conducted 35 surgeries in 34 patients (18 female, median age 68.4 ± 11.4 years) with robot-assisted pedicle screw placement. Indications included degenerative spine disease (n=8 patients), spondylodiscitis (n=9), metastases (n=10), chondrosarcoma (n=1) and fracture (n=6), with mean follow up of 7 months. 9 surgeries were performed in thoracic spine, 13 in lumbar and lumbosacral spine and 13 in thoracic and lumbar spine. Workflow included intraoperative computed tomography (iCT) imaging with automatic registration, fusion with preoperative imaging and review of the preplanned screw trajectories, robotic-assisted insertion of K-wires, followed by a fluoroscopy-assisted insertion of pedicle screws (first 12 surgeries) or insertion of navigated screws (latter 23 surgeries), with control iCT scan. The mean surgery time was 233.11 ± 45.1 minutes and mean robotic time was 37.4 ± 8.5 minutes. Mean time per screw for fluoroscopy-assisted robotic screws was 8.27 ± 6.54 minutes and for navigated robotic screws was 4.55 ± 2 minutes, the difference which was statistically significant ($p<0.05$). 229 screws were clinically acceptable (GRS A, B and C), out of this number 211 were GRS A screws (90.2%). A total of 5 screws (2.1%) were GRS D and E screws, from this number 1 screw was removed and 4 underwent intraoperative revision. For 2 out of 4 revised screws, robot surgery was abandoned and iCT-based navigation was used. All revised screws were GRS A screws following revision. A total of two screws experienced loosening during follow up, which prompted revision and extension of the spinal construct. Complications included wound healing deficits in 2 patients and cerebrospinal fluid fistula in two further patients.

Conclusion

Brainlab"s Cirq® Robotic Alignment module feature enables placement of pedicle screws in thoracolumbar spine with high accuracy. Learning curve is shown through improvement of time per screw.

Robotik, Präzision und maschinelles Lernen/*Robotics, accuracy & machine learning*

V104

Roboter navigierte Laser Kraniotomie. Die Erste in-vivo recovery Tierstudie.

A novel navigated, robot-driven laser craniotomy tool. The first in-vivo recovery animal study.

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[3]Advanced Osteotomy Tooly, Basel, Schweiz

Objective

To test a novel frame-less navigated, robot-driven laser tool in an in-vivo recovery animal study. We recently introduced a frame-less navigated, robot-driven laser tool for depth electrode implantation as an alternative to frame-based procedures. So far, this method has only been performed in cadaver and non-recovery studies.

Methods

A preoperative computed tomography (CT) scan was conducted to plan trajectories in sheep specimen. Burr hole craniotomies were performed with a frame-less navigated, robot-driven laser tool. Depth electrodes were implanted after cut-through detection was confirmed. The electrodes were cut at skin level postoperatively. Postoperative imaging was performed to confirm accuracy. Histopathological analysis was performed on bone, dura, and cortex samples.

Results

A total of 14 depth electrodes were implanted in two sheep specimens. Anesthesiologic protocols did not show any irregularities intraoperatively. One sheep had to be euthanized after 6 hours postoperatively due to food neglect. The other sheep stayed alive for more than a week without neurological deficits. Postoperative MRI and CT scans showed no intracerebral bleeding, infarction, or unintended damage. The average bone thickness was 6.2mm (range 4.1 – 8.0mm). The angulation of panned trajectories varied from 65.5° to 87.4°. Deviation of entry point performed by the frame-less laser beam varied from 0.27mm – 2.24mm. Histopathological analysis did not show any unintended damage correlated to the laser beam.

Conclusion

The novel robot-driven laser craniotomy tool showed promising results in this first in-vivo recovery study. These findings indicate that laser craniotomies can be performed safely and that cut-through detection is reliable.

Robotik, Präzision und maschinelles Lernen/*Robotics, accuracy & machine learning*

V105

Die graduelle Veränderung der stereotaktischen Korridore zum Gehirn seit der Einführung der Robotertechnologie.

The silent transformation of stereotactic corridors to the brain by the introduction of robotic technology.

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[1]Eberhard Karls Universität, Department für Neurochirurgie und Neurotechnologie, Tübingen, Deutschland

Objective

There are only a few basic principles for trajectory selection in stereotactic neurosurgery (e.g., avoiding sulci). In frame-based stereotaxy, however, the geometry of the frame and the corresponding patient positioning are limiting the accessible surgical corridors. We hypothesize that the introduction of the robotic stereotaxy might have widened these corridors while remaining safe.

Methods

We analyzed 427 frame-based (FRAME, n=201) and robotic (ROBOT, n=226) stereotactic trajectories in 272 patients undergoing stereotactic biopsy or stereoelectroencephalography between 03/2009 and 03/2021. Trajectories were planned on a 3D-MR image in all patients. For inter-subject comparison of the entry (EP) and target (TP) point (X,Y,Z) coordinates and trajectory angles about the x- and y-axis (α1,α2), we co-registered and normalized the patients" individual MRI to the standard MNI space. Additionally, we analyzed the diagnostic yield (DY), the risk of hemorrhage (HR) in both groups.

Results

There were no significant differences in TP coordinates. However, EP variability was larger in the ROBOT group with a significant lateral and posterior shift of the X- (46±19 and 37±15mm) and Y- (-15±42 and 5±38mm) coordinates. In line, there was a significant decrease of α1 (44±27° and 37±1°) and α2 (44±27° and 66±18°) angles in ROBOT trajectories. Notably, there was also a decrease of trajectory length (43±19 and 52±19mm). There were no significant group differences in the DY (97% and 98%) or HR (3.8% and 4.5%)

Conclusion

The robotic technology facilitates EP selection and has led to an unnoticed, gradual changed of the stereotactic corridors, in particular to temporal, cerebellar and brain stem targets. This represents a clinical benefit of robotics in complement to conventional stereotaxy.

Robotik, Präzision und maschinelles Lernen/*Robotics, accuracy & machine learning*

V106

Präzision in humanen Gehirnbiopsien mit patientenindividuellen 3D-gedruckten stereotaktischen Navigationsgeräten auf der Grundlage von MRT Daten- eine Kadaverstudie-

Precision in human brain biopsy using patient personalized 3D printed stereotactic navigation devices based on MRI data- a cadaveric study -

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[2]Fraunhofer Institut, Fakultät für Werkzeugmaschinen und Umformtechnik, Dresden, Deutschland

Objective

To date, conventional stereotactic frames are clinically used for biopsies and offer the highest possible precision. Unfortunately, they implicate some unsolvable technical and logistical limitations like storing, maintenance and calibration. Therefore, new types of navigation devices and manufacturing processes are entering the medicine market. The aim of the present paper is to determine the clinical precision in human brain needle biopsy by using a patient individual stereotactic navigation setup based on rapid prototype manufacturing.

Methods

T1 weighted MRI data sets of human cadaveric heads were used to plan 32 intracranial virtual biopsy target points. Based on this data, 16 individualized stereotactic navigation devices were created and manufactured from PA12 using MJF 3D print technique. Following the intraoperative stereotactic device application on cadaveric head, real needle position was evaluated using intraoperative CT scanning for each biopsy target.

Results

Thirty-two cerebral targets underwent a successful biopsy with the mentioned technique. The average weight of the navigation devices was 62.4 ± 6.0 g. The statistical target point precision was 1.05 ± 0.63 mm in euclidean deviation compared to the virtual planned biopsy target. The highest target point deviation was found in the coronal plane, the lowest in the transversal plane.

Conclusion

3D printed personalized stereotactic devices are a potential alternative for conventionally used frame-based and frameless navigation systems. Potential advantages can be observed in terms of accuracy, reduced medical imaging, manufacturing costs and intraoperative handling. Nevertheless, this technology cannot compensate for a lack of anatomical knowledge and clinical experience of the neurosurgeon.

Robotik, Präzision und maschinelles Lernen/*Robotics, accuracy & machine learning*

V107

Automatisierte Risikobewertung in der Hirntumorchirurgie mit KI-basierten Methoden: eine Pilotstudie
Towards an automated risk assessment in brain tumor surgery using AI-based methods: a pilot study

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[1]Charité - Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Deutschland
[2]Hasso Plattner Institute for Digital Engineering, Digital Health & Machine Learning Research Group, Potsdam, Deutschland

Objective

Recently, regression tree analysis using data from navigated transcranial magnetic stimulation (nTMS) and diffusion tensor imaging (DTI) has been established to predict postoperative motor outcome in brain tumor surgery. However, clinical application requires human resources, technical requirements and expertise. The aim of our study was to establish an automated pipeline using advanced methods as well as deep learning-based models, providing automated risk assessment for the motor outcome.

Methods

This pilot study included a consecutive, prospectively collected cohort of 49 patients with gliomas in proximity to the motor cortex and/or corticospinal tract (CST). All patients underwent MRI and nTMS motor mapping prior to surgery. The automated pipeline is structured as follows: 1) preprocessing of MRI data (skull stripping, co-registration) using Freesurfer, nibabel, ANTs and FSL, 2) automated tumor segmentation using deep learning-based models (Vnet), 3) automated motor cortex segmentation using FastSurfer, 4) preprocessing of DTI data including denoising, gibbs-ringing removal and bias correction using MRtrix3, 5) automated tractography of the CST using TractSeg and MRtrix3 and 6.) automated measuring of the tumor-tract-distance (TTD) and estimating motor cortex infiltration.

Results

Preoperative nTMS motor mapping prior to tumor resection was performed successfully in all patients (median age: 54; female: 18). Of those, 32 suffered from glioblastoma (WHO IV), 12 from WHO II/III astrocytoma, 4 from oligodendroglioma and 1 from dysembryoplastic neuroepithelial tumor. Peritumoral edema was detected in 39 cases. 29 patients have gone through our proposed automated pipeline. Tractography with automated measuring of the TTD was performed successfully in 21 patients. For 4 patients, the automatically generated segmented bundles or beginning and ending ROIs by TractSeg were manually dilated for performing proper tractography. Tractography was not successful in 4 patients due to large lesion.

Conclusion

Automated risk stratification in brain tumor surgery is a use case for standardizing clinical patient care, improving treatment quality, and economizing medical resources. Through the pipeline, more patients will benefit from differentiated preoperative planning that has been shown to lead to better functional and oncologic outcomes, not least by assigning patients to the right treatment pathway (based on their individual risk profile).

Robotik, Präzision und maschinelles Lernen/*Robotics, accuracy & machine learning*

V108

Phasendetektion in neurochirurgischen Operationen mittels Deep Learning
Phase detection in neurosurgical operations using deep learning

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Objective

With more sensors being deployed and extensive growth of collected data in the modern operating room deep learning methods are becoming more and more important in many areas of surgery. Surgical phase recognition is the task of automatically segmenting surgical videos into phases and has shown promising results in research when applied to endoscopic surgery. However, it remains to be evaluated where the investigated methods can successfully be transferred to a neurosurgical setup. Neurosurgery, in particular, provides a complex setup with less standardized surgical approaches due to high variety in location and type of lesions and complex human anatomy. Every day, many hours of video material from neurosurgical interventions are recorded, but it has not yet been evaluated whether this can be analyzed in a meaningful way. In this first pilot study, we evaluated whether microscopic video material of a standardized operation can be segmented into meaningful surgical phases using deep learning.

Methods

38 microscopic recordings of resection of vestibular schwannomas (single center, single surgeon) were manually annotated with eight phases (open dura, dura attachment, open basal cisterns, open Tübingen line, open internal auditory canal, tumor resection, endoscopic control, closing dura). The dataset was randomly divided into training data (18 videos), a validation set (4 videos) and a test-set (6 videos). A cascaded network consisting of a convolutional neural network (CNN, ResNet 50) and a Long Short-Term-Memory network (LSTM) was set up and end-to-end trained on 20-second subsequences of the training data set. Overall training accuracy was evaluated on the test dataset. The model was qualitatively analyzed by visual inspection of model predictions and frame input.

Results

The technique was implemented on all complete video recordings. Overall, a good test set result could be obtained (mean balanced accuracy: 81,2% +- 7,8%). Confusion was found in adjacent and visually similar phases. Qualitative analysis revealed that phases with strong visual cues, like different types of medical instruments or sutures, could be recognized with a higher accuracy than others.

Conclusion

With the evaluated technology individual operational phases can be recognized with high accuracy given the small amount of training data. In the post-hoc analysis, coherent characteristics for the classification could be determined, suggesting that useful information could be learned.

Neuroonkologie experimentell I/*Experimental Neuro-oncology I*

V109

Blockade von TIGIT in *in vitro* expandierten NK-Zellen resultiert in einer erhöhten Zytotoxizität gegen primäre Glioblastomzellen

Blocking TIGIT to improve the cytotoxicity of in vitro expanded NK cells towards primary glioblastoma cells

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Objective

NK cells and chimeric antigen-receptor modified NK cells are considered as the next wave in cellular immunotherapy to fight cancer. In contrast to T cells, NK cells are devoid of recombined immunoreceptors and recognize tumor cells by a set of inherited natural cytotoxicity receptors as well as activating and inhibitory receptors of the immunoglobulin and lectin superfamilies. Expression of inhibitory NK cell ligands on glioblastoma (GBM) cells, such as CD155/poliovirus receptor (PVR) can block NK cells with expression of the cognate inhibitory "T cell immunoreceptor with Ig and ITIM domains" (TIGIT). Of note, TIGIT expression has been shown to be upregulated on activated NK cells but also on NK cells from cancer patients. This study investigated whether antibody-mediated blocking of TIGIT can result in improved cytotoxicity of NK cells towards glioblastoma cells.

Methods

Primary NK cells were isolated from the blood of 12 healthy donors. On the day of isolation and after 10 days in co-culture with a PC-3 feeder cell line constitutively expressing IL-2, membrane-bound IL-15 and 4-1BBL, NK cells were analyzed by flow cytometry for immune checkpoint molecules and activating and inhibitory receptors. Subsequently, the cytotoxicity of the *in vitro* expanded NK cells against the CD155+ glioblastoma cell lines HT7606 and HT18584 was investigated by chrome release assays with and without the use of TIGIT-blocking antibodies.

Results

NK cells co-cultured with PC-3 feeder cells were successfully expanded using a NK cell to feeder cell ratio of 5:1 (expansion factor: median 24.5-fold, range 15.4 - 39.8). Analysis of immune checkpoint related markers revealed neglectable PD-1 and LAG3 expression, whereas TIGIT expression increased. A high significant increase in NK cell-mediated specific cell lysis of glioblastoma cell lines HT7606 and HT18584 could be observed when TIGIT was blocked using antibodies (HT7606: median 24.2%, HT18584: median 30.0%) when compared to non-treated cells (HT7606: median 6.5%, HT18584: median 16.5%) irrespective of KIR:KIR-ligand settings.

Conclusion

The results demonstrate that TIGIT blockade leads to an improved cytotoxicity of *in vitro* expanded primary NK cells towards glioblastoma cells by overcoming the immunosuppressive effect of CD155 on tumor cells. Therefore, TIGIT serves as promising target structure for future studies and clinical approaches.

Neuroonkologie experimentell I/*Experimental Neuro-oncology I*

V110

Erfolgreiche Reprogrammierung von aus Glioblastomgeweben stammenden M2-polarisierten Microglia/Macrophagen durch GW2580-vermittelte CSFR1 Inhibition

Successful reprogramming of patient-derived M2-polarized glioblastoma-associated microglia/macrophages via GW2580-mediated CSF1R inhibition

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Objective

Targeting immunosuppressive and protumorigenic glioblastoma-associated macrophages and microglial cells (GAMs) holds great potential to improve patient outcomes. Although CSF1R has emerged as a promising target to reprogram anti-inflammatory M2-like GAMs, relevant treatment data on human, tumor-educated GAMs and innovative patient-derived 3D tumor organoid models to study the influence on adaptive immunity and the effectiveness of treatment in a complex and entirely autologous setting are largely lacking.

Methods

We performed a comprehensive phenotypical, and transcriptional analysis of primary, patient-derived CD11b-sorted GAMs upon treatment with the CSF1R-targeting drugs PLX3397, BLZ945, and GW2580 by flow cytometry and RNAseq. Functional effects were studied in phagocytosis, transmigration and T cell killing assays as well as in a patient-derived glioblastoma tumor organoid model.

Results

The most effective reprogramming of GAMs was observed upon GW2580 treatment, which led to a downregulation of M2-related markers (CD163) and signaling pathways (Il6), while M1-like markers (HLA-DR), phagocytosis, and T-cell killing were substantially increased. Moreover, treatment of patient-derived glioblastoma organoids with GW2580 confirmed successful reprogramming together with reduced tumor cell proliferation.

Conclusion

Altogether, our data indicate that treatment with GW2580 could be an important pillar in the future therapy of GBM.

Neuroonkologie experimentell I/*Experimental Neuro-oncology I*

V111

Antitumorale in vitro Synergie von Aprepitant (ein Neurokinin-1-Rezeptor-Antagonist) und 5-ALA in Glioblastom

The in vitro anti-cancer synergy of neurokinin-1 receptor antagonist, aprepitant, and 5-Aminolevulinic acid in Glioblastoma

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Objective

5-Aminolevulinic acid (5-ALA)-based treatment modalities have been recently proven to be of utmost significance in the management of glioblastoma multiforme (GBM), a highly aggressive and fast-growing Grade IV brain tumor. Accordingly, there is great interest in finding effective pharmacologic adjuvants to improve the efficacy of 5-ALA. Therefore, in this study, we aim to examine the anti-cancer synergy of 5-ALA with a safe and clinically approved neurokinin -1 receptor (NK1R) antagonist, aprepitant in a human glioblastoma cell line.

Methods

Cell viability and cytotoxicity were evaluated by WST-1 assay. Flow cytometry was employed to assess cellular apoptosis. mRNA expression levels of apoptosis-associated genes were evaluated by quantitative real-time PCR (qRT-PCR). GBM cells' migratory behavior was determined by wound-healing assay and matrix metalloproteinases (MMP-2 and MMP-9) activity was assessed by zymography. The fluorescence intensity of Protoporphyrin IX (PpIX), a highly pro-apoptotic and fluorescent photosensitizer, was also visualized with confocal microscopy.

Results

We found that both aprepitant and 5-ALA reduced GBM cell viability in a dose and time-dependent manner and that combinational treatment exhibited potent synergistic growth inhibitory effects as indicated by combination index analysis. Moreover, aprepitant and 5-ALA induce apoptosis and modified the levels of apoptosis-related genes (up-regulation of Bax and P53 along with downregulation of Bcl-2). Furthermore, aprepitant and 5-ALA increased the PpIX fluorescence intensity. We also observed that aprepitant and 5-ALA effectively inhibited GBM cells' migratory phenotype and decrease MMP-2 and MMP-9 activities. Importantly, the combined use of these agents was significantly superior to the use of each drug alone for the induction of these effects

Conclusion

Collectively, our findings indicated that combining 5-ALA-aprepitant synergistically modulate the apoptotic, proliferative, and migrative phenotypes of GBM cells and offer new insight for further development of this combination as a novel anti-GBM therapy.

Neuroonkologie experimentell I/*Experimental Neuro-oncology I*

V112

Dielektrischen Eigenschaften von intrakraniellen Tumoren – potenzielle Rolle des Myelingehalts
Dielectric properties of intracranial tumors – role of myelin content

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Objective

Recently, tumor treating fields (TTFields) were established for the treatment of newly diagnosed glioblastoma (GBM). One of the most crucial parameters defining the treatment efficacy of TTFields is the electric field intensity, which depends on the dielectric properties of the tumor tissue. In this study, we determined the dieclectric properties of brain tumors by analyzing resected tissue following a fast acquisition protocol. In GBM patients, histological analysis for cellularity, vascularization, and myelin content was performed. In addition, sensitivity analyses for specific parameters (tissue hydration, temperature, and saline irrigation) were conducted.

Methods

A cohort of 130 patients with tumors of different histology and malignancy grade have been recruited (meningioma: n=36; brain metastases n=29; low grade glioma n=7; anaplastic glioma = 12; other= 7; glioblastoma n=39, all treated with TTFields). Tissue samples were placed into a cylindrical cell with a known diameter. The impedance was recorded at frequencies 20Hz-1MHz using a software specifically developed for this study. The measured impedance was translated into dielectric properties of the sample (conductivity and relative permittivity) based on the parallel plate model. Myelin, which is the most powerful electric isolator in the brain, was assessed in GBM samples by luxol fast blue staining, and quantified in a three-tier scale. To assess the impact of tissue conditions on the measurements, probes were warmed to 35 degrees Celsius, dehydrated or irrigated with 0.9% saline solution.

Results

We found significant differences between the conductivity of different types of tumors, with meningiomas showing the lowest and GBM tissue exhibiting the highest conductivity values. GBM samples with very high median conductivity values displayed a consistently lower myelin content. In addition, GBM patients with particularly high conductivity had a significantly shorter overall survival (log rank analysis, p = 0.024). While tissue temperature had no effects on the dielectric properties in GBM, saline irrigation and tissue hydration significantly affected the results.

Conclusion

The dielectric properties of intracranial tumors depend on histological class and malignancy grade. GBM patients with high conductivity values showed a significantly poorer prognosis, indicating this parameter as a potential marker for TTF efficacy.

Neuroonkologie experimentell I/*Experimental Neuro-oncology I*

V113

Intrazerebral (aber nicht intravenös) injizierte EpCAM-gerichtete CAR T-Zellen weisen potente anti-tumoröse Funktionen und in vivo Dynamiken gegen Hirnmetastasen des Lungenkarzinoms auf

Intraparenchymal (but not intravenously) injected EpCAM-directed CAR T-cells exhibit potent anti-tumor effects and in vivo dynamics for brain metastases from lung cancer

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Objective

Patients with lung cancer are at risk for brain metastases, and affected patients often succumb to their intracranial disease despite controlled systemic disease. Chimeric Antigen Receptor (CAR) T-cells emerged as an effective cell-based immunotherapy for hematological malignancies; but it remains unclear whether CAR T-cells represent a viable therapeutic avenue for brain metastases.

Methods

An orthotopic, fully immunocompetent cerebral metastasis model was established in mice by combining a chronic cranial window with repetitive intracerebral two-photon laser scanning microscopy. Intraparenchymal injection of Lewis lung carcinoma cells (expressing the tumor cell-antigen EpCAM) was performed. EpCAM-directed CAR T-cells (EpCAM-CAR T-cells) were injected either intravenously or into the adjacent brain parenchyma. This approach enabled the in vivo-characterization of fluorescent CAR T-cells and tumor cells on a single-cell level over weeks.

Results

All mice had visible tumor take with exponentially growing lesions following intracranial tumor cell injection. In mice receiving EpCAM-CAR T-cells intravenously, we neither observed substantial CAR T-cell accumulation within the tumor nor relevant anti-tumor effects. Local CAR T-cell injection, however, resulted in intratumoral CAR T-cell accumulation compared to controls treated with T-cells lacking a CAR. This was paralleled by lower velocities of EpCAM-CAR T-cells, characterizing antitumor cytotoxicity due to 'immune cell'-'tumor cell' contacts. Consequently, treatment with intraparenchymal EpCAM-CAR T-cells resulted in reduced tumorous growth as determined per in vivo-microscopy (median tumor area on day 10: 1.8 versus 10.8 mm2; p=0.001) and immunohistochemistry of excised brains. However, the number of intratumoral EpCAM-CAR T-cells within the tumor markedly decreased during the observation period, pointing towards insufficient persistence. Accordingly, survival was prolonged in mice receiving EpCAMCAR T-cells but long-lasting remission was rare (median survival: 15 versus 13 days; p=0.012). No CNS-specific or systemic toxicities of EpCAMCAR T-cells were observed in our immunocompetent model.

Conclusion

Our findings indicate that locally (but not intravenously) injected EpCAMCAR T-cells may safely induce relevant anti-tumor effects in brain metastases from lung cancer. Strategies improving the CAR T-cell persistence within brain metastases may potentially further boost the therapeutic success.

Neuroonkologie experimentell I/*Experimental Neuro-oncology I*

V114

Die Therapie mit dualen CAR-T Zellen kann Antigen Escape im *ex vivo* Glioblastom Modell überwinden

A combination of CAR-T cell specificities can overcome antigen escape mechanisms in ex vivo glioblastoma models

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Objective

Glioblastoma (GBM) is considered one of the most challenging tumors to conquer as tumor heterogeneity and antigen escape mechanisms suppress the effects of recent immunotherapeutic approaches. Genetically modified T cells expressing a chimeric antigen receptor (CAR) are retargeted to recognize tumor associated antigens (TAA). When activated, these cells initiate the triad of cytokine release, T cell proliferation, and target cell apoptosis. In order to overcome antigen escape due to tumor heterogeneity, we combined CAR-T cells in a dual targeting approach. We evaluated the performance of treatment with a combination of two CAR-T cell products versus a single CAR-T cell approach in GBM patient derived *ex vivo* organoids (PDOs).

Methods

PDOs were generated from freshly resected GBM tissue and cultured successfully up to several months. CAR-T cells were generated from peripheral blood mononuclear cells of healthy donors via lentiviral transduction of isolated T cells. The transduction rate was assessed by flow cytometry prior to application. PDOs were incubated with a defined number of CAR-T cells at an effector to target ratio of 1:4, while untreated PDOs served as controls. Morphological integrity was assessed microscopically before treatment and after 20 h and 48 h. Immunofluorescence staining was used to detect apoptosis in TAA expressing cells after 16h (TAA+/CC3+). Cytokine release of IFNγ was detected via ELISA after 16 h.

Results

PDOs generated from three different GBM patients showed an expression of our TAAs of interest of 62 %/1 %, 59 %/9 %, and 46 %/8 %, respectively. All treated PDOs presented clear disintegration of their circular shape until total dissolving after 48 h, whereas controls stayed intact. Treated PDOs showed significantly higher apoptosis than controls in both dual and monotreatment (p = 0.01 and p = 0.03, respectively). However, 46 % of tumor cells were apoptotic after administration of two CAR-T products, compared to only 30 % in the mono therapeutic approach and 1 % in the untreated controls. All treated PDOs showed higher levels of IFNγ than controls with significance in combined treatment (p = 0.04).

Conclusion

Despite the disparity of target expression in GBM, the efficacy of CAR-T cells was enhanced by a dual targeting approach overcoming antigen heterogeneity and antigen escape mechanisms. Suitable TAA combinatory therapies are subject to further research.

Trauma SDH/*Trauma - subdural hematoma*

V115

Neurokognitive Beeinträchtigung und Lebensqualität bei Patienten mit chronischem Subduralhämatom - ein prospektives Patientenregister

Neurocognitive impairment & quality of life after treatment of chronic subdural hematoma (cSDH) – a prospective patient registry

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Objective

Chronic subdural hematoma (cSDH) is one of the most common neurosurgical conditions and often caused by unnoticed minor trauma to the bridging veins in elderly patients. Besides age, various risk factors are discussed. Clinical presentation comprises neurological symptoms, deficiencies in neurocognition and quality of life. Therapy approaches range from conservative watch and wait or medical intervention and surgical treatments. The aim of this registry is to collect data from a large cohort of cSDH patients to learn about impact of risk factors and optimal therapy strategies.

Methods

Patients with radiological diagnoses of cSDH are eligible for inclusion. Epidemiological data, risk factors and medication as well as trauma history, NIHSS, Montreal-Cognitive-Assessment-Test (MOCA) results of radiological imaging and quality of life aspects (SF-12) are collected. Furthermore, therapy strategies, interventions and complications are documented.

Results

The registry is still recruiting, so far 90 patients (60 male and 30 female) have been included since 01/2020. Mean age of cohort was 82 years. At baseline, most common symptoms were headache (55.6%), vertigo (22.2%) and nausea (7.8%). Recent trauma was reported in 78.7% (n=89) of patients. Platelet aggregation inhibitors (33.3%) and oranticoagulants (32.2%) were most common risk factors (n=87). 12.8% of patients reported daily alcohol consumption (n=86). 88 patients underwent surgery via burrhole trepanation, subdural drainage was placed in 96% (n=86). Most common complication were postoperative seizures. Mean NIHSS at baseline (n=88) was 2.41 and improved to 0.4 at discharge (n=80) and further to 0.33 at first follow-Up(fFU) (n=36). Mean MOCA at baseline (n=54) was 20.2 and improved to 27.2 at fFU (n=10), accordingly mean SF-12 phys (45.1) and ment (50.9) (n=66) improved to 52.1 and 54.6 at fFU (n=17).

Conclusion

Patients with cSDH benefit of surgery, particularly in regard to neurocognition. Improvements can also be seen in neurological examinations (NIHSS) and quality of life (SF-12). Correlations between prevalence of radiological or clinical residual cSDH and therapy strategies as well as anamnestic medications remain to be seen.

Trauma SDH/*Trauma - subdural hematoma*

V116

Das chronische Subduralhämatom bei jüngeren Patienten (≤50): Demographische, klinische und Ergebnisanalyse

Patients ≤ 50 years old presenting with a chronic subdural hematoma: Demographic, clinical and outcome analysis

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Objective

Chronic subdural hematomas are a common diagnosis in the elderly but a rare pathology in patients younger than 50 years old. Therefore, we aimed to describe possible underlying factors that resulted in the cSDH of patients aged ≤ 50 years and analyzed their outcome.

Methods

All patients with a surgically treated chronic subdural hematoma presenting to a german university hospital between 2006 and 2017 were retrospectively assessed and only adult patients aged ≤ 50 years were included for further analysis. Demographic and clinical variables were collected and outcomes at discharge as well as the rate of recurrence within 90 days were analyzed.

Results

Over a period of 11 years, 44 younger cSDH patients (mean age 42±10 years, 69% (n=30) male) could be identified, which represented 5% of all surgically treated cSDH patients during this period. Their most common comorbidity was a neoplastic disease (n=8; 18%). Only 21 patients (48%) reported a trauma 33±32 days prior to the cSDH diagnosis. Neurological deficits were rare (2%; n=12). However, most patients suffered from headaches (n=30, 68%). Evacuation of the cSDH was performed via burr hole trephination in 91% (n=40) and via craniotomy in only 9% (n=4). 43% of cSDHs (n=19) were right hemispheric, 19 (43%) patients presented with a frontal cSDH and 20 (45%) had the maximal diameter parietally. Surgical and medical complications were rare (16% and 18%, respectively). After a mean hospital stay of 7,8±8,5 days, 86% (n=38) of patients were discharged with a Glasgow coma scale (GCS) of 15 and 77% (n=34) had benefited from surgery clinically. Only nine patients were re-admitted to the hospital with a recurrent cSDH within 90 days of discharge, three of them presenting with headaches and nausea and six with new neurological symptoms.

Conclusion

Surgically treated chronic subdural hematomas are a rare pathology in patients under the age of 50 years and represent only 5% of the overall cSDH population. Of note, the rate of neoplastic diseases in the younger cSDH patients is relatively high and further analysis into the pathophysiology of this co-occurrence might be needed.

Trauma SDH/*Trauma - subdural hematoma*

V117

Outcome nach Kraniotomie zur Evakuation eines akut subduralen Hämatoms bei über 80-jährigen Patienten
Outcome after craniotomy for acute subdural hematoma in patients aged 80 and older

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Objective

The objective of the study was to evaluate if surgical evacuation of acute subdural hematoma (aSDH) is a sensible treatment option patients aged 80 or older.

Methods

Patient records, imaging studies and surgical protocols of patients who underwent craniotomy for acute subdural hematoma (purely acute, acute on chronic and subacute SDH) as main diagnosis at our institution between January 2013 and August 2022 were retrospectively reviewed. Status on admission was documented with the Glasgow Coma Scale (GCS). Cardiovascular comorbidities were recorded using the CHA2DS2-VASc-Score, further data collection comprised history of malignant tumor and intake of anticoagulants. Primary outcome measure were in-hospital mortality and favorable functional outcome defined as Glasgow Outcome Scale (GOS) of 4 or 5 points.

Results

A total of 41 patients (39% female) aged 83.0 ± 3.0 years were included into analysis. Mean inpatient stay was 13.8 ± 10.5 days, in-hospital mortality was 48.8%. A favorable outcome could be achieved in 8 patients (19.5%) resulting in a number needed to treat of 5.125. Mean GCS at admission was 12 ± 3.9, 14 patients (34.1%) were intubated and 14 (34.1%) presented with preoperative anisocoria. Mean hematoma diameter was 17.4 ± 4.6 mm with a corresponding midline shift of 11 ± 4.9 mm. Anisocoria (p=0.009, Cramer"s V=0.43, OR=7.3, 95%CI=1.63-33.1) as well as a greater midline shift on preoperative CT-scan (p=0.009) increased the risk for death. CHA_2DS_2-VASc-Score (p=0.83) or intake of antithrombotic medication (p=0.66, Cramer"s V=0.08) were not associated with in-hospital mortality, whereas patients with a history of malignant disease (p=0.003, Cramer"s V=0.47, OR=0.38, 95%CI=0.25-0.59) had a higher risk to die. Diameter of hematoma (p=0.83), diameter of craniotomy (p=0.32) or initial GCS of less than 9 points (p=0.72, Cramer"s V=0.07, OR=1.4, 95%CI=0.3-6.3) were not associated with mortality. Considering hematoma subgroups, acute on chronic as well as subacute SDH were not associated with mortality (p=0.34, Cramer"s V=0.28). However, outcome was favorable in patients with subacute SDH (p=0.008, Cramer"s V=0.57).

Conclusion

Based upon a number needed to treat of 5.125 in our study, we suggest to critically evaluate the contraindications for evacuation of acute subdural hematoma via craniotomy in patients aged 80 and older. Patients with preoperative anisocoria did not benefit from surgical treatment.

Trauma SDH/*Trauma - subdural hematoma*

V118

Der GALT-Score: Eine neues Instrument zur Einschätzung des Rezidivrisikos neu diagnostizierter und mittels Bohrlochevakuation behandelter subakuter und chonischer subduraler Hämatome

The GALT-Score: A new tool to evaluate the risk of hematoma recurrence for primary diagnosed subacute and chronic subdural hematomas treated with burr-hole evacuation

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Objective

The demographic change and the increasing consumption of antiplatelet drugs respectively anticoagulants lead to rising incidences of subacute and chronic subdural hematomas worldwide. One of the most challenging aspects of the treatment are high rates of hematoma recurrence. Burr-hole evacuation is still the gold standard for primary diagnosed subacute and chronic subdural hematomas. Based on the new GALT-Score a preoperative assignment into low-risk and high-risk hematoma is feasible.

Methods

GALT is an acronym for gender, acuity, location, and thickness. The score is made up of four simple items, which include well known risk factors for hematoma recurrence. This study presents the characteristics of 101 patients either with subacute or chronic subdural hematomas treated with burr-hole evacuation plus subdural drain in a single center between January 2017 and December 2021. The Score was rated as follows: Gender (female=0, male=1), acuity (chronic subdural hematoma=0, subacute hematoma=1), location (right=0, left=1, bilateral=2), thickness of the hematoma (≤20 mm=0, >20 mm=1). Based on the total score, we evaluated the risk of recurrence and defined low-risk (0-2 points) and high-risk hematomas (3-5 points).

Results

Between January 2017 and December 2021 101 consecutive patients (28 women, 73 men) underwent surgery in our department. The acuity divided into 53 subacute (52,5 %) and 48 chronic (47,5 %) subdural hematomas. In 28 cases (27,7 %) the hematoma was located right. 33 hematomas (32,7 %) were left sided. Bilateral hematomas were observed in 40 patients (39,6 %). Hematoma thickness up to 20 mm was found at 52 individuals (51,5 %). 49 patients (48,5 %) were operated on hematomas with a thickness of more than 20 mm. 40 patients (39,6 %) were assessed as low-risk hematoma (LRH). We assigned 61 cases (60,4 %) into high-risk hematoma (HRH)-group. 15 patients (14,9 %) had to be reoperated on due to symptomatic hematoma recurrence. Those revision surgeries included 2 LRH and 13 HRH (13,3 % versus 86,7 %; p=0,024). The mean time to recurrence was 3,3 weeks (± 1,7). HRH had a significant higher recurrence rate compared to LRH (OR 5,15; 95% CI 1,09-24,2). The mean follow-up was 10,4 months (± 14,6).

Conclusion

The GALT-Score is the first preoperative risk assessment tool for subacute and chronic subdural hematomas treated with burr-hole evacuation. The differentiation between LRH and HRH may lead to purposeful management including surgical strategy, medication and close follow-up.

Trauma SDH/*Trauma - subdural hematoma*

V119

Wirksamkeit von subperiostalen Drainagen beim chronischen Subduralhämatom: eine prospektive randomisierte kontrollierte Studie.

Efficacy of subperiosteal drains in chronic subdural hematoma: a prospective randomized controlled single-center study

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Objective

Recent advances have led to an improved understanding of the pathophysiology and development of new treatment strategies for chronic subdural hematoma (cSDH). However, these lesions are most frequently treated by evacuation via a small craniostomy procedure. Subperiosteal drains have recently been introduced as alternatives to standard subdural devices but only a few prospective studies have explored their efficacy. Thus, a prospective randomized controlled trial was designed to assess the use of subperiosteal drains for the treatment of cSDH.

Methods

The study enrolled patients with newly diagnosed surgically amenable cSDH. These patients were randomized into two groups. The first group underwent cSDH evacuation via a burr-hole craionstomy procedure followed by placement of a subperiosteal drain; the second group underwent the identical procedure without drain placement. Patients were then followed for three months. Patient demographics, drain volumes, duration of drainage, cSDH recurrence, and postoperative outcomes were recorded. The data were evaluated and subjected to statistical analysis.

Results

Eighty-eight patients presenting with cSDH (12 with bilateral findings) from a total of 100 surgical cases were enrolled prospectively over 19 months.The mortality rate was 6.8%, severe postoperative morbidity was 1,1%. Nine patients were lost to follow-up resulting in a total of 79 patients and 90 procedures that remained eligible for ongoing evaluation. Of all procedures, 37 were carried out with drain placement and the remaining 53 without. There were 5 recurrent cases (13,5%) in the drain group and 17 (32,1%) in the control group without drain placement. This resulted in a statistical significance (OR 0.33; $p<0.05$) favoring the use of a drain. No other major difference between both groups could be established.

Conclusion

Subperiosteal drain placement can be used safely and effectively to treat cSDH in conjunction with a burr-hole craniostomy procedure. While it may not improve the overall outcome, subperiosteal drain placement was directly associated with reductions in disease recurrence and the need for a second surgical procedure. While this is the first study specifically designed to provide a prospective evaluation of the addition of subperiosteal drains, the findings are consistent with previously-published results concerning the use of drains in general as adjuncts to cSDH surgery.

Trauma SDH/*Trauma - subdural hematoma*

V120

Die langfristige Verwendung von diagnostischen subduralen EEG-Elektroden bei SubduralhEmatomen (DISEASE): Eine prospektive nicht-randomisierte kontrollierte Studie

The Long-Term Use of DIagnostic Subdural EEG electrodes And SubduralhEmatoma (DISEASE): A Prospective Nonrandomized Controlled Trial

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Objective

Seizures and status epilepticus (SE) are frequent complications of acute subdural hematoma (aSDH) associated with increased morbidity and mortality. Therefore, we aimed to evaluate whether invasive subdural electroencephalogram (EEG) recording leads to earlier seizure detection and treatment initiation in patients with aSDH.

Methods

The DISEASE trial was a single-center, prospective, non-randomized trial in 76 patients with aSDH. 31 patients (40.8%) were assigned to the electrode group and 45 patients (59.2%) to control group. The primary outcomes were the prevalence and time to detected epileptiform discharges (ETPs), seizures/SE occurrence, and SE incidence. Secondary outcomes included neurological outcomes assessed using the Glasgow Outcome Scale (GOS) at discharge and 6-month follow-up and the prevalence of focal structural epilepsy within 2years after discharge.

Results

The trial was stopped after a study committee meeting when the prespecified criteria were met. The electrode and control groups were well-matched for clinical characteristics at admission. ETPs were detected significantly more frequently in the electrode group than in the control group (77.4% vs 26.4%, p<.001). Frequencies of seizures and SE detection were significantly higher in the electrode group than in the control group (61% vs 15.6%, p<.001; 38.7% vs 11.1%, p=.005). Time to seizure and SE detection was significantly earlier (median 29.2 vs 83.8h, p=.018; 17.2 vs 83.8h, p=.033) in the electrode group than in the control group. Favorable outcomes (GOS 4-5) were more frequently achieved in the electrode group than in the control group (58% vs 31%, p=.065). One minor complication without clinical sequelae (3.3%) occurred in the electrode group. No significant differences were detected in long-term mortality or post-traumatic epilepsy (p>.05).

Conclusion

Invasive subdural EEG monitoring is valuable and safe for early seizure/SE detection and treatment, with improved outcomes in the neurocritical care of patients with aSDH.

Trial Registration: Clinicaltrials.gov NCT04211233

Abb. 1

Adulter Hydrocephalus und SIH/*Adult hydrocephalus and SIH*

V121

Der Headache Impact Test 6 (HIT-6) als Prädiktor für das Outcome bei Spontane Intrakranielle Hypotension (SIH)

The Headache Impact Test 6 (HIT-6) score as a predictor of outcome in Spontaneous Intracranial Hypotension (SIH)

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Objective

Introduction

Spontaneous intracranial hypotension (SIH), caused by a spinal CSF leak, may cause many clinical symptoms, the most common being disabling headaches. Patients report a high impact on their quality of life because of their symptoms. However, follow-up is usually complicated and might be subjective when assessing headaches and post-operative SIH-related symptom improvement. A novel way of evaluating outcomes is using PROMs ("patient-reported outcome measures").

Objectives: The study aimed to analyse the outcome of patients" headaches using the HIT-6 Score (Headache Impact test 6) in a daily routine for patients treated surgically for a spinal CSF leak.

Methods

All consecutive patients treated at our institution with SIH, according to ISHD, between January 2020 and November 2022 were included. Patients were asked to complete different questionnaires on the Heartbeat medical solution software on a tablet at the admission, post-operative at 14 days, 3,6,12 and 24 months, respectively.

Statistical analysis was performed using R software [version R 4.0.4] through the studio interface Version 1.4.1106. A multivariate analysis using a logistic regression model was performed as appropriate. Patients" loss of follow-up were censored at the recorded date of the last filled questionnaire.

Results

In total, we identified 80 patients that filled out the questionnaire and were included in the analysis. The median age was 45,3 years old (IQR 29-61). The median HIT-6 Score before surgery was 65, IQR (57-73) interpretable as severely disabling headaches. The score improved at three months to a median score of 49 (IQR 36-64) and, respectively, to a median score of 48 at one year and 46 at two years, considered as having little to no impact on patients" quality of life at this time. No difference was found between the tree month score and two year score (P>0.08).

Conclusion

Due to disabling symptoms, SIH notably impacts the patient"s quality of life. Therefore, PROMs are reliable and applicable in a daily surgical routine in order to asses clinical improvement. The use of new technologies such as tablets is a complementary alternative to clinical follow-up. The three-month assessment could give us a clear picture of the patients' outcomes and reflect their evolution.

Adulter Hydrocephalus und SIH/*Adult hydrocephalus and SIH*

V122

Sicherheit, Nebenwirkungen und Effektivität des Clippings von Nervenwurzeln bei Patienten mit Spontane Intrakranialle Hypotension (SIH)

Safety, sequelae and effectiveness of nerve root clipping in patients with Spontaneous Intracranial Hypotension (SIH)

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Objective

Introduction

Spinal CSF leaks may cause a myriad of clinical symptoms, the most common being orthostatic headache. Leaking cysts (Type II) and CSF venous fistulas (Type III) are a subgroup of spinal CSF leaks representing about 1/3 of spinal CSF leaks. In order to achieve optimal surgical management, the respective nerve root may be microsurgically clipped using aneurysm clips in order to seal the diverticula or the CSF venous fistula.

Objectives:

For specific lateral spinal CSF-leaks, nerve root clipping is regarded as the treatment of choice. The study aimed to analyse this procedure's safety, efficacy and side effects of this procedure.

Methods

All consecutive patients in whom the surgeon decided to clip a nerve root as the treatment of choice for SIH were included at our Neurosurgical institution from Mai 2018 to November 2022. Patients were evaluated clinically for post-operative hypesthesia, motor deficits, headaches and neuropathic pain. The latter was assessed using the DN4 questionnaire and the Pain detect questionnaire.

Results

In Total we identified 31 Patients with Type II spinal CSF leaks and 9 type III CSF venous leaks representing 40 patients treated using nerve root clipping. 29 were female (72.5%), and median age was 46,6 years old (IQR 35-55). Level of clipped roots were located between T1 and L1 with a predominance in T10-T11 (N=10, 25%), T11-T12 (N= 9, 22.5%), T9-T10 (N=7, 17.5%), and T12-L1 (N=7, 17.5%). The mean follow-up was 22 months. SIH-linked symptoms improved in 89% of patients. 35% of patients had post-operative hypesthesia in the respective dermatome. Only 1 patient had a transient minor motor deficit after a T1 nerve root clipping. Interestingly, only 2 (5%) patients were screened positive for non-disabling neuropathic pain with a DN4 score of >4. Only one patient required therapy with Pregabaline under which the symptoms improved.

Conclusion

Our findings suggest that nerve root clipping in the context of a spinal CSF leak is safe and did not lead to permanent motor deficits. The prevalence of neuropathic pain was 5% and was reported as non-disabling without the need for long-term medication. The procedure was highly effective, with the permanent improvement of SIH symptoms in 89% of the cases.

Adulter Hydrocephalus und SIH/*Adult hydrocephalus and SIH*

V123

Shuntscope-assistierte Katheterimplantation bei der Behandlung von Hydrocephalus bei Erwachsenen- Erfahrung mit 63 Proceduren

Shuntscope- guided Catheter Implantation in Adult Hydrocephalus – Experience of 63 Procedures

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Objective

Ventricular catheter placement in the selected subset of adult hydrocephalus can be highly challenging due to abnormal anatomical configuration or the need for transaqueductal stent placement. Transluminal endoscopy with the Shuntscope has been invented to increase the rate of successful catheter placements. This presentation evaluates Shuntscope system, achieved intraoperative image quality, related radiological and surgical outcomes in adults.

Methods

A retrospective analysis of all adult patients undergoing ventricular catheter placement using the Shuntscope from 11/2011 to 07/2022 in the author"s department was performed. Demographic, clinical, and radiological data were evaluated. The visualization quality of the intraoperative endoscopy was stratified into the categories; excellent, medium, and poor, compared to the postoperative catheter tip placement. Follow-up evaluation included the surgical revision rate due to proximal catheter misplacement.

Results

A total of 63 Shuntscope-assisted surgeries have been performed on 60 adults. The mean age was 48.43 years. The most common underlying pathology was a tumor- or cyst-related CSF impairment in 38.33 %, followed by pseudotumor cerebri in 21.66%. Achieved image quality was excellent in 39.68%, medium in 47.62%, and poor in 12.7%. Ideal catheter placement was achieved in 79.37%. There were no intraoperative complications associated with the Shuntscope. The revision rate due to suboptimal proximal VC placement was 4.76% during a mean follow-up period of 27.75 months. Statistical correlation between image quality grade and accuracy of catheter position was observed (p-value < 0,001).

Conclusion

The Shuntscope can be considered a valuable addition to standard surgical tools in treating a selected subset of adult hydrocephalus. Even suboptimal visualization contributes to high rates of correct catheter placement.

Adulter Hydrocephalus und SIH/*Adult hydrocephalus and SIH*

V124

Endoscopische dritt Ventriculostomie vs. Ventriculoperitoneal shunt fuer die Behandlung von Normal Druck Hydrozephalus, randomisierte Studie

Preliminary results: Endoscopic third ventriculostomy versus Ventriculoperitoneal shunt for treating normal pressure hydrocephalus, randomized approach

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Objective

Diagnosis and selecting the best treatment option for idiopathic normal pressure hydrocephlus (iNPH) is challenging. Ventriculoperitoneal shunt (VPS) and endoscopic third ventriculostomy (ETV) are part of the surgical options.

OBJECTIVE: To report a minimum 2-year outcome after ETV or VPS in patients with iNPH.

Methods

Prospective Randomized, parallel, open-label trial included patients over 65 years with iNPH, and with positive response to the tap test (TT) or lumbar drain trial (LDT) from 2016 to 2022. The functional outcomes were assessed according to the Kiefer index (KI). Dynamic gait index and mini-mental state exam (MMSE) were also used. The minimum follow-up time was 2 years. ETV was performed with a rigid endoscope with a 30° lens (Storz), and VPS was performed with a fixed-pressure valve (ProGAV 2.0 Miethke).

Results

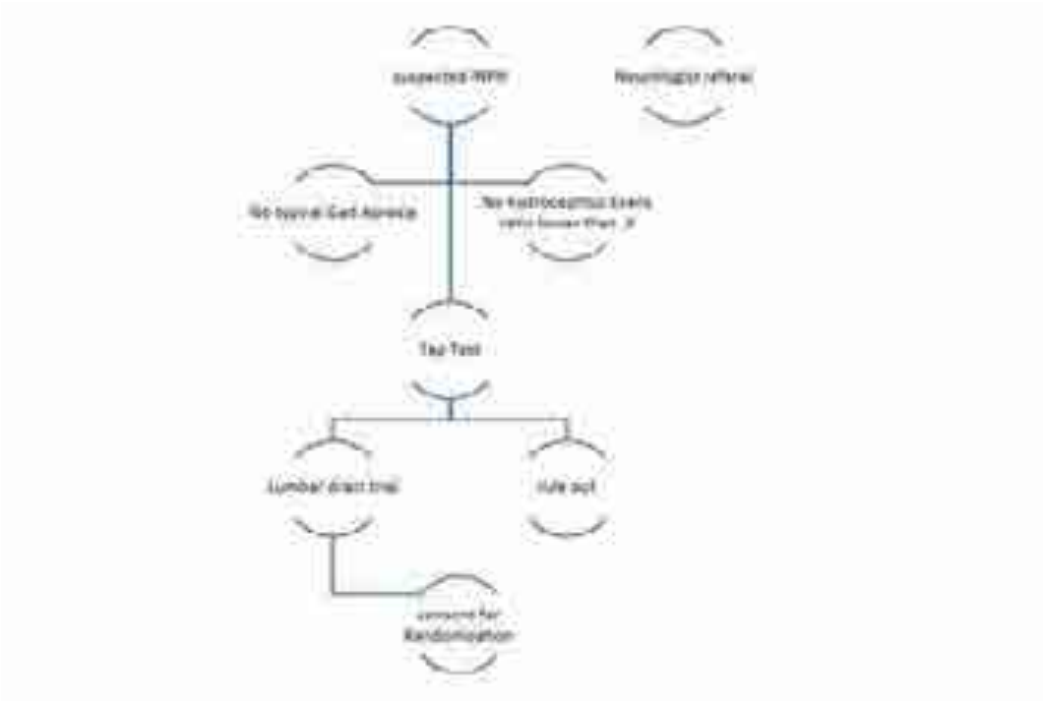
32 Patients were included, and the randomization elicited 17 ETV Group and 14 VPS Shunt. Nine patients from the ETV Group received VP Shunt due to failure of improvement after the procedure.

The outcome in VPS Group showed statistically significant improvement compared to ETV within the first year. Interestingly, VPS showed a secondary worsening or return to baseline after 2 years of the operation. The patinets who received both treatments had the best outcome. This study was stopped in 2022.

Conclusion

VPS was significantly better in treatment than ETV especially in the early phase after treatment. However, some patients treated with VPS showed a secondary worsening in outcome after a long follow-up. This could be part of progressive nature of the disease.

Abb. 1



Adulter Hydrocephalus und SIH/*Adult hydrocephalus and SIH*

V125

Abweichungen bei Druck und Flussmessung von explantierten Shuntventilen im Vergleich mit baugleichen Referenzventilen

In vitro pressure and flow measurement of explanted shunt valves deviate from reference valve

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[2]Universität Stuttgart, Institut für Medizingerätetechnik, Stuttgart, Deutschland

Objective

Shunt valves (SV) for cerebrospinal fluid diversion are precision devices. Failure of SV could lead to devastating outcomes. A meta-analysis found mechanical shunt failure the commonest shunt complication, with reported failure rate between 8 – 64 %.(1,2)

Following a series of SV revisions, exchange led to clinical improvement of patients. We propose a setup for in vitro SV testing in the operating room (OR).

Methods

The setup is built from low budget parts (Fig. 1).

(1) Syringe infusion pump with 50 ml 0.9 % saline solution set to a flow rate of 20 ml/h.

(2) Three-way valve mounted on a metal ruler at zero. Ruler is set vertically and the top is attached to a stand.

(3) A 30 cm extension line is fixed to the ruler and connected with the up facing port of the three-way valve. A 10 cm long catheter connected to the syringe via three-way valve.

(4) SV connected to a distal catheter on same height as three-way valve.

(5) Precision balance to control output flow rate (optional).

Measurements started when steady dripping at the distal end started. Pressure values in cmH2O were noted after 1-, 3- and 5-minutes. Mean pressure and flow rate (ml/h) were calculated.

A new Codman Certas Plus with Siphonguard (CPS) and Miethke ProGAV2.0 SV were tested in equal settings as reference valve (RV). Additionally, 10 explanted valves were tested with the setup; underdrainage was the most common indication (7/10).

Results

Pressure was 2.98 cmH2O higher in the Certas RV compared to ProGAV2.0 RV (Fig. 2).

In the setup "underdrainage" relates to higher pressure of the defective SV compared to RV and/or a lower flow. While infection could lead to underdrainage due to protein concretion.

7/10 valves differed more than ±10 % from baseline pressure of equal RV setting.

Conclusion

(1) Pressure difference of 2.98 cmH2O for equal settings of RV remains unclear and could hint that one RV malfunctioned. 70 % of SV differed more than 10 % from RV pressure. SV malfunctioning is a common problem, but its causes still need to be discovered.

(2) This simple and inexpensive setup could be used as a routine procedure in the OR prior to shunt implantation and may lead to a lower incidence of SV revision.

1. Wong JM, Ziewacz JE, Ho AL, et al. Patterns in neurosurgical adverse events: cerebrospinal fluid shunt surgery. Neurosurg Focus 2012;33(5):E13.
2. Paff M, Alexandru-Abrams D, Muhonen M, Loudon W. Ventriculoperitoneal shunt complications: A review. Interdiscip Neurosurg 2018;13:66–70.

Abb. 1

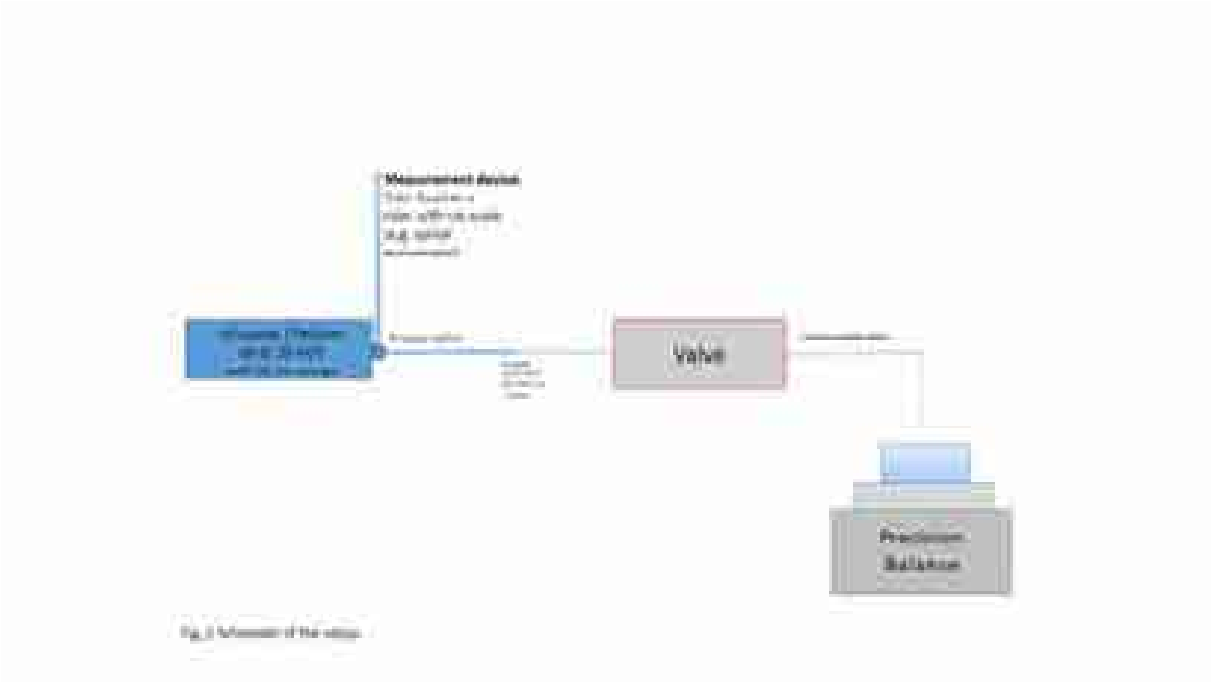

Abb. 2

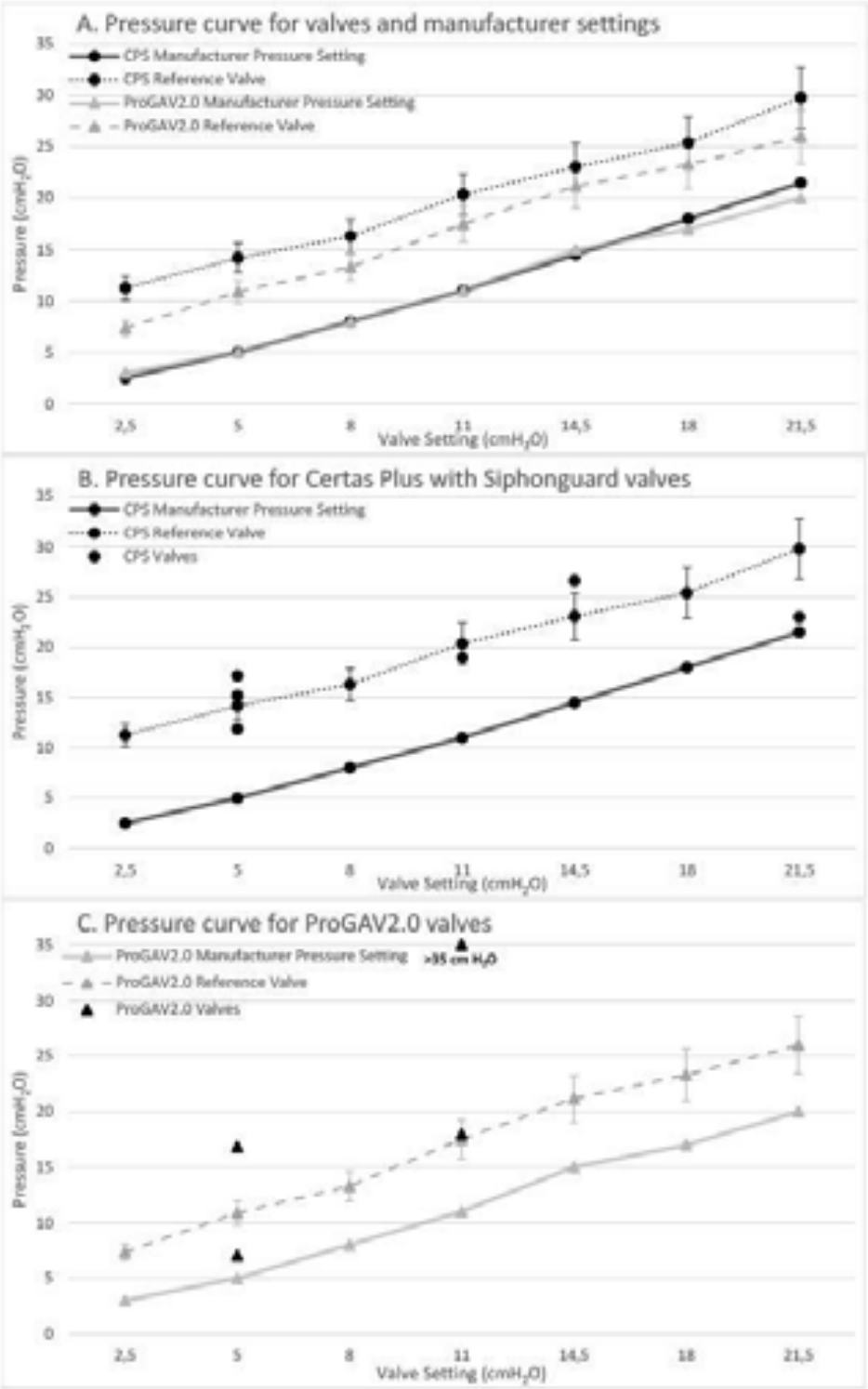

Fig. 2 Pressure curves for tested valves.

Adulter Hydrocephalus und SIH/*Adult hydrocephalus and SIH*

V126

Erfahrungsbericht nach 138 Implantationen eines telemetrischen Shuntsenors bei Shuntversorgten Patienten mit Hydrocephalus.

Lessons learned from 138 telemetric sensor implantations in cases of shunt treated patients with hydrocephalus.

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Objective

Telemetric intracerebral pressure (ICP) measurements have been established over the last years. The m.Scio Sensor (Miethke, Germany) is an inline device for the telemetric evaluation of the intraluminal pressure within the shunt system. We hereby report our clinical experience after 138 implantations.

Methods

A retrospective analysis from 2015 until August 2022 in our Department was performed. All patients, who underwent a m.Scio implantation, were evaluated for indication, medical history, postoperative course and long term follow.

Results

Indications were benign intracranial hypertension (n=34), normal pressure hydrocephalus (n=29), malresorptive hydrocephalus (n=25), occlusive hydrocephalus (n=17) and others (n=33). Children and adolescents were included in 10 cases. The m.Scio was mainly selected in complicated cases, who whether had multiple valve adjustments, distorted communication or were unsatisfied with the shunt treatment. Major complications were wound healing problems 3 of the first 16 patients. After adopting the implantation strategy, no further wound healing related issues occurred. The sensor measurement were helpful in the detection of over- and/or underdrainage problems as well as shunt occlusions.

Conclusion

The m.Scio is a versatile tool for the long term follow up and treatment of complex cases of hydrocephalus. The measurement can be perfomed quick and easy in the outpatient clinic and supports the decision making process.WE were able to establish a routine setup for follow up course of shunt treated patients in our department.

Gliome Adjuvante Therapie und follow-up/*Glioma - adjuvant treatment and follow-up*

V127

Zusammenhang des Erkrankungsalters mit dem molekularen Profil und Überleben bei Patienten mit *IDH*-Wildtyp Glioblastom

Association of age with the molecular profile and outcome in patients with IDH-wildtype glioblastoma

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Objective

The molecular landscape as well as prognosis of many cancer subtypes is associated with patients´ age. However, the impact of patient"s age on molecular and clinical features in *IDH*-wildtype glioblastoma, (GB-*IDH*wt) is not yet fully understood. Here, we aim for a comprehensive molecular characterization of GB-*IDH*wt in young adults (YA) and older adults (OA), to investigate age-related molecular and clinical features in GB-*IDH*wt.

Methods

We report molecular characterization of 94 GB-*IDH*wt tumor samples, using whole-exome sequencing (WES) in 53 and targeted next generation sequencing (NGS) in 41 cases. In addition, Sanger sequencing was performed to address *TERT*-promoter (*TERTp*) mutations. Moreover, clinical data on, progression-free and overall survival (PFS, OS), adjuvant treatment- and tumor features were collected.

Results

Patients" median age was 56.3 yrs. (20.8-80.9 yrs.). YA was defined as patients younger than 45 yrs. (n=22) based on quartiles of the cohort (<Q1: 45.8 yrs.). OA comprised the rest of the cohort (n=72). The median OS was 14.9 mos. with a median PFS of 9.5 mos. The frequency of the most common genomic alterations, i.e. *TERTp* mutations (81.9%), *EGFR* alterations (amplification: 47.9%, mutation: 27.6%), *CDKN2A* deletions (44.7%), *PTEN* mutations (28.7%), *TP53* mutations (26.6%), *ATRX* alterations (mutation: 5.4%, loss: 10.6%) and *PIK3CA* mutations (3.2%) matches previously reported numbers. *ATRX* alterations and *PIK3CA* mutations were individually associated with younger age (p=0.033 and p=0.036, respectively) whereas *TERTp* mutations were marginally correlated with older patients (r=0.23, p=0.028). While patients" age correlated with OS (r=-0.25, p=0.043), YA and OA did not differ significantly in OS (median: 18.7 vs 16.4 mos., p=0.37), even if YA was compared to patients >70 years (median: 18.7 vs. 11.5 mos., p=0.142). Importantly, individual molecular alterations were not significantly associated with clinical outcome. In contrast, radio-chemotherapy was a strong indicator for a longer survival (median OS: 3.5 vs. 17 mos., p<0.0001) and a methylated *MGMT* promoter status was associated with a higher PFS (12.5 vs. 9.5 mos., p=0.019).

Conclusion

A young age at first diagnosis of a GB-*IDH*wt is neither associated with an improved outcome nor with a certain molecular profile. Therefore, cautious should be taken when predicting survival of patients with GB-*IDH*wt based on age or age-related molecular profiles.

Gliome Adjuvante Therapie und follow-up/*Glioma - adjuvant treatment and follow-up*

V128

Lösliche zirkulierende Immun-Checkpoint-Moleküle in bösartigen Hirntumoren
Soluble circulating immune checkpoint molecules in malignant brain tumors

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Objective

Glioblastoma (GBM) has a detrimental prognosis and thus far, no effective therapy with long lasting efficacy has been established. The breakthrough of immune checkpoint therapy has been shown to be effective in other immunogenic cancers, so immune activation and memory formation directed against the tumor, are of great hope especially for long-term control of glioblastoma. Thus, understanding the immunobiology of GBM is essential to enable a more targeted switch to an immunotherapeutic approach. Our goal was to discover alterations in the circulating immunome of GBM compared to other cerebral tumor entities (metastases, meningioma) in order to identify soluble immune markers as potential biomarkers and therapeutic targets.

Methods

We performed flow cytometry of peripheral blood in 208 patients with the following entities: 1) **primary GBM** (n=68), 2) **recurrent GBM** (n=25), 3) **cerebral metastases** (non-small cell lung cancer (NSCLC), n=61; breast cancer, n=19), 4) **meningioma** (n=15) as well as 5) **healthy donors (HD)** (n=20). For this purpose, we used three different immunological bead-based multiplex assays. The study was approved by the local ethics committee (PV4904).

Results

We detected a distinct immune signature of exhaustion in the peripheral blood of patients with GBM. Exhaustion was defined by an increased prevalence of soluble immune checkpoint markers (sCD27, sPD-L2, sGal-9), whereas soluble chemokines (CX3CL, CXCL12) were underrepresented. This distinct immune signature was similar in primary and recurrent GBM and differed markedly from other cerebral tumor entities as well as HD. However, primary GBM, but not their recurrent counterparts, additionally exhibited increased levels of neurotrophic factors (BDNF, b-NGF) and signs of immune activation with significantly increased levels of Interleukin-18.

Furthermore, primary GBM with higher levels of the immune activation marker TNFa showed a significantly longer survival than those with lower levels ($p=0.043$). In non-small cell lung cancer, higher levels of the chemokine Il-6 were associated with significantly poorer survival ($p<0.001$).

Conclusion

Taken together, our results were able to delineate a specific immune profile of soluble markers in GBM compared to other cerebral tumor entities and healthy individuals.

Gliome Adjuvante Therapie und follow-up/*Glioma - adjuvant treatment and follow-up*

V129

Überwachung des Tumorstatus in Glioblastom Patienten über die Porphyrinbiosynthese – ein vielversprechender Ansatz

Monitoring of the tumor status in glioblastoma patients via Porphyrin biosynthesis – a promising approach

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Objective

Fluorescence-guided resection (FGR) maximizes the extent of resection during high-grade glioma (HGG) surgery. Due to administration of 5-aminolevulinic acid (ALA), Protoporphyrin IX (PpIX) accumulates selectively in malignant glioma cells. Human cells naturally produce porphyrins, but their synthesis is boosted when the prodrug ALA is administered. PpIX is a tissue marker during HGG resection. Alterations in porphyrin pattern after ALA administration were described for bladder and prostate cancer. Moreover, PpIX was identified in extracellular vesicles in plasma of HGG patients. This work aimed to explore whether PpIX is elevated in primary and recurrent glioma patients' sera and could thus serve as a marker for the tumor burden.

Methods

Serum PpIX levels were quantified via liquid chromatography coupled to mass spectrometry. Serum was taken from 23 patients with primarily diagnosed glioblastoma and five recurrent HGG. All 28 patients underwent FGR; blood was collected before, during, and after surgery. Likewise, blood was taken from eight healthy volunteers after ALA administration for comparison. Descriptive statistics and receiver operating characteristics (ROC) analysis were run to determine differences between healthy and patients to elucidate the biomarker potential of PpIX.

Results

Time-kinetics of serum PpIX accumulation were different between groups. In primary HGG serum, PpIX peaked significantly ($p < .001$) later than in healthy volunteers (8.9 *vs*. 5.0 h after ALA). More importantly, peak serum PpIX levels were about 3-fold higher in primary ($p = .001$) and recurrent HGG ($p = .011$) patients compared to healthy volunteers, who showed an average maximum serum PpIX of 1,032 ± 385 pmol/ml. During ROC analysis, PpIX levels within the time frame of maximum serum PpIX showed good separation between healthy volunteers and primary HGG (AUC = 0.943, CI95% = 0.884-1.000, PPV = 91 %, NPV = 84 %, Accuracy = 87 %). No evidence was found that surgery had any effect on extent of PpIX synthesis.

Conclusion

Evaluation of PpIX serum levels in 28 patients and eight healthy volunteers after ALA administration showed sufficient discrimination between glioma patients and healthy volunteers with satisfying diagnostic parameters, e.g., PPV, NPV, and accuracy. These results indicate the possibility of developing a blood test using PpIX for HGG diagnosis to support, e.g., the progress controls. Concerning the limited number of individuals, further studies are needed.

Gliome Adjuvante Therapie und follow-up/*Glioma - adjuvant treatment and follow-up*

V130

Regorafenib-eine praktikable Option für die Drittlinienbehandlung des rezidivierenden Glioblastoms?
Regorafenib-A feasible option as third-line therapy of recurrent glioblastoma?

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Objective

Recurrent glioblastoma has a devastating prognosis and limited treatment options. Evidence beyond second line therapy remains scarce. Since the REGMOA trial, Regorafenib has been introduced as a new treatment for recurrent glioblastoma. The aim of this study is to investigate the efficacy and impact of Regorafenib on PFS and OS as a third line therapy in recurrent glioblastoma.

Methods

Data collection was performed as a single-center retrospective analysis. From January 1st, 2016, to December 31th, 2022 patients with recurrent IDH wild-type glioblastoma (CNS WHO grade 4) had received alkylating chemotherapy as first-line therapy, were reviewed. Inclusion criteria were histological diagnosis, gross total resection in the primary and recurrent situation, prior first-line therapy according to STUPP protocol or CeTeG and ECOG performance status score ≤2. OS after first- and second-line therapy was assessed. Therapeutic effect was evaluated according to RANO criteria. NCI-CTCAE 5.0 was used to evaluate adverse events.

Results

A total of 96 patients (42.7% females) with a median age of 56 y (range 30-86 y) were enrolled in the study. MGMT promotor methylation was found in 43 (44.8%) patients. 19 patients (42.1% female) received Regorafenib 160 mg once daily for the first 3 weeks of each 4-week cycle as 3rd line therapy during the course of treatment. The mOS for all patients was 420 d (95% CI 363.0-506.0). Those who received Regorafenib as salvage therapy had a significantly longer OS (895 d, 95% CI 471.0-813.0) (p=0.021). Patients who received second-line therapy with CCNU as salvage therapy, had significantly shorter median OS (376 d, 95% CI 330.0-441.0) than those who were switched to regorafenib after second progression. Mean time from disease progression to start of regorafenib was 48.4±23.3 d. Delays were attributed to late tumor board recommendations and lengthy application processes due to off-label use in this indication. Adverse effects of any CTCAE grade were noted in 10 patients (52.6%), with 5 patients (26.3%) presenting with CTCAE °III-IV reactions. No death was considered to be drug-related.

Conclusion

MOS was significantly longer in patients who received Regorafenib as 3rd line chemotherapy after disease progression. The time from progression to initiation of therapy is prolonged by off-label use application barring patients in need from necessary treatment. However, adverse events are common suggesting a good ECOG status as prerequisite prior to the start of therapy.

Gliome Adjuvante Therapie und follow-up/*Glioma - adjuvant treatment and follow-up*

V131

Die Alcatraz-Strategie: ein neuer multimodaler Therapieansatz in der Therapie des Glioblastoms
The Alcatraz-Strategy: a novel multimodal therapeutic approach for glioblastoma

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Objective

Several discoveries both on the morphological and functional cellular level have fundamentally changed our understanding of glioblastoma biology over the last years. Most notably, tumor microtubes (TMs) as ultralong membrane protrusions enable glioblastoma cells to assemble to a syncytial microinvasive communicating network. TM-supported neurogliomal synapses (NGS) have been shown to integrate glioblastoma cells into neural circuits which foster malignant growth and cellular invasiveness. The authors speculate to what extent these novel insights into the malignant network might impact future standard of care and attempt to conceive a multimodal treatment regime based on current translational efforts and ongoing clinical trials.

Methods

A therapeutic outlook was conceptualized with regard to the following basic principals deduced from abovementioned discoveries: 1) Morphological isolation on the single cell level via inhibition of TM-based spatial network architectures. 2) Functional isolation on the single cell level via inhibition of TM-mediated intercellular cytosolic exchange and inhibition of NGS activation. 3) Greatest possible removal of the microinvading tumor cell front far beyond MRI-detectable abnormalities.

Results

Three multicenter clinical trials in the light of abovementioned principles are being designed, are recruiting or are at the stage of initiation: The "MecMeth"-phase I/II trial evaluates meclofenamate (MFA) as a potential TM-targeted drug. MFA has recently been shown to exert a morphological and functional breakdown within TM-based glioblastoma networks by an inhibition of TM outgrowth and TM-mediated intercellular cytosolic traffic. The PERSURGE-trial will analyze the effects of perampanel as a NGS-inhibitory drug regarding functional connectivity and radiological tumor growth kinetics. The ATLAS-trial is designed as the first prospective trial to evaluate supramarginal resection for a potential survival benefit compared to a gross-total resection regime in temporal glioblastoma.

Conclusion

Reminiscent of the Alcatraz Federal Penitentiary, where inmates had to face 1) a spatial isolation in single cells, 2) a functional isolation by the ban of interpersonal communication and 3) a safety-margin to the mainland by the sea as an insuperable barrier, the authors propose the Alcatraz-Strategy as a multimodal therapeutic approach – aimed at fighting glioblastoma"s long-distance connectivity and microinvasive capacity.

Gliome Adjuvante Therapie und follow-up/*Glioma - adjuvant treatment and follow-up*

V132

FGFR3-TACC3-Fusionen beim Glioblastom sind mit einem geringeren Alter bei Diagnose und längerem Gesamtüberleben assoziiert

FGFR3-TACC3-fusion in glioblastoma is associated with younger age and longer overall survival

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Objective

Oncogenic fusion genes like the BCR-ABL fusion in lung cancer or the Philadelphia chromosome in leukemia are successfully used for targeted therapy. In glioblastoma, fusion of the fibroblast growth receptor 3 and the transforming acidic coiled coil containing protein, FGFR3-TACC3-fusion (F3T3-fusion), is the most frequent oncogenic fusion and reported to be prevalent in 3-4% of glioblastoma (GBM). The F3T3-fusion leads to constitutively activated kinase signaling of FGFR3 and could serve as a predictive marker for the benefit of FGFR3-kinase inhibitor therapy. Little on the expression of F3T3- fusions in GBM is known. The aim of this analysis is to provide data on the epidemiology and molecular characteristics of GBM patients with F3T3- fusion in our own collective.

Methods

We collected data of 107 patients who were operated between January 2019 and December 2021 in our department for neurosurgery and received the integrated diagnosis of GBM WHO ZNS grade 4. In all cases methylation epic arrays and full molecular analysis was available. Clinical data was collected from patient records. F3T3 positive patients were compared with F3T3 negative patients by t-test. Overall survival (OS) and progression free survival (PFS) were calculated by Kaplan-Meier-analysis.

Results

F3T3-fusion was present in 10.3% of GBM patients. Mean age at diagnosis for F3T3-fusion positive patients was significantly lower (52.8 ±11.8 vs. 63.2 ±11.6) years compared to 63.17 (±11.59) years in negative patients (p=0.018). A non significant trend towards a shorter PFS in F3T3-fusion positive patients (397 ±117 days) compared to negative patients (236 ±137 days) was observed (p=0.14). OS was significantly longer in F3T3 positive patients (412 ±172 days) compared to negative patients (251 ±176 days; p=0.011). All F3T3 positive GBM had a gain on chromosome 7 and loss at chromosome 10 and 80% of F3T3 positive GBM were classified as RTKI or RTKII phenotype. F3T3 fusion was exclusive with amplifications in MET, MYCN and MDM2 as well as with deletions of RB, NF1 and NF2.

Conclusion

F3T3-fusion is present in a small number of GBM patients and is associated with a significantly better OS. Presence of the oncogenic fusion is further associated with RTKI or RTKII methylation class. As the F3T3-fusion could serve as a therapeutic target, the molecular characteristics of F3T3 fusion positive tumors and the functional relevance of the fusion gene should be further investigated.

V133

Die deutsche Version des Neurofibromatosis 2 Impact on Quality of Life Questionnaire (NFTI-QOL-D) korreliert mit Depression und Krankheitsschwere

The German Version of the Neurofibromatosis 2 Impact on Quality of Life Questionnaire Correlates with Severity of Depression and Physician-Reported Disease Severity

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Objective

Neurofibromatosis type 2 (NF2) is a rare genetic disease that causes a wide range of disabilities leading to compromised quality of life (QOL). There is clear need for a validated disease-specific tool to assess quality of life among German-speaking patients with neurofibromatosis type 2 (NF2). The NFTI-QOL questionnaire has produced useful results in English-speaking cohorts. The aim of this study was to produce and validate a German version of the NFTI-QOL (NFTI-QOL-D) and to correlate QOL scores with a depression score (PHQ-9) and clinical disease severity.

Methods

The original English-language NFTI-QOL was translated into German and then back-translated in order to preserve the questionnaire"s original concepts and intentions. A link to an online survey encompassing the NFTI-QOL-D and the PHQ-9 depression questionnaire was then sent to 97 patients with NF2 by email. The respondents" scores were compared to clinician-reported disease severity scores.

Results

77 patients completed the online survey in full. Internal reliability among NFTI-QOL-D responses was strong (Cronbach"s alpha: 0.74). Both PHQ-9 and clinician disease severity scores correlated with NFTI-QOL-D scores (Pearson"s rho 0.63 and 0.62, respectively).

Conclusion

The NFTI-QOL-D is a reliable and useful tool to assess patient-reported QOL in German-speaking patients with NF2. The correlation of QOL with both psychological and physical disease parameters underlines the importance of individualized interdisciplinary patient care for NF2 patients, with attention paid to mental well-being as well as to somatic disease manifestations.

V134

Stellen minderjährige Kinder eine Ressource für PatientInnen mit malignen Hirntumoren dar?
Underaged children– a resource for patients suffering from malignant brain tumours

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Objective

Brain tumours are often associated with significant burden for patients and their relatives. Patients with malignant brain tumours and underaged children might be particularly affected. However, the proportion of patients with underaged relatives who are affected by neuro-oncological diseases to date is unknown. The aim of the present work was to determine the proportion of neuro-oncologic patients with underaged children and assess the burden for patients.

Methods

Within a 22-month period, all outpatient brain tumour patients were asked to fill in a short questionnaire including epidemiological data, the EORTC-qlq-C30 and -BN20 questionnaire, the distress-thermometer, and a modified variant of a palliative-care screening tool (MIDOS). For analysis, WHO° 2-4 Gliomas, WHO° 2-3 meningioma, other WHO° 3 and 4 tumours, cerebral metastases and lymphoma were considered as potentially life-threatening. Data were collected and analysed using the Prism 9 for macOS (Version 9, GraphPad Prism). Continuous data are presented as means ± standard error of mean.

Results

Our analysis includes 881 brain tumour patients. 540 patients were female and the median age was 61 years (16 – 88 years). Thereof, 252 patients suffered from glioma, 339 from meningioma, 196 patients from pituitary gland tumours, 64 from cerebral metastases and 30 from other tumours.

665 patients (75.5 %) had 1269 children in total. 150 brain tumour patients (17%) had 196 children under the age of 18 at presentation to our outpatient clinic.

For malignant brain tumour patients, mean distress as assessed by the distress thermometer was 4.6 ± 0.08. Patients with underaged children had significant lower distress values ($p = .006$), a higher quality of life during the week before ($p < .0001$), better family life ($p = .02$), but more financial worries ($p < .0001$) compared to malignant brain tumour patients without underaged children.

Conclusion

About 17.5% of patients with potentially malignant brain tumours have underaged children in our cohort. However, underaged children might be a positive resource more than a burden as patients with malignant brain tumours and children under 18 years of age show lower distress values and a better a quality of life.

Versorgungsforschung & QoL I/*Health Care Research & QoL*

V135

Depressionen bei Patienten mit Glioblastom beeinträchtigen Lebensqualität und Neurokognition
Depression in glioblastoma patients affecting quality of life and neurocognition

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Objective

The diagnosis of a malignant glioma impacts the patient's mood and health related quality of life (HRQoL) due to the disease-related psychological burden or to the tumor itself. Moreover, depressive symptoms can negatively influence the neurocognitive performance, altogether affecting adjuvant therapy and survival outcome. The aims of this study were to describe the prevalence and time course of depression in glioblastoma patients, and to examine its interactions with HRQoL and neurocognitive performance.

Methods

226 patients with previously untreated, supratentorial glioblastoma as well as 61 age- and sex-matched controls were tested with a battery of eleven standard neurocognitive tests complemented by standard questionnaires to assess depression (Becks Depression Index) and HRQoL (SF-12). Depression was defined as a BDI score >13. Patients were examined prior to neurooncological treatment (surgery), as well as after three and six months follow-up time. A cluster analysis was performed to group tests together based on their similarity and normalized mean cluster scores were calculated. Cluster scores were compared between patients with versus without depression using Wilcoxon tests. Spearman correlations were calculated to examine relationships between neurocognitive performance, depression and different aspects of quality of life. FDR correction was applied for multiple comparisons.

Results

Preoperatively, 14.3% suffered from depression and showed significantly higher BDI scores than controls ($p=0.046$). Depression rates increased strongly in the follow-up period and were significantly higher than in the control group (3 months: 34%, $p=0.002$; 6 months: 35%; $p<0.001$). All HRQoL-subdomains correlated significantly with depression. Patients with depression tended to need more time to complete the recall trials testing visual and verbal memory ($p=0.069$). Moreover, HRQoL subdomains correlated with distinct neurocognitive domains including processing time, visuospatial abilities and language functions.

Conclusion

The elevated prevalence of depression in glioblastoma patients showing a sharp and plateau-shaped rise in the follow-up period highlights the demand for timely diagnosis and psycho-oncological interventions. The interactions between depression and neurocognitive functioning affecting daily living activities and HRQoL should be considered for the interpretation of the functional status and for the recommendations of supportive interventions.

V136

Cognitive Reserve Index bei neuro-onkologischen Patienten
Cognitive Reserve Index in neuro-oncological patients

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Objective

Neuro-oncological diseases are often associated with brain damage and subsequently neurological impairments. Cognitive reserve is a measure of the resilience to neuropathological damage and its compensation mechanisms. Patients with a higher education level, working with high cognitive input or engaged in cognitively stimulating activities during "leisure time" have better compensation for brain damage. The Cognitive Reserve Index Questionnaire (CRIq) is a validated tool to assess the level of cognitive reserve but has not been introduced in neuro-oncology yet.

The aim of our present work was to introduce the Cognitive Reserve Index Questionnaire (CRIq) in neuro-oncology.

Methods

In this pilot series, all patients treated in our neuro-oncologic outpatient clinic were routinely asked to answer the CRIq during a 3-month period (10/2022 – 12/2022). The questionnaires were analysed according to the "Instructions for the administration of the CRIq" and correlated with epidemiological data. Data were collected and analysed using the Prism 9 macOS (Version 9, GraphPad Prism). Continuous data are presented as means ± standard error of mean.

Results

The present analysis includes a cohort of 103 neuro-oncologic patients. 65 patients were female, 38 male. The mean age was 54.9 yrs. 31.1% of patients were married and 65.1% had children.

The mean length of schooling was 10.4 ± 0.4 yrs and the mean working years were 19.7 ± 1.3 yrs. Neuro-oncological patients participated in 3.5 ± 0.1 leisure time activities with weekly frequency (of maximum 5 possible activities), 1.6 ± 0.1 activities with monthly frequency (possible maximum 6), 1.1 ± 0.1 with annual frequency (possible maximum 3) and 2.4 ± 0.1 (possible maximum 3).

49/103 questionnaires were filled out correctly so that CR could be calculated. 86.7% patients suffered from an intracranial tumor and 49% had a malignant disease. 6.1% of patients had a low, 2.1% a medium-low, 6.1% a medium, 8.2% a medium-high and 83.7% a high CRI.

Conclusion

The CRI could be a promising tool in determining cognitive reserve in neuro-oncological patients. In our setting ca. 90% had a medium-high to high CRI. However, this probably is not a true reflection of the CRI of our entire patient collective, since only 47.6% of the questionnaires were filled in correctly and hence more than half need help answering its questions.

V137

Soziales, Familienleben und Partizipation neuro-onkologischer PatientInnen
Social contacts, family life and participation of neuro-oncological patients

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Objective

In addition to extending lifespan, maintaining and improving quality of life is an important goal of any neuro-oncological treatment. In addition to extending lifespan, maintaining and improving quality of life is an important goal of any neuro-oncological treatment. In addition to physical and psychological complaints, quality of life is also determined by the question of participation, friendships, family life and sexuality. There are hardly any systematic surveys on this for neuro-oncological patients.

The aim of the present work is therefore a survey of how social interaction is impaired by neuro-oncological diseases.

Methods

All patients with cerebral tumours treated in our neuro-oncologic outpatients office between 02/2021 and 11/2022 were included in the present analysis. Neuro-oncological patients were routinely asked to answer a battery of different questionnaires including epidemiological data, the EORTC-qlq-C30 and -BN20 questionnaire, the distress-thermometer, and a modified variant of a palliative-care screening tool (MIDOS). The Likert scale of the EORTC and MIDOS were dichotomized into a "favourable" (no or minor burden) or "unfavourable" (major or severe burden) quality of life. Data were collected and analysed using the Prism 9 for macOS (Version 9, GraphPad Prism). Data are presented as means ± standard error of mean.

Results

The present analysis includes data from 3106 consultations and 881 patients encompassing the entire range of benign and malign neuro-oncological diseases. 540 patients were female and the median age was 61 years (16 – 88 years). 138 patients (15.7 %) stated that they lived alone, 665 patients (75,5 %) had totally 1269 children.

Median distress was 4.5 ± 0.06. Neuro-oncological disease significantly affected everyday family life in 28%, activities with relatives or friends in 27% and in 46% the overall quality of life within the last week. About 27% of patients worried about the future or their family life. Patients reported to have sexual problems in 15% and neuro-oncologic disease led to a significant burden on the relatives in 38% and to care problems in 15%.

Conclusion

Impairment of social contacts, family life and participation are a significant problem in nearly 30 % of neuro-oncological patients. Moreover, neuro-oncologic disease led to a significant burden on the relatives in 38% and to care problems in 15%.

V138

Geriatrische Screening älterer neuro-onkologischer PatientInnen
Geriatric screening of elderly neuro-oncologic patients

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Objective

Assuming that elderly patients suffer more from side effects of standard therapies, less aggressive treatment protocols have been established, e.g. the NOA-8 study. This practice has been questioned by several retrospective studies using standard protocol. However, routine geriatric assessment has not yet been established. Aim of the present pilot series was to establish a routine geriatric screening in our neuro-oncologic outpatient office.

Methods

Elderly neuro-oncologic patients (aged ≥ 65 years) were routinely asked to answer the ISAR questionnaire during a 22-month period (02/2021 – 11/2022) during their neuro-oncological outpatient appointment. The tool uses 6+1 questions, dichotomising patients into two groups with low (0 - 1) and high ISAR values (2 - 6). According to the recommendations of the German Society for Geriatrics, a special geriatric treatment should be implemented if patients have two or more complaints (ISAR ≥ 2). The patient´s daily performance was assessed using the Karnofsky performance scale (KPS), Neurological Assessment in Neuro-oncology (NANO) and the Distress thermometer. Data were collected and analysed using the Prism 9 programme (GraphPad Prism).

Results

429 elderly neuro-oncologic patients were included in this analysis. 146 patients suffered from malign and / or life-threatening neoplasms, 283 from benign lesions. 248 patients were female. Median age was 72 years (65 – 89 years). 388 / 429 elderly patients (90.4%) were able or willing to participate in geriatric screening and answered 5.95 of the 6 + 1 questions, completing 870 questionnaires in total (patients were seen multiple times).

Patients suffered from a high geriatric burden (ISAR values 2-6) in 356 consultations (40.9%) and should therefore be considered for a geriatric referral. The most frequent symptoms were the need of hospital admission within the last 6 months (41.8%) and polymedication (>5 different medications per day, 40.7%). High ISAR values correlated highly significant with high distress, a worse quality of life, an impairment of family life and reduced participation (each $p < .0001$) as well as financial problems ($p = 0.009$).

Conclusion

Elderly neuro-oncologic patients suffered from high geriatric burden in 40% of consultations and should be considered for a specialist geriatric referral. High geriatric burden correlates with high distress, a worse quality of life, an impairment of family life and reduced participation.

Vestibularisschwannome II Genetik, Biologie und Histologie/*Vestibular schwannomas II genetics, biology and histology*

V139

Einfluss immunmodulatorischer Zytokine auf die Progression des Vestibularisschwannoms
Impact of immunomodulatory cytokines on the progression of vestibular schwannoma

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Objective

Vestibular schwannoma (VS) is a benign tumor arising from the eighth cranial nerve. Approximately 50% of sporadic VS do not increase in size, but some tumors do exhibit rapid progression. There is currently no pharmacological treatment available to inhibit the growth of these tumors, and the therapeutic options are limited to surgical resection and radiation therapy. Previous studies showed an influence of tumor-associated macrophages (TAM) infiltration on tumor progression. Macrophages could be attracted by various cytokines and differentiated to the TAM subtype. Therefore, the aim of this study was to elucidate the mechanisms of macrophage attraction and differentiation in the VS.

Methods

172 VS samples from patients who had at least one preoperative MRI have been examined. Irradiated patients and patients with recurrence or hereditary neurofibromatosis were excluded from the study. Tumor size and tumor growth rate were volumetrically determined using the preoperative MRI images. To examine the expression of nine immunomodulatory cytokines, RNA was isolated from tumor samples and transcribed in cDNA. Currently 66 VS samples were quantified using qPCR. The correlation between tumor volume and tumor growth rate with macrophage markers and cytokine expression was analyzed with the Spearman's rank test.

Results

Correlation analysis revealed positive correlation of cytokine expression among each other. CCL2 expression ($r=-0.27$, $p=0.04$) showed a weak positive correlation with tumor volume. CCL5 ($r=0.46$, $p<0.001$), TGF-β ($r=0.28$, $p=0.04$) and IRF4 ($r=0.44$, $p<0.001$) expression displayed a moderate positive correlation with tumor volume. VS growth rate showed a moderate negative correlation with CCL2 ($r=-0.45$, $p=0.03$) and a moderate positive correlation with IRF4 ($r=0.48$, $p=0.02$) expression. Furthermore, tumor size revealed a very strong positive correlated with growth rate ($r=0.85$, $p<0.001$).

Conclusion

Our previous results demonstrated a positive correlation between tumor size and macrophage amount. Based on the preliminary results of the present study, it is possible that macrophages are attracted by CCL5 and TGF-β. The increased expression of CCL5, IRF4, and TGF-β may cause these macrophages to polarize towards the TAM subtype. This could potentially contribute to tumor volume increase. In addition, IRF4 may have a direct effect on the growth rate of VS. These new findings confirm the impact of TAM infiltration in VS progression and could lead to a new diagnostic and therapeutic approach.

Vestibularisschwannome II Genetik, Biologie und Histologie/*Vestibular schwannomas II genetics, biology and histology*

J-SPNC005

Role of immune cell infiltration and inflammation in the growth of cystic vestibular schwannoma and cystic degeneration: a single cohort.

Role of immune cell infiltration and inflammation in the growth of cystic vestibular schwannoma and cystic degeneration: a single cohort.

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Objective

While most vestibular schwannoma (VS) are sporadic, solid and slow-growing, the cystic counterpart exhibit an unreliable clinical and pathological behavior, hampering treatment strategies. Cystic tumors" management is challenging since observation and/or radiation therapy might not be suitable, while harmless complete microsurgical resection may be difficult to achieve. Pathophysiological mechanisms of VS tumorigenesis, cystic degeneration and growth are not precisely defined, but it has become clear that inflammation might play a pivotal role and also be therapeutically useful. The objective of present work, is to evaluate immune cell infiltration in cystic tumors, and correlate it with tumor cell proliferation, COX2 expression, volumetric tumor size and growth.

Methods

We conducted a retrospective review of 1143 consecutive primary sporadic VS surgically treated at a single center from 2003 to 2017. After withdrawal of cases meeting exclusion criteria, 756 patients were elegible for study. From this sample, a cohort of 90 (12%) cystic VS were selected for analysis. Patient demographics, preoperative radiological images, volumetric analysis and tumor growth rate were scrutinized and correlated with immunohistochemical evaluation for tumor cell proliferation (MIB1), expression of the enzyme cyclooxygenase 2 (COX2), lymphocyte (CD3, CD8) and macrophage (CD68, CD163) infiltration.

Results

Mean tumor volume was 9.1 cm3, ranging from 0.31 to 51.10 cm3. MIB1 ranged from 0% to 3.7%, with a mean of 1.20%. Correlation between preoperative volumetric tumor size and immunohistochemistry did not find any significant result for the ANOVA. We observed a trend for larger preoperative tumor size with increased expression rates of CD163. Volumetric tumor growth was accessed for 23 cases (23/90 = 25.6%). Mean volumetric tumor growth was 4.32 cm3/year, ranging from 0.07 to 29.24 cm3/year. Percentual volumetric tumor growth was calculated as a more representative marker for growth dynamic independent of the initial preoperative tumor volume. Mean percentual volumetric tumor growth was 0.93% ranging from 0.03 to 3.17%. We observed volumetric tumor growth (cm3/year) with significant ANOVA for CD3 and CD68, however there was no significant difference in percentual volumetric tumor growth. In 3 (3.3%) patients, solid tumors degenerated into cystic.

Conclusion

We conclude that inflammatory cell infiltration and COX2 enzyme expression are not associated with cystic VS volumes or growth.

Vestibularisschwannome II Genetik, Biologie und Histologie/*Vestibular schwannomas II genetics, biology and histology*

V140

Das Tumormikroenvironment bei Vestibularisschwannomen mit und ohne Neurofibromatose Typ 2
Tumormicroenvironment in Vestibular schwannoma with and without NF2

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Objective

Vestibular schwannoma (VS) are benign tumors growing bilaterally in most cases of neurofibromatosis type 2 (NF2). In these cases, a systemic approach is urgently needed due to different tumors in other locations and the high recurrence rate, invasiveness and functional deficits in patients. However, until these days long lasting medical treatments are missing. The tumor microenvironment is an important aspect for tumor growth, response and recurrence in immunotherapeutic approaches. Therefore, we investigated the tumor microenvironment in patients with VS with and without NF2 in order to develop a new therapeutic approach for these tumors.

Methods

Tissue samples of 40 patients with VS with and without NF2 were analysed for expression of CD4, CD8, CD7, CD14, CD68, CD163, CCR2, CD25 and iNOS by immunohistochemistry and in comparison with two health vestibular nerves as control group. Fast and slow growing VS were distinguished by MRI imaging and evaluated separately. Five representative areas of each slide were manually evaluated to compare antigen expression between different tissues for each antigen.

Results

The M2 macrophages marker CD 163 showed a significant higher expression (p= 0.04) in NF2 VS (14%) than in sporadic VS (6.2%). CD68 as general macrophages marker showed a similar expression level in both groups, significantly higher than in control group. CD4, CD7 and CD8, marker for T- lymphocytes, showed a low expression level in both groups with no significant difference. CD14 a marker for monocytes showed a high expression level in NF2 VS and sporadic VS in comparison to the control group (13.5-10.2% vs. 5.0%), but the difference was not significant. CCR2, a chemokine receptor for monocyte chemotaxis showed a significant (p=0.03) higher expression in sporadic rapid growing VS (2.5%) than in the control group (0.2%). CD 25 was although significantly overexpressed in sporadic VS (5.9% vs. 0.3%). iNOS showed no increased expression levels.

Conclusion

T cells are a very small part of the tumor microenvironment in VS. Macrophages especially the M2 subtype, monocytes and their chemotaxis are a relevant part of the tumor microenvironment in vestibular schwannoma with interesting differences between sporadic and NF2 VS. These results make an immunotherapeutic approach possible.

Vestibularisschwannome II Genetik, Biologie und Histologie/*Vestibular schwannomas II genetics, biology and histology*

V141

Das natürliche Wachstumsverhalten von NF2-assoziierten Vestibularisschwannomen während der Kindheit, dem Jugend- und jungen Erwachsenenalter.

Natural growth behavior of NF2-associated vestibular schwannomas during childhood, adolescence, and young adulthood.

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Objective

To evaluate the natural tumor volume and growth rate of vestibular schwannomas without any treatment (e. g. surgery, bevacizumab) or during the treatment-free interval in young patients with NF2.

Methods

We retrospectively reviewed 36 patients (72 tumors) with NF2 younger than 25 years at the time of diagnosis. Tumor volumetric measurements were performed using thin-slice (< 3 mm) T1-weighted contrast-enhanced magnetic resonance imaging (MRI) using the BrainLab software. The growth rate was calculated by volume changes over time and significance was tested with two independent sample t-tests and paired sample t-tests (SPSS Version 24).

Results

813 volumetric measurements were performed in 53 selected tumors during the treatment-free period. The mean age at the time of diagnosis was 11 ± 6 (range 1–22) years and the mean follow-up time was 37.64 (range 12–167) months. The period between 2 and 25 years of age was observed. A saltatory growth dynamic was seen throughout this lifetime with several peaks, declines, and periods of stable growth. The mean natural growth rate was 0,69 ± 1,30 cm3/year (yr) and the mean natural tumor volume was 3,34 ± 4,97 cm3/year. There was no significant difference in natural growth rate between the genders (female mean growth rate 0.91 +/- 1.71 cm3/yr, male growth rate 0.46 +/-0.73 cm3/yr, $p > 0.05$).

Conclusion

Regarding natural growth rate and non-influenceable factors such as sex or tumor side, our results correspond to previously described findings. During their lifetime, NF2-associated VS in children and young adults exhibit a different growth dynamic probably influenced by hormones, puberty, peripuberty, or growth factors. Further investigations (clinical, neuroendocrine, and receptor dependency) and long-term natural history studies are needed for further evaluation.

Vestibularisschwannome II Genetik, Biologie und Histologie/*Vestibular schwannomas II genetics, biology and histology*

V142

Metastasis associated in colorectal cancer 1 (MACC1) mRNA Expression in Vestibularisschwannomen
Metastasis associated in colorectal cancer 1 (MACC1) mRNA expression in vestibular schwannoma

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Objective

Vestibular schwannoma (VS) are benign cranial nerve sheath in the cerebellopontine angle, which could lead to hearing loss. In about 4% are caused by neurofibromatosis type 2 (NF2) as a genetic disorder, in the other cases VS are sporadic. Metastasis associated in colon cancer 1 (MACC1) is known to contribute to angiogenesis, cell growth, invasiveness, cell motility and metastasis of solid malignant cancers, and non-syndromic hearing impairment. Therefore, we evaluated, whether MACC1 may be involved in the pathogenesis of VS.

Methods

MACC1 mRNA and protein expression were analysed by quantitative polymerase chain reaction and immunohistochemistry in sporadic VS (n = 49), recurrent sporadic VS (n = 8), NF2-associated VS (n = 5), recurrent NF2-associated VS (n = 6), and healthy vestibular nerves (n = 4), respectively. MACC1 mRNA expression level were correlated with the patients" clinical course and symptoms.

Results

There was no significant overexpression on the protein level evaluated by immunohistochemistry. Although there was a significant MACC1 mRNA overexpression in sporadic VS in comparison to healthy nerves or NF2 associated VS. Recurrent tumors showed similar MACC1 mRNA expression levels than primary tumors. MACC1 mRNA expression was significantly correlated with deafness in sporadic VS patients.

Conclusion

Our results demonstrate for the first time, that MACC1 could be a new molecular marker involved in VS pathogenesis.

Vestibularisschwannome II Genetik, Biologie und Histologie/*Vestibular schwannomas II genetics, biology and histology*

V143

Unterschiede in der Methylierung von Vestibularisschwannomen und den zugehörigen Nerven
Differences in the methylome between vestibular schwannoma and the respective nerve

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Objective

The analysis of the methylome plays a major role in the molecular pathological diagnosis of brain tumors. In some cases, this analysis is crucial for therapy. In benign vestibular schwannoma (VS), which arises from Schwann cells surrounding the eighth cranial nerve, less information has been known about the tumor methylome so far. Since there is no pharmacological treatment for VS now, an analysis of tumor biology at the methylation level is of particular interest. In order to make more precise predictions about the origin of the VS and about possible pharmacological targets, the aim of our study is to compare the methylation profile of the VS with the corresponding nerve.

Methods

For CpG site methylation analysis, DNA from four VS and their respective associated nerves was isolated from samples obtained during surgical removal. The methylome was determined using classic bisulfite conversion followed by Infinium MethylationEPIC BeadChip array. Detailed analysis was performed using the GenomeStudio Software.

Results

Evaluation revealed an overlap of 15 hypermethylated genes, which are more than 3-fold higher CpG-methylated in the tumor tissue compared to the corresponding nerve. Interestingly, the most of these are known as tumor suppressor genes from other tumor entities. DAXX and ZIC1 were identified as tumor suppressor genes in breast cancer. In addition, USP13 and TCF7L2 are tumor suppressor genes that have been detected in bladder cancer and colon cancer. Likewise, the MHC class 1 related-protein A, which leads to poorer survival in most tumors when expressed at higher levels, and better survival only in colon carcinoma. The hypermethylated gene COL11A2 , encoding collagen type XI alpha 2, is involved in fibrillogenesis and enzyme modification. COL11A2 loss of function can lead to hearing loss in affected patients.

Conclusion

The detection of hypermethylated genes in the VS compared to the corresponding nerve suggests that these genes are downregulated in the VS. This sheds lights on the genesis of the VS. In particular, the detection of different tumor suppressor genes, which have already been detected in other tumors, could represent new putative pharmacological targets to prevent the progression of VS.

Hypophysenadenom I/*Pituitary adenoma I*

V144

Prädiktiver Wert des frühen postoperativen Wachstumshormon-Serum-Wertes nach transsphenoidaler Operation bei Akromegalie: Entwicklung einer SOP.

Predictive value of early postoperative serum growth hormone levels after transsphenoidal surgery for acromegaly: suggestion of a standard operating procedure.

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Objective

Objective Transsphenoidal surgery (TSS) is the first line therapy in the management of acromegaly. Generally accepted parameters for remission of hypersecretion are dependent on serum growth hormone (GH) and insuline like growth factor 1 (IGF-1) 12 weeks after surgery. However, reoperation in cases without remission after that time is more difficult than early secondary surgery due to scar formation. Therefore, in cases with resectable tumor remnants early secondary surgery during the same hospital stay seems to be meaningful. The aim of this study is to identify thresholds of serum GH in the early postoperative course as an indicator for early secondary surgery.

Methods

Methods Between 04/2008 and 07/2019 86 adults (41 female, 47 male, mean age 49.65) with acromegaly underwent 88 TSS for resectable pituitary adenomas (PA). Using logistic regression, the correlation of two early postoperative GH levels (GH_1 on the first day and $GH_{3/4}$ at the 3rd or 4th day) to remission during the first year after surgery was retrospectively analyzed. Thresholds for failed remission were identified using ROC-analyses and Youden-Indices. These thresholds were than used for development of a standard operating procedure (SOP) for clinical application (Figure 1), and predictive values were estimated.

Results

Results Remission was achieved in 71.6 % of cases during the first year after surgery. As expected, there was a significant ($p < 0.05$) influence of GH_1, $GH_{3/4}$ and radicality of resection for the outcome. Thresholds determined for failed remission were $GH_1 \geq 1.42$ ng/mL and $GH_{3/4} \geq 0.58$ ng/mL. Implementation to a SOP leads to determination of $GH_{3/4}$ in cases with GH_1 over the threshold and interdisciplinary discussion of early reoperation, when $GH_{3/4}$ also is over the threshold. The positive predictive value of this SOP amounts to 78.3 %, the negative predictive value is 89.2 %.

Conclusion

Conclusion For resectable PAs, our SOP with postoperative evaluation of GH_1 and $GH_{3/4}$ enables early determination of postoperative remission or surgical failure, and thus is a safe indicator for early secondary surgery within the same hospital stay in cases of postoperative persistence of GH hypersecretion.

Abb. 1

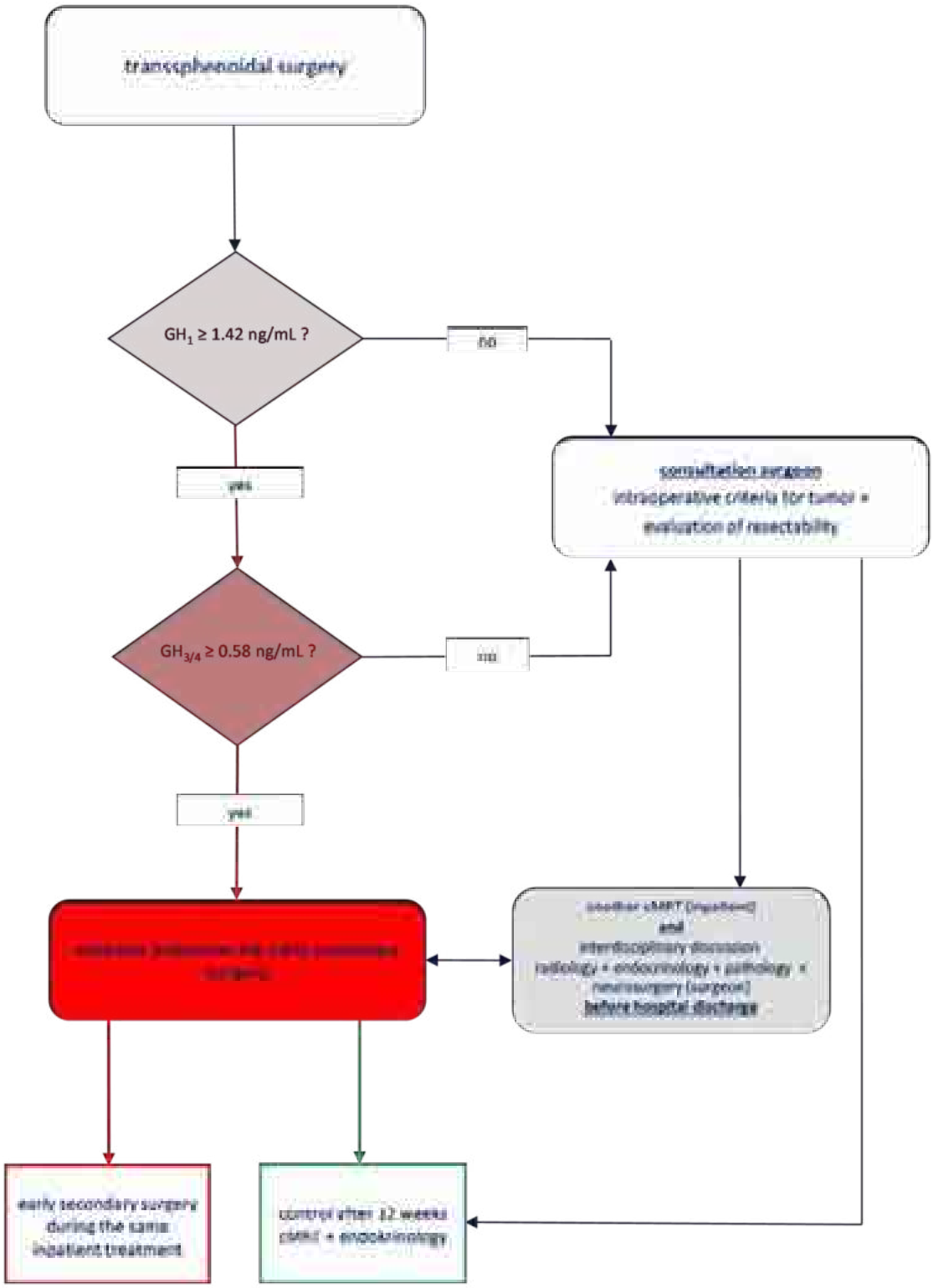

Figure 1. Standard operating procedure (SOP) for early secondary surgery within the same hospital stay in cases of postoperative persistence of GH hypersecretion

Hypophysenadenom I/*Pituitary adenoma I*

J-SBNC021

Primäre radiochirurgische Behandlung klinisch relevanter Hypophysenadenome
Primary radiosurgical treatment for clinically relevant pituitary adenomas

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Objective

To determine whether there is reasonable evidence to support stereotaxic radiosurgery (SRS) as an initial treatment of pituitary adenomas (PA) with prior surgical indication.

Methods

Integrative review of papers published between 2013 and 2023 in LILACS, PubMed and Cochrane Library.

Results

The most recent and comprehensive evidence found revealed that, in the last 35 years, only 24 retrospective studies were performed addressing SRS as a primary treatment for PA with surgical indication. The main indications were patient refusal or ineligibility for surgery, cavernous sinus invasion, and intolerance or resistance to dopaminergic agonists. The literature empathizes SRS as an effective treatment for pituitary adenomas, with 97% of tumoral control in a 5-year pool. For endocrine response, the SRS stabilizes about half of the cases. Non-transient complications were uncommon, the main ones being new hypopituitarism, present in approximately 1 in 10 cases, vision disturbance and oculomotor nerve palsy. As this was based on retrospective studies, it is exposed to selection and bibliographic biases.

Conclusion

In selected cases, initial SRS can be an effective and safe alternative for tumoral and biochemical control in patients with clinically relevant PA, especially in those clinically inoperable or who refuse resection. Attention should be paid to late adverse effects of radiation such as hypopituitarism, optic neuropathy, and radiation-induced malignancies. However, the available evidence still has important limitations, such as limited post-intervention follow-up, variable periods of neuroendocrine assessments between studies, and the heterogeneity of nature and data collection.

References:

Palmisciano P et al. Endocrine disorders after primary gamma knife radiosurgery for pituitary adenomas: A systematic review and meta-analysis. Pituitary. doi:10.1007/s11102-022-01219-x

Mehta GU et al. Management of hormone-secreting pituitary adenomas. Neuro Oncol. doi:10.1093/neuonc/now130

Hypophysenadenom I/*Pituitary adenoma I*

V145

Chronisch-entzündliche und infektiöse Hypophysenpathologien bei transsphenoidal operierten Patienten
Characteristics of inflammatory and infectious diseases of the pituitary gland in patients undergoing transsphenoidal surgery

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Objective

Inflammatory and infectious diseases of the pituitary gland (IPD) are rare and represent only 1-3% of all surgically treated lesions. Immediate surgery is indicated, especially in cases of neurological impairment, but chronic inflammatory and infectious processes can mimic other pituitary tumors, such as adenomas. Limited data are available on the characteristics of patients with this pathology. We report our findings in 25 patients and compare these with a matched pituitary adenoma control group.

Methods

25 patients with histologically confirmed IPD were identified from our database of 1336 patients treated surgically from 2003-2022. All patients were operated on transnasal/transsphenoidal. Clinical characteristics, radiographic findings, and laboratory parameters were analyzed (Pi). Furthermore, we extracted data from a sex-, age- and tumor volume-matched control group (Pc) and compared findings between both groups.

Results

IPD was encountered in 1.9% (n=25; 72% female, 28% male) of all 1336 patients. Patients of group Pi most commonly presented with endocrine dysfunction (14/25) and oculomotor nerve palsy (6/25). One patient reported mildly decreased visual acuity after surgery, and no surgical mortality occurred. Pathology revealed septic infection in 9/25 cases, most commonly caused by bacteria (3/9) and fungi (2/9). In the aseptic group, lymphocytic hypophysitis (8/25) and granulomatous inflammation (3/25) were most frequently observed. Preoperative radiographic findings (cystic/solid tumor mass, contrast enhancement) did not significantly differ. Six of the 25 patients in the Pi group had a history of immunosuppression (p=0.01). Interestingly, no significant differences in infection-related laboratory parameters (CRP, PCT, leukocyte count) were observed. At follow-up (mean 741 days), 12 patients required hormone substitution.

Conclusion

IPD is a rare entity and affected merely 1.9% of all patients in a large surgical cohort. Preoperative diagnosis remains challenging, as neither radiographic findings nor preoperative laboratory workup correctly predicted these lesions. Surgical treatment enables decompression of supra- and parasellar structures. Furthermore, this low-morbidity procedure enables the identification of pathogens or inflammatory diseases requiring targeted medical treatment, which is crucial for these patients. Establishing a correct diagnosis through surgery and histopathological confirmation is thus of high value.

Hypophysenadenom I/*Pituitary adenoma I*

V146

Korrelation zwischen der iMRT-Bildgebung und neuer corticotroper Insuffizienz sowie (passagerem) Diabetes insipidus bei transsphenoidaler Resektion von Hypophysenmakroadenomen

Correlation between iMRI imaging and new adrenocortical insufficiency as well as (transient) diabetes insipidus in transsphenoidal resection of pituitary macroadenoma

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Objective

A new adrenocortical insufficiency as well as (transient) diabetes insipidus occurring postoperatively after tanssphenoidal resection of pituitary macroadenoma are potential complications and require adequate therapy. Based on this, we investigated a possible relationship between the morphologic characteristics of the pituitary gland and the sellar region with a focus on intraoperative MRI imaging and the occurrence of clinically relevant adrenocortical insufficiency as well as diabetes insipidus during transspheonidal resection of macroadenoma.

Methods

A retrospective evaluation was performed. Patients who underwent transsphenoidal surgery for macroadenoma at our department between 2014 and 2020 were analyzed provided that complete records were available up to 12 months after resection. Morphological aspects regarding the pituitary gland as well as the sellar region in iMRI imaging and after three months were analyzed. The endpoint was a new adrenocortical insufficiency at the time of endocrinological control nine months postoperatively as well as (transient) diabetes insipidus during the hospital stay. Analysis was performed with SPSS 28.

Results

48 resections of macroadenomas were included in the final analysis. There was a statistically significant correlation with increased intercarotid artery distance (ICD) at C4 segment with new adrenocortical insufficiency (18.2 vs. 22.4 mm, p = .003). Also, there was a correlation between thickening of the pituitary stalk at the junction with the gland on sagittal imaging and new insufficiency (2.8 vs. 3.2 mm, p = .04). In addition, there was a statistically significant association between intraoperative thickening of the stalk and the occurence of new (transient) diabetes insipidus (2.7 vs. 3.2 mm, p = .025). At three months, the stalk thickening was regressive (2.9 vs. 2.2 mm). However, an improvement in adrenocortical insufficiency did not correlate with this aspect (p = .078).

Conclusion

ICD at the C4 segment is an easily determined parameter that significantly correlates with new postoperative adrenocortical insufficiency. A larger diameter of the pituitary stalk is associated with new insufficiency as well as (transient) diabetes insipidus and supports the frequent intraoperative impression of edematous distension of the stalk. Thickening regressed postoperatively, with morphologic improvement not associated with improvement in adrenocortical insufficiency. All parameters could be assessed using standard MRI sequences.

Abb. 1

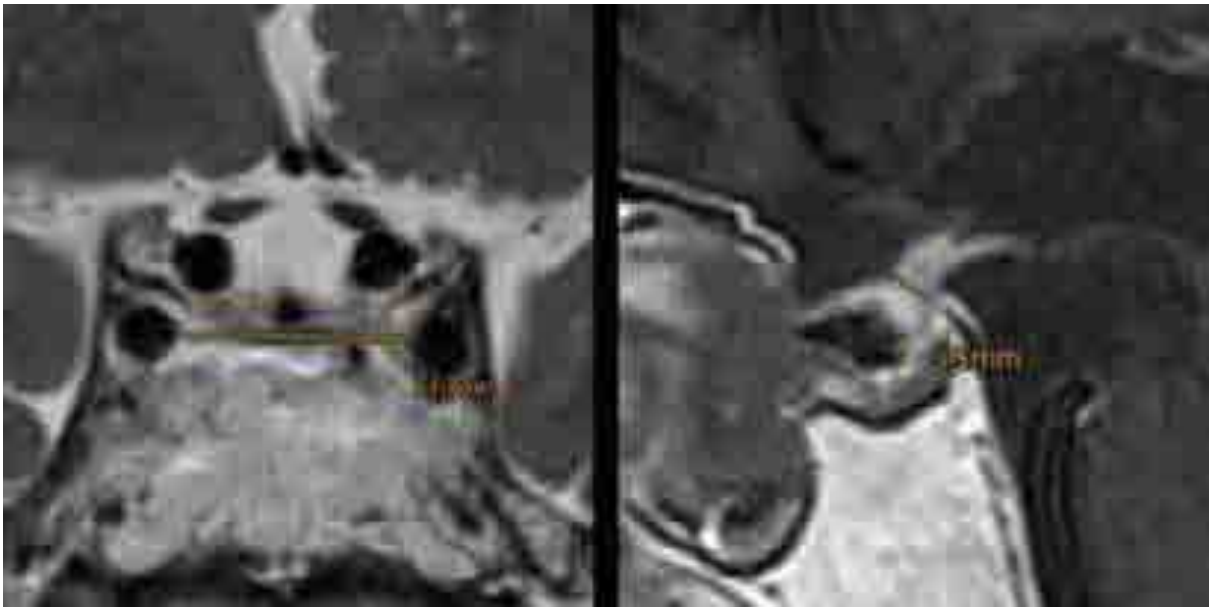
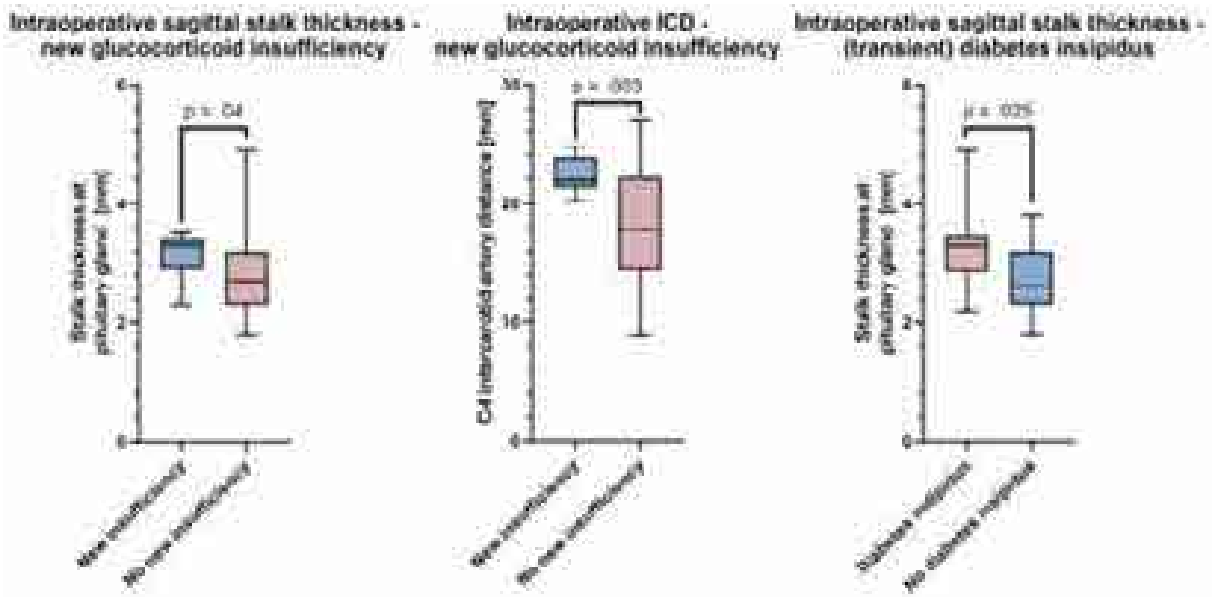


Abb. 2


Intraoperative sagittal stalk thickness - new glucocorticoid insufficiency
Intraoperative ICD - new glucocorticoid insufficiency
Intraoperative sagittal stalk thickness - (transient) diabetes insipidus

Hypophysenadenom I/*Pituitary adenoma I*

V147

Vergleichende Analyse von intraoperativen und bildgebenden Merkmalen für invasives Wachstum von Hypophysenadenomen

Comparative analysis of intraoperative and imaging features of invasive growth in pituitary adenomas

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Objective

Most pituitary adenomas are benign in nature and can be treated effectively by microsurgical resection, medical treatment and/or radiotherapy. However, invasive growth can be an important feature of a more aggressive behavior and adverse prognosis. Extension of pituitary adenomas into the cavernous sinus can be categorized according to the Knosp criteria on magnetic resonance imaging (MRI). The prognostic significance of intraoperatively detected invasive growth is unclear and comparative analyses of MRI features and intraoperative findings are still scarce.

Methods

We performed a retrospective analysis of 764 pituitary adenomas that were surgically treated between October 2004 and April 2018. Invasive growth was assessed according to the surgical reports and preoperative MR-imaging (Knosp criteria). Clinical data such as age at diagnosis, patient gender, histopathological subtype as well as recurrence-free survival on follow-up imaging, were collected.

Results

Invasive growth (Knosp grade 3A – 4) was seen in 24.35% (186/764) of the cases and based on intraoperative assessment in 42.41% (324/764). Overall, 19.07% of pituitary adenomas showed a recurrence. Invasion by intraoperative assessment was associated with older age (p=0.0374), male gender (p=0.0390), sparsely granulated corticotroph adenomas (p=0.0433), null cell adenomas (p=0.0368) and a shorter recurrence-free survival (p=0.0493) in the univariate analysis. Radiographic invasion was correlated with age (p=0.0018), sparsely granulated corticotroph adenomas (p=0.0264), null cell adenomas (p=0.0275) and a shorter recurrence-free survival (p=0.0008). Only radiographic invasion was an independent prognostic factor in the multivariate analysis. (p=0.0134).

Conclusion

Only MRI invasion but not intraoperative evidence of invasion is an independent prognostic factor for inferior recurrence-free survival. MRI invasion as assessed by Knosp criteria can be used for prognostic evaluation and clinical decision-making.

Hypophysenadenom I/*Pituitary adenoma I*

V148

Morbus Cushing – eine lebenslange Erkrankung trotz Remission?
Cushing´s Disease – a lifelong disease despite remission?

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Objective

Cushing's disease (CD) is caused by an ACTH-secreting pituitary adenoma and should be treated immediately after diagnosis by transsphenoidal adenoma resection. Since recent studies provide increasing evidence that even after successful surgery an impairment of quality of life persists, our study aims for objectifying these deficiencies.

Methods

Patients with CD, who were operated between 2007 and 2019 received a set of disease related questionnaires dealing with their disease-related history and health. The responses were compared with those of a healthy normative collective.

Results

Surprisingly, the greatest impairment was found in the psycho-cognitive domain in the SF-36. Patients in almost all age groups indicated an impairment in the area of emotional role understanding (n=64/79), as well as in physical role function (n=36/79). A major influencing factor for this impairment could be the pronounced limitation of cognitive performance, where in the Tuebingen CD-25 all female age groups except the group of 41–50-year-old women (whose z-score was -0.99, n=14/69) felt highly impaired. Among the male subjects, subjective impairment in this area was significantly lower. It is striking that when analyzing the correlating parameters, in most cases a high educational degree correlates with a higher quality of life. Among the patients who expressed no cognitive impairment (n=19), 42.1% reported a completed university degree and 20.8% a secondary school degree. Among the maximally impaired patients, this ratio was the other way round. Overall, 29.9% (n=26) of the total study cohort had a college degree while 18.4% (n=16) had a secondary school degree.

Conclusion

Cushing's disease not only requires hormonal normalization of the corticotrope hormone axis as a therapeutic measure. The effect of the disease on the quality of life of the affected persons is still present after years compared to the healthy normal population, especially in the cognitive-functional area, despite laboratory-chemical recovery. This finding should be taken into account in the follow-up and support should be offered to the patients.

Päd. Epilepsie Funktionell Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Ped. Epilepsy Functional Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V149

Modifizierte vertikale parasagittale Hemisphärotomie bei pädiatrischen Patienten mit Hemimegalenzephalie und therapieschwieriger Epilepsie

Modified vertical parasagittal hemispherotomy in infants with hemimegalencephaly and drug-resistant epilepsy

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Objective

Hemispheric disconnective techniques (HDT) are known to be the most effective tool for seizure control in patients with hemimegalencephaly (HME). However, surgical interventions in this entity are challenging and associated with a high risk of complications. Reports about the overall seizure-free rate after HDT in patients with HME range from extremely from 40 - 90%. Up to date, surgical technique (lateral vs. parasagittal hemispherotomy) does not seem to infuence the post-operative outcome.

Methods

We retrospectively analyzed seizure outcome classified according to the Engel Epilepsy Surgery Outcome Scale (ENGEL) in all patients who underwent modified vertical parasagittal hemispherotomy (MVPH) for HME performed by one neurosurgeon from 2009-2020.

Results

Out of 142 patients who underwent vertical parasagittal hemispherotomy, MVPH was performed in 15 children (f: 8) with HME. The median age at time of surgery was 25 months (range: 7 months - 17 years). The whole cerebral hemisphere was affected in 11 / 15 patients, whereas 4 / 15 patients showed segmental HME. The contralateral hemisphere was considered normal in 12 / 15 patients, 2 / 15 patients presented with isolated focal cortical dysplasia contralateral to HMG and 1 / 15 patient showed additionally suspected idiopathic epilepsy contralateral to HMG. Out of the 12 unilaterally affected patients, 11 / 12 were seizure free (ENGEL class 1a) at last-follow up (range: 6 months – 5.2 years, median: 2.1 years). There was no surgery-related mortality or major unexpected morbidity expect hydrocephalus.

Conclusion

Modified vertical parasagittal hemispherotomy is a safe surgical technique to treat patients with HME and pharmaco-resistant epilepsy. This technique tends to result in a better postoperative outcome especially for this etiology.

Päd. Epilepsie Funktionell Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Ped. Epilepsy Functional Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V150

Vertikal, parasagittale transventrikuläre Hemisphärotomie bei therapieresistenter Epilepsie im Kindesalter - monozentrische retrospektive Erfahrungen.

Vertical, Parasagittal Transventricular Hemispherotomy in Pediatric Drug Resistant Epilepsy - Single Center Retrospective Experience

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Objective

Drug resistant epilepsy in hemispheric pathology represent favorable candidates for epilepsy surgical treatment. For this group of patients, we report our experience with the minimal invasive technique for hemispherotomy in a single center pediatric case series.

Methods

In the time period between 1/2018 until 12/2022 a retrospective review according to our in-house data base was performed to collect clinical data form patients who underwent minimal invasive, AR guided hemispherotomy epilepsy surgery. Indication for surgery was given during an interdisciplinary case discussion in a tertiary pediatric medical center. The peri-operative data was evaluated for surgical time, intensive care unit and hospital stay, possible complications and seizure outcome during follow-up.

Results

A total of 32 patients (mean age: 6.6±4.5yrs; range: 0.2-15) received vertical parasagittal transventricular hemispherotomy at our institution with a mean follow up time of 2.1±1.3 yrs. were included in this study. Underlying disease for epilepsy was perinatal ischemia or hemorrhage (n=16), hemispheric dysplasia (n=10); Rassmussen encephalitis (n=4), Sturge-Weber Syndrom (n=2). Mean surgical time was 187±43 minutes (120-297). Median hospital stay was 9 (range: 6-63) days while ICU and IMC stay was 2±2.4 and 1.7±3.5 days, respectively. Six patients needed additional subsequent surgeries including 2 ETV, 3 shunt placements and 1 decubitus revision. New shunt rate was 9.4%. One of these patients had and previous premature IVH and another suffered from a coagulopathy with postoperative hemorrhage. Seizure outcome was generally favorable according to Engel classification (Engel Ia: 84%, Ib: 9.4%, Id: 3.1%, III: 3.1%).

Conclusion

Vertical, parasagittal transventricular hemispherotomy is a challenging but feasible and effective technique to beneficially control drug resistant epilepsy in unilateral hemispheric pathologies. The complication rate was experienced to be acceptable with a comparable secondary rate of hydrocephalus development. Future perspective investigations are under way to evaluate neurocognitive development after hemispherotomy.

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V151

Was ist die beste Resektionsstrategie für kindliche LEATS mit medikamentöser refraktärer Epilepsie
Towards a better definition of a resection strategy in pediatric LEATs causing refractory epilepsy

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Objective

Resection strategy in pediatric long-term epilepsy associated tumors (LEATS) consists of pure lesionectomy, ECoG guided tailored resection or even partial/complete lobectomy. To propose an evidence based appropriate surgical strategy, we retrospectively analysed our consecutive institutional series of surgically treated pediatric LEATs.

Methods

Twenty-two children suffering from medically intractable seizures harbouring suspected LEATs were investigated at the pediatric epilepsy monitoring unit using clinical and video EEG monitoring, extended MRI epilepsy protocol and FDG and Methionine (MET) PET examinations. Additionally, 2 stereo-EEGs were performed. In 17/22 patients ECoG was used for intraoperative pre-and postresection EEG assessment and when feasible for tailoring the amount of resection. Additionally, neuronavigation and intraoperative MR imaging in recent cases were used for guiding the surgery.

Results

In temporal LEATS, mainly antero-temporal resections or temporal lobectomies were performed (15 patients), whereas in extratemporal LEATS lesionectomies or tailored resections guided by ECoG were achieved (7 patients). Histological diagnosis was GG in 20 and DNET in 2 patients. Preoperative MRI contrast enhancement was present in 10 GG (45%) and FDG PET showed a hypo-metabolic area in 6 GG (27%). Intensiv Methionine (MET) PET uptake was found in 13 GG, weak MET enhancement in 6 GG and no tracer uptake in 1 GG. However, MET PET uptake did not correlate neither with MR contrast uptake intensity, nor with extent of the tumor defined by FLAIR images. Thus, diagnostic sensitivity of MET PET for GG was 100%, specificity 95% in our patients. In temporal resections, ILAE Class 1 seizure outcome was achieved in 75%, which was improved to ILAE Class 1 in 94% by performing 6 repeat surgeries with antero-temporal lobectomies after unsuccessful lesionectomies. The extratemporal patients experienced ILAE Class 1 seizure outcome in 86% without additional surgeries (mean follow-up 28 month).

Conclusion

In childhood LEATs amino acid PET was found to have high diagnostic sensitivity for GGs. In surgical therapy, for extratemporal LEATs a pure lesionectomy or tailored resection may be an appropriate strategy. On the contrary, for temporally located LEATs an antero-temporal resection or even temporal lobectomy may be necessary to achieve seizure freedom and avoid recurrences.

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V152

Ergebnisse nach konservativer oder chirurgischer Behandlung bei Neu auftretende Epilepsie bei Kindern mit zerebraler kavernöser Malformation

Outcome after Conservative or Surgical Treatment for New-Onset Epilepsy in Children with Cerebral Cavernous Malformation

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Objective

This study aimed to investigate and compare the outcome of conservatively or surgically treated children with cerebral cavernous malformation (CCM) and new-onset epilepsy during a 5-year period.

Methods

Our institutional database was screened for CCM patients treated between 2003 and 2020. Patients £18 years of age with complete magnetic resonance imaging dataset, clinical baseline characteristics, and diagnosis of new-onset CCM-related epilepsy (CRE) were included. Definite seizure control was classified as International League Against Epilepsy (ILAE) class <2. Functional outcome was assessed using the modified Rankin Scale (mRS) score. CRE patients were separated into two groups according to their treatment modality. Seizure control, intake of antiepileptic drugs (AED), and functional outcomes were assessed. Systematic literature research was performed to identify cases of new-onset CRE in children

Results

39 pediatric CRE patients were analyzed. 18 (46.1 %) patients were conservatively treated, while 21 (53.8 %) underwent surgical CCM removal. While the functional outcome was similar in both groups at the last follow-up, definite seizure control was better in the surgical group (77.8 %) than in the conservative group (25.0 %) both after 5-years of follow-up (p = 0.038), and at last follow-up with 85.7% vs 50% respectively (p = 0.035). We found substantially higher rates of discontinuation of AED treatment at the last available follow-up in patients undergoing surgical resection (p = 0.009).

Conclusion

Surgical treatment of pediatric patients with new-onset CRE had higher rates of complete seizure control and early discontinuation of AED treatment than conservative treatment. Functional outcomes of patients managed surgically or conservatively were comparable. Such findings may give insight into early surgical treatment for such patients.

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V153

Intraoperative Hochfeld MRT (3 Tesla) für Epilepsie- und Tumorchirurgie in pädiatrischer Neurochirurgie
Intraoperative high field MR (3Tesla) imaging for epilepsy and tumors in pediatric neurosurgery

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Objective

Intraoperative high field MR (3 Tesla) imaging is an elaborate task, especially when used in children. On the other hand, advantages on prognosis may be significant, especially in pediatric epilepsy and tumor surgery.

Methods

Thus, we searched our intraoperative MRI database to identify all children operated at the Neurosurgical Department, Vienna Medical University during the last 16 months.

Results

Altogether, 73 children in 86 surgeries were operated on using the 3 Tesla intraoperative MRI suite. Of those, 39 epilepsy surgeries (patients median age 6, 0-16) and 34 tumor surgeries (patients mean age 8, 0-18) were performed. The epilepsy surgery cases consisted of 18 resections, 12 disconnections, 9 depths electrode implantations and 10 LITT procedures. For the tumor cases, 33 resections, 2 stereotactic biopsies and 2 open biopsies were performed in the iop MRI suite. Intraoperative assessment of the extension of lesional epilepsy (FCDs, LEATS, Cavernomas) and tumor borders were feasible in every case. Due to the intraoperative MR imaging results, second look surgeries were performed in 20-30% of the cases, dependent on the specific diagnosis. Highest numbers of second look surgeries were performed in diffuse gliomas and in FCDs. No adverse effects like intraoperative anaesthesia instability or postoperative infection occurred.

Conclusion

Intraoperative high field MRI in pediatric neurosurgery (especially in epilepsy and tumor surgery) seems to be beneficial in increasing extent of resection at least in 20-30% of the cases and may thus contribute to improve outcome in pediatric tumor and epilepsy cases.

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Bericht über Technik und Ergebnisse der ventralen und dorsalen Rhizotomie zur palliativen Behandlung schwerer Dystonie bei Zerebralparese

Report of technique and results of ventral and dorsal rhizotomy for palliative treatment of severe dystonia in cerebral palsy

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Objective

Dystonia due to cerebral palsy is a serious entity with a high impact on the child's quality of life and extreme difficulty for caregivers. Clinical treatment with medications has partial results. Some patients refractory to clinical treatment will require surgical treatment. Modulation procedures such as baclofen pump placement and deep brain stimulation have limitations and high cost. The authors describe 5 cases of children who underwent ventral and dorsal rhizotomy to relieve spasticity and dystonia.

Methods

Five patients with cerebral palsy GMFCS V with severe spasticity and significant dystonia who underwent ventral and dorsal rhizotomy were studied. The children initially underwent clinical treatment with physical rehabilitation. Medications such as: baclofen, tizanidine, diazepam, trihexyphenidyl and botox were used. Treatment options were evaluated and a decision was made to perform a ventral and dorsal rhizotomy, with a section of 50% of the motor roots and 80% of the dorsal roots. Initially in the lumbar region and in the second time in the cervical region. Patients were assessed using the modified Asworth scale and family members' assessment of improvement in care. Complications were also analyzed.

Results

Patients' ages ranged from 10 to 18 years. In all five patients there was decrease of one grade on the modified Asworth scale. In two patients the improvement was 3 degrees and in 1 patient the improvement was 1 degree. As these were patients with severe neurological sequelae, surgical complications were studied. Two patients had mild to moderate temporary dyspnea. One case had wound dehiscence and a second patient a deep wound infection after a fistula.
Caregivers reported significant improvement in care and reported that they would perform the procedure again. There was little improvement in cervical and trunk dystonia.

Conclusion

The initial treatment of dystonia is with drugs, but in severe cases the response is limited. Faced with this situation, surgical options are divided into ablative procedures and dystonia and spasticity modulating procedures. Patients unable to undergo modulating surgeries may benefit from ablative surgeries. Rhizotomy is an extensive surgery, but the patients had good results, mainly in improving palliative care for children.

Diversität und Frauen in der Neurochirurgie/*Diversity and women in neurosurgery*

V154

Wie divers sind die klinischen Neurowissenschaften? Eine Querschnittsstudie der Autorenschaften hinsichtlich der Geschlechterverteilung (und des kulturellen Hintergrunds) in der Neurologie, Neurochirurgie und Psychiatrie

How diverse is Clinical Neuroscience? A cross-sectional analysis on female participation and cultural diversity in academic Neurology, Neurosurgery, and Psychiatry

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Objective

Gender disparity within the medical scientific field has previously been demonstrated, and its causes and consequences have been subject to debate and speculation. The aim of this study was to provide a current status quo of the participation of women in clinical neuroscience and to identify similarities as well as differences between neurological, psychiatric and neurosurgical papers.

Methods

Original articles, commentaries and letters published in the official journals of the European and American societies of neurology, neurosurgery and psychiatry between July 2020 and December 2020 were included (European Journal of Neurology, Neurology, Neurosurgery, Acta Neurochirurgica, Journal of Neurosurgery, European Psychiatry and American Journal of Psychiatry). Metadata including authors" sex, affiliation and medical degree were collected.

Results

1775 articles were included for analysis, which consisted of 780 neurosurgical, 848 neurological and 147 psychiatric publications. Of 15.080 authors, 4365 (29%) were female. Neurosurgical papers had significantly lower female participation compared to neurology and psychiatry, with 19% female authors (vs. 39% and 45), 18% female first authorship (vs. 48% and 51%), 9.5% female last authorship (vs. 29% and 39%). Also, significantly less female neurosurgical first and last authors were medical doctors compared to their male counterparts (76% and 76% vs. 82% and 87%). Especially invited articles showed significantly lower female authorships across all specialties (13% vs. 31% vs. 35%).

Conclusion

The analyzed data reflect the still existing gender disparity in academic neuroscience, which is particularly pronounced within neurosurgery. Among all specialties, the relatively low ratio of women in senior positions and invited publications is conspicuous. An open, constructive approach is needed to identify and implement measures to increase diversity within both clinical and scientific field. A more diverse environment may contribute to an increase of medical and scientific quality.

Diversität und Frauen in der Neurochirurgie/*Diversity and women in neurosurgery*

V155

Neurochirurgie in der Schwangerschaft: Aktueller Status-quo und Empfehlungen im Falle einer operativen Tätigkeit

Neurosurgery during pregnancy: Current Status-quo and recommendations in case of surgical activities

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Objective

The medical field is turning into a female dominated area. Nevertheless, there are still enormous gender gaps: Particularly, certain specialties are affected. Further, leadership positions still are male-dominated. For the future, it is important to open the entire medical sector to females. Thus, inadequate barriers have to be addressed. The institutional interpretation of the German Mutterschutzgesetz (MuSchG) regularly results in the fact that expectant mothers are prohibited from working (Beschäftigungsverbot). Here, we summarize the current data on female neurosurgeons´ perspective, legal status-quo and possible solutions.

Methods

In order to document the current attitude of female neurosurgeons toward the continuation of work (particularly of performing surgeries) while being pregnant, a survey was carried out in 2022. Further, data was collected by searching literature and contacting persons experienced in the legal framework and its scope of interpretation. Finally, a recommendation based on the data was put down.

Results

95% of the respondents declared the wish to continue to perform surgeries while being pregnant. The minority of female neurosurgeons were allowed to perform surgeries when the institutional or legal authorities noticed pregnancy. A formal objection failed in all cases (100%). Recommendations for pregnant neurosurgeons are presented in order to assure the best protection possible but also adequate autonomy (when there is the wish to continue to perform surgeries). We present conditions allowing the continuation of surgical activities and a list of possible surgeries.

Conclusion

In order to facilitate female neurosurgeons (who wish to do so) the continuation of surgical activities while being pregnant a framework of the current data and summarizing recommendations are presented.

Wirbelsäule degenerativ und Chiari Malformation/*Spinal degenerative and Chiari malformation*

V156

Auswirkungen der COVID-19-Pandemie auf die Frailty bei hospitalisierten Wirbelsäulenpatienten in einem deutschlandweiten Netzwerk aus 76 Krankenhäusern

Changes in frailty among patients admitted for spine pathologies during the COVID-19 pandemic in a nationwide hospital network in Germany

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Objective

In spine care, frailty is associated with poor outcomes. During the COVID-19 pandemic, frailty increased in the general population. We examined changes in frailty among patients hospitalized for spine pathologies during the COVID-19 pandemic and whether they were associated with changes in surgical management and outcomes.

Methods

This retrospective observational study used administrative data from a nationwide network of 76 hospitals managing 7% of all in-hospital cases in Germany. All patients hospitalized for spine pathologies in 2019 (pre-pandemic period) and between March 5, 2020, and May 17, 2022 (pandemic period) were included. Patient demographics, types of surgery (decompression, discectomy, kyphoplasty, spine fusion), and in-hospital mortality rates were compared between pandemic and pre-pandemic periods and changes examined for associations to frailty. Frailty was assessed using the hospital frailty risk score. Ethics approval was granted by local authorities (490/20-ek).

Results

Of the 223,418 included patients with spine pathologies, 151,766 were admitted during the pandemic and 71,652 in 2019 (pre-pandemic period). During the pandemic, the proportion of high frailty patients increased from a range of 5.1%-6.1% to 6.5%-8.8% ($p<0.01$), compared to 2019 levels. At the same time, the proportion of low frailty patients decreased from a range of 70.5%-71.4% to 65.5%-70.1% ($p<0.01$). The most consistent changes in rates of surgery were observed in spine fusion, which showed increases throughout the pandemic by a range between +1.6 to +2.7%. Changes in decompression, discectomy, and kyphoplasty were less pronounced. The extent of the changes in spine fusion rates differed across frailty groups, with consistent increases among low frailty patients, ranging between +2.2% and +3.5%, versus comparably mild increases by 0.1%-0.3% or decreases by 0.3%-0.8% among high frailty patients. Rates of in-hospital mortality were not associated with frailty but increased significantly during the pandemic by a range of +0.4 to +1.4%.

Conclusion

We present the largest study on frailty among spine patients in Germany so far. Frailty increased significantly during the COVID-19 pandemic. At the same time, the way spine pathologies were treated changed as well, most prominently represented by a significant increase in spine fusion rates among low frailty patients. Whether this was due to an increased burden of symptoms or organizational changes during the pandemic is up for discussion.

Wirbelsäule degenerativ und Chiari Malformation/*Spinal degenerative and Chiari malformation*

V157

Prä- und postoperative funktionelle Anpassungsvorgänge innerhalb des somatosensiblen Kortex bei degenerativer zervikaler Myelopathie

Pre- and Postsurgical Functional Adaptations within the Somatosensory Cortex in Degenerative Cervical Myelopathy

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Objective

Degenerative Cervical Myelopathy (DCM) is the most common cause of spinal cord dysfunction in adults. Despite extensive multimodal diagnostic possibilities, conclusive outcome predictors for surgical therapy are still lacking. Somatosensory deficits are a common early symptom of DCM. Here, the functional adaptation in the somatosensory system was investigated before and after surgical decompression using functional magnetic resonance imaging (fMRI).

Methods

The trial involved 11 DCM patients (age 58 ± 14 years, 8 male) planned for surgical decompression and (until now) 9 age- and gender-matched control subjects (age 57 ± 12 years, 7 male). All participants underwent a clinical examination and a block design fMRI (3T) session consisting of alternating, passive somatosensory stimulation of the subjects' hands and feet. The presurgical BOLD response was analyzed in MATLAB® 2019a and SPM12 at the group level using a three-way ANOVA with the factors "group" (patients/controls), "limb" (hand/foot) and "side" (left/right). For three patients which already completed follow-up examinations after 3, 9 and 24 months a single subject GLM analysis was performed addressing the postsurgical BOLD changes.

Results

Preoperatively, the patient group featured reduced activation in the somatosensory cortex compared to the control group ($p \leq 0.001$, uncorrected). Also, the three patients with complete follow-up data individually revealed reduced BOLD response prior to surgery. One of those patients showed a continuous clinical improvement in the follow-up examinations (pre-op: JOA 10, 24 months post-op: JOA 17). This is consistent with an increased cortical response in the postoperative fMRI sessions, involving a larger volume of activation ($p \leq 0.05$, FWE corrected) in the somatosensory cortex than at baseline. The other two patients with only mild clinical impairment (pre-op: JOA 14 and 16.5) neither showed a relevant clinical improvement nor an increase of cortical response.

Conclusion

DCM patients showed reduced cortical responsiveness to somatosensory stimuli preoperatively. In addition, it was shown on a single patient level that BOLD responses might increase in parallel with clinical improvement after surgery. In other clinically less impaired patients, cortical activation and clinical status remained reduced. This points towards a differential functional network responsiveness to surgery, dependent on individual factors such as the severity of preoperative symptoms.

Wirbelsäule degenerativ und Chiari Malformation/*Spinal degenerative and Chiari malformation*

V158

Depression und Angststörung sind pathogene Faktoren für die Entwicklung von Rückenschmerz - Ergebnisse einer machine learning-gestützten Auswertung einer großen Kohortenstudie

Machine-learning based exploration of a large cohort study data set reveals depression and anxiety as major pathogenic factors of back pain

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Objective

Development of back pain is multifactorial and it is not well understood which factors are the main drivers of the disease. We therefore applied a machine-learning approach to an existing large population-based cohort study data set and sought to identify and rank the most important contributors to the presence of back pain amongst the documented parameters of the cohort.

Methods

399 participants (age 39 to 73 years) were randomly selected from the population of a region in southern Germany and prospectively enrolled in the KORA-MRI (Cooperative Health Research in the Region Augsburg) cohort. MRI images of the whole body, including the spine, as well as metabolic, sociodemographic, anthropometric and cardiovascular data were obtained. Presence of back pain was one of the documented items in this data set. Applying a machine-learning approach using a logistic regression model with *least absolute shrinkage and selection operator* (LASSO) regularization, we sought to identify the variables that were most strongly associated with backpain. Causal mediation analysis was performed to evaluate the underlying mechanisms of the identified associations.

Results

We found that depression and anxiety were the two most selected predictors for back pain in our model. Additionally, BMI, spinal canal width and disc generation, medium and heavy physical work as well as cardiovascular factors were among the top 10 most selected predictors. Using mediation analysis, we found that the effects of anxiety and depression on the presence of back pain are direct effects which are not mediated by any factor, especially not by spinal imaging.

Conclusion

Mental health was the most important component in the pathogenesis of back pain in our cohort. Interestingly, the effects of anxiety and depression on the presence of back pain were direct, i.e. not mediated by any other factor. The association of physical factors like BMI and spinal degeneration with back pain was weaker, albeit still

present. This supports the notion, that back pain has to be treated in a personalized multidimensional framework which addresses the specific pathogenic factors present in each individual patient.

Wirbelsäule degenerativ und Chiari Malformation/*Spinal degenerative and Chiari malformation*

V159

Langzeit funktionelle Behandlungsergebnisse von Patienten, die sich einer unilateralen Laminotomie mit Undercutting unterzogen zur Behandlung einer zervikalen spondylotischen Myelopathie - Ergebnisse einer prospektiven Studie

Long-term functional outcome in patients undergoing unilateral laminotomy and decompression for cervical spondylotic myelopathy – results of a prospective study

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Objective

Cervical spondylotic myelopathy (CSM) can lead to up to 60% of neurological deterioration. Both anterior and posterior approaches have been demonstrated to achieve comparable results. Standard posterior approaches are either laminectomy and fusion or laminoplasty. Both have the disadvantage of bilateral muscle detachment. In 2015, our group described posterior bilateral decompression by means of laminotomy and undercutting to the contralateral side (OLD). In this study, we report long-term functional follow-up of this novel technique.

Methods

Patients undergoing OLD for CSM were prospectively enrolled in this study. Their functional status was assessed by means of the modified JOA score (mJOA) preoperatively, at three months, six months and one year after surgery. Primary endpoint was a significant improvement in functional status, defined as an increase of at least 2 points in the mJOA score, otherwise known as minimal clinically important difference (MCID). Secondary endpoint was improvement in the Neck Disability Index (NDI).

Results

A total of 64 patients had long-term follow-up at one year. Mean age was 65 years (range: 43-81). Most patients were male (42/64, 66%). Mean preoperative mJOA=12 (SD=3.4). A total of 27/64, 42% had MCID. Among these patients, the mean preoperative mJOA=10 (SD=3.3), with a statistically significant improvement to mJOA=14 (SD=2.9) (p<.001). On the other hand, 22/64, 34% patients did not have MCID: their mean mJOA=13 (SD=3) both preoperatively and at one-year follow-up (p=.771). Finally, 15/64, 23% patients suffered clinical deterioration, with drops of ≥2 points in the mJOA: mean preoperative mJOA=14 (SD=2.2), and mean mJOA=11 (SD=3) at one-year follow-up (p<.001). NDI improved in 34/64, 53% patients: mean preoperative NDI=28 (SD=10) and NDI=19 (SD=8) at one-year follow-up (p<.001). On the other hand, n=11/64, 17% did not experience any changes in NDI, with mean being 23 (SD=7.8) (p=.160); and n=19/64, 30% experienced worsening from mean NDI=19 (SD=6.5) preoperatively to NDI=28 (SD=7.8) at one-year follow-up (p=.001).

Conclusion

OLD achieves a similar rate of MCID in CSM to laminectomy and laminoplasty, as quoted in the literature (44-52%). OLD thus constitutes an equipoise surgical method in the treatment of CSM.

Wirbelsäule degenerativ und Chiari Malformation/*Spinal degenerative and Chiari malformation*

V160

Chiari Malformationen Typ I: Ein Update über das seltene Krankheitsbild, dessen individueller Therapie und neuer Aspekte

Delving into profound Decision Making in Neurosurgical Care of Chiari Malformation Type I

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Objective

The goal of this study is to offer a tool containing objectifiable parameters, including a validation of the Chicago Chiari Outocome Scale (CCOS) for deciding when surgical intervention in Chiari malformation type I is beneficial in children and adults.

Methods

We evaluated 111 patients from 0 to 63 years [73 female (65.7 %), 38 male (34.3 %)] who underwent surgical decompression of the posterior fossa due to Chiari malformation type I in a single neurosurgical center. 46 presurgical clinical and radiographic factors were selected. The outcome was investigated using the Chicago Chiari Outcome Scale (CCOS) and Clinical Outcome Score. The mean postoperative follow-up period was 3.5 years. All factors regarding the outcome were tested individually and in small subgroups to reflect the diversity of clinical presentation. In addition a validation of the CCOS was performed using SPSS.

Results

An excellent ability of the CCOS to correctly predict individual patient outcome was represented with an area under the ROC curve of 0.861. We found that a favorable outcome, defined as CCOS ≥11, was achieved in 93 % (n=93) of all patients who underwent the follow-up examination. Different subgroups were analyzed e.g. early onset Chiari in young children (ages 0-5), or elderly patients (≥ 50 years) presenting with Chiari. The most frequent surgical intervention was decompression of the posterior fossa with laminectomy of C1 and duroplasty (n=83, 74.8 %). Headaches were observed preoperatively in 48 patients (43.2 %). Numbness in extremities showed a notable disproportion in children (n=6, 18.2 %) compared to adults (n=8, 10.3 %) with an OR (95% CI): 1.94 (0.62;6.13). Radiographically, we found the highest correlation with a good outcome in patients with a tonsillar herniation distance of more than 10 mm [OR (95% CI): 4.15 (1.34;12.87)].

Conclusion

Our analysis of children and adults enlightens the diverse manifestations of Chiari malformation type I faced in daily neurosurgical practice. The CCOS in addition is a valuable tool to categorize outcome after surgery and helps to further investigate the rare cases of neurosurgical intervention in patients with Chiari malformation.

Wirbelsäule degenerativ und Chiari Malformation/*Spinal degenerative and Chiari malformation*

V161

Neueste Entwicklungen in der Behandlung von Chiari-Malformation Typ I: Ein Expertenupdate
Experts' update on the management of Chiari Malformation Type I

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Objective

Controversy about the surgical management in cases of symptomatic Chiari type I has been previously discussed but without a clear global consensus regarding the different surgical techniques and outcomes. We aim here to obtain the expert Neurosurgeons' opinion and experience on the different surgical strategies they adopted in their practice through the last decades.

Methods

A questionnaire consisting of 30 questions was sent to Neurosurgeons globally in the form of an online form. The data were then exported in an excel table and the different responses were analyzed. Questions tackled information about the experience of the neurosurgeon taking part in the survey, common and uncommon presentations, surgical technique, and postoperative outcomes.

Results

Responses were collected from 46 consultant neurosurgeons from 11 different countries located in 4 different continents with an estimated total number of 1595 cases. The respondents agreed to an extent of 71.7% that at least posterior fossa decompression is a must and to 80.4% that duroplasty and 78.3% that arachnoid dissection should accompany the decompression. However, they disagreed regarding the necessity of shrinking the tonsils and method of dural closure. They reported that syringomyelia was more commonly encountered than hydrocephalus. They agreed that all cases witnessed clinical and radiological improvement following surgery and rarely accompanied with major complications.

Conclusion

Posterior fossa decompression with duroplasty and arachnoid dissection happens to be the surgical technique of choice for most neurosurgeons globally with favorable results and low rate of major complications.

V162

Eine vorangehende Thrombektomie hat keinen Einfluss auf die Frühkomplikationsrate der dekompressiven Hemikraniektomie zur Behandlung eines malignen Hirninfarktes

Prior thrombectomy does not affect the surgical complication rate of decompressive hemicraniectomy in patients with malignant ischemic stroke

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Objective

Even though mechanical recanalization techniques have dramatically improved acute stroke care since the pivotal trials of decompressive hemicraniectomy for malignant courses of ischemic stroke, decompressive hemicraniectomy remains a mainstay of stroke treatment. However, it is still unclear, whether prior thrombectomy, which in most cases is associated with application of antiplatelets and/or anticoagulants, affects the surgical complication rate of decompressive hemicraniectomy and if conclusions derived from prior trials of decompressive hemicraniectomy are still valid in times of modern stroke care.

Methods

A total of 103 consecutive patients, who received a decompressive hemicraniectomy for malignant middle cerebral artery infarction, were retrospectively evaluated. Surgical and functional outcomes of patients, who had received mechanical recanalization before surgery (thrombectomy group, n=49), and of patients, who had not received mechanical recanalization (medical group, n=54), were compared.

Results

The baseline characteristics of the two groups did significantly differ with regards to preoperative systemic lysis (63.3% in the thrombectomy group vs. 18.5% in the medical group, p<0.001), the rate of hemorrhagic transformation (44.9% vs. 24.1%, p= 0.04) and preoperative Glasgow Coma Score (median of 7 in the thrombectomy group vs. 12 in the medical group, p=0.04) and were similar to prior randomized controlled trials of decompressive hemicraniectomy. There was no significant difference in the rates of surgical complications (10.2% in the thrombectomy group vs. 11.1% in the medical group), revision surgery within the first 30 days after surgery (0.4% vs. 5.6%, respectively) and functional outcome (median modified Rankin Score of 4 at 5 and 14 months in both groups) between the two groups.

Conclusion

A prior mechanical recanalization with possibly associated systemic lysis does not affect the early surgical complication rate and the functional outcome after decompressive hemicraniectomy for malignant ischemic stroke. Patient characteristics have not changed significantly since the introduction of mechanical recanalization; therefore, the results from former large randomized, controlled trials are still valid in the modern era of stroke care.

Schlaganfall und SAB/*Stroke and SAH*

V163

Der zerebrale Sauerstoffpartialdruck während Spreading Depolarization beeinflusst das klinische Ergebnis bei malignem Schlaganfall

Tissue partial pressure of oxygen during spreading depolarization in malignant stroke is associated with outcome

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Objective

Prevention of secondary lesion progression within peri-infarct tissue is one of the most important treatment targets in ischemic stroke. Spreading depolarization (SD) describes a propagating neuronal mass depolarization within the cerebral cortex that likely represents a relevant mechanism of secondary lesion progression. In the present study, we investigated the influence of SD on brain tissue partial pressure of oxygen ($PtiO_2$) within the peri-infarct tissue of patients suffering malignant hemispheric stroke (MHS).

Methods

Between 2008 and 2015, this prospective observational study included 25 patients with MHS that underwent decompressive hemicraniectomy (DC) followed by subdural placement of an electrocorticography (ECoG) strip electrode and cortical implantation of a $PtiO_2$ probe within in the periinfarct tissue. Continuous and simultaneous ECoG and $PtiO_2$ recordings were obtained at bedside for five days postoperatively. Post hoc, recordings were analyzed for the occurrence of SD and SD-associated $PtiO_2$ changes, as well as their association with clinical outcome at 6 months, determined by the mRS score.

Results

The overall simultaneous ECoG and $PtiO_2$ recording time was 2603 hours, during which 796 SDs were detected. Most SDs occurred within the first 72 hours after surgery and less SDs were detected in large infarcts. The overall SD duration and SD frequency did not correlate with outcome. During the observation period, the overall $PtiO_2$ baseline changed significantly with an almost linear increase that reached a peak around 100 hours (*p=0.0055), followed by a $PtiO_2$ drop until the end of the monitoring period (*p=0.0048). Accordingly, low baseline $PtiO_2$ (<15mmHg) was mainly noted during the first 24 hours but did not correlate with outcome (p=0.916). On the other hand, 20 out of 25 patients showed SD-associated $PtiO_2$ changes in 363 out of 796 SDs (45.6%), which were categorized as biphasic (222), hypoxic (119) and hyperoxic (22). Among these SD-associated $PtiO_2$ responses, a high occurrence rate, biphasic response pattern and high amplitude correlated significantly with favorable outcome (mRS 1-3) at 6 months.

Conclusion

SD-associated $PtiO_2$ coupling in patients suffering hemispheric stroke appears to be associated with clinical outcome and could reflect the presence of viable and metabolically less impaired peri-infarct tissue.

Schlaganfall und SAB/*Stroke and SAH*

V164

Management der spontanen Subarachnoidalblutung: Ergebnisse einer deutschlandweiten Umfrage
Management of spontaneous subarachnoid hemorrhage: results of a german-wide survey

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Objective

There is no clear consensus on best clinical management modalities with regards to cerebral vasospasm prophylaxis (CVP) and follow-up imaging for perimesencephalic nonaneurysmal subarachnoid hemorrhage (NASAH).

This survey aims to evaluate the clinical management among neurosurgical departments in Germany.

Methods

135 departments received a hardcopy questionnaire, evaluating the incidence of NASAH patients treated annually as well as the estimated complication rate. Further, clinical vignettes of minor, moderate and severe NASAH on CT-scans questioning the in-hospital treatment including initial observation, blood pressure management, CVP and the need for digital subtraction angiography (DSA) were included.

Results

80 departments (59.2%) answered the questionnaire. Centers providing a higher case load state an elevated complication rate applying the Phi coefficient (Φ=1.17, $p<.05$).

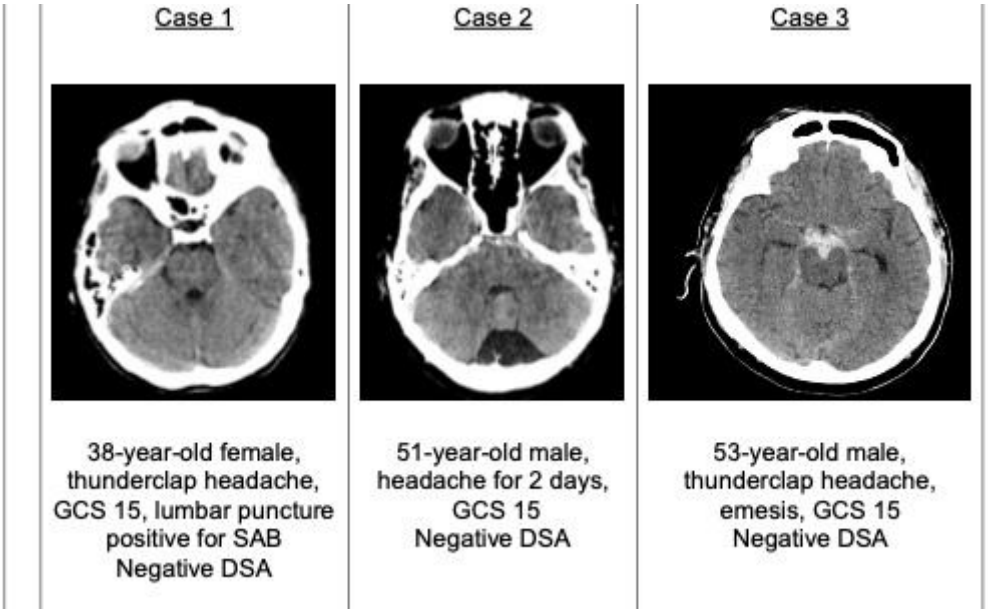
Initial observation on the intensive care unit is performed in 51.3%; 47.5%, 70.0% in minor, moderate and severe NASAH, respectively. Invasive blood pressure monitoring is performed more often in severe cases (52.5%, 55.0%, 71.3% minor, moderate, severe).

CVP and transcranial doppler ultrasound are performed in 41.3%, 45.0%, 63.8% in minor, moderate and severe bleeding, respectively. Indication for a second DSA is set in the majority of centers, whereas after two negative ones a third DSA is less often indicated (2nd: 66.2%, 72.5%, 86.2%; 3rd: 3.8%, 3.8%, 13.8% minor, moderate, severe).

Conclusion

This study confirms treatment differences of patients suffering from NASAH within Germany and that treatment options are influenced by the initial bleeding severity. Therefore, we suggest to conceive new treatment guidelines including this finding.

Abb. 1


Case 1
Case 2
Case 3
38-year-old female, thunderclap headache, GCS 15, lumbar puncture positive for SAB Negative DSA
51-year-old male, headache for 2 days, GCS 15 Negative DSA
53-year-old male, thunderclap headache, emesis, GCS 15 Negative DSA

V165

Hyperkapnie – ein therapeutisches Instrument bei hemikraniektomierten Patienten mit Subarachnoidalblutung?
Hypercapnia – a possible therapeutic tool in hemicraniectomized subarachnoid hemorrhage patients?

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Objective

Recent clinical studies have shown that inducing hypercapnia can be used to enhance cerebral perfusion (CBF) in ventilated patients with spontaneous subarachnoid hemorrhage (SAH). However, some clinicians have the concern that hypercapnia could lead to elevations of intracranial pressure or reduced blood pressure. In hemicraniectomized patients, in who a hypercapnia-induced increase in ICP is unlikely, hypercapnia could be an interesting tool to optimize CBF. The aim of this retrospective study was to analyze whether periods of hypercapnia were associated with elevated ICP or higher doses of vasopressors in a cohort of ventilated, hemicraniectomized SAH patients.

Methods

We analyzed a 10 year period of a single center SAH database for patients with spontaneous SAH who underwent hemicraniectomy. Blood gas analyses and physiological parameters (ICP, CPP), as well as doses of vasopressors were derived from the electronic charts and analyzed 24 h before and after hemicraniectomy. Hypercapnia was defined as an arterial $pCO_2 \geq 45$ mmHg.

Results

Of 479 patients with spontaneous SAH, 39 underwent hemicraniectomy. Of the hemicraniectomized patients, 27 were female. Initial H&H score was V in 24, IV in 5, III in 5, II in 1, and I in 4 patients. An aneurysm was identified as bleeding source in 38 patients. 26 patients underwent hemicraniectomy within 24, 4 within 48, and 9 within 72 hours after admission. 1 patient was suffering from COPD. Hemicraniectomy significantly reduced ICP (pre- vs. post-hemicraniectomy: 22.8±5.5 vs. 13.4±4.3 mmHg, $p< 0.01$). Before hemicraniectomy, the pCO_2 had been kept low with only 3 periods of hypercapnia in 2 patients. Interestingly, these were not associated with critical ICP elevations above 20 mmHg. After hemicraniectomy, we identified 19 periods of hypercapnia in 14 patients. In the hemicraniectomized patients, elevated pCO_2 was not associated with elevated ICP (mean ICP during hypercapnia 10.0±2.9 mmHg). A relevant impact of hypercapnia on the doses of vasopressors was not apparent.

Conclusion

We did not observe an elevated ICP or increased need for vasopressors, or other apparent adverse events during periods of hypercapnia. This indicates that inducing hypercapnia could be used safely in ventilated, hemicraniectomized SAH patients with ICP-monitoring. Controlled studies are warranted to examine whether elevated pCO_2 targets or periods of hypercapnia influence secondary brain injury and clinical outcome positively.

V167

Leichte Hyperglykämie (140-160 mg/dL) bei Patienten mit aneurysmatischer Subarachnoidalblutung korreliert mit schlechtem funktionellem Outcome

Mild hyperglycemia (140-160 mg/dL) during aneurysmal subarachnoid hemorrhage is independently associated with poor outcome

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Objective

Hyperglycemia in critically ill patients is strongly linked with poor outcome. Current guidelines recommend insulin treatment for blood sugar levels exceeding 180 mg/dL. We analyzed the clinical impact of different levels of hyperglycemia occurring during the treatment of patients with aneurysmal subarachnoid hemorrhage (SAH).

Methods

For the consecutive series of 626 SAH patients treated between 01/2005 and 06/2016, daily maximal blood sugar levels during 2 weeks after SAH were recorded. The cohort was subsequently divided into four groups: normoglycemic (<140 mg/dL, n=242), mild hyperglycemic (140-160 mg/dL, n=113), severe hyperglycemic (160-200 mg/dL, n=132) and stress-hyperglycemic (>200 mg/dL, n=139). Primary study endpoints were the occurrence of cerebral infarctions, in-hospital mortality and poor outcome at 6 months after SAH (defined as mRS>3). Secondary endpoints included the development of different adverse events during disease.

Results

Normoglycemic SAH individuals showed the lowest rates of cerebral infarction (34.2%/52.7%/58.3%/54.3%), in-hospital mortality (8.3%/16.8%/18.9%/23.7%), and poor outcome (18.1%/34.6%/44.2%/55.7%) as compared to mild, severe and stress-hyperglycemic patients (respectively). In univariate analyses, significant differences were observed for cerebral infarction (p=0.001), in-hospital mortality (p=0.027), and poor outcome (p=0.001) when comparing normoglycemic with mild hyperglycemic patients. In multivariate analysis, the difference remained significant for poor outcome (aOR=1.90, p=0.040) and cerebral infarcts (aOR=1.84, p=0.017). Moreover, mild hyperglycemia (vs. normoglycemia) independently increased the risk for intracranial hypertension requiring decompressive craniectomy (aOR=2.02, p=0.039) and symptomatic angiographic vasospasm (aOR=1.76, p=0.038). In the analysis comparing different hyperglycemic subgroups, only stress-hyperglycemia (vs. mild or severe hyperglycemia) was independently associated with poor outcome (aOR=1.70, p=0.035). The remaining correlations revealed no significant results.

Conclusion

Hyperglycemia during disease affects two-thirds of SAH patients and is significantly linked with poor outcome. This effect might be related to disturbed autoregulation of intracranial pressure and promotion of neuroinflammation. The clinical relevance of mild hyperglycemia might speak in favor of lower threshold for hyperglycemia treatment after SAH than currently accepted.

Neuroonkologie Studien/*Neurooncology - Studies*

V168

Intraoperatives MRT verglichen mit 5-ALA Fluoreszenz bei der Resektion von neu diagnostizierten Glioblastomen: Ergebnisse einer prospektiven kontrollierten Mulitcenterstudie

Intraoperative MRI-guided resection compared to 5-ALA-guidance in newly diagnosed glioblastoma: A prospective controlled multicenter clinical trial

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Objective

Prospective studies suggest the superiority of intraoperative MRI (iMRI) over 5-aminolevulinic acid (5-ALA) for achieving complete resections of contrast enhancement in glioblastoma. We investigated whether this assumed superiority proofs to be true in a prospective controlled trial.

Methods

A prospective controlled multicenter parallel-group trial with two center-specific treatment arms (5-ALA and iMRI) and blinded evaluation was performed. Safety measurements, including propensity scores, were used to ensure comparability between arms. Main inclusion criteria were unifocal completely resectable glioblastomas. Independent blinded review of pre- and post-operative MRI was performed to assess resectability and extent of resection. The primary endpoint was complete resection in early postoperative MRI. Clinical outcome parameters, including progression-free survival (PFS), overall survival (OS), and quality of life status, were also analyzed.

Results

314 patients with newly diagnosed glioblastomas were recruited at eleven German centers. We evaluated 127 patients in the 5-ALA and 150 in the iMRI arm in a modified intent to treat analysis. A complete resection, defined as a residual tumor ≤0.175 cm³, was achieved in 90 (78%) of patients in the 5-ALA and 115 (81%) in the iMRI arm (p=0·79), with comparable small mean (median was 0cm³ in both cohorts) residual tumor volumes of 0.187 and 0.267cm³ respectively. Significantly longer incision-suture times (p<0·001) were seen in the iMRI arm (316 minutes) than in the 5-ALA arm (215 minutes). Perioperative patient characteristics, adjuvant treatment

and median PFS (4.7 and 5.6 months) and OS (24.1 and 22.7 months) were comparable between the 5-ALA and iMRI arms. Complete resections resulted in a significantly longer median OS (27.9 versus 19.4 months) and PFS (6.9 versus 3.8 months) compared to incomplete resections, respectively.

Conclusion

We could not confirm superiority of iMRI for achieving complete resections. Neurosurgical interventions in newly diagnosed glioblastoma must aim for a safe complete resection of contrast-enhancing residual disease, irrespective of the technology used. Due to high acquisition and maintenance costs, 5-ALA might be superior to iMRI from an economic point of view.

Neuroonkologie Studien/*Neurooncology - Studies*

V169

Randomisierte, kontrollierte Studie zur anterioren temporalen Lobektomie im Vergleich zur Gross Total Resektion bei neu diagnostiziertem temporalem Glioblastom - Studienprotokoll der ATLAS-Studie

Randomized, controlled trial of anterior temporal lobectomy versus gross total resection in newly-diagnosed temporal glioblastoma – the ATLAS trial study protocol

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Objective

With the discovery of cellular tumor networks in glioblastoma with evidence of communicating malignant cells far beyond the enhancing tumor tissue, the conception of supramarginal resection strategies has gained growing attention. Thus, supramarginal resection might provide superior long-term disease control. However, with regard to adjacent eloquent brain tissue and critical vasculature at risk, supramarginal resection regimes are restricted to a selected group of tumor localizations, e.g. temporal glioblastoma. Known as an anatomically highly standardized neurosurgical procedure commonly performed in patients with pharmacoresistant temporal lobe epilepsy, anterior temporal lobectomy (ATL) might constitute a paradigm for such supramarginal resection strategies in temporal glioblastoma surgery.

Methods

Based on previous retrospective studies suggesting ATL to result in a significant survival benefit compared to a conventional gross-total resection (GTR) approach, the authors designed a prospective, randomized (1:1) multicenter controlled trial aimed at evaluating ATL for a potential superiority compared to a GTR approach in patients suffering from glioblastoma located solely within the temporal lobe.

Results

Superiority will be defined as significant differences in the primary endpoint overall survival (OS) and non-inferiority regarding the co-primary endpoint quality of life. Secondary endpoints include progression-free survival, functional and neurocognitive outcome among others. An interim safety analysis 6 months after recruitment of 1/3 of the patients will be performed to make sure that the postoperative clinical status is not significantly worse in the experimental (ATL) arm compared to the standard (GTR) arm as measured by the rate of patients with inferior mRS of 4-6. The trial will randomize 170 patients in 22 German and Austrian Unversity centers over 3 years with a follow-up of 3 years after inclusion of the last patient. Assuming a prolongation of median survival time from 17 months to 27.5 months for the ATL approach and constant recruitment, this sample size provides a power of above 80% for the intended two-sided stratified log-rank test (level of 5%) to detect differences in OS between the arms.

Conclusion

This trial harbors the potential to show superiority of ATL versus GTR in temporal glioblastoma surgery and may thus introduce ATL as the surgical approach of choice for isolated temporal glioblastoma.

Neuroonkologie Studien/*Neurooncology - Studies*

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Stereotaktische interstitielle photodynamische Therapie neu diagnostizierter IDH-Wildtyp Glioblastome: Zwischenauswertung der GL-01 Studie

Stereotactic Interstitial Photodynamic Therapy in Adult Patients with Newly Diagnosed Supratentorial IDH Wild-Type Glioblastoma: Preliminary Report on the GL-01 Study

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Objective

Stereotactic interstitial photodynamic therapy (iPDT) is a promising local therapy option for malignant gliomas. A photochemical reaction leads to accumulation of reactive oxygen species that trigger cell death mechanisms and microenvironmental immune responses. Here, we report preliminary results of the first phase II study on patients with newly diagnosed IDH wildtype glioblastoma.

Methods

The GL-01 Study (NCT04121455) is an open, multicenter, uncontrolled, explorative pilot phase II study that aims to include a maximum of 20 adult patients with histologically proven, newly diagnosed, supratentorial glioblastoma. Study sponsor is Photonamic GmbH & Co.KG (Pinneberg, Germany). Patients are treated with iPDT using 20 mg 5-ALA as a photosensitizer precursor. Primary study objective is to determine safety and tolerability. Secondary objectives are to evaluate overall survival, progression free survival as well as to determine patients' mental and physical condition after iPDT.

Results

So far, 11 patients were included. A planned internal interim safety analysis after treatment of 10 patients found no safety or toxicity issues and the study was continued. In all patients early postoperative MRI 48 hours post iPDT objectified adequate tumor coverage of diffusion restriction signaling as a surrogate for photochemical reaction effectiveness and early follow-up demonstrated marked tumor involution on imaging in all patients.

Conclusion

According to preliminary data from the GL-01 study, iPDT is a safe and minimally invasive local therapy option for newly diagnosed IDH-Wildtype Glioblastoma with marked early tumor response. Survival data analyses are pending and will be reported after study completion.

Neuroonkologie Studien/*Neurooncology - Studies*

V171

Sicherheit und Wirksamkeit der TTFields-Therapie vor und während der Radiotherapie im neudiagnostizierten Glioblastom – die PriCoTTF Phase I/II Studie

Safety and efficacy of TTFields therapy prior and concomitant to radiotherapy in newly diagnosed glioblastoma – the PriCoTTF phase I/II trial

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Objective

The combination of TTFields and radiotherapy has shown a synergistic inhibiting effect on glioblastoma cell proliferation. Based on these preclinical data, we conducted the phase I/II PriCoTTF trial in adult patients with newly diagnosed glioblastoma investigating the safety and efficacy of TTFields therapy initiated prior and concomitant to radiochemotherapy.

Methods

TTFields therapy was started after surgery upon completed wound healing and sustained throughout radiochemotherapy and adjuvant chemotherapy for approximately 9 months in total. Arrays remained applied on the patients' scalp during radiotherapy. At recurrence, TTFields rechallenge was possible.

Primary endpoints were safety and tolerance, based on a selection of pre-specified treatment-limiting toxicities (TLTs).

Results

Thirty-three patients have been enrolled with mostly typical characteristics for a glioblastoma cohort, except for a rather low fraction of patients with gross total resection (GTR, 22.5 %). We found a distribution of adverse events of common toxicity criteria (CTC) grade 3 or higher comparable to that of recognized glioblastoma trials. Notably, skin toxicity of CTC grade 3 or higher occurred rarely (2,6 %) and no patient developed TLTs. Median TTFields treatment duration was 8.4 months.

A definite conclusion about the overall survival lacks mature enough data (event rate 48 %). Remarkably, the number of days with TTFields usage >23 h was independently associated with overall survival shown by multivariable Cox regression (HR 0.96, 95 % confidence interval 0.93 - 0.99, p = 0.008).

Conclusion

The PriCoTTF trial met its primary endpoint indicating that combined TTFields and radiotherapy is safe and well tolerated. High-grade skin toxicity was rare and patients with high TTFields usage seem to perform particularly well. For first estimates on putative efficacy, an extended follow-up is necessary. At that time point, the shorter overall TTFields therapy duration and fraction of patients with GTR need to be taken account of.

Neuroonkologie Studien/*Neurooncology - Studies*

V172

Kurzer Blick auf die NOA 11 Studie- Klinisch kontrollierte Studie zur Evaluation der Sicherheit und Wirksamkeit derstereotaktischen, 5- Aminolävulinsäure gestützten, photodynamischen Therapiebeim Rezidivglioblastom

Quick look on NOA 11 trial- controlled clinical trial to evaluate the safety and efficacy of stereotactical photodynamic therapy with 5 aminolevulinic acid in recurrent glioblastoma

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Objective

There are limited possibilities in treatment of recurrent glioblastoma patients, therefor the NOA 11 trial to investigate the efficacy and safety of interstitial photodynamic therapy (iPDT) in recurrent glioblastomas was initiated.

Methods

The trial was started in February 2021. Four centers had been initiated. Up to know 13 patients have been enrolled in the study who met the current inclusion criteria and tumor size was not more than 2,5 cm in diameter. The patients were randomized 1:1 controlarm vs. iPDT arm.

While hospitalization AE s were recorded, physical examination, blood sampling, clinical scores, quality of life, and MRI response was evaluated. After discharge, the patients were followed every two months with MRI, Quality of life and AE documentation.

Results

Momentarily 7 patients were randomized in the i PDT arm and 6 patients were randomized in the control arm. Until now 10 AEs had been reported, 7 in the i PDT group, and 3 in the controlgroup. None of the AEs were evaluated as therapy associated. In detail we saw pulmonary embolism, seizure and Cerebral hygroma in the iPDT group and cerebral edema, pneumonia and hemiparesis in the controll arm. Now SAE or SUSAR occured. We detected direct response in MRI after i PDT.

Conclusion

Photodynamic therapy seems to be a save and promising option in treatment of recurrent glioma patients.

We are looking forward to the interim analyses to give a statement about progression free and overall survival as well as tolerability and quality of life.

Neuroonkologie Studien/*Neurooncology - Studies*

V173

Eine multizentrische, retrospektive Analyse der prognostischen Faktoren bei intrakraniellen diffusen Mittelliniengliomen mit H3 K27M-Mutation bei Erwachsenen

A multicenter, retrospective analysis of prognostic factors in intracranial H3 K27M-mutant diffuse midline glioma in adults

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Objective

H3 K27M-mutant glioma was first described as a new grade 4 entity in the 2016 WHO classification of brain tumors. Current studies have focused on its common pediatric appearance, increasing the need to better understand this entity in adults. However, there are only few reports on tumor behavior in adults so far. Here we report a multicentric, retrospective analysis of 71 diffuse midline glioma (DMG) in adults.

Methods

In this multicentric study cases of molecularly confirmed H3K27M-mutant glioma (n=71) between 2015 and 2022 with minimum age of 18 were included. Clinical, radiological and surgical features were analyzed to identify prognostic factors. The study was approved by the local ethics committee (PV4904).

Results

Overall, 71 patients were identified, with a mean age of 36.21 ± 13.77 years at the initial diagnosis of H3K27M-mutant glioma and a median overall survival (OS) of 8.5 ± 14.16 months. Female to male ratio was 1:1.4. Tumors were located in the following sites: **diencephalon** (n=38, 53.5%), **metencephalon** (n=13, 16.9%), **mesencephalon** (n=10, 14.1%), **myelencephalon** (n=6, 8.5%), and **telencephalon** (n=4, 5.6%). Gross total resection (GTR) was achieved in only 14.5% of all patients (n=10), 29.5%% (n=21) showed a subtotal resection (STR) and 55.1% (n=38) received a biopsy. Intraoperative cryo section resulted in low-grade glioma in 29.7% (n=11), high-grade glioma in 62.2% (n=23) and no tumor was found in 8.1% (n=3). Surgical approaches were used as follows: 1) **convexity** (n=35, 50%) 2) **stereotaxy/VarioGuideTM** (n=14, 20%) 3) **suboccipital** (n=11, 15.7%) 4) **paramedian** (n=6, 8.6%) and 5) **retrosigmoidal** (n=4, 5.7%). Tumors located in telencephalon/diencephalon/myelencephalon were associated with a poorer OS, while a location site in the mesencephalon/metencephalon showed a significantly longer survival (8.1 vs. 18.5 months, p=0.0067). Furthermore, a postoperative Karnofsky Performance Score (KPS) below 80 showed a significantly reduced OS (5.8 vs. 12.5 months, p=0.006). Patients, who received resection (GTR/STR) showed no significant survival benefit compared to biopsied patients (9.6 vs. 6 months, p=0.46).

Conclusion

The present study describes surgical features of diffuse midline glioma with H3K27M mutation in one of the largest existing multicentric studies in adult patients. Our data shows that location and postoperative KPS impact

OS significantly. Furthermore, resection of H3 K27M-mutant glioma was found to provide no significant survival benefit compared with biopsy.

Gliome Imaging II/*Glioma Imaging II*

V174

Auf tiefen neuronalen Netzen basierende Visualisierung der Deformation der weißen Substanz bei Gliompatienten

Deep neural network based visualization of white matter deformation in glioma patients

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Objective

Streamline tractography is based on diffusion MRI (dMRI) data and is used to delineate the brain"s white matter (WM). Gliomas can affect white matter structure, causing either disruption or displacement. These structural impairments may lead to functional impairments. Here, we aimed to detect and visualize the streamlines" deformation in brain tractography using a deep learning-based method. This further reveals insight into how glioma-induced structural alterations in WM can lead to functional impairment.

Methods

We included 40 healthy subjects (age: 26-35 years) from the Human Connectome Project (HCP) for training. Four left- or right-hemispheric motor glioma patients (age range: 47-73 years, WHO grades III and IV) were included for streamlines" anomaly detection and visualization. We preprocessed the dMRI data using MRtrix3 and applied constrained spherical deconvolution (CSD) to estimate fiber orientation distributions (FODs). Subsequently, we generated whole-brain tractograms (~1M streamlines) using Trekker with parallel transport tractography (PTT). We trained and validated a deep learning model based on a convolutional autoencoder using streamline"s geometric positions, to learn streamline low dimensional representation (embedding). We further used our trained model to detect and visualize the anomalies in the whole brain tractograms of glioma patients at the streamline level. The anomaly score was calculated for each test streamline"s embedding based on its minimum Euclidean distance to all training data embeddings. Subsequently, we obtained an anomaly map based on the given streamline"s anomaly scores for each test subject.

Results

We could detect and visualize the deviations in streamline"s geometry that arise due to brain tumor. Figure 1 illustrates the T1w image (left) of two test patients with their corresponding anomaly map (right). Streamlines" deformation around the tumor can be seen in these two patients with noticeable contrast.

Conclusion

Here, we present an analysis pipeline for anomaly detection in streamline"s geometry. First, we learn a representation of tractography streamlines using a convolutional autoencoder by capturing their spatial information. Subsequently, we successfully detect and visualize the streamline"s deformation in glioma patients.

Abb. 1

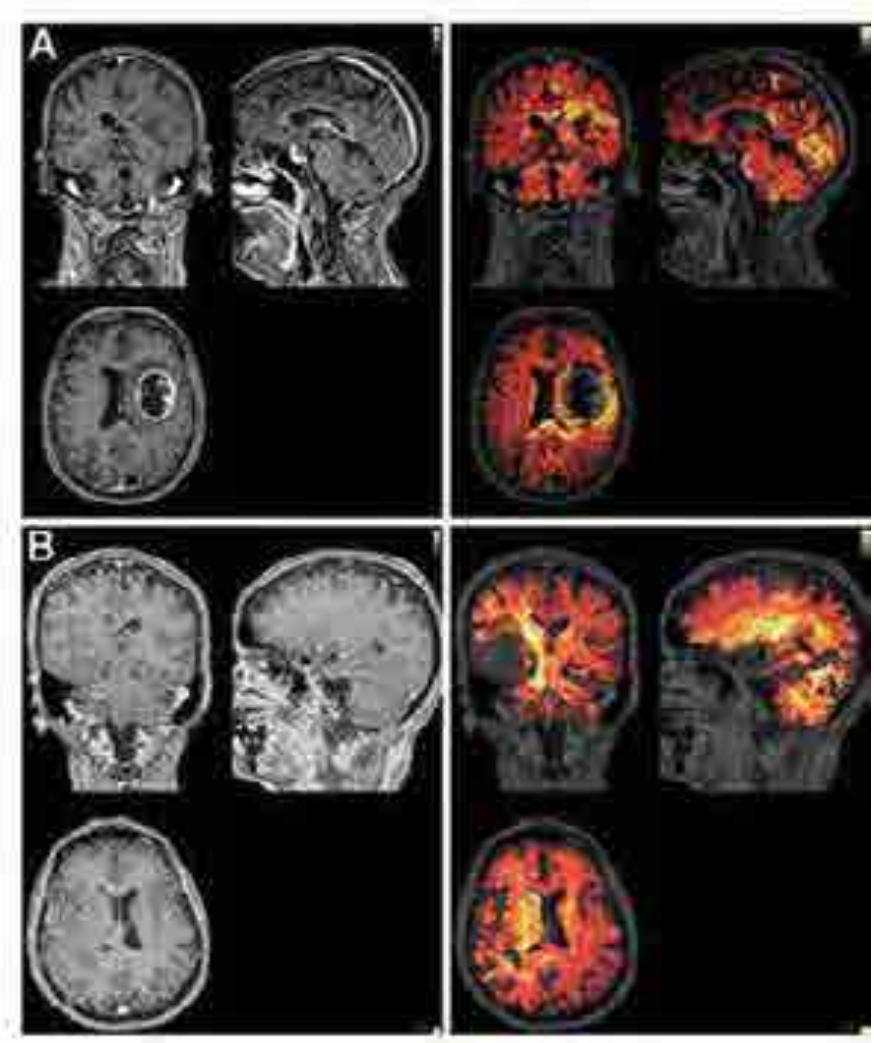

Figure1 Demonstration of the T1w images and obtained anomaly map. A) 73 years old female patient with glioma WHO grade IV. B) 57 years old male patient with glioma WHO grade III

Gliome Imaging II/*Glioma Imaging II*

V175

Multi-task fMRT-informierte Traktografie für die Resektionsplanung sowie zur Leitung von dynamischem intraoperativen Mapping und Monitoring bei Gliomresektionen im Wachzustand

Multi-task fMRI-informed tractography to inform resection planning and intraoperative mapping and monitoring during awake glioma surgery

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Objective

In brain tumour surgery, the need of maximised resection has to be balanced against the risk of functional damage. Lesions to important white matter connections are critical with regard to permanent deficits, e.g. of communication functions. Here, we present the clinical experience of using multi-task fMRI-informed tractography to plan resection of brain tumours adjacent to cognitive networks and to guide task selection during awake surgical mapping and monitoring.

Methods

A consecutive series of 25 patients with intrinsic brain tumours in eloquent locations were investigated preoperatively by 3T fMRI and diffusion imaging (DTI). Patients underwent two language / cognitive tasks: overt picture naming (PN) and forced choice (i.e., selection of a semantically related object) via left-handed button press triggered by an auditorily presented sentence. The BOLD activations were analysed in SPM 12 to calculate the laterality indices whenever clinically relevant, and to define the starting/ending regions of interest (ROIs) for tractography. DWI data were preprocessed in FSL. Tractography was performed using a probabilistic algorithm in MRtrix.

Results

Feasibility was excellent, i.e., exams were well tolerated and could be performed adequately by all patients. The results pointed towards a relatively robust identification of language laterality using the combined clusters of the inferior frontal gyrus (IFG) and the angular gyrus (ANG) based on the forced choice (semantic decision) task. Moreover, we observed an overall very good agreement between our preoperative results and the intraoperative findings during awake surgery, using cortical and subcortical direct electrical stimulation. However, more subtle language-related neurocognitive functions such as verbal fluency and verbal working memory are more difficult to monitor, although relevant, and call for dynamic adjustment of the monitoring tasks, dependent on the network structures at risk during the respective surgical step. This was illustrated by a subset of three patients where fMRI-informed tractography depicted the frontal aslant tract at high surgical risk.

Conclusion

Based on our preliminary experience, multi-task fMRI-informed tractography could represent a powerful tool to optimise surgical decision making and intraoperative guidance, even in cases where the complexity of the functions at risk pushes towards the limits of intraoperative monitoring.

Gliome Imaging II/*Glioma Imaging II*

V176

Resting state fMRT als Ersatz für aufgaben-basiertes fMRT in der Operationsplanung für Gliompatienten?
Resting state fMRI as a substitute for task-based fMRI in treatment planning for glioma patients?

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Objective

The preservation of white matter tract integrity during brain surgery is essential for preserving the patient's cognitive functions. Fiber tracking, using diffusion weighted MRI, informed by cortical mapping, e.g. using functional MRI (fMRI), has been established to explore individual structural connectivity for treatment planning. Task-related fMRI, however, demands active participation by the patients as well as special technical and personnel resources. Applying resting state fMRI (rs-fMRI) instead, can greatly reduce those demands. Therefore, we here explored the usability of rs-fMRI to inform tractography and treatment planning as compared to task-based fMRI.

Methods

Twelve patients scheduled for glioma surgery (6 females, 6 males, age 45 ± 15 yrs) underwent fMRI including two language task-related fMRIs (7 mins & 111 scans each), a rs-fMRI (6 min, 300 scans) and diffusion imaging. One task required overt production of language triggered by object drawings from the CoNaT battery (i.e., picture nam- ing). In the other task patients were asked to listen to a sentence and select one of three presented images matching to the sentence via button press. Task fMRI was an- alyzed using SPM12. Diffusion image processing and rs-fMRI analysis was done in FSL. Similarity between fMRI task activation and resting state network (RSN) maps was as- sessed by Dice coefficient. To compare the utility of both maps for fiber tracking, indi- vidual clusters of each seeded probabilistic tracking using MRtrix, and the trajectories of the resulting tracts of each group were compared.

Results

Dice similarity between the language network map derived from ICA and language task activation maps reached 18±4%. RSNs provided less differentiation between individual regions, depicting comparatively extensive functional network clusters. How- ever, RSN also revealed functional networks to which the task-related fMRI analysis was blind, such as the default mode network. In summary, task-related fMRI allowed for a more specific information of the structural network analysis by seed-based tractography.

Conclusion

Rs-fMRI analysis is a straight-forward tool to examine a wide variety of functions in a single examination of minimized demands. Compared to task fMRI, results are less specific to very particular functions and more challenging to interpret. Where a general overview is sufficient, or patients are not eligible for task-related fMRI, rs-fMRI can be a valuable alternative.

Gliome Imaging II/*Glioma Imaging II*

V177

Störung der funktionellen Konnektivität zum Zeitpunkt der Diagnose ist prognostisch für progressionsfreies und Gesamtüberleben bei Glioblastompatient:innen

Disturbance in whole brain functional connectivity at diagnosis is prognostic of progression free and overall survival in glioblastoma patients

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Objective

Glioblastoma is a systemic brain disease with tumor cells infiltrating the brain far beyond the macroscopically visible tumor. This leads to disturbance in global functional connectivity (fc). Here, we investigated whether the degree of disturbed fc at diagnosis was indicative of whole brain disease burden and thus prognostic of progression free and overall survival (PFS and OS).

Methods

26 patients with newly diagnosed glioblastoma (WHO 2021) were prospectively enrolled. All patients underwent resting-state functional MRI (rsfMRI) and disturbance of whole brain fc was quantified using our recently published marker called the dysconnectivity index (DCI). Higher DCI values indicated more disturbance of functional connectivity. Furthermore, clinical data was recorded.

Results

Mean age was 64 years, 8 patients were female, 16 male. Median follow-up was 13.6 months. 24 patients had tumor progression during the observation period, median PFS was 8.2 months. 19 patients died during the observation period, median OS was 13.4 months. 9 patients had a stereotactic biopsy, 17 were resected. Univariate cox regression models showed that higher disturbance of global fc in both the lesional and the contralesional hemisphere were associated with lower PFS ($p<0.0001$) and lower OS ($p<0.0001$). This held true in multivariate analyses which accounted for potential confounders (age, KPS, tumor volume, resection status, MGMT promoter methylation).

Conclusion

The degree of disturbance of fc in glioblastoma patients at diagnosis as determined by our imaging maker (DCI) was associated with PFS and OS in a highly significant manner. This suggests that higher DCI values at diagnosis could indicate more advanced disease burden of the whole brain which in turn results in worse PFS and OS. We therefore propose to conduct further prospective and longitudinal studies to investigate how fc-based technologies could be used to tailor tumor-specific therapy to the individual disease burden of glioblastoma patients.

Gliome Imaging II/*Glioma Imaging II*

V178

Analyse der präoperativen Wachstumsrate von Glioblastomen - Korrelierende Faktoren und Auswirkungen auf das postinterventionelle Überleben

Analysis of the preoperative growth rate of glioblastoma – Correlating factors and impact on postinterventional survival

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Objective

Patients with lesions suggestive for glioblastoma (GBM) are usually referred to surgical therapy rapidly. Little is known about the natural growth of these tumors. The aim of this study was to analyze preoperative growth rates, correlating factors and the possible impact on overall survival in GBM.

Methods

Data from 749 adult patients with a diagnosis of glioblastoma, IDH-wildtype, CNS WHO grade 4, operated on in our hospital during 2010-2020 were analyzed for the availability of 2 preoperative cerebral MRI scans with untreated, contrast-enhancing tumor and a maximum slice thickness of 1 mm (3D-data). The shortest interval between MR-imaging was set at 7 days. Tumors were segmented semi-automatically with manual correction and volumes were calculated. Growth between MRI-examinations was assumed to be exponential, and the growth rate was calculated accordingly as volume doubling time (VDT; in days) and specific growth rate (SGR; percent growth per day). Potential correlating parameters and impact on postoperative survival were investigated.

Results

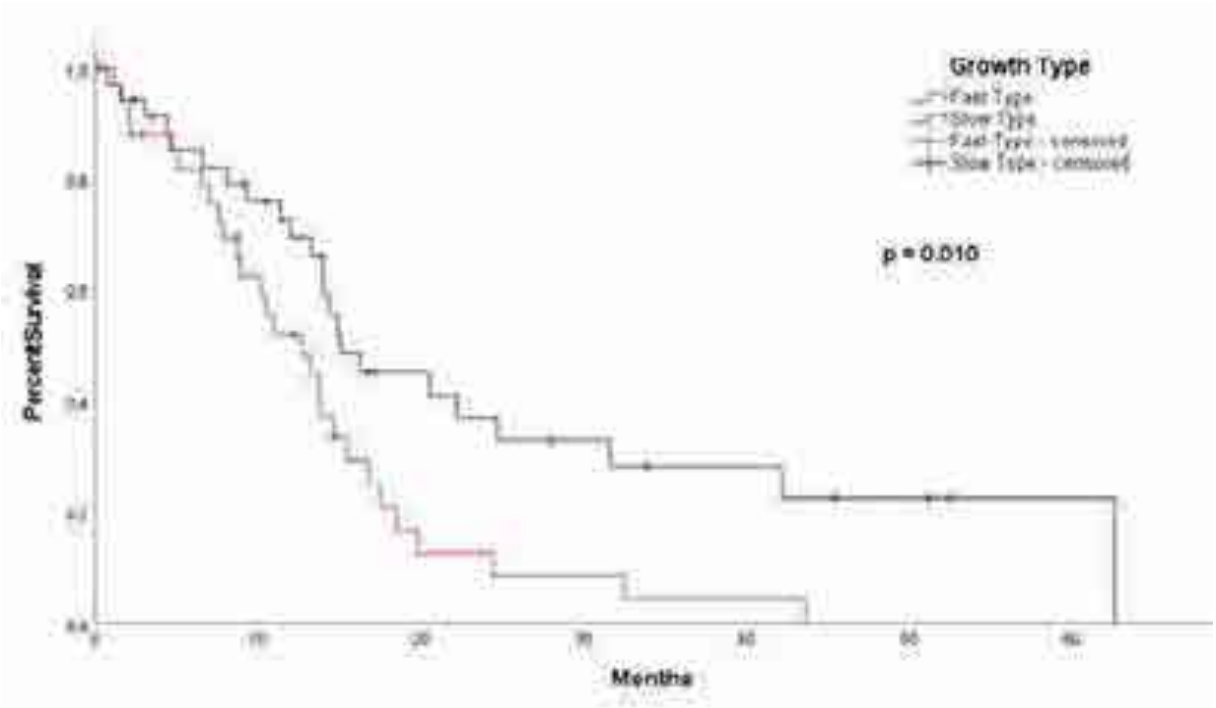
70 patients met the inclusion criteria. Median VDT was 30.6 days, median SGR was 2.2%. SGR showed a negative correlation with tumor size. Two groups of growth rate were determined according to the median SGR. Overall survival after intervention was significantly longer in the group with slow growth (mean: 18.6 months), compared to the fast group (mean: 11.5 months). Kaplan-Meier Curves showed significant survival benefit for patients in the slower growth type group. In subanalysis, this superior survival could only be shown for patients with resection, but not for patients undergoing biopsy and adjuvant therapy without any tumor debulking. Higher SGR was independently associated with shorter overall survival in multivariable Cox-regression models, including extent of resection and MGMT status.

Figure 1: Survival for growth groups "Slow Type" (n=35) and "Fast Type" (n=35) after surgical intervention on GBM (log-rank test: p = 0.010)

Conclusion

The data from this study suggest that early referral for surgery is critical for newly detected contrast-enhanced lesions suggestive of GBM, especially in smaller tumors. Preoperative growth rate was significantly associated with survival after surgical resection, independently of additional factors analyzed. With these findings, additional subclassifications and molecular analysis with highly relevant predictive values might be possible in the future.

Abb. 1


Growth Type
Fast Type
Slow Type
Fast Type - censored
Slow Type - censored
p = 0.010
Percent Survival
Months

Gliome Imaging II/*Glioma Imaging II*

V179

Exponentielles Tumorwachstum bei humanen Glioblastomen - Eine MRT-volumetrische Studie
Exponential tumor growth in human glioblastoma - A MRI-volumetric study

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Objective

Tumor growth of various tumor types has been studied and found to be exponential or gompertzian with a natural limitation. However, this may not be true for an infiltrating tumor with a necrotic, non-vital component such as glioblastoma (GBM). As the untreated life expectancy of these tumors is very poor, patients are usually referred to therapy rapidly. Therefore, only little is known about untreated human GBM growth in vivo to date. With this study, we aimed to investigate the natural tumor growth of GBM before treatment using tumor volumes of patients who had at least 3 preoperative sequential MRI examinations.

Methods

749 adult patients operated in our hospital between 2010-2020 for confirmed supratentorial GBM, IDH-wildtype, CNS WHO grade 4, were screened for the availability of 3 or more preoperative MRI scans with contrast-enhancing lesions. Patients with any surgical treatment between scans were excluded. Tumors were segmented, and volumes were calculated. Growth curves of absolute and relative tumor volumina were visualized and the coefficient of determination R^2 was calculated for trendlines (linear and exponential).

Results

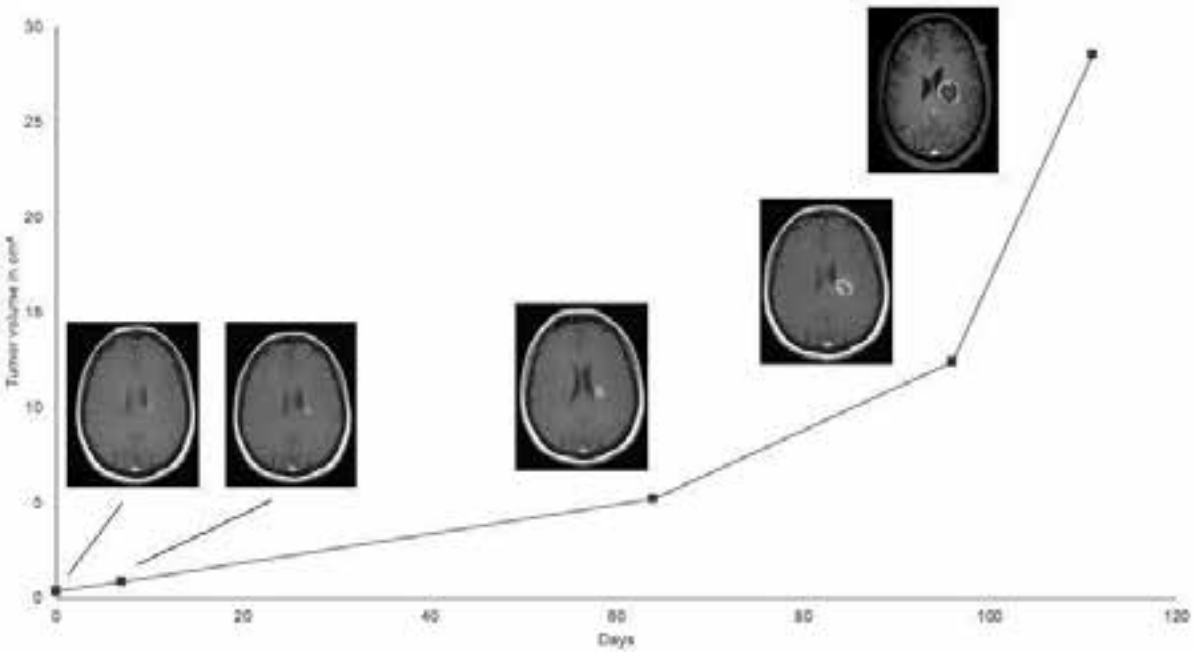
13 patients were identified with 3 or more sequential MRI scans without any treatment in-between. 11 patients had 3 preoperative MRI scans, 2 patients had 5 sequential MRI examinations each. Tumor volume curve graphs visually showed exponential growth in 11 patients with a good fit of the exponential trend lines. Volumes of all but one of the tumors were rather small (< 3cm³, median: 0.68 cm³; range: 0.10 cm³ – 39.96 cm³) at the first MRI examination. Reasons for multiple preoperative MRI examinations varied among patients, such as initial wrong differential diagnosis or postponement of surgery at patients' request. Comparison of growth rates between tumors showed strong variability, with tumor volume doubling rates between 5.7 and 192.5 days.

Figure 1: Example of exponential growth of a GBM in a patient, initially diagnosed with multiple sclerosis.

Conclusion

This is the first study to prove an exponential tumor growth in untreated human GBM in vivo with highly variable growth speeds. Further analysis with larger cohorts and additional molecular analysis might enable subgrouping of GBMs according to their growth speed, which might be a relevant predictive factor.

Abb. 1



Neurovaskuläres Imaging/*Neurovascular Imaging*

V180

Der Einfluss von Läsionstyp und Läsionsort auf die Vorhersage von Sprachlateralisierung bei Patienten mit zerebralen vaskuläre Läsion anhand von funktioneller Magnetresonanztomographie (fMRT)

The influence of lesion type and lesion location on the prediction of language laterality in patients with cerebral vascular malformations using functional magnetic resonance imaging (fMRI)

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Objective

The prediction of language lateralisation in patients with cerebral vascular malformations close to language areas prior to intervention is essential for diagnostic and treatment decisions, as well as it improve patients" outcome. Different works raise drawbacks influencing the prediction of language dominance in patients showing cerebral vascular lesions close to language critical areas using fMRI because of potential remodelling processes or hemodynamic phenomena. This study further compares language laterality indices (LIs) in patients with arterial venous malformations (AVM) and cavernoma in dependency of lesion location in order to investigate a potential impact of lesion type and lesion location on language laterality prediction using fMRI.

Methods

22 patients with AVM (5 patients with lesion in the frontal lobe), 11 patients with cavernoma (4 patients with lesion in the frontal lobe) and 15 healthy control subjects were included in this study. During language fMRI patients performed a subvocal verb generation task. Data analysis was conducted by using SPM12 comprising realignment, coregistration and smoothing for preprocessing. Whole brain analysis was performed using the general linear model approach on individual level. Laterality indices (LIs) calculated using the LI-toolbox implemented in SPM independently on the basis of the frontal, the temporal and the parietal lobe. Differences between lesion type and lesion location (frontal and non-frontal lesions) were assessed by using non-parametric t-tests.

Results

Qualitatively, the absolute LIs showed values above 0.2 independently of lesion location in all groups. On individual level, calculated LIs were below 0.2 in 3 (6.3 %), 9 (18.8 %) and 2 (4.2 %) patients referring to the frontal, temporal and parietal lobe respectively. Between the patient groups there were no significant difference in absolute LIs according to lesion type. Compared to healthy controls only patients with frontal AVMs showed significantly lower LIs when LIs were calculated for the frontal lobe ($p=0.019$, $r=0.43$) and for the parietal lobe ($p=0.015$, $r=0.44$). Patients with lesions in other locations than the frontal lobe did not significantly differ from healthy controls.

Conclusion

The results of this study suggest a mild influence of lesion location on language laterality prediction where patients with frontal lesions exhibit lower LIs than healthy controls, but no influence of lesion type on language laterality prediction.

Neurovaskuläres Imaging/*Neurovascular Imaging*

V181

Präoperative Planung bei AVMs: Bildgebung und 3D Visualisierung
Preoperative Planning in AVM surgery: Imaging work-up and 3D visualization

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Objective

Surgery of arteriovenous malformations of the brain (avm´s) are challenging due to their complex angioarchitecture, hemodynamics and potential location close to eloquent regions. Therefore, surgical indication and successful treatment is largely dependent on a thorough understanding of the avm´s vascular anatomy and its relationship to eloquent brain regions and fiber tracts on preoperative imaging. In this study, we show our preoperative work-up for brain avm´s on the bases of cases from daily practice including 3D visualization (3D) and virtual reality (VR) visualization for superior image data presentation.

Methods

3D digital subtraction angiography (3D-DSA), time resolved MRI (TWIST), functional MRI (fMRI) and diffusion tensor imaging sequences (DTI) were acquired from six patients suffering from brain avm´s at our institution during preoperative workup. Segmentations of brain tissues and skull were done with FAST (FMRIB's Automated Segmentation Tool, Oxford, UK) and Amira (Thermo Fisher Scientific, Massachusetts, US). Composition and 3D visualization was performed with our newly in-house developed software. A cross platform game engine (Unity Technologies, San Francisco, US) was used to create a 3D environment for VR.

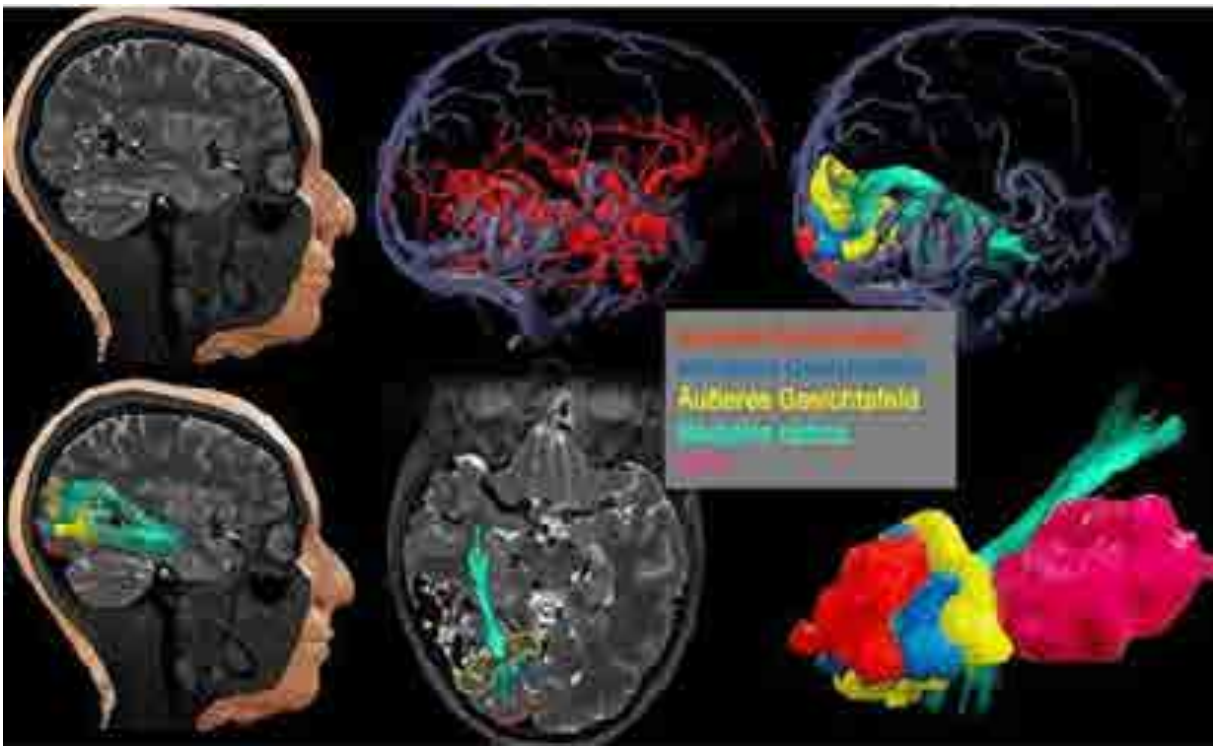
Results

3D-DSA allowed for superior 3D segmentation of the avm´s angioarchitecture, TWIST was used to differ arterial feeders from venous drainage, fMRI and DTI revealed eloquent speech, motor and visual networks. By the means of six concrete avm case-studies we illustrate the advantages of planning in 3D and VR: intuitive and fast understanding of complex anatomical and functional relations, in particular arterial feeders, nidus, related aneurysms, venous drainage and eloquent regions. Intraoperative findings by photos, videos and Doppler ultrasound document the correlation of preoperative planning and surgical reality.

Conclusion

Due to the outstanding presentation of complex image data, 3D and VR is particularly suitable for individual surgical planning of avm´s. It can improve the understanding of the complex angioarchitecture and its relationship to critical structures. We propose a routine imaging workup for the surgery of avm´s including 3D-DSA, TWIST-MRI, fMRI and DTI. This data should be segmented and visualized in a 3D or VR viewer to provide anatomical angioarchitecture and functional information at best. This helps the neurosurgeon to make an indication, to select the right approach and dissection strategy and to avoid pitfalls.

Abb. 1



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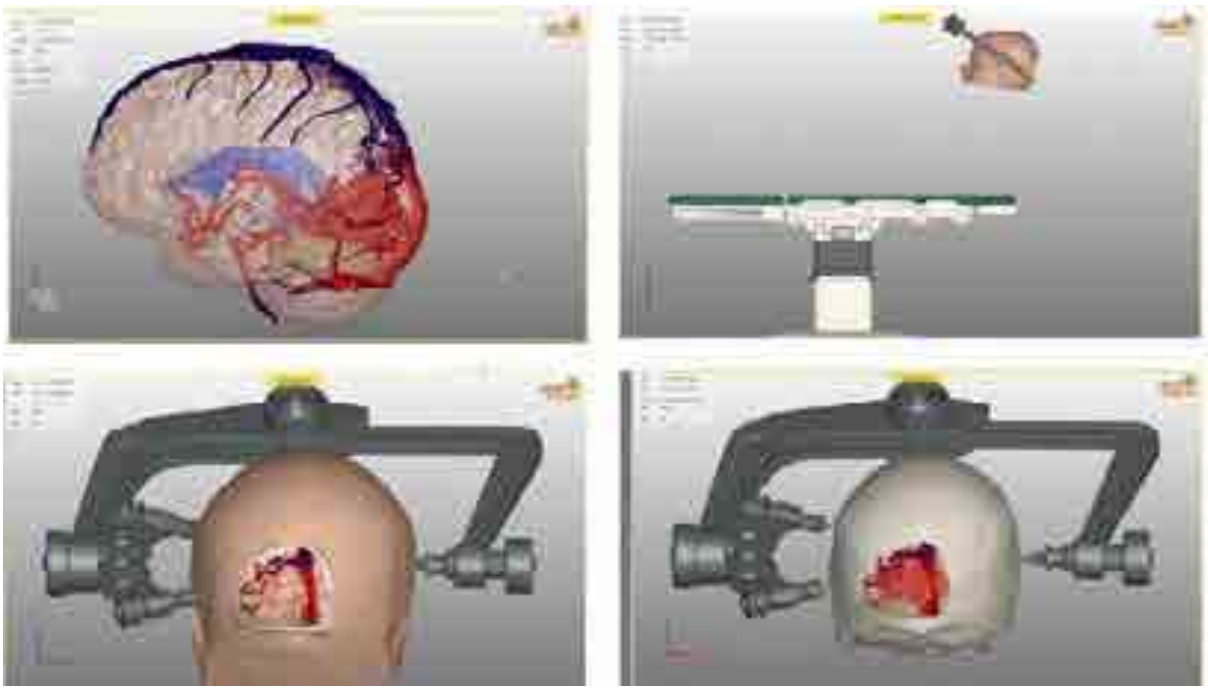

Neurovaskuläres Imaging/*Neurovascular Imaging*

V182

Deep Learning basierte ganzhirnvolumetrische Analyse bei erwachsenen Patienten mit Moyamoya Angiopathie und altersentsprechender Vergleich mit einem Normkollektiv

Deep learning based whole-brain volumetric analysis in adult patients with Moyamoya angiopathy and age-matched comparison with healthy controls

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Objective

Moyamoya angiopathy (MMA) may lead to perfusion deficits, stroke and brain atrophy in the long term. To date only very little is known about quantification of brain-volumetric changes in MMA patients. We aimed to analyze whole brain volumetrics of a large cohort of MMA patients compared to healthy controls by deep learning based algorithms and to correlate the results with other imaging modalities and clinical data.

Methods

3D T1w MRI sequences of all adult MMA patients treated at our center between 2016-2022 without prior revascularization were analyzed for whole-brain segmentation (AssemblyNet) and compared age-matched to a healthy collective. In total, 133 different regions of interest (ROI) were examined in each patient by structure and tissue type separately for subcortical and cortical localization. All segmentations were subjected to manual quality control.

Results

82 adult patients with MMA and 129 healthy controls were analyzed. 22.0% of all MMA patients did not show any infarctions on MRI and had comparable brain volumes to the healthy cohort. Significant decrease of brain volume was seen for cortical (2.79% [CI95% 1.08–4.49]) and subcortical gray matter (5.31% [CI95% 1.54–9.09]), as well as white matter (2.76% [CI95% -0.28 – 5.80]) analysis in MMA patients. The largest decrease in total cerebral volume was found in MMA patients between 30-45 years with a mean loss of 2.65% [CI95% 0.67–4.63], between 45-60 years with 2.79% [CI95% 0.85–4.73] and 9.00% (CI95% 0.20-17.81) for hemispheres with ischemia. We saw a mean increase of external CSF space of 16.7% (CI95% 7.8-25.7) as an indirect sign of brain atrophy, which did not correlate with the Suzuki grade, while the decrease in white matter correlated with grade of infarctions seen on FLAIR (Fazekas score) ($p<0.05$). 42.7% of MMA patients were affected unilaterally and showed a significant mean cerebral volume loss of 2.3% in the affected hemisphere compared with the unaffected contralateral side. The validity check with infratentorial ROIs did not show significant volume deficits, as expected.

Conclusion

MMA patients exhibit significant brain volume differences of local and global ROIs compared with healthy controls. Deep learning segmentation enables such volumetric analysis quickly and will provide a broader understanding of disease dynamics. This might also support decision-making when indicating bypass surgery and help to understand differences of outcome after revascularization.

Neurovaskuläres Imaging/Neurovascular Imaging

V183

Deep Learning basierte Ganzhirnvolumetrie bei erwachsenen Patienten mit Moyamoya-Angiopathie und Korrelation mit neuropsychologischen Defiziten

Deep learning based whole brain volumetrics in adult patients with Moyamoya angiopathy and correlation with neuropsychological impairment

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Objective

Adult patients with Moyamoya angiopathy (MMA) have an increased incidence of neuropsychological impairment (NI), primarily of executive functions. Preliminary work showed a correlation with the affected vascular territories. However, NI has not yet been analyzed in context of brain volumetric changes. Therefore, we aimed to correlate NI results of a large European cohort of MMA patients with a comprehensive data-set of their respective whole-brain volumetric (WBV) analyses.

Methods

All adult MMA patients treated at our center between 2016 and 2022 without previous revascularization and availability of our standardized routine NI assessment, as well as 3D T1w MRI sequences were included. In these patients 133 distinct regions of interest (ROIs) were evaluated using deep learning based WBV (AssemblyNet). For executive function testing, the NI battery included the Trail Making Test A (TMTA, psychomotor processing speed)) and B (TMTB, mental flexibility), as well as the d2 test (d2, selective attention) and the Chapuis Maze (ChL, problem-solving ability). Dysexecutive syndrome (DCS) was defined as ≥ 2 abnormal test results.

Results

A total of 62 adult MMA patients (female-to-male ratio 2.4:1, median age 46 years (16-47), mean IQ 102.7 ±14.2, median NIHSS 0 (0-8)) with baseline neuropsychological assessment underwent WBV testing. DCS was present in 50.8% of cases and was statistically independent of neurological functioning (NIHSS). In contrast, WBV revealed a significant ($p<.001$) loss of mean cerebral volume of 4.9% (CI95% 2.2-7.5) in patients with DCS, which was aggravated when analyzing the mean cerebral white matter only (cWM) with a loss of 7.9% (CI95% 3.4-11.1; $p<0.001$), compared to patients without DCS. Interestingly, DCS was found significantly ($p<.01$) more likely in patients with volume loss in the right transverse temporal gyrus (20.4% (CI95% 4.8-35.9)), compared to the left side. Significant volume reductions ($p<.05$) were observed for the right versus left side of patients with abnormal TMTA, TMTB and ChL test results, particularly in temporal and temporomesial ROIs.

Conclusion

Impaired executive function in adult MMA patients is commonly seen. Interestingly, neurological function (NIHSS) did not correlate, but volumetric changes and the resulting brain atrophy did. This is the first time to show such association in a large data-set of MMA patients. Further research will help to better understand NI and to possibly prevent its development by timely revascularization.

Neurovaskuläres Imaging/*Neurovascular Imaging*

V184

Die klinische Auswirkung von nTMS basierte DTI in chirurgischer Therapie von pontinen cavernösen Malformationen

The clinical impact of nTMS based DTI in pontine cavernoma surgery

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Objective

Introduction: Brainstem cavernous malformations (BSCMs), mostly located in the pons, are challenging to treat due to their anatomical proximity to different cranial nerve nuclei and ascending and descending neural tracts. The current study aims to evaluate the utility and clinical impact of nTMS DTI in the resection of pontine cavernoma.

Methods

Methods: We analyzed retrospective data of 38 patients (mean age 38 years, range 19-72 years; 18 female) operated on pBSCM in our department. The resting motor threshold (RMT), recruitment curve (RC) and the cortical representation area of hand, leg and facial function were determined MEP-positive stimulation spots were then imported into the fiber tracking software and set as seed points for tractography. All surgical approaches were tailored based on preoperative nTMS-DTI examination.

Results

Results: This study proves that through the preoperative visualization of motor tracts by nTMS -DTI, an individually tailored approach is associated with a favorable postoperative outcome (mean mRS score of 1,37 at 3 months follow up). Higher preoperative RMT values were associated with a postoperative motor deficit ($p<.05$). Also, a higher RMT level correlated with a lower FA threshold ($p<.05$) revealing structural impairment of the CST already prior to surgery.

Conclusion

Conclusion: NTMS based fiber tracking enables objective somatotopic tract visualization on the pontine level and provides a valuable instrument for preoperative planning, intraoperative orientation and individual risk stratification. NTMS, thus, may increase safety of surgical resection of brainstem cavernomas.

Neurovaskuläres Imaging/*Neurovascular Imaging*

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

V187

Tiefe Hirnstimulation im Nucleus Subthalamicus - Vorteile oder Wunder der direktionalen Elektroden?
Deep Brain Stimulation of the Subthalamic Nucleus – Advantages or Miracles of Directional Leads?

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Objective

Deep brain stimulation (DBS) with directional leads has recently been reported to provide wider therapeutic windows and to be the preferred variant in a cross-over study with blinded patients and clinicians in STN DBS for Parkinson"s Disease (PD). This study focusses on the clinical and programming differences in omnidirectional versus directional leads.

Methods

A consecutive group of 43 patients implanted with pulse generators with multiple independent current control (MICC) and comparable lead constructions, either conventional omnidirectional (c-lead, 19 patients) or directional leads (d-lead, 24 patients) and comparable disease characteristics were analyzed for lead position, motor outcome and programming parameters.

Results

Comparison of both groups showed significant difference of age (c-lead 55.9y vs d-lead 64.4 y; p<0.01). In both groups similar precision of lead position was achieved (p=.366). Disease severity was comparable for both groups with pre-operative UPDRS-III Med-off at 40.9 vs. 41.6 points. Patients" UPDRS-III scores improved to similar extents in both groups with a Stim-ON/Med-OFF improvement of 75% of the initial levodopa response. At one year follow-up, 20 of 48 D-leads were activated in ring mode and 28 in directional mode (57%). Besides horizontal steering, 11 d-leads were activated also in vertical steering mode. C-mode stimulation needed larger stimulation amplitudes than d-mode (3.7 vs. 2.9 mA, p = .04) and larger stimulation frequencies (160 to 169 Hz vs. 144 Hz, p 0.004).

Conclusion

This retrospective analysis provides a first comparison of conventional versus directional DBS leads with MICC. The overall clinical outcome by UPDRS-III was well comparable; this is nonetheless remarkable, as the d-lead group was significantly older and suffered at a longer disease duration. In view of smaller lead contacts and higher electrode impedances in d-leads, the stimulation amplitude was smaller in this group, similar to some previous results. Further this is one aspect contributing to a larger therapeutic window by directional stimulation, besides the more individual shaping of VTAs. In the d-lead group, in 75% of the patients at least one lead with horizontal steering was used for the best clinical effect at one year f-u indicating a benefit of this programming option. Still, the option of applying lower DBS stimulations rates in d-leads, appears as an interesting factor, possibly resulting from a more efficient stimulation mode.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

V189

Vorläufige Daten suboptimaler Ausrichtung von stereotaktischen Lokalisierungsscans unter Verwendung einer mobilen CT-Anwendung

Preliminary Data on suboptimal planar alignment of stereotactic localizing scans with the use of a mobile CT application

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Objective

Localizing scans (LSC) are essential for stereotactic procedures. The transportation to stationary CTs is accompanied with associated risks as well as prolongation of the procedure. Correct planar alignment of LSC can cause further time delay. Hence, we sought to develop a LSC workflow with a mobile CT (mCT) in an experimental Operating Room to investigate the process time and the influence of planar alignment on target accuracy.

Methods

The workflow was carried out in an experimental Operating Room using a stereotactic frame (Leksell Vantage, Elekta, Stockholm, Sweden) a stereotactic phantom (Brainlab, Munich, Germany) and the Brainlab Airo-CT. The total process time (TPT) from frame mounting to localizing scan was measured and segmented to quantify individual parts of the workflow. To measure accuracy of the LSC, computed deviation of the Brainlab planning software was used. Test trajectories were planned and visualized with the mCT while a biopsy needle was inserted. By default, LSC were leveled in every plane. Intentional alignment errors (IAE) were created through coronal or sagittal tilt as well as a series only aligned by sense of proportion.

Results

The LSC workflow was completed 27 times with TPT data included from n=23. The mean TPT was 10.8 min with a mean/max deviation of 0.25/0.69 mm. TPT was inversely correlated with the number of LSC workflow sessions (NLR, Exponential Plateau: R^2= 0.81; TPT0= 13.8 min; TPTM=9.81 min). TPT reduction showed subtle association with higher mean deviation (SLR: R^2= 0.27, p=0.01) but not with maximum deviation. Computed deviations were sufficient to hit the target with test trajectories (n=27/27). IAE (coronal/sagittal and sense of proportion) caused significant increase in mean deviation (p=002, p=0.001, p≤0.001) but no increase in max deviation (p>0.5) compared to a set (n=10) of identical aligned LCS. The mean deviation remained below 0.3 mm regardless of the scenario.

Conclusion

The relative time reduction of 29% (TPT0/TPTM) shows that implementation of a mCT LSC workflow offers a fast learning curve. Potential time savings may benefit the patient as well as hospital economics. Even though IAE affected the mean deviation, absolute values were rather small. Moreover, no influence on maximum deviation was seen, leaving LCS with suboptimal planar alignment adequate for stereotactic use. This preliminary data indicates that suboptimal planar alignment of LSC can be compensated and has negligible impact on stereotactic accuracy.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

V190

Perivaskuläre Räume als Risikomarker für intracerebrale Blutungen bei DBS-Implantation – eine retrospektive Analyse

High burden of perivascular spaces as a potential risk marker for intracerebral hemorrhage in DBS surgery – a retrospective investigation

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Objective

Cerebral intraparenchymal hemorrhage due to electrode implantation (CIPHEI) has been associated with higher age, use of microelectrode recording and directional DBS electrodes (Sajonz et al. in preparation). Perivascular spaces (PVS) have been associated with spontaneous intracerebral hemorrhage (Duperron et al. 2019) and vascular events (Gutierrez et al. 2017) and may signal a general vascular vulnerability. We thus investigated the role of PVS as a risk indicator for CIPHEI.

Methods

Retrospective analyses of suitable (3 Tesla, no artifacts) preoperative MRI prior to DBS implantation (01/2013-12/2021) comprised PVS burden quantification by the commonly used Frangi-filter for tubular structures (smin=0,4mm, smax=2,0mm, scale ratio=2, α=0,1, β=1, c=0,01) on the normalized T2w isotropic data (Frangi et al. 1998) (Fig. 1). A PVS index was computed by a simple summation of all non-negative filter responses within supratentorial white matter separately for both hemispheres. Postoperative CT scans were assessed for hemorrhages. Data analysis was based on the generalized linear model for binomial responses (BR-GLM) using the bias reduction approach developed by Firth (1993) to account for sparse sampling of CIPHEI. Adjustments of PVS for non-linear effects of age and other potential confounds were performed using a generalized additive model.

Results

305 suitable cases were included with 17 CIPHEIs observed in 13 procedures (Fig. 2). The corresponding odds ratio for CIPHEI is 2.89 [95% confidence interval 1.09-9.66, $p = .041$] for adjusted PVS above average. The odds ratio for adjusted PVS below average as baseline reference is 0.02 [0.01-0.04, $p < .001$]. Extending the BR-GLM model of above-average PVS by the multiplicative term of above-mentioned risk factors the odds ratio is 23.59 [8.69-81.59, $p < .001$].

Conclusion

Our findings indicate that high burden of PVS may represent a further risk factor for CIPHEI. The risk factor combination, namely higher age, use of microelectrode recording and directional DBS electrodes, with a high burden of PVS should be carefully evaluated considering the risk for CIPHEI.

Abb. 1

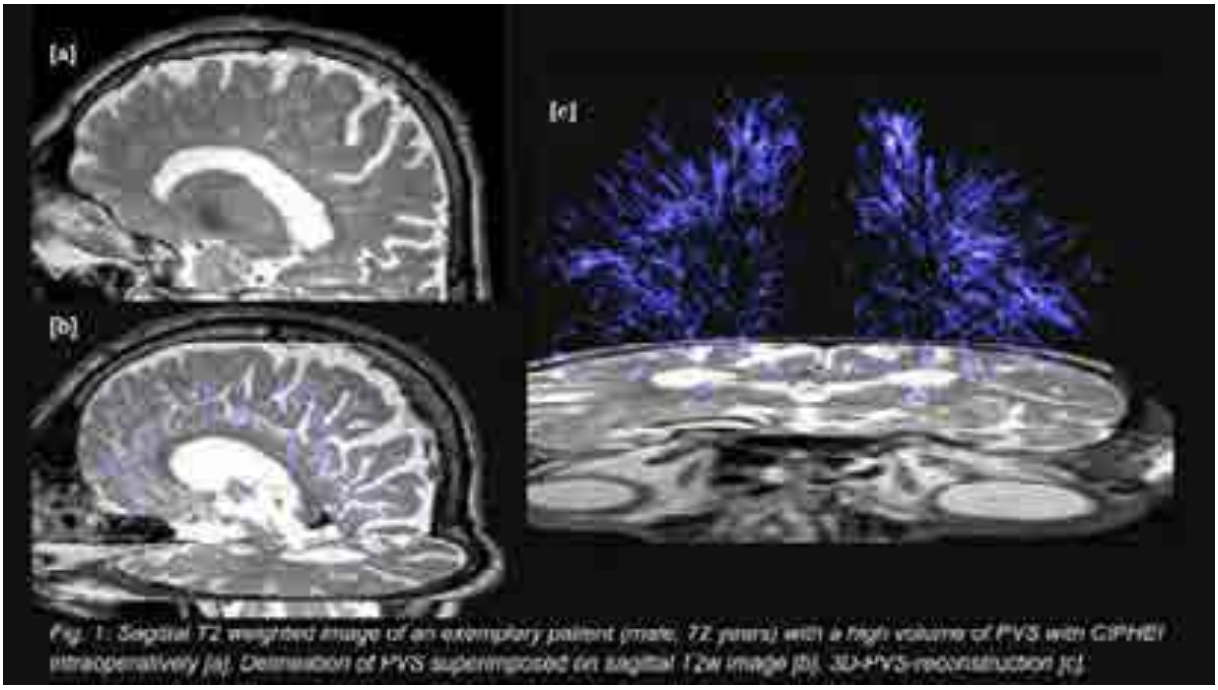

Fig. 1: Sagittal T2 weighted image of an exemplary patient (male, 72 years) with a high volume of PVS with CIPHEI intraoperatively (a). Delineation of PVS superimposed on sagittal T2w image (b). 3D-PVS-reconstruction (c).

Abb. 2

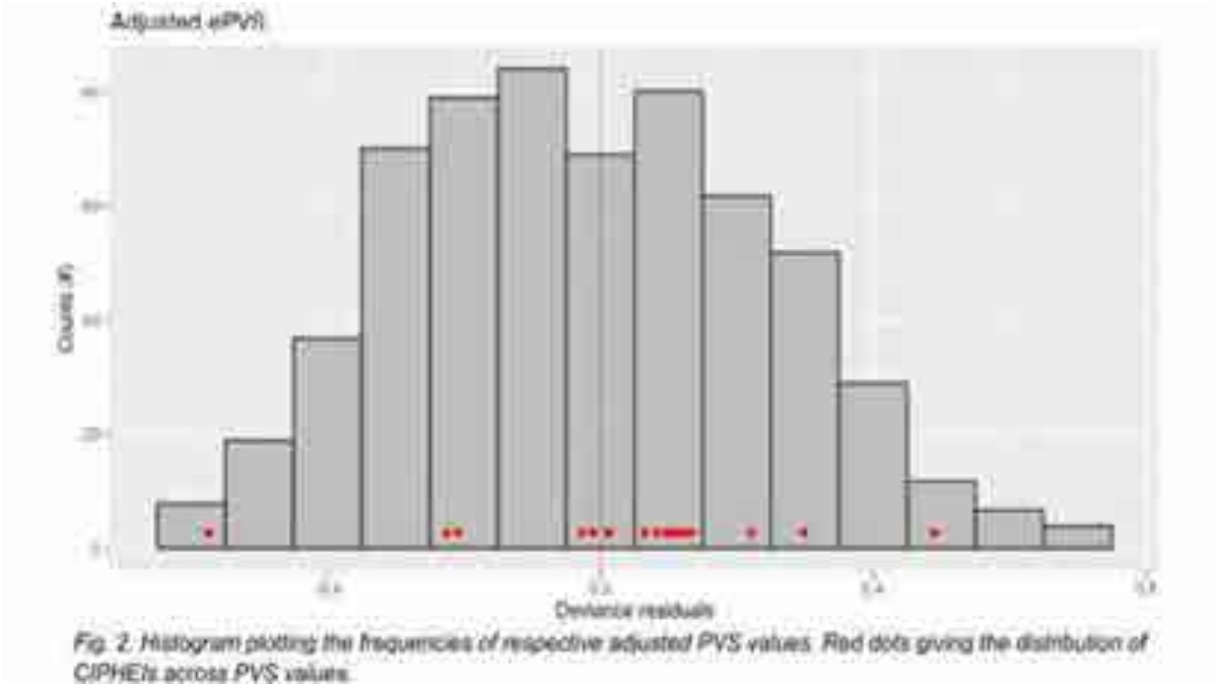

Fig. 2: Histogram plotting the frequencies of respective adjusted PVS values. Red dots giving the distribution of CIPHEIs across PVS values.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

V191

Idiopathisches Peri-Elektodenödem nach Tiefer Hirnstimulation – retrospektive Analyse
Idiopathic peri-electrode edema after deep brain stimulation – a retrospective analysis

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Objective

Though being a safe procedure, postoperative idiopathic peri-electrode edema (IPEE) edema surrounding the implanted deep brain stimulation (DBS) lead has been repeatedly reported in the literature and remains a phenomenon of unknown cause. This study is a retrospective analysis to identify the incidence, clinical features and possible underlying mechanisms or commonalities of (IPEE).

Methods

We performed data analysis including of all patients who underwent DBS implantation in the last 20 years at our department and identified all cases of IPEE as detected on postoperative imaging within the first 28 days of implantation. Demographic, clinical, radiological and surgery-associated data was collected and evaluated for association with IPEE.

Results

13 (5 female, 8 male; mean age 61 years) patients were identified with IPEE. 9 patients received bilateral STN DBS for Parkinson"s Disease and 4 patients received bilateral Vim DBS for essential tremor. IPEE occurred unilaterally in five patients and bilaterally in eight patients. In cases of unilateral edema IPEE was always observed around the first implanted electrode. The majority of patients (n=10) developed IPEE subcortically, whereas edema along the entire course of the electrode was present in 3 patients. Hemorrhagic transformation of IPEE was found in 3 cases. IPEE patients were implanted with leads from 3 different manufacturers. In 3 cases IPEE was asymptomatic. In the remaining cases patients presented with seizures (n=7), confusion (n=3) or speech difficulty (n=4). Symptomatic cases were detected usually in the early postoperative course (mean 9,9 days, range 4-23). 4 patients were treated with dexamethasone, 2 patients were treated with antiepileptic drugs and 2 patients were treated with both. 5 patients did not receive medical therapy, 3 of which were asymptomatic cases. Complete resolution of IPEE occurred within several weeks independently of treatment or location of edema. None of the cases showed any signs of infection or required surgical revision.

Conclusion

IPEE is a rarely reported complication of DBS implantation, presenting within the first weeks following surgery and a symptomatic or asymptomatic course. We could not identify common potential factors favoring the occurrence of IPEE although we have noticed a higher incidence in the last few years. Rigorous reporting and multicentric analysis might help to identify underlying factors to better understand the etiology of IPEE.

Chiari Verschiedenes Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Chiari Miscellaneous Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V192

Intrakranielle Arachnoidalzysten: Was ist die geeignete Operationstechnik? Eine retrospektive Vergleichsstudie mit 61 pädiatrischen Patienten

Intracranial arachnoid cysts: what is the appropriate surgical technique? A retrospective comparative study with 61 pediatric patients

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Objective

Symptomatic intracranial arachnoid cysts (ACs) should be treated either through microsurgical (MS) or endoscopic surgical (ES) fenestration, implantation of cysto-peritoneal shunt (CPS) system is another treatment option with decreasing indication. In our study, we compared the complication and revision rates between the three operative techniques in pediatric patients.

Methods

Patients below 18 years with symptomatic intracranial ACs operated between 2004-2021 were included. Initial symptoms, location, complication rate, clinical and radiological improvement, postoperative events and revision rate were compared retrospectively.

Results

Sixty-one patients; 33 (54.1%) MS operated (mean age 7.6 years), 18 (29.5%) ES operated (mean age 6.2 years) and 10 (16.4%) with CPS (mean age 3.0 years) were identified. The most common initial symptom was headache in 45.9%. 20 (32.8%) postoperative events were documented. The highest revision rate (60%) was seen in the CPS group compared to 33.3% in MS group and 16.7% in ES group. 31 patients harbored perisylvian ACs, 89% remained event-free after ES, 71% after MS and 20% after CPS. Clinical improvement immediately after surgery was observed in 58 patients (96.9 MS, 88.9% MS and 100% CPS). A radiological volume reduction could be proven postoperative in 51 patients (78.8% MS, 88.9% ES and 90% CPS).

Conclusion

Endoscopic or microsurgical fenestration of AC are both safe and efficient techniques. However, endoscopic technique showed longer event free survival compared to microsurgical one, especially in perisylvian arachnoid cysts. CPS shows on long terms the highest revision rate but carries the least surgical risks.

Chiari Verschiedenes Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Chiari Miscellaneous Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V193

Nicht-Invasive Erstdiagnostik und Monitoring in Patienten mit Pseudotumor cerebri.

Non-invasive first-line and follow-up diagnostic of patients with idiopathic intracranial hypertension (IIH)

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Objective

Idiopathic intracranial hypertension (IIH) is a disease associated with increased intracranial pressure (ICP) under absence of hydrocephalus or space-occupying lesion. For initial diagnosis and follow-up repetitive invasive lumbar punctures are often necessary to evaluate therapy success. Combined ultrasound-based measurement of optic nerve sheath diameter (ONSD) and third ventricle Diameter (TVD) is an ideal first-line tool, to diagnose possible ICP increases and exclude hydrocephalus. After treatment, repetitive ONSD determination can be used for control of therapy success.

Methods

12 adults (age-range 22-49 years) and 33 children (age-range 4-17 years) diagnosed with IIH were investigated. Ultrasound-based transorbital ONSD and transtemporal TVD measurements were performed initially and during the course of the disease repetitively. Individual ONSD values were compared to invasively measured ICP values to create inter- and intra-individual ONSD-ICP-correlation-curves and calculate ICP values according to ONSD.

Results

Initial ONSD mean value was 5.95 ± 0.34mm in the pediatric (normal values < 5.3mm) and 6.15± 0.41mm in adult (normal value < 5.5mm) patients. TVD values were always below 5mm in children and adults, excluding hydrocephalus. After any kind of therapy mean ONSD decreased quickly and significantly ($p< 0.01$) in the entire cohort and increased again with rising ICP. Intra-individual correlations of ONSD and ICP were outstandingly linear ($r= 0.95 - 1$, $p < 0.01$). We present a general equation to approximately calculate individual ICP values after ONSD determination.

Conclusion

Combined ultrasound-based ONSD and TVD measurement is an optimal first-line screening tool for IIH in pediatric and adult patients. ONSD can detect ICP increase, TVD can exclude hydrocephalus as underlying reason. Repeated ONSD measurements during IIH therapy can be used for control of therapy success as ICP values of individual patients can approximately be calculated using a general mathematical formula, we provide. Thus, repeated lumbar punctures can be avoided.

Chiari Verschiedenes Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Chiari Miscellaneous Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V194

Nicht-invasive quantitative Beurteilung des ICP im pädiatrischem Pseudotumor cerebri durch ultrasonographische Bestimmung des Optikus-Nerven-Scheiden-Durchmessers.

Noninvasive quantitative approximation of ICP in pediatric idiopathic intracranial hypertension based on point-of-care ultrasound optic nerve sheath diameter

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Objective

Diagnosis and follow-up in children with idiopathic intracranial hypertension (IIH) often require repetitive lumbar punctures (LPs). This study investigates the inter- and intraindividual relationships between ONSD and ICP in childhood IIH and evaluates whether an individualized mathematical regression equation obtained from two paired US-ONSD/ICP values can be used to approximate ICP directly from ONSD values to avoid further LPs.

Methods

159 ultrasound examinations and 53 invasive ICP measures via lumbar puncture were performed in 28 children with IIH. US-ONSD was measured using a 12-Mhz linear transducer and compared to ICP values. In 15 children a minimum of 2 paired US-ONSD/ICP measures were performed and repeated-measures correlation (rmcorr) as well as intraindividual correlations were analyzed.

Results

Over the entire cohort, the correlation of ONSD and ICP was moderately good ($r=0.504$, $p<0.01$, Rmcorr $r=0.91$, $p<0.01$). In contrast, intra-individual correlations of ONSD and ICP were outstanding(r ranging from 0.956-1). A mathematical regression equation obtained from two paired US-ONSD/ICP values can be calculated and applied for the individual patient to approximate ICP from US-ONSD.

Conclusion

Point-of-care US-ONSD is a noninvasive, quick and reliable method to control treatment efficacy in pediatric IIH. An individualized regression formula can be established from two US-ONSD/ICP value pairs for each patient, for example during initial lumbar puncture before and after withdrawal of CSF; This formula can then be used to directly approximate ICP from ONSD values. Thus, invasive follow-up methods can potentially be avoided.

Chiari Verschiedenes Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Chiari Miscellaneous Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

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Der aktuelle Status des ESPN Pediatric Craniectomy and Cranioplasty Registry (PedCCR)
Current status of the ESPN Pediatric Craniectomy and Cranioplasty Registry (PedCCR)

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Objective

In the pediatric age group the evidence regarding decompressive craniectomy (DC) is weak. Literature on pediatric cranioplasty is even more limited. Concerns are resorption of autologous bone flaps, skin breakdown and growth-related problems associated with synthetic implants. The relevance of DC and subsequent cranioplasty and the need for accurate and systematic data have led to the creation of the Pediatric Craniectomy & Cranioplasty Registry (PedCCR) under the auspices of ESPN.

Methods

After thorough literature review, gaps in knowledge and evidence were identified and the following aims for PedCCR were defined: 1) Compare surgical practices regarding indication, timing and operative technique in a large multicenter cohort. 2) Provide outcome data in a large multicenter cohort. 3) Establish risk factors for complications and cranioplasty failure based on systematic data reaching back as far as the initial injury.

Results

The PedCCR is a prospective, multicenter, open registry enrolling children (≤16 years) undergoing DC and/or cranioplasty for any pathology. A steering committee will assure good scientific practice. Standardized questionnaires were designed and data will be collected online in an electronic joint database, which is currently in the testing phase. The core set of data comprises case report forms for DC, cranioplasty and follow-up visits for at least 24 months, with follow-up forms being recommended until adulthood. Incident reporting forms can be submitted for any incident or unscheduled operation. All forms allow reporting of basic data even in the absence of the patient, i.e. by telephone interview or written contact to parents/carers/treating physicians/rehabilitation clinic.

Conclusion

The PedCCR sets out to answer highly relevant open questions regarding pediatric DC and cranioplasty by using a high-quality prospective approach. The registry proposal was designed to maximize scientific yield at reasonable effort for participating centers. Collaboration is highly appreciated to advance this project together, as the registry is now actively recruiting and can be accessed on pedccr.com.

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Einfluss von Tumorlokalisation und Resektion auf kommunikationsbezogene Neurokognition in Glioblastompatienten

Influence of tumor location and resection on communication related neurocognition in glioblastoma patients

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Objective

Deficits in communication related neurocognition can heavily affect the quality of life of brain tumor patients and can even impact survival. So, a thorough resection causing only minimal damage to those neurocognitive parameters should be achieved. This study aims at investigating which tumor locations may predispose patients to postoperative deficits in communicative neurocognition to provide further evidence for guiding surgical decision making and neuromonitoring strategies.

Methods

139 Patients with newly diagnosed glioblastoma (61 ± 11 years, 65% male) underwent a standardized neurocognitive assessment within 7 days prior to tumor resection and 3-6 days afterwards. Part of this examination were a lexical word fluency test and a verbal learning test which together informed a summarizing language memory score. The test scores were transformed into percentile ranks (PR), correcting for age, gender and educational level. Postoperative changes in communicative functions were defined by an in-/decrease of >1 standard deviation (i.e., 20.6 PR). The contrast-enhancing (CE) tumor lesions were segmented based on the preoperative CE-T1-weighted 3 Tesla MRI, and were normalized to a standard brain template. A voxel-based lesion symptom mapping (VLSM) was performed using the segmented tumor volumes and the standardized language memory scores to identify brain locations corresponding to significant deficits. The resulting lesion maps were interpreted by intersection with a standard brain atlas.

Results

Overall, there was no significant postoperative change in communication functions over time (average deterioration: 0,92 PR ± 20,57 PR). 19 patients (14%) showed relevant postoperative functional improvement, most of them with left hemispheric tumors (left: 58%; right: 42%). Interestingly, most of the 21 patients (15%) with postoperative functional deterioration had right hemispheric lesions (left: 38%; right: 62%). The VLSM could associate the postoperative deteriorations with left temporal structures, especially the inferior fronto-occipital fasciculus (IFOF) and the cingulum.

Conclusion

Although left hemispheric ventral stream components like the IFOF are at specifically high risk regarding communication functions, right hemispheric structures should not be neglected. The left ventral stream association of with verbal fluency and memory should be considered not only for perioperative diagnostics but also for intraoperative monitoring during awake surgeries.

Versorgungsforschung II/*Health Care Research*

V197

Die Machbarkeit eines App-basierten Patient*innen zentrierten Outcome Assessments (neuro-) onkologischer Patient*innen im molekularen Tumorboard – TRACE Studie

Feasibility of patient-reported outcome assessment in the Molecular Tumor Board – App-based assessment of (neuro-)oncological patients under targeted therapy (TRACE)

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Objective

Comprehensive genomic profiling and biomarker-based therapies are currently used in clinical trials and in innovative health care systems including the center for personalized medicine network. Systematic assessments of patient-reported outcomes (PRO) are warranted to gain insight into the perspective of patients during biomarker-based therapies. In the present study, we focused on health-related quality of life (HRQoL), psychosocial situation, and physical symptoms in patients treated at our center.

Methods

Based on a retrospective evaluation of symptom burden in 265 neuro-oncology patients in the Molecular Tumor Board (MTB), we developed an app by 14 expert rounds including validated assessments of HRQoL, symptom and psychological burden and tested it in a pilot study.

After informed consent, patients were introduced to the app by study staff and completed subsequently patient-reported outcomes at several time points. We conducted a structured interview with health care personnel and the patients as users after 3 months to assess the app"s usability and feasibility. The interview was transcribed and analyzed according to Mayring´s qualitative content analysis regarding handling, feasibility and applicability in daily routine.

Results

So far, 14 patients and caregivers have been enrolled, (9 female, 5 male). Median age was 50 years (range 28 - 79), 3 out of 14 patients dropped out due to death.

A total of 4 study staff members, 9 patients and one caregiver were interviewed regarding the usability and feasibility of the app, which were both evaluated as good (study staff members in total n=40 quotes, patients/caregivers n=112 quotes). Main advantages were the possibility to complete questionnaires at home and the easy implementation in daily life. Compliance to PRO assessment was high (80% of questionnaires were

adequately completed), we observed a median Distress score of 3.5 (range 0-10, n=158, weekly assessed) and a median Global Health score of 75.77, (n=44, EORTC QLQ-C30, question 29 and 30, monthly assessed).

Conclusion

This pilot study proved feasibility, acceptance of the app and might enable PRO assessment during biomarker-guided therapies.

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Der Einfluss neurokognitiver Defizite auf die Wahrnehmung erhaltener sozialer Unterstützung bei Patienten mit hirneigenen Tumoren

The impact of cognitive impairment in patients with high-grade gliomas on the perception and contribution of social support

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Objective

Cognitive impairment is frequent in patients with high-grade gliomas. Social support is required throughout the course of the disease straining patients and their supporters. It remains to be determined how cognitive impairment affects the extent and perception of provided social support. Thus, we investigated the relationship between cognitive impairment and social support.

Methods

Adult patients with high-grade glioma (WHO °III / °IV) eligible for complete tumor resection were prospectively evaluated before (t1) and three months after surgery (t2) for neurocognitive deficits using the Montreal Cognitive Assessment (MoCA) between 7/2018 and 3/2021. To assess received and provided social support patients and their supporters completed the Berlin Social Support Scales (BSSS) at t1 and t2 with higher scores indicating greater perceived/provided support. Patients were dichotomized based on MoCA scores (Group A ≤ 23, Group B > 23). Descriptive and correlation analysis were conducted.

Results

73 predominantly male patients (m:f = 67.1% : 32.9%) with a median age of 59.7 years [range: 29-86 years] were recruited at three centers. Participating supporters (n=59, 80.8%) were mainly female first degree relatives (spouse: n=42 (57.5%), child: n=11 (15%), sibling: n=4 (5.4%); m:f = 23.7% : 76.3%). MoCA scores were comparable at t1 and t2 (t1: median = 23 [11-30] vs. t2: median = 25, range [15-30], p=0.14), while perceived social support measured with the BSSS decreased over time (t1: median = 113, range [100-129] vs t2: median = 108, range [89-123], p = 0.03). BSSS scores did not differ between groups at t1 (Group A: median = 115 [100-129] vs. Group B: median = 111.5 [100-113], p=0.16). At t2 patients with better cognitive function perceived less social support (Group A: median = 114 [91-122] vs. Group B: median = 106.5 [89-120], p=0.049) with a weak, but significant negative correlation (p=0.047, *r* = - 0.172). Provided support based on the supporters assessment was stable over time (t1: median = 40 [31-44] vs. t1: median = 39 [31-40], p=0.16).

Conclusion

Provided social support for patients with high-grade gliomas is stable during the first three months of the disease trajectory. Yet, patients´ perception of received support changes, particularly in those without cognitive impairment, who feel less supported three months after the diagnosis. Further studies are needed to assess possible causes for the discrepancies to maintain a healthy social network.

V199

Affektive Symptome bei Patienten mit hochgradigen hirneigenen Tumoren – Zusammenhang zwischen psychischer Belastung, Tumorlokalisation und neurokognitiven Defiziten

Burden of affective symptoms in high-grade glioma patients - association with tumor location and neurocognitive deficits

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Objective

Patients with high grade gliomas suffer from affective symptoms throughout the course of the disease and often present with neurocognitive deficits. The diagnosis of a malignant disease, tumor location and the presence of neurocognitive dysfunction may influence the presence of affective symptoms. We investigated the association between tumor location, cognitive function and affective symptoms.

Methods

Adult patients with high-grade glioma (WHO °III / °IV) eligible for complete tumor resection were prospectively evaluated before (t1) and three months after surgery (t2) for neurocognitive deficits applying the Montreal Cognitive Assessment (MoCA) and affective symptoms (depression, anxiety) using the Hospital Anxiety and Depression Scale (HADS) between 7/2018 and 3/2021. Five groups were defined for tumor location (fontal, temporal, basal ganglia, limbic system, parieto-occipital). Demographic and clinical data was analyzed descriptively. The correlation between HADS- and MoCA-scores as well as tumor location and changes in HADS scores over time were assessed.

Results

73 patients were recruited aged 60.3 ± 12.4 years (m:f = 67.1% : 32.9%) at three centers. Temporal (n=34, 41.0%) and frontal (n=23, 27.7%) location were most frequent. HADS scores were comparable between tumor locations (p=0.75) and showed no significant change over time (t1: 9 [range: 0-29]; t2: 9.5 [range: 0-27], p=0.69). Tumor location had no impact on change in HADS scores between assessments (p=0.34). Cognitive impairment (<26 points) was noted in 72/119 (60.5%) assessments. MoCA scores were comparable across tumor locations (p=0.43). HADS scores were not significantly different among patients with and without cognitive impairment (p=0.25; median HADS: 8 (impaired cognitive function) vs. 11 (normal cognitive function)) with a trend towards a greater frequency of pathologic HADS scores in patients with preserved cognitive function (HADS > 8: 39.9% vs. 26.6%, p=0.16).

Conclusion

In our cohort, cognitive impairment and tumor location did not significantly influence the severity and frequency of affective symptoms in patients with high-grade gliomas. A trend toward a greater burden of affective symptoms in patients with preserved cognitive function indicates a more reactive cause of affective symptoms. Further investigation is needed to determine risk factors for affective symptoms in glioma patients to tailor effective treatment.

Versorgungsforschung II/*Health Care Research*

V200

Longitudinale neurokognitive Untersuchung von Patienten mit niedrig gradigen Gliomen
Longitudinal neurocognitive assessment in patients with low-grade glioma

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Objective

Low-grade gliomas (LGG) are rare cerebral tumors that mostly develop in young adults with an active lifestyle at the time of diagnosis. Early and repeated treatments for LGG, including surgical resection, have been shown to postpone malignant transformation and thus maximize survival benefit. However, it has been recognized that tumor- as well as surgically-induced impairments of neurocognitive functioning negatively affect patients" health-related quality of life (HRQOL). In this study we aim to assess the short- and long-term neurocognitive sequelae from the tumor and its treatment in a total of 50 LGG patients over a time course of 10 years.

Methods

LGG patients received neurocognitive testing on the day before surgery as well as within one week after surgery. Follow-up neurocognitive testing was performed in a 6-month interval matched with clinical follow-ups and imaging. Whenever patients required repeated surgery, they were again tested pre- and postoperatively. The neurocognitive test battery consisted of 9 standardized tests covering a wide span of neurocognitive domains. In addition, participants completed questionnaires for HRQOL, fatigue, depression and distress.

Results

Initial analysis (n=27) of neurocognitive test results revealed significantly worse postoperative results in comparison to preoperative testing concerning Moca Score (p= .001), selective attention (p= .017), concentration performance (p= .029), verbal learning performance (p= .002), supraspan (p = .025) and delayed recall (p= .046), digit span forward (p= .032) and backward (p= . 002), word retrieval (p= .018) as well as semantic (p= .007) and formal-lexical (p= <.001) word fluency, while visual-spatial memory (p= .185) and auditory speech comprehension (p= .375) remained unchanged. Comparison of postoperative and 6-month follow-up neurocognitive test results showed that patients performed significantly better concerning Moca Score (p= .014), concentration performance (p= .049), verbal learning performance (p= .014), supraspan (p= .011) and digit span backward (p= .005) while other scores did not show significant improvement.

Conclusion

On the base of this initial analysis, it can be assumed that surgery in LGG patients may indeed cause initial impairment of different neurocognitive functions. However, the results also show that the preoperative level of some neurocognitive functions is regained over a 6-month period, possibly due to processes of neural plasticity and functional reorganization.

Versorgungsforschung II/*Health Care Research*

V201

Video-basiert angewiesene Heim-Testung versus krankenhausgebundenes, analoges Assessment neurokognitiver Funktionen

Video-instructed home testing versus analogue hospital-based assessment of neurocognitive functions

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Objective

Neurocognitive disorders are a relevant problem for brain tumour patients and are often overlooked due to the limited access to adequate assessments in clinical routine. Beyond personnel and logistic constraints, analogue testing in the hospital setting is also compromised by the stressful situational context and limited mobility of the patients. Here, the remote administration of cognitive assessments might be a promising alternative to overcome part of the aforementioned obstacles. We, therefore, set out to test the feasibility and reliability of video-instructed home testing of neurocognitive functions compared to the analogue setting in a hospital environment.

Methods

A neurocognitive assessment including eleven paper-pencil tests with six parallel versions was administered to two groups of healthy subjects which were stratified by age, gender and educational level. All six test versions were applied to the participants on six separate days within two weeks in pseudo-randomised sequence. The first group (A; n=29) received standardised, analogue instructions in a quiet hospital room. The other group (V; n=34) performed the tests at home guided by video-based instructions from the same investigators as group a. Beyond the neurocognitive test results per se, the total time to complete the test battery as well as the likert-scaled levels of motivation, stress, fun, exertion, and overstrain were assessed. Reliability was calculated using intraclass correlation coefficients. Group results (A versus V) were compared using Wilcoxon tests. P-values were FDR-corrected for multiple comparisons.

Results

Interim analysis from n=14 (A; age 48±19 yrs) vs. n=28 (V; age 41±18 yrs) showed a higher fun level for the V group (8.8±1.2 vs. 8.1±1.1; $p<0.05$) whilst V patients reported less overstrain (2.5±2.1 vs. 3.1±2.1; $p<0.05$). Regarding the neurocognitive test results, there were no significant differences between groups except for slighly better performance of the a group in the digit span test forward (A: 5.3±0.9 vs. V: 4.6±1.2 digits; $p<0.001$) and lexical word fluency (a: 17.4±4.2 vs. V: 15.2±4.5; $p<0.001$) as opposed to a more complete copying of the complex figure in the V group (A: 34.3±2.1 vs. V: 35.2±1.2; $p<0.001$).

Conclusion

Video-based remote instructions allow for a representative and comparatively little overstraining neurocognitive testing. The concept is particularly interesting for monitoring brain tumour patients with reduced mobility in the follow-up period.

Vasospasmus/*Vasospasm*

V202

Vasospasmuserkennung bei schwerer aneurysmatischer Subarachnoidalblutung: Perfusions-CT nach Schema oder nur bei TCD-Auffälligkeiten?

Detecting vasospasm in severe SAH: Scheduled imaging or TCD triggered perfusion CT?

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Objective

Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating disease, which often is associated with dismal prognosis and severe complication, like delayed cerebral ischemia (DCI). Unfortunately, patients with high WFNS and Fisher grades are often intubated and ventilated ergo neurological decline is difficult to detect. To date, vasospasm resulting in DCI is mostly detected by regular transcranial duplex sonografies (TCD) and cranial perfusion computed tomografies (PCT), followed by angiography. TCDs have a high underlying interrater discrepancy, and therefore might miss a certain percentage of severe vasospasm, resulting in DCI.

Methods

We introduced a paradigm of scheduled PCTs (schePCT) on patients with severe aSAH, which were performed on day 1, 5, 7 and 10 after aneurysmal rupture. The aim of this study was to analyze whether a schematized schedule for PCTs in severe aSAH was feasible and improved the detection rate for vasospasms, compared to PCT performed solely after detection of flow acceleration in TCD (TCD-PCT). Statistical analysis was performed with the Man Whitney Test, using GraphPad Prism 9.

Results

37 patients with aSAH and a GCS of 3 were included into the study. 86% were female. Median age was 60 years. 65% of the patients were treated by clipping, 35% inteventionally. 76% of patients developed DCI. Median mRS at discharge was 4,9.

Detection of perfusion deficits in a CT was more frequent in TCD-PCT when compared to sche-PCT, with significantly higher rates between the days 3-6 and 10-12 post rupture. The rate of vasospasm detected in angiography following a positive PCT was higher in schePCT on day 3-10, but higher in TCD-PCT on day 1+2 and 13-15.

The total number of treated patients with angiographic vasospasms, which only were found after schePCT, was 9.

Conclusion

We conclude that performing PCTs following a schematized schedule on day 1, 5, 7 and 10 post rupture results in a higher detection rate for angiographic vasospasms during the core spasm phase between day 3 and 10, when compared to TCD-triggered PCTs. Although the probability of finding a perfusion deficit in PCT was higher when this was triggered by flow accelerations in TCD, the rate of perfusion deficits related to acute angiographic vasospasm was higher if the CT was scheduled. Scheduled PCTs should therefore be performed in severe aSAH especially during the core spasm phase from day 3-10 to prevent to miss vasospasms.

Vasospasmus/*Vasospasm*

V203

Der Oxygen Reactivity Index signalisiert gestörte lokale Perfusionsregulierung vor verzögerten zerebralen Ischämien bei Patienten mit aneurysmatischer Subarachnoidalblutung

The Oxygen Reactivity Index indicates disturbed local perfusion regulation before delayed cerebral ischemia in patients with aneurysmal subarachnoid hemorrhage

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Objective

Cerebral autoregulation (CA) can be impaired in patients with delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage (aSAH). The Pressure Reactivity Index (PRx, correlation of blood pressure and intracranial pressure) and Oxygen Reactivity Index (ORx, correlation of cerebral perfusion pressure and brain tissue oxygenation, PbtO2) are both believed to estimate CA, but PRx is more commonly used in studies on aSAH and DCI. Whether there are regional differences in the functionality of CA within the brain, for instance in areas with disturbed physiology, is unclear. We hypothesized that CA could be poorer in hypoperfused territories during DCI, and that ORx and PRx may not be equally effective in detecting such local variances.

Methods

In this observational cohort study, ORx and PRx were compared daily in 76 patients with aSAH with or without DCI until the time of DCI diagnosis. The ICP/PbtO2-probes of DCI patients were retrospectively stratified by being in or outside areas of hypoperfusion in the CT perfusion image used to diagnose DCI, resulting in three groups: DCI+/probe+ (DCI patients where the probe was located inside the hypoperfused area), DCI+/probe- (probe located outside the hypoperfused area), DCI- (no DCI).

Results

PRx and ORx were not correlated (r=-0.01, p=0.56). ORx but not PRx was highest when the probe was located in a hypoperfused area (ORx DCI+/probe+ 0.28±0.13 vs. DCI+/probe- 0.18±0.15, p<0.05; PRx DCI+/probe+ 0.12±0.17 vs. DCI+/probe- 0.06±0.20, p=0.35). This discrepancy between PRx and ORx was observed on day 3 after hemorrhage and persisted until DCI diagnosis. ORx and PRx did not differ between patients with DCI, whose probe was located elsewhere, and patients without DCI (ORx DCI+/probe- 0.18±0.15 vs. DCI- 0.20±0.14; p=0.50; PRx DCI+/probe-0.06±0.20 vs. DCI- 0.08±0.17, p=0.35).

Conclusion

PRx and ORx measure different physiological components of autoregulation. ORx may detect local perfusion disturbances during DCI after SAH more readily than PRx. Further research should investigate the robustness of ORx and PRx to detect DCI and to serve as a basis for autoregulation-targeted treatment after aSAH.

Vasospasmus/*Vasospasm*

V204

Endovaskuläre Behandlung der verzögerten zerebralen Ischämie nach aneurysmatischer Subarachnoidalblutung - eine retrospektive Kohortenanalyse

Endovascular treatment of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage – a retrospective cohort analysis

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Objective

Delayed cerebral ischemia (DCI) is one of the main outcome-determining complications after aneurysmal subarachnoid hemorrhage (SAH). If euvolemic induced hypertension (iHT) is unable to sufficiently increase cerebral blood flow, ischemia can progress into DCI-related infarction. Endovascular treatment by means of intra-arterial nimodipine infusion has demonstrated promising results in patients suffering from refractory DCI. Mostly applied as a last resort option able to quickly resolve angiographic vasospasm, the effect of endovascular DCI treatment on infarct prevention and outcome remains insufficiently examined.

Methods

We performed a retrospective cohort analysis of all patients with SAH treated in a single university hospital between 2011 and 2020. Patients were diagnosed with DCI based on clinical criteria, multimodal neuromonitoring (brain tissue oxygen tension / microdialysis) and imaging (perfusion CT). Endovascular DCI treatment was primarily reserved as a last tier option for DCI refractory to iHT. Primary outcome was the occurrence of DCI-related infarction. Secondary endpoint was favorable outcome after 12 months defined as extended Glasgow outcome scale (GOS-E ≥ 5).

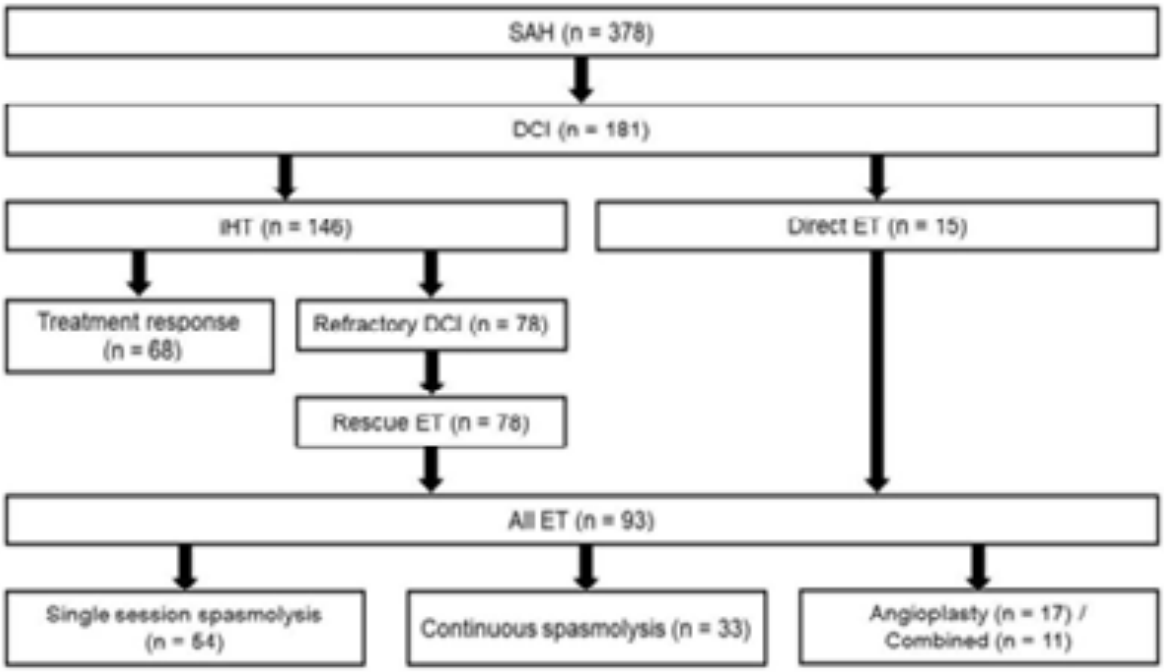
Results

A total of 378 consecutive SAH patients were treated during the inclusion time frame of which 181 (47.9%) suffered DCI. Eighty-seven (23.0%) patients received endovascular DCI treatment after exhausted iHT. DCI-related infarction was observed in 45 (47.4%) patients who underwent last tier spasmolytic treatment. Long-term clinical outcome was available for 67 patients, and favorable outcome was reached in 29 (43.3%) patients after 12 months.

Conclusion

Endovascular DCI treatment is a safe treatment option for delayed cerebral ischemia, refractory to induced hypertension. Complications of endovascular treatment can be severe but remain rare. As endovascular DCI treatment was reserved as last tier, data cannot reliably be compared to patient not suffering refractory DCI.

Abb. 1


SAH (n = 378)
DCI (n = 181)
IHT (n = 146)
Direct ET (n = 15)
Treatment response (n = 68)
Refractory DCI (n = 78)
Rescue ET (n = 78)
All ET (n = 93)
Single session spasmolysis (n = 54)
Continuous spasmolysis (n = 33)
Angioplasty (n = 17) / Combined (n = 11)

Vasospasmus/*Vasospasm*

V205

Interaktion des optimalen zerebralen Perfusionsdruck mit früher Hirnschädigung nach aneurysmatischer Subarachnoidalblutung und Einfluss auf ischämische Komplikationen sowie auf die Prognose

Interaction of optimal cerebral perfusion pressure with early brain injury and impact on ischemic complications and outcome after aneurysmal subarachnoid hemorrhage

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Objective

Cerebral autoregulation is impaired in the early phase of aneurysmal subarachnoid hemorrhage (aSAH). The study objective was to explore pressure reactivity index (PRx) and cerebral perfusion pressure (CPP) in the earliest phase after aneurysm rupture and to address the question whether a CPPopt - (optimal CPP)-targeted management is associated with less severe early brain injury (EBI).

Methods

aSAH-patients admitted in the time from 2012 to 2020 were retrospectively included. PRx was calculated as the correlation coefficient between ICP and MAP in a four-hour time window. By plotting PRx versus CPP, CPP correlating the lowest PRx value, was identified as CPPopt. EBI was assessed applying the SEBES (Subarachnoid Hemorrhage Early Brain Edema Score) score on day 3 after ictus, a SEBES ≥ 3 was considered severe EBI.

Results

In 90 out of 324 consecutive aSAH-patients ICP monitoring was performed ≥ 7 days allowing PRx-calculation and CPPopt-determination. Mean age was 54.2 ± 11.9 years. Severe EBI was associated with a larger mean deviation of CPP from CPPopt 72 h after ictus (r=0.2204, p=0.03). Progressive edema with indication for decompressive hemicraniectomy (DHC) were associated with larger deviation of CPP from CPPopt on day 2 (r=0.2325, p=0.02). The higher the difference of CPP from CPPopt on day 3 the higher the mortality rate (r=0.3166, p=0.04).

Conclusion

Patients with CPP near to the calculated CPPopt in the early phase after aSAH experienced less severe EBI, received less frequently DHC, and exhibited a lower mortality rate. A prospective evaluation of CPPopt-guided management starting in the first days after ictus is needed to confirm the validity of this concept in clinical practice.

Vasospasmus/*Vasospasm*

V206

Evaluation der Heterogenität der Mean Transit Time der Perfusions-CT-Bildgebung in Early Brain Injury Phase: Ein Einblick in die Pathophysiologie der aneurysmatischen Subarachnoidalblutung

Evaluation of Mean Transit Time Heterogeneity of Perfusion CT Imaging in the Early Brain Injury Phase: An Insight Into aSAH Pathophysiology

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Objective

The concept of early brain injury (EBI) is based on the assumption of a global reduction in brain perfusion following aneurysmal subarachnoid hemorrhage (aSAH). However, the heterogeneity of computed tomography perfusion (CTP) imaging in EBI has not yet been investigated. In contrast, increased MTT-heterogeneity, a possible marker of capillary-transit-time-heterogeneity, in the delayed cerebral ischemia (DCI) phase has recently been associated with poor neurological outcome after aSAH. The present study therefore examines the cvMTT in the EBI phase and whether it is a predictor of outcome at this early stage.

Methods

We retrospectively analysed data from 124 patients with aSAH. The heterogeneity of the MTT of CTP imaging performed within 24 h after haemorrhage was analysed using the coefficient of variation (cvMTT). We analysed the total patient population and formed two subgroups: patients with and patients with and without external ventricular drainage. We used linear and logistic regression to model the mRS outcome (treated as numerical and dichotomised values). We analysed linear dependency between variables with the use of linear regression. The evaluation of the means between two groups was performed with Student´s *t*-test.

Results

The heterogeneity of MTT, as defined by cvMTT in early CTP imaging during the EBI phase of aSAH, does not significantly correlate with the dichotomized outcome after 6 months for the entire study population (p = 0.15) nor for any of the subgroups (without EVD: p = 0.21; with EVD: p = 0.3). There is no significant difference in mean heterogeneity of MTT, as defined by mean cvMTT, between patients with and without EVD at the time of early CTP imaging. The heterogeneity of MTT, as defined by cvMTT at early CTP imaging, does not significantly correlate with initial WFNS (p = 0.23) or Fisher grade (p=0.07).

Conclusion

In the present cohort of 124 patients with aSAH, heterogeneity of MTT (cvMTT) of early cerebral perfusion imaging did not correlate with the initial WFNS grade, Fisher grade, or outcome after six months. Therefore, the present study suggests that capillary transit time heterogeneity, as measured by cvMTT, may not be clinically or physiologically relevant in the early brain injury (EBI) and therefore does not represent a predictor for the 6-month outcome following aSAH.

Vasospasmus/*Vasospasm*

V207

Wirkung der multimodalen SAH-Therapie auf die MTT und MTT-Heterogenität der Perfusions-CT-Bildgebung spiegelt die Pathophysiologie der DCI wider

Effect of multimodal SAH therapy on MTT and MTT heterogeneity of perfusion CT imaging reflects the pathophysiology of DCI

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Objective

Capillary transit time heterogeneity is one important feature of delayed cerebral ischemia and can clinically be assessed by the mean transit time heterogeneity (cvMTT) of CT perfusion (CTP) imaging. The cvMTT in the DCI phase correlates with the neurological outcome of aneurysmal subarachnoid haemorrhage (aSAH) patients. The combined multimodal therapy consisting of intra-arterial nimodipine administration (spasmolysis) and elevation of blood pressure (BP) are standard treatment for DCI-related cerebral perfusion restriction and neurological deterioration. The aim of the present study was to evaluate the effect of spasmolysis and elevation of BP on MTT and cvMTT during DCI.

Methods

Of all patients treated with aSAH in our neurovascular centre between 5/2012 and 12/2019, those who suffered from clinical deterioration and/or perfusion impairment were retrospectively included. CTP-based perfusion impairment (MTT, cvMTT) on the day of DCI diagnosis was compared with the follow-up CTP on the following day after initiation of combined multimodal therapy. Data were correlated with clinical epidemiological data and the BP and statistically analysed by our statistician using paired t-test and linear regression with R. Continuous data are presented as means ± standard deviation.

Results

Eighty-one of 535 patients with aSAH suffering from clinical deterioration and/or perfusion impairment were included. The meanMTT was significantly reduced in follow-up CTP as compared to the first CTP (in sequence of imaging: 3.7±0.7s vs 3.3±0.6s; p<0.0001). No significant reduction of the cvMTT in the follow-up CTP compared to the first CTP was observed (in sequence of imaging: 0.16±0.06 vs 0.15±0.06; p=0.35). The mean arterial pressure (MAP) increased significantly between the time of the follow-up CTP and the first CTP (in sequence of imaging: 98±17mmHg vs 104±15mmHg; p<0.0001). When testing for a possible dependence of mean MTT and MAP, no significant relationship was found in the linear regression analysis (p = 0.58, R^2 = -0.009).

Conclusion

The results show a clear significant effect of the combined multimodal therapy on meanMTT but not on cvMTT. We therefore hypothesise that the combined multimodal might effectively address the general perfusion impairment but not the pathophysiological mechanisms underlying the capillary transit time heterogeneity, for example microvascular dysfunction or microthrombosis.

Meningeome I/*Meningioma I*

J-SBNC037

Bewertung der Lebensqualität bei Patienten mit chirurgisch behandelten parasagittalen Meningeomen
Quality of life assessment in patients with surgically treated parasagittal meningiomas

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Objective

Surgery remains the primary treatment for parasagittal meningiomas (PSM). Given that most surgical series assess individuals from a functional point of view, the quality of life (QoL) among these patients has been poorly evaluated.

Using the previously described scales, the present study therefore aimed to assess the QoL in patients with PSM who underwent surgical treatment and identify risk factors for different levels of QoL.

Methods

Patients were contacted and interviewed via telephone. A total of 136 patients with PSM underwent surgery at our institution between 1984 and 2020. Among them, 45 had agreed to participate in the research. The scales utilized included the Functional Assessment of Cancer Therapy General (FACT-G), Brain (FACT-Br), and Meningioma (FACT-MNG). Medical records were also reviewed

Results

The mean KPS was 93.3 (70–100). Overall, the mean scores for the FACT-G, FACT-Br, and FACT-MNG scales were 98.4/108 (55–108; SD: 12.9), 179.3/200 (98–200; SD: 22.4), and 219.3 (119–248; SD: 29.7). Considerable variability in scales scores was observed among those with the same KPS score. Preoperative KPS score was significantly associated with both FACT-Br [−21.64; 95% CrI (−34.04, −9.59)] and FACT-MNG [−31.88; 95% CrI (−47.24, −15.25)]. Preoperative KPS was identified as a risk factor for QoL impairment

Conclusion

Variability in the scale scores among those with the same KPS score highlights the importance of structured assessment. Moreover, KPS may overlook impairments in QoL. To date, this has been the first study to assess QoL in PSM patients.

Meningeome I/*Meningioma I*

V208

Prädiktive Faktoren spinaler Meningeome.
Predictive factors in spinal meningiomas.

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Objective

The first choice of treatment for spinal meningiomas is microsurgical resection. Available data suggest that the postoperative outcome of these meningiomas is more favorable compared to intracranial meningiomas. To optimize the treatment of patients with spinal meningioma, it is essential to generate a more detailed knowledge about risk stratification.

Methods

We present the analysis of spinal meningiomas of our institutional meningioma cohort treated between October 2003 and March 2017. Clinical characteristics and outcome parameters of spinal meningiomas are compared to cranial meningiomas.

Results

206 spinal meningiomas were evaluated. 82.8% (n=168) could be resected with a Simpson grade 3 or less, corresponding to a complete resection. 96.1% (n=198) of the resected meningiomas could be classified as WHO grade 1. In contrast, the proportion of WHO grade 1 among intracranial mengingiomas was 78.35% (n=1393). On average, the follow-up was 30.5 months for spinal tumors compared with 39.5 months for cranial meningiomas. The recurrence rate was only 4.9% (n=8) for spinal meningiomas. In comparison, 23.9% (n=378) of patients with intracranial meningioma developed recurrence. Kaplan-Meier analysis demonstrated a significantly more favorable recurrence-free survival for spinal tumors (p=0.0001). Multivariate analysis of spinal meningiomas showed that Simpson resection grade was the only independent prognostic parameter (p=0,0012). In contrast male gender (p=0,0190), high WHO grade (p=0,0001) and resection of a recurrent tumor (p=0,0001), were independently associated with worse prognosis in intracranial meningiomas in addition to the negative prognostic impact of high Simpson grade (p=0001).

Conclusion

Compared to intracranial meningiomas, spinal meningiomas have a more favorable prognosis. A crucial factor is complete resection, corresponding to Simpson grade £ 3. However, it should be emphasized that resection of spinal meningiomas is challenging and, due to the location in proximity to critical structures, such as the spinal chord, complete resection is not always possible.

Meningeome I/*Meningioma I*

V209

Automatisiertes und gemultiplextes Medikamenten-Kombinationsscreening identifiziert synergistische Medikamentenpartner für die Behandlung von aggressiven Meningeomen

Automated and Multiplexed Combinatorial Drug Screening of FDA-Approved Drugs Identifies Potential Synergistic Drug Partners for the Treatment of Aggressive Meningiomas

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Objective

The goal of combinatorial therapy is to improve the effectiveness of treatment by targeting multiple aspects of cancer cells or by overcoming resistance to single drugs. In search of effective synergistic drug combinations for the treatment of aggressive meningiomas, we performed an automated and multiplexed combinatorial drug screening of 166 FDA-approved anticancer drugs in three grade 3 meningioma cell lines.

Methods

Three grade 3 meningioma cell lines (NCH93, IOMM-Lee, and KT21-MG1) were stably transduced with blue, green, and red fluorescence proteins mTagBFP2, mNeonGreen, and tdTomato. The cell lines were multiplexed into 384-well plates and treated in 5x5 dose-response matrices with drug concentrations ranging from 0, 1, 10, 100, and 1 000 nmol/L for 48 hours by the automated liquid handler Hamilton MicroLAB STAR®. The drug library AODX from the National Cancer Institute was used consisting of 166 FDA-approved anticancer drugs. To demultiplex cell viability from a single well, fluorescence as a surrogate marker for viability was measured before adding ATP-based end-point viability assay CellTiterGlo 2.0 (Promega), which served as an independent combined result of all cell lines (combined group). Synergism was calculated by the ZIP Synergy model in the software R (v4.2.2). Drug-drug synergism was defined as a ZIP score over 10.

Results

This drug screening effort generated 13 695 unique drug-drug combinations per cell line. Most synergistic combinations were observed in the combined group (n=188, 1.37%), followed by IOMM-Lee (n=157, 1.14%), and KT21-MG1 (n=122, 0.88%). The lowest number of synergistic drug-drug combinations was observed in NCH93 (n=75, 0.54%). Interestingly, 86 combinations were uniquely found in IOMM-Lee, 54 in KT21-MG1, and 20 in NCH93, indicating specific tumor vulnerabilities. When analyzing all synergistic combinations, 19 drug combinations were observed in all cell lines and the combined group. Of those, the drugs Temsirolimus, Gemcitabine, and Romidepsin were highly enriched. As an example, mTOR inhibitor Temsirolimus concordantly showed strong synergism with the androgen receptor antagonist drug Darolutamide in all cell lines (average ZIP score: 27.75, $P < .0001$).

Conclusion

This comprehensive combinatorial drug screening identified synergistic drug-drug partners for the treatment of aggressive meningiomas. Further validation studies in patient-derived meningioma organoids are ongoing.

Meningeome I/*Meningioma I*

V210

Ein perifokales Ödem ist ein Risikofaktor für präoperative Epilepsie bei Patienten mit Meningeom WHO Grad 2 und 3

Perifocal edema is a risk factor for preoperative seizures in patients with meningioma WHO grade 2 and 3

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Objective

Approximately 25% of patients with intracranial meningiomas have a history of seizures prior to initial diagnosis, impacting patients" quality of life. We aimed to elaborate on incidence and predictors for seizures in a patient cohort with molecularly well-defined atypical and anaplastic meningiomas.

Methods

We retrospectively searched our institutional database for patients with meningioma WHO grade 2 and 3 according to the 2021 WHO classification undergoing microsurgical tumor resection. Clinical, histopathological, and imaging findings were collected and correlated with preoperative seizure development. Tumor and edema were volumetrically quantified.

Results

90 patients were screened with 54 patients fulfilling the inclusion criteria. Median age of 62.8 years and male-to-female ratio was 1:1.3. Most tumors (44/54, 81%) were classified as atypical meningioma WHO grade 2, and 10/54 tumors (19%) as anaplastic meningioma WHO grade 3, including five patients harboring a TERT promoter mutation. Brain invasion was detected in 31/54 patients (57%) and strongly correlated with WHO grade 3. Meningiomas were most frequently located at the convexity in 33/54 patients (61%), at the skull base in 19/54 patients (35%) and rarely intraventricularly (2/54 patients, 4%). Importantly, 25/54 patients (46%) experienced preoperative seizures. Preoperative peritumoral edema was detected in 39/54 patients (72%) with a median edema volume of 19.5 cm^3 (range: 0.0-171.9 cm^3). Median tumor volume was 27.6 cm^3 (1.6-223.3 cm^3). The incidence of preoperative epileptic seizures was independent of age, tumor location, TERT promoter mutation, brain invasion and WHO grading. In multivariate analysis, only presence of peritumoral edema but not edema volume itself was associated with preoperative seizure development.

Conclusion

Preoperative seizures were frequently encountered in about every second patient with meningioma WHO grade 2 or 3. Patients presenting with peritumoral edema on preoperative imaging are at particular risk for developing epileptic seizures. Prophylactic antiepileptic drug management should be carefully evaluated in these patients.

Meningeome I/*Meningioma I*

J-SBNC038

Zirkulärer zugang mit mehreren bohrlöchern zur resektion eines zusätzlichen und intrakraniellen meningioms: technischer hinweis

Circular approach with multiple burr holes for resection of an extra and intracranial meningioma: technical note

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Objective

The circular approach with multiple burr holes for resection of extracranial and intracranial parasagittal meningiomas aims to resect the tumor, minimizing the risks of reaching and injuring the superior sagittal sinus (SSS). The aim of this study is to describe this specific technique and present a case where it was performed.

Methods

With the patient already positioned in a Mayfield three-pin skull fixation device, the incision is marked around the bulging tumor and a horseshoe incision is performed. Since the meningioma is extensive, it is necessary to leave about three centimeters for visualization of the meningioma margin when opening. Then, burr holes are made encircling the bone meningioma as close as possible to each one, avoiding the SSS. The next step is to interlock the burr holes incising the dura mater affected by the tumor along the periphery of the extracranial meningioma. After total isolation of the affected part of the bone and the dura mater, these parts are separated from the intradural part, which will be removed later due to the greater care with the SSS, coagulating the veins that drain the tumor and dissecting the meningioma away from the brain parenchyma.

Results

Using the circular approach with multiple burr holes, a total resection of the extra and intracranial meningioma was achieved, without injuring the SSS. The degree of resection on the Simpson scale was I. Complete removal of the meningioma was certified by postoperative axial computed tomography. In addition, the patient's postoperative period obtained excellent results with improvement of the patient's optical disorder and interruption of generalized tonic-clonic seizures.

Conclusion

The circular approach with multiple burr holes in this note is performed safely and effectively. The technique is very useful when the meningioma is extensive and, it has numerous advantages, such as a lower risk of injury to the SSS with a satisfactory resection of the meningioma. Although it is a recognized option, it has been insufficiently documented and described in detail, therefore it is important to expand the knowledge and proper use of this technique among neurosurgeons.

Meningeome I/*Meningioma I*

V211

Die Rolle der stereotaktischen Radiochirurgie bei WHO-Grad II Meningeomen: Ergebnisse einer großen europäischen multizentrischen Beobachtungsstudie.

The role of stereotactic radiosurgery in WHO grade II meningiomas: results of a large European multicenter observational study.

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Objective

In recent years, stereotactic radiosurgery (SRS) has gained an increasing role in controlling recurrence or progression of atypical World Health Organization (WHO) grade II meningiomas. This study evaluates a large, multi-institutional database of European radiosurgery centers to present the outcomes of WHO grade II meningiomas treated with SRS. Our aim was to investigate the long-term tumor control rate and morbidity of SRS.

Methods

At 15 participating centers, 217 consecutive patients with 304 WHO grade II meningiomas treated between 1992 and 2003 were screened for inclusion. Clinical and imaging data were collected independently by each center and uniformly entered into a multicenter database by a visiting research fellow.

Results

Detailed results of 168 patients and 255 meningiomas (83,9%) were analyzed. The median age of the patients upon SRS treatment was 57 years. The median tumor volume was 6.1 cm³ and the median dose at the tumor margin was 15 Gy (50% isodose). All tumors were treated by surgery before SRS. The median imaging follow-up was 48 months. The volume of treated tumors decreased in 99 (38.8%), remained unchanged in 70 (27.5%), and increased in 86 lesions (33.3%), corresponding to a tumor control rate of 66.3%. The five-year progression-free survival (PFS) rate was 45.0%. The morbidity rate was 6.7% at last follow-up.

Conclusion

The data analysis shows that SRS for WHO grade II meningiomas has a reasonable tumor control rate in the medium term which controls favorably to the literature. We also observed a low morbidity rate. Our study suggests that SRS may be an effective option for managing WHO grade II meningiomas. However, it should be noted that those kind of meningiomas can vary widely in their behavior and response to treatment, and the best approach depends on the specific characteristics of the tumor and the individual patient's situation.

Moyamoya und cerebrale Revaskularisation/*Moyamoya and cerebral revascularization*

V212

Postoperative Langzeitergebnisse von 22 Patienten mit atherosklerotischer, steno-okklusiver Vaskulopathie behandelt mit zerebraler Bypass-Chirurgie: Ein single-center, retrospektive Analyse

Postoperative long-term outcome of 22 patients with atherosclerotic steno-occlusive vasculopathy treated with cerebral bypass surgery: a single-center, retrospective analysis

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Objective

The goal of our study was to evaluate the long-term clinical outcome of our patient with cerebral hypoperfusion secondary to chronic atherosclerotic steno-occlusive vasculopathy treated with extra-intracranial bypass (EC-IC Bypass).

Methods

The clinical records of patients were analyzed who underwent EC-IC Bypass operation between January 2019 and December 2020. Modified Ranking score (mRS) and the results of multimodal imaging of cerebrovascular reserve capacity and digital subtraction angiography were retrospectively analyzed.

Results

A total of 27 surgical revascularizations were performed in 27 patients within the examined period. The 2 years clinical follow up could be performed in 22 patients due to compliance reasons. Only these patients were included in our analysis. 13 patients had symptomatic chronic cervical internal carotid artery occlusion, in 9 patients bypass surgery was performed due to cerebral hypoperfusion secondary to middle cerebral artery occlusion. Six indirect and 16 direct, superficial temporal artery to middle cerebral artery EC-IC Bypasses were performed. Immediate postoperative worsening was observed in 3 patients (13%) with complete recovery at the long-term follow up. The mean long-term mRS was 1.3 preoperatively and postoperatively as well. In 2 cases (0.9%) direct bypass graft stenosis could be observed without hemodynamic relevance. Long-term graft occlusion was not observed. Significant increase of the cerebrovascular reserve capacity could be observed in all of the operated patients using dynamic CT-Perfusion with acetazolamide-challenge, BOLD fMRI with Apnoe Paradigm and transcranial doppler sonography.

Conclusion

In our series of patients treated with direct or indirect EC-IC bypass we could observe significant improvement of the long-term outcome. Bypass surgery for selected group of steno-occlusive vasculopathy remains an important and effective treatment in a high-volume neurovascular center.

Moyamoya und cerebrale Revaskularisation/*Moyamoya and cerebral revascularization*

V213

Arteria cerebri anterior Revaskularisation bei erwachsenen Europäischen Moyamoya Patienten mit direkten und indirekten kombinierten Bypässen

Anterior cerebral artery revascularization in European adult Moyamoya patients with combined direct and indirect bypass techniques

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Objective

Cerebral revascularization with EC-IC bypass is the treatment of choice for Moyamoya patients with cerebrovascular insufficiency. While anterior cerebral (ACA) revascularization with direct or indirect bypasses is commonly performed in pediatrics, it is only scarcely used in adults. We report our experience with ACA revascularization in adult Moyamoya patients.

Methods

This is a retrospective analysis of adult patients who have received an ACA revascularization at our center. If cerebrovascular insufficiency is detected in PET/CT for the ACA territory, we routinely indicate ACA revascularization. We have analyzed direct and indirect STA-ACA revascularization with the known techniques (encephalo-duro-arterio-synangiosis [EDAS], encephalo-duro-synangiosis [EDS] and encephalo-galea-periost-synagiosis [EGPS]). Perioperative complications were graded by the Clavien-Dindo classification, revascularization success was rated on postoperative digital subtraction angiography (DSA).

Results

We analyzed 70 ACA revascularizations in 41 patients with a median age of 36 (range 17-68) years, 73.1% were females. 29 (71%) patients had bilateral ACA revascularizations (of which 26 were placed primarily within one surgery), 12 (29%) unilateral. A total of 4 direct and 151 indirect (41 EDAS, 41 EDS, 69 EGPS) revascularizations were performed as combined indirect procedures. Relevant complications (Clavien Dindo grade ≥3) were seen in 8 (11%), whereat 5 (63%) of these were local wound-healing problems. Postoperative DSA was available for 31 patients (53 bypasses) with a mean follow-up time of 12.9 months since surgery. Successful revascularization was proven for 47 (89%) patients in total. We saw local filling around the bypass in 13 (28%), partial filling in 24 (51%) and complete filling of the ACA territory in 10 (21%). All direct bypasses were patent. Of the indirect ones most likely EDAS (17 bypasses), followed by EDAS combined with EDS (13), EDS (11), EGPS combined with EDS (3) and EGPS (1) supplied additional blood.

Conclusion

ACA revascularization in adult patients is a safe procedure bringing additional blood flow to the hypoperfused brain. The high success rates of indirect bypasses in this series prove that this technique also works in adults for this specific indication, although some time is needed until new vessels are sprouting sufficiently. We propose to always perform direct bypasses if feasible, if not EDAS seems to be to most effective method, followed by EDS.

Moyamoya und cerebrale Revaskularisation/*Moyamoya and cerebral revascularization*

V214

De-novo kontralaterale Krankheitsprogression in europäischen Moyamoya-Patienten
De-novo contralateral disease progression in European moyamoya patients

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Objective

Objective: Moyamoya disease (MMD) leads to occlusion of the distal internal carotid arteries and proximal circle of Willis. In some patients with unilateral MMD, contralateral disease progression (CDP) can be seen. Aim of this study was to identify the clinical features and incidence of CDP in a large European cohort of Moyamoya patients with primary unilateral surgical treatment.

Methods

Methods: We retrospectively reviewed all moyamoya patients treated only unilaterally at our center for unilateral MMD or bilateral MMD with predominantly unilateral clinical relevance and unilaterally impaired hemodynamics. Patients without at least one postoperative follow-up examination were excluded. We evaluated the initial symptoms of CDP, secondary treatment or intention to treat, findings leading to the diagnosis of CDP, time to secondary treatment and the clinical course.

Results

Results: We identified 38 patients receiving primarily only unilateral EC-IC bypass surgery, 24 patients had unilateral MMD and 14 patients bilateral MMD. The median patient age was 41 years. Initial surgical revascularization was a direct STA-MCA bypass in 37 of 38 (97,4%) patients. CDP was diagnosed in 12,5% in unilateral MMD patients (n = 3) and in 57,1% of the unilaterally treated bilateral MMD patients (n = 8) during an average follow-up period of 2,54 years. 54,5% developed novel symptoms leading to the diagnosis of CDP with these manifestations of CDP being predominantly transient ischemic attacks (66,6%) and headaches (33,3%). The average time until secondary surgical treatment was 3,9 years (range from 0,36 to 18,63 years) and included a direct STA-MCA bypass in 100% of the cases.

Conclusion

Conclusion: The rate of CDP leading to secondary surgical revascularization of the contralateral side was 12,5% in unilateral MMD and 57,1% in unilaterally treated bilateral MMD patients in our European cohort. All MMD patients with initial need for only unilateral treatment should be followed up clinically and by MRI to timely identify and treat CDP.

Moyamoya und cerebrale Revaskularisation/*Moyamoya and cerebral revascularization*

V216

Quantifizierung des Bypass Wachstums bei langfristigem Follow-up von Moyamoya Patienten nach Revaskularisations Operation

Quantification of Bypass growth in long-term longitudinal follow-up after surgical revascularization in Moyamoya patients

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Objective

Evaluation of bypass patency after surgical revascularization is an important quality control in patients with moyamoya angiopathy (MMA). Aim of this study was to quantify and understand bypass vessel-growth dynamics seen on MRI in of MMA patients.

Methods

This retrospective study included patients after direct and indirect extracranial-intracranial revascularization with availability of magnetic resonance time-of-flight angiography (MR-TOF) preop, 3-months and 12-months postop. The vessel size of the common superficial temporal artery (STA), ramus frontalis (RF) and ramus parietalis (RP), were obtained using ImageJ software for vessels used as donor and vessels without surgical intervention. Vessel dynamics were compared to correspondingly obtained [15O]water PET with acetazolamide challenge and infarction patterns in the affected vascular territory quantified by a modified Fazekas score (FS).

Results

Twenty-seven adult patients had a total of 56 revascularizations with 38 direct STA-MCA bypasses (11 bilateral, 16 unilateral) and 18 indirect STA-ACA bypasses (7 bilateral, 4 unilateral). Vessel growth seen on MR-TOF at the 12-month follow-up indicated a universal growth in vessel size:The main trunk of the STA increased by 1.08mm2 (67.08%) on the left side and 1.06mm (54.92%) on the right side in the entire cohort (p=0.041; CI 0.09-1.38). If the RP was used as donor vessel for direct bypass, the size increased by 1.34mm2 (89.33%), if it was not used (negative control in unilateral patients) it only gained 0.19mm2 (12.34%) (p=0.002; CI 0.63-1.84). For the RF used as a donor for indirect revascularization, the growth was 0.90mm2 (58.4%), if it was not used (negative control) the growth was 0,18mm2 (12%).Bypasses were divided into two groups of "strong" and "weak" growth according to the median change in size. Interestingly, the strong bypass growth cohort had less infarctions and lower Fazekas scores, as well as less severe perfusion deficits seen on PET/CT, but both did not reach statistical significance likely due to the size of the cohort.

Conclusion

Bypass growth can reliably be monitored by quantification of MR-TOF. The negative correlation to infarctions and PET/CT might explain variable results in growth dynamics of bypasses, as patients with brain atrophy caused by infarctions might have a much smaller demand for blood. These findings must be validated in a larger cohort and might help to better understand hemodynamics before and after revascularization.

Moyamoya und cerebrale Revaskularisation/*Moyamoya and cerebral revascularization*

J-SBNC039

Bilateraler Ursprung der vorderen Hirnarterien im Augenabschnitt, der das Moyamoya-Syndrom nachahmt: eine seltene Anomalie - Fallbericht

Bilateral ophthalmic segment origin of anterior cerebral arteries mimetizing Moyamoya syndrome: a rare anomaly – Case Report

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Objective

The main objective of the present study is to report a bilateral ophthalmic segment origin of anterior cerebral arteries mimetizing Moyamoya syndrome, a rare anomaly to incrise literacture.

Methods

Case report of a patient with bilateral ophthalmic segment origin of anterior cerebral arteries mimetizing Moyamoya syndrome and compare it with findings in present literature.

Results

23-year-old female patient presenting with working memory and attention deficit, associated with headache, and episodes of transient focal deficits. She also had cardiac valvulopathy, associated with rheumatic fever, in treatment. During the investigation, MRI was performed and suggested Moyamoya syndrome diagnosis. Then, a cerebral angiography was performed, which showed no evidence of Moyamoya disease pattern, excluding the diagnosis, but, in the other hand, showing a rare anatomic pattern – a bilateral ophthalmic segment origin of anterior cerebral arteries. The ACA gives rise to a ventral ophthalmic artery that courses caudally and laterally, medial to the supracavernous internal carotid artery, where it enters the optic canal. This ventral ophthalmic artery originates from the Al-ACoA-A2 junction. This pattern is seen in the dog. An anastomosis occurs between the dorsal ophthalmic artery and the supracavernous ICA under the ipsilateral optic nerve. The proximal segment of the primitive ophthalmic artery regresses, and the primitive ophthalmic artery will now arise from the internal carotid artery. Obviously, these steps and the events leading to the maturation of the ophthalmic artery will contribute to the development of some anatomical variations. Infraoptic A1 is unilateral in most cases with only three cases of a bilateral infraoptic course reported in the anatomic and neurosurgical literature.

Conclusion

Variations of the anterior cerebral artery are common findings, usually of little clinical significance. But, sometimes, it might lead to misdiagnosis and change of the outcome or therapeutic plan. It is important to be able to recognize and make the right differentiation, in order to offer to the patient the best information, treatment and follow-up.

Vestibularisschwannome III Facialisfunktion und -regeneration/*Vestibular schwannomas III Facial function and recovery*

V217

Die Fazialisfunktion bei Vestibularisschwannomen – welches Konzept bewährt sich langfristig?

Facial nerve outcome in vestibular schwannomas – which concept holds true at long-term?

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Objective

Good facial nerve function is the most important goal in vestibular schwannoma treatment. This has led to a general change of concept favoring incomplete tumor resection. Here we investigate the influence of clinical and surgical factors on early and long-term functional outcome.

Methods

In a consecutive series of 686 VS surgeries, all patients were operated under neuro-monitoring via a retro-sigmoid approach by an interdisciplinary oto-neuro-surgical team led by three experienced neurosurgical skull base surgeons and two oto-surgeons. Parameters of analysis were facial nerve function by House-Brackmann-Scale, tumor extension with and without brainstem involvement, the extent of resection and the need for additional treatment. Objective documentation was based on photo-video-documentation of facial nerve function and on MRI for tumor resection, with a minimum follow-up of 12 months. Tumor resection was graded as complete resection CR, with sub-groups TR total resection and GTR gross total resection (capsule or tiny residual at cranial nerves VII or VIII), as opposed to partial resection PR.

Results

From 2005 to 2020, in 686 VS, CR was performed in 640 operations (93%), PR in 46 (7%); a change was noted from 96% CR in the first 11 years towards a more conservative approach with 85% in the most recent 4 years in 189 cases. In case of normal pre-operative facial nerve function (591 patients), outcome was good in 85% (HB°1-2) and moderate in 14% (HB°3), at a minimum follow-up of 1 year. Tumor size, tumor extension with brainstem involvement and pre-operative facial nerve function were significant outcome factors with good outcome HB°1-2 in 89% in small tumors versus 83% in large tumors with extensive brainstem contact or compression. Analysis of the most recent 189 cases identified the major causes for incomplete resection in 28 patients, previous surgery and radiosurgery, extensive adhesion at brainstem level and neurofibromatosis. It also revealed a much less favorable long-term outcome with only 64% HB°1-2 at 1 year and a higher risk of secondary recurrence within few years. On the contrary, in 6 patients planned staged surgery within a few months was performed with very good functional outcome.

Conclusion

Previous (radio)surgery carries a high risk of secondary partial tumor resection and further regrowth impacting facial nerve function. Facial outcome at long-term is best the smaller the tumor and the higher the extent of tumor resection at the first surgery.

Vestibularisschwannome III Facialisfunktion und -regeneration/*Vestibular schwannomas III Facial function and recovery*

V218

Bedeutung der kortiko-bulbäre motorisch evozierte Potentiale in der Vestibular Schwannoma Chirurgie für die Prädiktion einer Fazialisparese.

Significance of cortico-bulbar motor evoked potential (coMEP) monitoring in vestibular schwannoma surgery (VSS) for prediction of postoperative facial nerve palsy

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Objective

Direct facial nerve stimulation during VSS allows preservation of the nerve in its continuity, but prognostication of a possible facial palsy in most cases is not possible. Cortico-bulbar transcranial motor evoked potentials (coMEPs) as a relatively new monitoring modality were investigated if a correlation of intraoperative amplitude reduction and postoperative severity of facial palsy is present.

Methods

In 49 patients (mean age 50yrs; 19-84) with unilateral VS (mean size 22mm; 10-50) were investigated. Intraoperative neuromonitoring consisted of auditory evoked potentials (AEPs), direct facial stimulation and cortico-bulbar MEPs. An anodal stimulation via subdermal corkscrew electrodes on position C3 or C4 and a cathode near Cz with a train of 6 pulses, each with a duration of 500µs, at a frequency of 500Hz and an interstimulus-interval (isi) of 2 was used.

Results

Complete resection was achieved in >90% of patients, with an overall useful hearing preservation rate of 32%, closely correlated to intraoperative AEP wave V monitoring. Additionally, MEPs could be monitored in every patient during the duration of the surgery. In 16% of the patients, a significant reduction of MEP baseline amplitude was recorded, correlating directly with a moderate to severe postoperative facial palsy (House Brackmann (HB) 3-5). No palsies without MEP amplitude reduction were observed. During 6 months FU, recovery of 1-2 HB Grades was observed in all cases. All patients with intraoperative MEP amplitude reduction had significant larger VS than patients without MEP amplitude reduction (27 vs 22 mm diameter).

Conclusion

Adding to direct facial nerve stimulation, intraoperative coMEP monitoring during VSS seems to be of high significance and value for intraoperative facial nerve preservation and postoperative short and long term facial palsy prognostication.

Vestibularisschwannome III Facialisfunktion und -regeneration/*Vestibular schwannomas III Facial function and recovery*

V221

App-basierte Fazialisrehabilitation - Innovation aktueller Therapieansätze bei postoperativer Fazialisparese
App-based facial nerve rehabilitation - innovating current therapeutic approaches for postoperative facial palsy

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Objective

Facial palsy after vestibular schwannoma surgery is temporary in many cases but can significantly affect patients" quality of life. Physical training - initially guided and subsequently performed by the patient - is of paramount importance for recovery of facial nerve function. The introduction of medical application software (apps) might improve therapy by maintaining motivation of daily home-based training and surveilling patients" rehabilitation progress.

Methods

We developed a mobile app for innovative and home-based facial nerve rehabilitation (FACEsemper) that instructs the patient on a daily training program consisting of 6 variable exercises and 3 repetitions. The app allows the user to determine the exercise intensity for different facial areas and integrates a reminder function for daily training. Further functions include photo documentation, a calendar and the generation of a training report, as well as the possibility of direct contact with the attending physician. The usability of the app was prospectively investigated on 30 subjects. 10 physicians, 10 patients with facial palsy and 10 healthy subjects tested the app features for two weeks. Usability was assessed by numerous self-rating questionnaires (i.e., mHealth App Usability Questionnaire, MAUQ; System Usability Scale, SUS; Adjusted Visual Aesthetics of Websites Inventory, aVisAWI) and scores were compared between groups.

Results

The participants reported a mean number of 14.4±5.9 years of smartphone use and 11.1±1.2 years of app use. 62.5% of subjects had former experience with the use of fitness apps. Each participant performed a mean number of 216.5 facial exercises. The averaged total scores of questionnaires were: MAUQ 5.7±0.9/7, SUS 88±12.4/100, aVisAWI 5.7±0.8/7 and specific rating 4.5(±0.5)/5. App content (4.6/5) and user comfort (4.6/5) were rated higher than esthetic features (4/5). There was no significant difference of usability scores between groups. A main limitation was malfunction of the daily reminder in some android versions leading to missed training sessions in some users.

Conclusion

This study revealed a positive user experience and a good to excellent usability of the FACEsemper app. However, we identified some limitations and suggestions useful for further development of the app. As a next step, the app should be evaluated in a large patient cohort with facial palsy to assess a potential medical benefit in terms of facial rehabilitation compared to traditional training.

Vestibularisschwannome III Facialisfunktion und -regeneration/*Vestibular schwannomas III Facial function and recovery*

Hypophysenadenom II/*Pituitary adenoma II*

V223

Die exoskopische Operationstechnik zur transsphenoidalen Operation von Rathkezysten - Ein retrospektiver Vergleich zum operationsmikroskopischen Vorgehen

Microscopic vs. exoscopic transsphenoidal surgery for Rathkes cleft cyst– a retrospective single center study of 131 patients

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Objective

In specialized neurosurgical pituitary centers microscopic or endoscopic transsphenoidal surgeries are routinely performed for sellar lesions. Exoscopic transsphenoidal surgery (ExTS) using 4K 3D orbital camera system is a novel operative technique for this indication. The utility of this system for the treatment of Rathke"s cleft cysts (RCC) has not been validated yet.

Objective was the comparison of exoscopic transsphenoidal surgery (ExTS) versus microscopic transsphenoidal surgery (MTS) regarding duration of surgery, length of postoperative hospital stay, remission rate and postoperative complications (diabetes insipidus, SIADH, pituitary insufficiency, CSF-leak, epistaxis, new visual impairment).

Methods

We performed a retrospective analysis using the electronic medical records of all transsphenoidal operated RCCs, conducted between Juli 2013 and Mai 2022 at a specialized pituitary center. Patients with histologically confirmed diagnosis of RCC with defined type of transsphenoidal surgery were included: 78 patients after MTS and 53 patients operated via ExTS.

Results

Mean(±SD) duration of surgery in minutes was comparable for both operative techniques (78.5 (±21.7) minutes vs. 73.1 (±26.7) minutes, p=0.2). Mean postoperative length of hospital stay was significantly shorter after ExTS comparing to MTS (7.9 days vs. 6.9 days, p<0.01) for both first surgeries (7.8 days vs. 7 days, p<0.01) and repeated surgeries (8.3 days vs. 6.4 days, p=0.016). Mean duration of follow-up was 32.5 (range 0-95) months for MTS and 10.6 (range 0-30) months after ExTS. There were no significant differences in recurrence rates after both surgical procedures (16.7% vs. 9.7%, p=0.24). The incidence of postoperative complications like CSF-leak (9% vs. 7.5%, p>0.99), diabetes insipidus (9% vs. 9.4%, p>0.99), SIADH (7.7% vs. 1.9%, P=0.24), new pituitary insufficiency (10.3% vs. 18.9%, p=0.2), epistaxis (1.3% vs. 1.9%, p>0.99), meningitis (3.8% vs. 3.8%, p>0.99), new visual field defect (0% vs. 0%, p>0.99) was not statistically significant different between both groups. Recurrence rate was 16.7% and 9.7% (p=0.24) for MTS and ExTS respectively.

Conclusion

Both MTS and ExTS were effective for the treatment of RCC. Duration of surgery, recurrence rate and procedure-related morbidity were not statistically significant between both operative techniques. Meanwhile the length of postoperative hospital stay after ExTS was significantly shorter than after MTS.

Hypophysenadenom II/*Pituitary adenoma II*

V224

Transsphenoidale Separationschirurgie als Teil eines primär interdisziplinären Therapieansatzes bei nicht resizierbaren Hypophysentumoren

Transsphenoidal Separation Surgery (TSSS) for Unresectable Pituitary Adenomas: Proof of Concept

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Objective

Invasive pituitary adenomas (PA, Knosp grade 4 and some grade 3 tumors) often cannot be resected completely (Micko et al. 2019). Separation surgery originates from surgery for spinal metastases. It aims to create a spatial separation of nervous tissue to enable radiosurgery (RS) instead of fractionated radiotherapy (FRT) for tumor control (Bate et al. 2015). This concept was adapted to TSSS as the rates of secondary hypopituitarism are lower after RS compared to FRT (Knappe et al. 2020).

Methods

We retrospectively analyzed the data for all patients undergoing microsurgical transsphenoidal surgery (TSS) for PAs in our institution from 10/2007 to 12/2020. The PAs were classified according to the modified Knosp classification on preoperative MRI. Inclusion criteria were Knosp grades 3 and 4, follow-up of at least 12 months, and surgery with concept of TSSS.

Results

A total of 94 (39 female) cases were included, 30 (32%) had prior surgeries for PA, 2 had prior FRT. Mean age 55 ± 16 ys., mean follow-up 62 ± 41 months, Knosp grades 3A N=63 (4 bilateral), 3B N=9, and 4 N=22 (3 bilateral), mean tumor 32.1 ± 13.8 mm. Thirty-seven of the adenomas were functioning (39%).

Six patients underwent staged TSS and transcranial surgery (TCS). In 21 cases postoperative imaging showed no tumor remnant (22%, Knosp grades 3A N=19, 3B N=2). These patients required no further treatment, 23 patients needed further surgeries: six early revision surgeries (TCS twice, four second-look TSS), 17 due to tumor progression later on.

Twenty-six out of the remaining 73 patients received RS (36%, two patients twice), 6 underwent FRT and one patient both. After radiotherapy five tumors (RS N=4 and FRT N=1) showed progression.

Prior to FRT 3 out of 7, prior to RS 4 out of 26 patients had panhypopituitarism. After FRT 2 out of 3 patients with partial hypopitutarism needed further hormone replacement, and one developed new hypogonadism and hypothyroidism. The need for hormone replacement remained unchanged after RS for all patients expect one (new hypogonadism), including 12 cases without any endocrinological deficit.

Conclusion

TSSS seems to be a valuable concept for interdisciplinary treatment of unresectable PAs. However, only 36% in our cohort underwent RS according to our concept.

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Hypophysenadenom II/*Pituitary adenoma II*

V225

Das Risiko perioperativer Blutungskomplikationen bei Patientin mit Hypophysenadenomen und endoskopischer endonasaler Operation bei einer notwendigen perioperativen Thrombozytenfunktionshemmung mit ASS 100

Risk of perioperative bleeding complications in patients with endoscopic endonasal surgery for pituitary adenomas and a compulsory indication for perioperative antiplatelet medication with ASS 100

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Objective

To analyse the risk of perioperative bleeding complications associated with continued perioperative platelet inhibitory medication using aspirin 100mg (ASS) when strongly indicated due to cardio- or cerebrovascular indications in patients undergoing endonasal transsphenoidal surgery (ETS) for treatment of pituitary adenoma (PA).

Methods

Single centre study of a series of consecutive patients with PA, who underwent ETS between December 2008 and June 2022. Patient data (age, sex, clinical endocrinology, tumor histology), were prospectively entered into a SPSS® database. Patients with ASS medication were interdisciplinary managed according to a standard protocol. ASS was paused at least 7 days prior to ETS in patients with primary prophylaxis (no previous myocardial ischemia, no stroke, no relevant peripheral artery disease). If a continued perioperative platelet inhibition with ASS 100mg was indicated after individual interdisciplinary case by case discussion. Perioperative discontinuation was grouped as less than 2 days, 2-4 days and 4<7 days.

Results

35 (11.5%) of 304 included patients were operated without preoperative withholding of ASS 100mg (14 (4.6%) patients <2 days, 8 (2.6%) patients 2-4 days, and 13 (4.3%) patients >4 day). 274 patients (90.1%) had primary surgery and 30 (9.9%) surgery for recurrent tumors. No difference (age, sex, suprasellar extension, tumor volume largest diameter) in baseline criteria were found for patients with perioperative ASS medication and patients with discontinued ASS. 1 patient (0.3%) suffered from postoperative intracranial haemorrhage but in this patient ASS was discontinued 7 days before surgery. 8 patients (2.6%) had postoperative epistaxis (1 patient [0.3%] in the perioperative ASS group and 7 patients [2.3%] in the ASS discontinued group), which was not statistically significant. No other cerebrovascular complications were encountered while discontinuing ASS.

Conclusion

Patients with a compulsory indication for antiplatelet therapy with ASS 100mg and the indication for surgery of a PA can be safely operated without increased risk of perioperative bleeding complications. An interdisciplinary case by case discussion with cardiologists and neurologists should take place prior to surgery and perioperative ASS cessation should be as long as justifiable with regard to potential cardiovascular or cerebrovascular complications.

Hypophysenadenom II/*Pituitary adenoma II*

V226

Die Basallamelle der oberen Nasenmuschel aus neurochirurgischer Sicht
The basal lamella of the superior turbinate from a neurosurgeon´s perspective

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Objective

The sphenoethmoidal recess and the superior turbinate should be protected in endoscopic transnasal neurosurgery due to their aerodynamic and olfactory function. The purpose of this study is to clarify the anatomical relationships of the superior turbinate´s basal lamella (4BL) around the posterior ethmoid with a focus on the superior turbinate, the sphenoethmoidal recess, the anterior sphenoid wall and its ostium to help neurosurgeons to perform a safe approach.

Methods

Cone beam CTs of 36 adults and 14 cadavers (total: 100 sides) were investigated with the 3DSlicer software (www.slicer.org) creating three-dimensional models of the 4BL and the posterior ethmoid. We established a segmenting method to accurately describe the geometry of each 4BL´s shape. We analyzed their relationship to neighboring structures.

Results

The most common 4BL was described as a monosegmental, nearly pentagonal plate in the frontal plane. We rarely observer a stringent "L"-shaped 4BL-appearance with an anterior frontal and a posterior horizontal portion in a lateral view, as usually reported.

On both sides it was built of 1.2 ± 0.4 segments (median: 1; range: 1–2). We identified a 2nd segment in 24.0% on both sides (total N=24). The 1st (cranial) segment was a frontal plate in 81.0% (N=81), a concave plate in 8.0% (N=8), a sigma plate in 5.0% (N=5), a convex plate in 4.0% (N=4), a frontal wave in 2.0% (N=2). The 2nd (caudal) segment was a horizontal plate in 45.8% (N=11), a convex plate in 29.2% (N=7), a frontal plate in 25.0% (N=6).

The 4BL adhered the anterior sphenoid wall in 95.0% (N=95) on a large surface. This adhesion was both direct and indirect through the lateral nasal wall´s common lamella. The 4BL partly comprised the basal lamella of the middle turbinate in 5.0% (N=5) and an Onodi-cell in 65.0% (N=65).

The sphenoid ostium´s lowest point was measured from the superior turbinate´s posterocaudal insertion at the anterior sphenoid wall (mean: 10 mm, range: 4.7-15.5) and found mostly superior (98.0%), medial (97.0%), anterior (51.0%). There were no significant differences between the sides.

Conclusion

The segmenting method is eligible to describe the 4BL´s morphology which mostly appeared as a nearly pentagonal frontal plate, fusing to the anterior sphenoid wall. This anatomical analysis should help

neurosurgeons´ orientation. An excessive dissection of the sphenoethmoidal recess and the anterior sphenoid wall may violate the 4BL and thus the stability and function of the superior turbinate.

Hypophysenadenom II/*Pituitary adenoma II*

V227

Psychische und körperliche Lebensqualität sowie assoziierte klinische Parameter bei Patienten mit Hypophysentumoren: eine fragenbogenbasierte Querschnittsstudie (QoL-Hypophyse)

Mental and physical quality of life and associated clinical parameters in patients with pituitary tumors: a questionnaire-based cross-sectional study (QoL pituitary)

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Objective

A pituitary disease and its treatment can cause a wide range of emotional and physical stress in patients. Our questionnaire-based study aims to examine the physical and psychological quality of life of patients with pituitary tumors and whether certain subgroups are particularly strained. In addition to patient surveys, the patient's overall situation is also described and correlated anatomically, in terms of laboratory chemistry, as well as ophthalmologically and rhinologically. Now we present our first descriptive data.

Methods

The local ethics committee approved this clinical study. The patients were recruited in the over regional, interdisciplinary (neurosurgery and endocrinology) consultation hour for pituitary tumors at our neurosurgical ambulance during one year. 159 patients (92 (57.9%) females and 67 (42.1%) males) were included. Enrollment was performed prospectively and the response rate is over 60%. Data about quality of life of patients with the mentioned pituitary tumors were accumulated using a variety of questionnaires (Distress Thermometer, SF-8, GAD-7, PHQ-9, WHOQOL, LBNQ-Pituitary, QLS-H, AcroQoL, Tübingen-CD 25 and an internal questionnaire).

Results

Based on the 159 answered questionnaires we distributed our patients in 5 groups: non-active pituitary adenomas (93, 58.5%), prolactinomas (26, 16.4%), ACTH-producing tumors (4, 2.5%), growth hormone-producing tumors (16, 10.1%) and a group of "other tumors" including Rathke cleft cysts and meningiomas (20, 12.6%). Rating their distress on a scale from 0-10 in the categories depression, anger and need of help most patients indicated low distress, almost half of the patients choosing a zero on the scale. Fear (mean: 2.96) and stress (mean: 4.15) were rated higher, indicating a stronger impairment in those categories. Doctors were named as their main source of information about their pituitary disease, followed by the internet. 28.3% of the patients wish for more endocrinological consultation. 44.7% stated to only think about their disease when going to the doctor.

Conclusion

Many patients with pituitary tumor suffer from a deterioration of life quality. More knowledge about this phenomenon helps to understand and adapt the supply according to the disease-specific stresses. This may not only improve the quality of life of the patient, but also indirectly improve the treatment and thus the outcome.

Hypophysenadenom II/*Pituitary adenoma II*

V228

Der Einfluss radiologischer Tumorwachstumsmuster auf die sinunasale Gesundheit und Lebensqualität bei Hypophysenadenomen

The influence of radiological tumor growth pattern on sino-nasal health and quality of life in pituitary adenomas

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Objective

Pituitary adenomas account for one of the most common mass lesions of the brain. While transsphenoidal tumor resection is the preferred surgical approach, the impact on quality of life (QoL) and sino-nasal health considering the radiological tumor size seems to be unclear. In our study, we examined the influence of the radiological KNOSP and Hardy score on QoL and sino-nasal health before and after endoscopic transsphenoidal tumor resection.

Methods

Prospectively collected data with informed consent between 1st August 2016 and 31st August 2021 were evaluated. KNOSP and Hardy classifications have been applied for pituitary adenomas on all preoperative MRI scans and have also been dichotomized in small and large lesions. QoL and sino-nasal health has been assessed immediately before and at follow-up examinations 3 to 6 months after surgery by using Short-Form (SF-36) and SNOT-NC surveys.

Results

159 KNOSP and Hardy scores were obtained. Values assessed by independent t-tests showed significant differences between small and large KNOSP tumors for the SNOT-NC total score (ρ = 0.05), sleep problems (ρ = 0.028) and for visual impairment (ρ = 0.021). Pre- and postoperative comparisons for the small KNOSP cohort showed an increase of nasal discomfort (ρ = 0,018), while large KNOSP score experienced improved visual impairment (ρ = 0,008) and sleep quality (ρ = 0,022) after surgery. Assessing the Hardy classification, differences for SNOT-NC nasal score (ρ = 0.044) and visual score (ρ = 0,034) were determined. Pre- and postoperative comparisons found an increase in nasal discomfort after surgery (ρ = 0,01) for small Hardy stage lesions, while for large suprasellar growth a significantly improved vision (ρ = 0.046) was shown. Contrary to the SNOT-NC findings SF-36 only showed incoherent results for KNOSP and Hardy classification.

Conclusion

Growth characteristics of pituitary adenomas based on KNOSP and Hardy classification may influence the visual impairment and sleep quality. Patients with smaller lesions were more prone to experience a decrease of sino-nasal health. These findings underline the importance of evaluation of QoL and sino-nasal health in patients with pituitary adenomas. Radiological classifications showed only minor influence on SF-36, suggesting that this survey does not depict sino-nasal health well.

Pädiatrischer Hydrocephalus Diagnostik Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Diagnostics Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V229

Überlegenheit des point-of-care Ultraschalls gegenüber der Fundoskopie zur Identifizierung eines mutmaßlich erhöhten intrakraniellen Druckes bei Kindern

Superiority of transorbital point-of-care ultrasound versus fundoscopic papilledema to identify potentially elevated intracranial pressure in children

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Objective

Fundoscopic papilloedema is missing in up to 50% of cases with raised ICP requiring treatment. Transorbital point-of-care-ultrasound techniques - optic nerve sheath diameter (ONSD) and optic disc elevation (ODE) - were compared to fundoscopic findings in children with symptoms rising suspicion of raised ICP.

Methods

72 children were included; 50 with proven pathology associated to raised ICP (e.g. pseudotumor cerebri, tumor, hydrocephalus), 22 with pathology excluded. Bilateral ONSD and ODE were quantified by US using a 12 MHz linear array transducer. This was compared to fundoscopic optic disc findings and, in 28 cases, invasively measured ICP values.

Results

Only 23/50 (46%) of children with potentially raised ICP had papilledema on fundoscopy. The diagnostic accuracy of cut-off values for potentially raised ICP for US-ONSD (5.73mm, AUROC 0.952) and US-ODE (0.43mm, AUROC 0.804) was considerably higher compared to fundoscopic papilledema (AUROC 0.730), see Fig 1. Repeatability and observer-reliability of US-ODE examination was eminent (Cronbach´s α = 0.978-0.989). Papilledema was only found in case ODE was > 0.67mm, an ODE > 0.43 had a positive predictive value for potentially raised ICP of 90%, see Fig 1. US-results were more appropriate to indicate decrease of ICP after treatment than fundoscopic papilledema, see Fig 2.

Conclusion

In our cohort transorbital point-of-care US determination of ONSD and ODE could more reliably detect potentially elevated ICP in children than fundoscopy. Sonographic determination of ONSD and ODE did indicate ICP decrease after treatment earlier and more reliably than fundoscopy. The established cut-off values for US-ONSD and US-ODE and a newly developed US-based grading of ODE can be used as an ideal first-line-screening tool to detect or exclude conditions with potentially elevated ICP in children.

Abb. 1

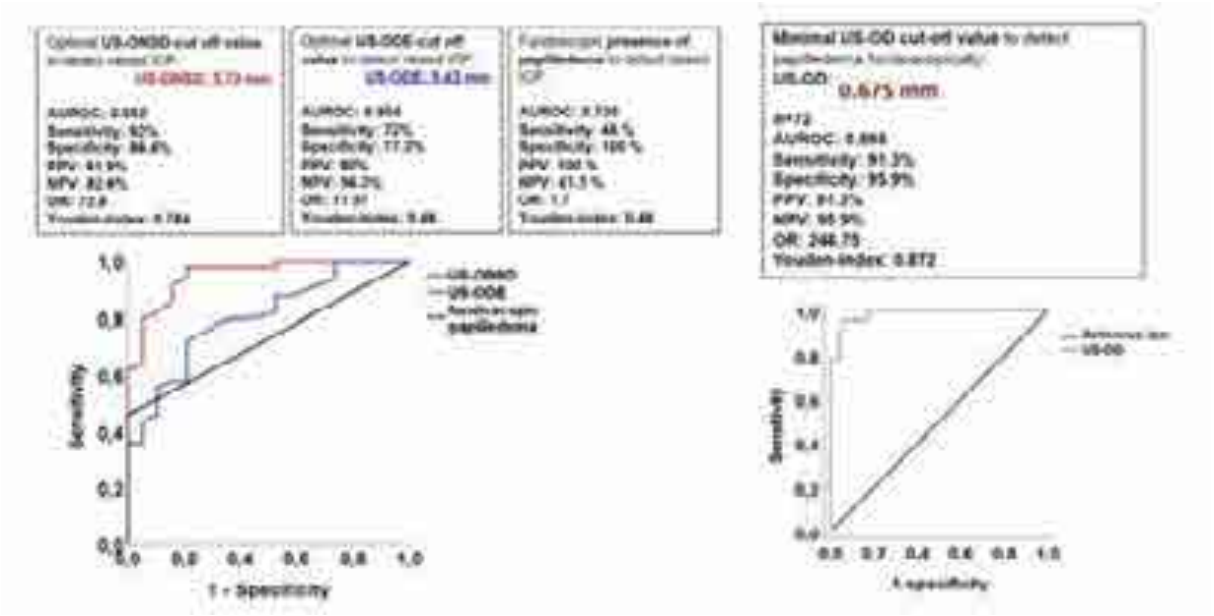
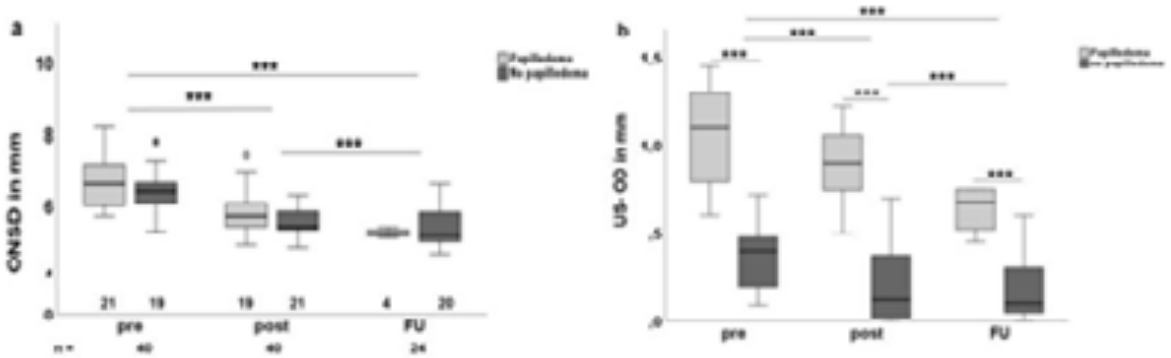

Minimal US-OD cut-off value
0.675 mm
Sensitivity
1 - Specificity

Abb. 2


a
CNSD in mm
pre
post
FU
b
US- OD in mm
pre
post
FU

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V230

Einfluss von Geschlecht und Ätiologie auf die Entwicklung von Papillenödem und Sehnervenscheidenerweiterung bei Kindern mit erhöhtem ICP

Influence of gender and etiology on the development of papilledema and optic nerve sheath extension in children with raised ICP

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Objective

To analyse if gender and type of pathology influence the development of papilledema and compare fundoscopic and point-of-care-ultrasound techniques (optic nerve sheath diameter (ONSD) and optic disc (OD) elevation) to detect pathologies with ICP increase in children.

Methods

72 children were included; 46 male, 26 female; 50 with proven pathology (e.g. pseudotumor cerebri (PTC), tumor, hydrocephalus), 22 with pathology excluded. Bilateral ONSD and OD were quantified by US using a 12 MHz linear array transducer. This was compared to ophthalmoscopic optic disc findings and in some patients with invasive ICP values.

Results

In patients with proven pathology, significant more girls (69%) had fundoscopic papilledema compared to boys (37%, $p<0.05$). Girls had also larger US- OD values (0.88±0.36mm vs. 0.65±0.4mm in boys). US ONSD revealed no gender-specificity. In tumor patients 80% had initial papilledema (100% girls, 79% boys), compared to 50% in pseudotumor cerebri (PTC) (83% girls, 30% boys). Initial US OD was larger in tumor compared to PTC. ONSD had no pathology specificity.

Conclusion

Papilledema seems to be a gender- and pathology-specific feature, whereas US ONSD is not. Girls rather seem to develop papilledema under similar conditions. Male sex and PTC are risk factors to remain undetected using ophthalmoscopic OD findings for diagnostics. US ONSD and OD can be useful additions to detect pathologies with possible raised ICP in children.

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V231

Externe Validierung eines Prädiktionsmodells für Hydrozephalus nach Resektion pädiatrischer Kleinhirntumore

External validation of a prediction model of postresection hydrocephalus in pediatric patients with posterior fossa tumorsPreliminary results of external validation of the modified Canadian Preoperative Prediction Rule for Hydrocephalus

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Objective

Persistent hydrocephalus after posterior fossa tumor (PFT) resection is a common phenomenon with incidences up to 40%. Hence the modified Canadian Preoperative Prediction Rule for Hydrocephalus (mCPPRH) score was developed to identify preoperatively those children who are at high risk for persistent hydrocephalus. Children at high risk are likely to benefit from an internal CSF diversion procedure prior to tumor resection, which has shown to reduce persistent hydrocephalus substantially. External validation is essential before implementing the mCPPRH in clinical practice. To date, adequate external validation in a European set of children is lacking. We performed an external validation analysis to gain more insight in the performance of the mCPPRH in pediatric patients in Western Europe.

Methods

We identified a cohort of pediatric with PFT and who subsequently underwent resection. The variables of the mCPPRH were collected including age, transependymal edema, moderate to severe hydrocephalus, metastasis, and preoperative tumor diagnosis. As defined by the modified CPPRH model, the outcome was persistent hydrocephalus within 6 months of tumor diagnosis, as defined by the occurrence of either ventricular shunting or endoscopic third ventriculostomy. To assess external validation, the performance of the mCPPRH was assessed with discrimination (*c*-statistic) and calibration (calibration slope and expected/observed number of events (E/O)) measures. Discrimination refers to the ability of a prediction model to discriminate between patients with and without the outcome and is quantified using the c-statistic. The c-statistic ranges from 0.5 to 1, 1 refers to perfect discrimination. Calibration refers to the agreement between predicted and observed outcome.

Results

114 children were included in the analysis. The median patient age was 7 years (IQR 3-11). 20 (17.5%) children suffered from persistent hydrocephalus. The externally validated c-statistic was 0.77. The calibration slope was 0.89 and the E/O ratio equaled 0.89 indicating promising performance measures. The calibration slope and E/O ratio should ideally be 1. A slope <1 is often seen in validation studies.

Conclusion

The mCPPRH shows potential to support decision-making on performing prophylactic internal CSF diversion procedure prior to PFT resection in Western European pediatric patients, although increasing the sample size is needed to obtain robust results. A multicentered study has been designed and planned.

Pädiatrischer Hydrocephalus Diagnostik Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Diagnostics Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V232

Verhältnis der Weite des 3. Ventrikels (TVD) und von Seitenventrikel-Indices zu Liquorvolumina und Gehirnvolumen beim Pädiatrischen Hydrocephalus

Relation of third ventricular diameter (TVD) and ventricular indices to cerebrospinal fluid volumes and brain volume in pediatric hydrocephalus

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Objective

Treatment decision and monitoring of treatment success in pediatric hydrocephalus is often based on changes in ventricular width. After closure of the fontanel, the ventricular width can be estimated either by determining the third ventricle diameter (TVD) by transtemporal ultrasound (US) or by measuring the common ventricular indices in cranial CT or MRI. The aim of our study was to investigate whether and to what extent TVD and the ventricular indices correlate with the actual volume of the inner and outer cerebrospinal fluid (CSF) spaces and brain volume.

Methods

83 children (newborn to 18 years) diagnosed with hydrocephalus were investigated. All patients underwent cranial MRI and using an automated segmentation algorithm the volumes of lateral ventricles, third and fourth ventricle as well as total internal/external CSF and brain volume were determined. Volumes were compared to TVD, Cella Media Index (CMI), Evans Index (EI) and frontal-occipital-horn-ratio (FOHR).

Results

TVD and all 3 ventricular indices correlated excellently and highly significant ($p<0.01$) to the volume of the lateral ventricles ($r= 0.666$-0.859), the third ventricle ($r=0.447$-0.849) and the total internal CSF spaces (0.668-0.871). All linear parameters correlated significantly negative ($r= -0.618$ - - 0.272; $p<0.01$) with external CSF volume. Brain volume and CSF volumes correlated negatively only depending on pathology. CMI was the only linear ventricular parameter to correlate significantly negative with brain volume ($r=-0.324$, $p<0.01$).

Conclusion

TVD and all three lateral ventricular indices reliably mirror the inner CSF volume and correlate negatively to the outer CSF volume. TVD was not inferior in its correlation to CSF volumes compared to lateral ventricular indices. Since TVD can be determined easily, precisely and reliably by transtemporal US, in contrast to ventricular indices demanding CT or MRI, it becomes a superior, reliable, non-invasive diagnostic bedside tool in pediatric hydrocephalus.

Pädiatrischer Hydrocephalus Diagnostik Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Diagnostics Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V233

Der Einfluss der Covid-19-Pandemie auf die Shuntrevisionsrate bei Kindern
The influence of the Covid-19 pandemic on the shunt revision rate in children

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Objective

During the first year of the Covid-19 pandemic we observed a decrease of our shunt revision rate. In order to investigate a possible correlation with an assumingly lower general infection rate in children in times of lock down and homeschooling, we performed a detailed analysis of our shunt and general pediatric patient population.

Methods

For this retrospective single institution study we performed an electronic patient charts retrieval for children admitted for shunt revision or infectious diseases for four time periods (study period April 2020 – March 2021, control periods from three previous years). A detailed analysis of all shunt revision and infectious cases including age and season specific evaluation followed. Possible correlations were investigated.

Results

A total of 318 shunt revision and 13,919 pediatric cases have been evaluated. The shunt revision rate during the study period was 29% less compared to the average rate of three previous years (p 0.061), the number of pediatric cases with main diagnosis infection dropped significantly ($p < 0.05$), whereas other pediatric admissions remained stable. Significant age or seasonal influences did not exist. The number of shunt revisions in association with a documented systemic infection or a primary shunt infection dropped significantly during the study period ($p<0.05$ each). This was not the case for underdrainage, overdrainage ($p>0.05$ each) or other indications. In general, infections of upper and lower airways, the gastrointestinal and nervous system decreased during the pandemic, urinary infection rates remained stable.

Conclusion

The decreased shunt revision rate during the first year of the pandemic seems to correlate with a decrease of the general infection rate in children and adolescents at the same time. Infection-associated shunt failures showed a significant decrease during this period compared to previous years.

Pädiatrischer Hydrocephalus Diagnostik Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Diagnostics Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

V234

Der Einfluss des COVID-19 Lockdowns auf die pädiatrische Neurochirurgie - Auswertung nationaler Daten.
Big data approach on the impact of COVID-19 lockdown on pediatric neurosurgery.

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Objective

COVID-19 led to lockdowns in 2020, significantly limiting activities of daily life. Data on the impact on healthcare systems is ambiguous: Some sources indicate no statistically relevant changes, whereas others reveal a decline in operations and hospitalisations. For some diagnoses, e.g. child abuse, conflicting results are relevant to future contingency plans. So far no data has been published for pediatric neurosurgery in Germany. We present the results of a big data approach.

Methods

We obtained anonymous data from the nationwide database of hospital statistics (German Federal Statistical Office, www.destatis.de) in August 2022. For the age group <18 years in 2016-2020, the following diagnoses (ICD-10 code) were analysed: Intracranial injury (S06), malignant (C71), benign (D33) and unspecified (D43) neoplasia, abuse (T74), violent attack (Y09) and, for comparison, forearm fracture (S52). The following operations (OPS code) were chosen: Operation of the central nervous system (CNS, 5-01-05), excision of intracranial lesion (5-015), shunt insertion (5-023), shunt revision (5-024), plastic operations of the spinal cord (5-036) and, for comparison, overall number of operations (OPS-5), spondylodesis (5-836) and functional neurosurgery (5-028) at all ages.

Results

The overall number of operations declined from 17.23 million in 2019 to 15.82 million in 2020 (8.2%). CNS operations in general declined by 5%. Shunt insertion declined by 8.1%, revision by 5.1% and spinal cord operations by 6.6%, whereas excisions of intracranial lesions increased by 1.7%. Spondylodesis and functional operations both decreased by 11.9%.

The hospitalisations for intracranial neoplasia declined by 8.8% compared to previous years. The number of inpatients with intracranial injury declined by 16%. Violent attack was also documented less often (-13.2%), but child abuse increased by 3.3%. Forearm fractures declined by 5.6%.

Conclusion

The COVID-19 lockdown in 2020 lead to reduction of operations, including pediatric neurosurgery. Neuro-oncological operations were not affected. In comparison, elective neurosurgery in adults decreased by 12%. Admissions for brain tumor declined by 9%. Intracranial injury even declined by 16%, reflecting limited activities and mobility. An increase in documented child abuse by 3.3% compared to the average of previous years was observed. These results help understand the impact of pandemics and political decisions and guide future decision-making.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

V235

Die Ko-Kultur von PBMC-Zellen und Organoiden optimiert das Tumormicroenvironment im Glioblastom
Co-culture of PBMCs and patient derived organoids enhances glioblastoma tumor microenvironment

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Objective

Glioblastoma (GBM) is the most common malignant brain tumor in adults and still a challenge for recurrent situations. Novel immunotherapeutic approaches have shown promising effects *in vitro* and in preclinical animal models. However, their clinical breakthrough is hampered by complex interactions with the tumor microenvironment (TME). Previous work in our group showed that the TME is still active in GBM patient-derived organoids (PDO) after one week of culture but declining rapidly after. To obtain a more realistic *ex vivo* model for immunotherapeutic testing, we aimed to introduce an enhanced TME by co-culturing peripheral blood mononuclear cells (PBMC) and GBM PDO.

Methods

We generated PDOs from freshly resected tissue from three different GBM patients. PBMCs were obtained from healthy donors. Subsequently, PDOs and PBMCs were co-cultured at a ratio of 1:20 (enhanced PDO [ePDO]). PDOs without PBMCs (normal PDO [nPDO]) as well as primary tissue (PT) were used as controls. Immunohistochemical analysis of numerous antigens of the TME (CD45+ myeloid cells, CD7+ natural killer (NK) cells, CD4+ T helper cells, CD8+ cytotoxic T cells, and CD68+ macrophages) was performed to investigate the composition of the TME in PT and PDOs with or without co-culture with PBMCs.

Results

In PT, CD45+ myeloid cells accounted for 2.95 % of TME, CD4+ T helper cells for 3.3 %, CD8+ cytotoxic T cells for 2.1 %, CD7+ NK cells for 0.8 % and CD68+ macrophages for 6.74 %. In nPDO, CD45+ myeloid cells ($p = 0.012$), CD4+ T helper cells ($p = 0.047$), CD8+ cytotoxic T cells ($p < 0.001$) and CD68+ macrophages ($p = 0.003$) were expressed significantly less compared to PT. CD7+ NK cells could not be detected in nPDO ($p = 0.18$). In contrast, ePDOs did not show any significant difference in TME expression in CD45+ myeloid cells ($p = 0.61$), CD4+ T helper cells ($p = 0.59$), CD7+ NK cells ($p = 0.74$) and CD68+ macrophages ($p = 0.22$). CD8+ cytotoxic T cells were found less (0.1 %, $p < 0.01$) compared to PT.

Conclusion

After 21 days, no TME could be detected in nPDOs, whereas ePDOs expressed a specific and distinct TME, which reflected the TME composition in PT even after 21 days. Thus, this enhanced *ex-vivo* PDO approach could reflect the interaction of tumor, TME and immunotherapeutic agents and, consequently, may represent a realistic model for individual immunotherapeutic drug testing in the future.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

V236

***Ex vivo* Organoide spiegeln das Tumormicroenvironment des Glioblastoms wider**
Ex vivo glioblastoma organoids reflect tumor microenvironment

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Objective

Glioblastoma (GBM) is one of the most challenging tumor entities to overcome. However, complex interactions with the tumor microenvironment (TME) impede their clinical breakthrough of new immunotherapeutic agents. Robust models for *ex vivo* trials of new therapeutic agents reflecting the TME-tumor interactions are desperately needed. Here, we present the composition of the TME in primary tissue (PT) and changes of the TME composition in an *ex vivo* organoid model.

Methods

Fresh tissue of ten different patients (nine GBM and one oligodendroglioma) was carefully minced to 500 µm sized pieces and cultured until round patient derived organoids (PDOs) formed. PDOs were obtained after day 7 (t2) and day 14 (t3). Analysis of different antigens (CD45+ myeloid cells, CD7+ natural killer (NK) cells, CD4+ T-helper cells, CD8+ cytotoxic T-cells, CD14+ monocytes, CD68+ macrophages, INOS+ M1 macrophages, CD163+ M2 macrophages and CCR2+ peripheral macrophages) was conducted in order to investigate TME composition in PT as well as the ability of PDOs to reflect primary TME features.

Results

In the PT (t1), macrophages were strongly represented in the TME and made up almost 40 % of the total cell count in the tumor, of which the largest proportion were M2 macrophages. The number of immune cells decreased from t1 to t3 for every cell type. CD45+ myeloid cells made up 3 % at t1 and only 0.51 % at t3. There were significant differences in CD4+ cells between t1 (2.2 %) and t3 (0.6 %) ($p = 0.04$). While CD8+ cells started with 0.6 % at t1, no CD8+ cells were left at t3. CD7+ NK cells decreased from 0.66 % at t1 to 0.003 % at t3. CD68+ macrophages decreased from 30.5 % at t1 to 22.8 % at t3 ($p = 0.001$). CD14+ monocytes decreased significantly from t1 (20.6 %) to t3 (7.5 %) ($p = 0.03$). M1 macrophages dropped from 1.2 % to 0.7 % from t1 to t3, as well as M2 macrophages from t1 (16.7 %) to t3 (8.4 %). CCR2+ peripheral macrophages declined from t1 (3.8 %) to t3 (0.7 %). However, even though the absolute count of immune cells decreased from t1 to t3, the relative distribution of TME did not change.

Conclusion

In summary, the relative composition of the TME in PDOs stayed representative for GBM PT. Therefore, PDOs might represent a promising *ex vivo* model for individual immunotherapeutic drug testing, that might work optimal during the first 7 days. Alternatively, the TME in GBM PDOs could be enhanced and altered in order to represent the TME in PT even better.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

V237

Der metastatische Phänotyp von B16 Melanomzellen wird nach ephrinB2-EphB4 Interaktionshemmung durch eine spezielle endotheliale Zellpopulation wiederhergestellt

A distinct endothelial cell population rescues the metastatic phenotype of B16 melanoma cells after ephrinB2-EphB4 interaction depletion

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Objective

Spinal metastasis remains a persistent challenge in the neurosurgical operating room. Patients need to undergo emergency surgeries on a regular basis due to rapid onset of neurological deficits. Driven by these challenges we aim to understand metastatic spread to the spinal bone on a molecular level in endothelial cells and tumor cells to facilitate improved therapeutic approaches and diagnostics.

Methods

We established a murine syngeneic spinal bone metastasis model. In vivo dissemination to different spinal segments was first evaluated using fluorescent beads, followed by murine cancer cell lines. We investigated short-term seeding and long-term growth behavior to identify correlations between seeding and tumor formation. EphrinB2-Eph4 interaction has been described as a crucial mediator of spinal bone metastasis. Transient (pharmacological) and permanent (genetical) interventions were performed.

Results

We found that dissemination of microbeads to distinct spinal segments depended on the segment and particle size/volume. Disseminated tumor cells on the contrary show less frequent arrest in the bone and equal distribution among segments independent of tumor cell type, while spinal metastases established more frequently in the B16 melanoma model. EphrinB2 intervention changed the dissemination behavior towards the lumbar segment. Interestingly, only transient intervention retained this distribution, permanent ephrinB2 depletion on endothelial cells (*efnb2i*ΔEC) resulted in equal dispersion of metastases. Histological staining revealed a reduction of Endomucin (Emcn) positive structures in combination with a reduction of Type H (Emcn high/CD31 high) endothelial cells in naïve *efnb2*iΔEC animals. In tumor tissue, these Type H endothelial cells were unaffected. However, an increase in CD31-expressing endothelial cells was observed under endothelial ephrinB2 depletion. These CD31-expressing endothelial cells have been recently described as Type E (Emcn low/CD31 high) and implicated in angiogenesis and osteogenesis.

Conclusion

We here describe a subpopulation of endothelial cells in *efnb2*iΔEC mice that seems to resemble pro-angiogenic and possibly pro-adhesive type E endothelial cells. Based on these finding we propose a compensatory pro-angiogenic mechanism in *efnb2*iΔEC mice that is highjacking pre-existing developmental pathways, which is critical for late-stage spinal metastatic growth independent of the initial seeding and extravasation of metastatic cells.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

V238

CUSP9v3 verfügt in vitro über eine starke antineoplastische Aktivität gegen das Medulloblastom

The drug repurposing approach CUSP9v3 has a strong antineoplastic activity against medulloblastoma in vitro

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Objective

Medulloblastoma represents one of the most common brain tumors in children. While current first-line therapy is associated with a five-year overall survival greater than 70% in standard-risk patients, high-risk patients face a significantly worse clinical course urging the need for novel therapeutic strategies. In this study, we examined whether the drug repurposing approach CUSP9v3 has antineoplastic activity in medulloblastoma models in vitro.

Methods

Preclinical drug testing including MTT assays, staining with annexin V/propidium iodide followed by flow cytometry, Western blot analyses and scratch assays were performed in high and low c-myc-expressing established and primary cultured medulloblastoma cells. Spheroids were used to assess effects on 3-dimensional growth.

Results

CUSP9v3 showed a strong and dose-dependent inhibitory effect on the cell viability of established (DAOY, HD-MB03, D425 and D458), primary cultured (PC322 and PC399) and stem-like (SC322 and SC399) medulloblastoma cells. Moreover, flow cytometric analyses showed a significant increase of the fraction of annexin V-positive (apoptotic) medulloblastoma cells following treatment with CUSP9v3. These findings were accompanied by enhanced cleavage of effector caspase 3. On the 3-dimensional level, the growth of tumor spheroids was significantly impaired by CUSP9v3. In addition, treatment with CUSP9v3 had a significant anti-migratory effect on DAOY, PC322 and PC399 medulloblastoma cells.

Conclusion

Our observations suggest that CUSP9v3 has a strong pro-apoptotic and anti-migratory activity against medulloblastoma cells in 2- and 3-dimensional settings. These effects were present in both, c-myc low and high expressing models. Overall, these data encourage further studies of CUSP9v3 as a potentially valuable therapeutic strategy against medulloblastoma.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

V239

TTFields verstaerken die Wirkung von CUSP9v3 auf das Glioblastom auf ueberwiegend synergistische Weise

TTFields empower the drug repurposing approach CUSP9v3 against glioblastoma in a predominantly synergistic manner in vitro

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Objective

Drug repurposing represents a promising strategy to safely accelerate the clinical use of therapeutics with antineoplastic activity. In this study, we examined whether Tumor Treating Fields (TTFields) enhance the biological effects of CUSP9v3, a treatment strategy including nine repurposed drugs, in an *in vitro* setting of glioblastoma.

Methods

We performed MTT-assays to examine effects of the combination treatment on the viability of different glioblastoma cells. Tumor spheroids were used as a model to examine effects of the combination treatment in a 3-dimensional setting. Staining with annexin V/propidium iodide or MitoTrackerTM followed by flow cytometry was done to assess pro-apoptotic effects. Specific protein expression of caspases and members of the Bcl-2 family of proteins was determined by Western blot analyses.

Results

TTFields had predominantly synergistic inhibitory effects on the cell viability of established (U251), primary cultured (PC38, PC40, PC128) and stem-like (SC38, SC40) glioblastoma cells when combined with CUSP9v3. In addition, flow cytometric analyses revealed that a simultaneous treatment with TTFields and CUSP9v3 significantly increased the fraction of annexin V-positive (apoptotic) glioblastoma cells. Moreover, the fraction of cells with a reduced mitochondrial outer membrane potential was significantly higher following a simultaneous treatment with TTFields and CUSP9v3. On the molecular level, these observations were associated with enhanced cleavage of effector caspase 3 and a reduced expression of the anti-apoptotic Bcl-2 family proteins Bcl-2 and Mcl-1.

Conclusion

These data suggest that TTFields enhance the susceptibility of glioblastoma cells towards CUSP9v3, potentially allowing significant dose reduction and decreased toxicity. This observation seems to rely at least in part on a caspase-dependent cell death mechanism. TTFields are widely used for the treatment of glioblastoma patients and CUSP9v3 was recently shown to have a favorable safety profile in a phase Ib/IIa trial (NCT02770378) which facilitates transition of a combined approach to the clinical setting.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

V240

Tumor Treating Fields (TTFields)-Effekte auf Glioblastom-, anaplastische Ependymom- und Oligodendrogliom-Proben in einem von Patienten abgeleiteten *ex vivo* Organoid-Modell

Effects of Tumor Treating Fields (TTFields) on glioblastoma, anaplastic ependymoma and oligodendroglioma samples in a patient-derived ex vivo organoid model

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Objective

TTFields are intermediate frequency (100-500 kHz) alternating electric fields of low intensity (1-3 V/cm). The use of TTFields at 200 kHz is effective and approved for the treatment of newly diagnosed glioblastoma (GBM) patients. However, more knowledge is needed to predict how individual tumors will respond to treatment. We have recently developed patient-derived three-dimensional GBM tissue culture models that could be used to screen patient tumors for treatment susceptibility. Our aim here was to extend these models to brain tumors beyond GBM, namely anaplastic ependymoma (AE) and oligodendroglioma, by culturing tumor-organoids as microtumors on murine organotypic hippocampal slice cultures (OHSCs) and subjecting them to TTFields treatment.

Methods

Brains of mice 5-8 days postpartum were sliced to a thickness of 350 µm using a vibratome in order to prepare OHSCs. Slices were cultured for 14 days. Freshly resected tumor tissue from a GBM, AE, and oligodendroglioma patient, each, was cultured for 14 days to obtain organoids. Afterwards, the organoids were placed onto the OHSCs. TTFields at 200 kHz and 1.5 V/cm were administered for 72 h using the inovitro™ laboratory research system before measuring microtumor growth via fluorescence imaging.

Results

Organoids from all entities grew into microtumors after being placed onto OHSCs. While microtumor size was significantly decreased after TTFields treatment in case of the GBM and AE sample, there was no significant reduction in the oligodendroglioma microtumor size.

Conclusion

Our patient-derived 3D model could be used to measure the effects of TTFields on different individual brain tumors. To our knowledge, we were the first to apply TTFields to patient-derived AE and oligodendroglioma samples. While TTFields led to a reduction in microtumor size in the case of the GBM and AE sample, effects on the oligodendroglioma sample might be due to different inter-patient sensitivity to TTFields or might require TTFields frequency optimization.

Komplikationen und Trauma/*Complications and trauma*

V241

Das deutsche Kranioplastie-Register – Eine prospektive multizentrische Kohortenstudie: Das langfristige neurologische Ergebnis und die Komplikationsrate nach Kranioplastie

German Cranial Reconstruction Registry – a prospective multicenter cohort study: long-term follow-up on outcome and complication rate

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Objective

The German Cranial Reconstruction Registry (GCRR) is a prospective multicenter cohort study, which investigates the primary surgical and neurological outcome of patients, who underwent cranioplasty after decompressive craniectomy (DC). This is the first report on the long-term neurological and surgical outcome.

Methods

Only medical centers, which initially participated in the GCRR and reported a minimal follow-up (FU) of at least 12 months on 50% of their respective patient cases, were included in this analysis. Parameters used in the register were investigated as factors for the long-term outcome. A favorable long-term outcome (FLTO) was defined as favorable if patients fulfilled both a Glasgow outcome score (GOS) of 4 or 5 and a modified Rankin scale (mRS) of less than 4. Complications and the rate of reoperation was also investigated. We used univariate analysis to identify variables that determine statistical correlation before multivariate analysis was performed using regression models.

Results

One-hundred sixty-six patient cases were included in this study for long-term analysis. The mean follow-up was 938.6 ± 532.2 days. Seventy-eight patients (47.6%) had a FLTO. The overall surgical revision rate of 22.3% (n=37). 35.5% and 25.3% of patients experienced an improvement in mRS and GOS respectively after CP **(fig. 1).** Multivariate logistic regression predicted the use of drains with suction as a significant factor in decreasing the rate of reoperation (p=0.022, OR = 0.328. 95% CI 0.126-0.853). Having diabetes (p=0.024, OR 0.118, 95% CI 0.018-0.759) and preoperative brain parenchyma that extended above the level of the skull bone (p=0.028, OR 0.237, 95% CI 0.066-0.855) predicted an unfavorable long-term neurological outcome **(tab.1).**

Conclusion

The perioperative risks of CP should be weighed against the chance of long-term neurological improvement. This study presents evidence that the operative use of drains with suction decreases the rate of reoperation, while diabetes and distended skin flaps at the time of surgery seem to have a negative impact on the long-term neurological outcome.

Abb. 1

	Sig.	OR	95% CI for OR Lower	Upper
Multivariate analysis of for dependent variable FLTO				
TBI	.453	1.653	.445	6.133
stroke	.306	.519	.148	1.829
any risk factor	.464	.614	.166	2.265
hypertension	.732	.821	.266	2.535
diabetes	**.024***	**.118**	**.018**	**.759**
coagulates	.256	.194	.011	3.288
Coagulates paused	.516	2.664	.138	51.374
Soft tissue above bone level	**.028***	**.237**	**.066**	**.855**
Autologous implant	.706	1.231	.418	3.620
Defect size in cm2	.731	.998	.987	1.009
Number of tiles	.365	.902	.721	1.128
Size of drain	.658	1.093	.737	1.620
Age at CP	.285	.982	.949	1.015
Multivariate analysis of for dependent variable reoperation				
existing VPS	.063	4.268	.924	19.718
anti-epileptic drugs	.223	1.879	.681	5.183
simultaneous implantation of VPS	.183	6.582	.410	105.642
Postoperative drain with suction	**.022***	**0.328**	**0.126**	**0.853**
time between DC and CP	.977	1.000	.998	1.002
length of stay	.698	1.005	.979	1.032
Discharge to home	.448	1.530	.510	4.589

Table 1: multivariate binary logistic regression of variables significant in univariate analysis for both long-term favorable outcome and reoperation with Odds ratio and 95% confidence intervals, CP – cranioplasty, DC – decompressive craniectomy, TBI – traumatic brain injury, OR – odds ratio, CI – confidence interval* represents a statistically significant value of $p < 0.05$

Abb. 2

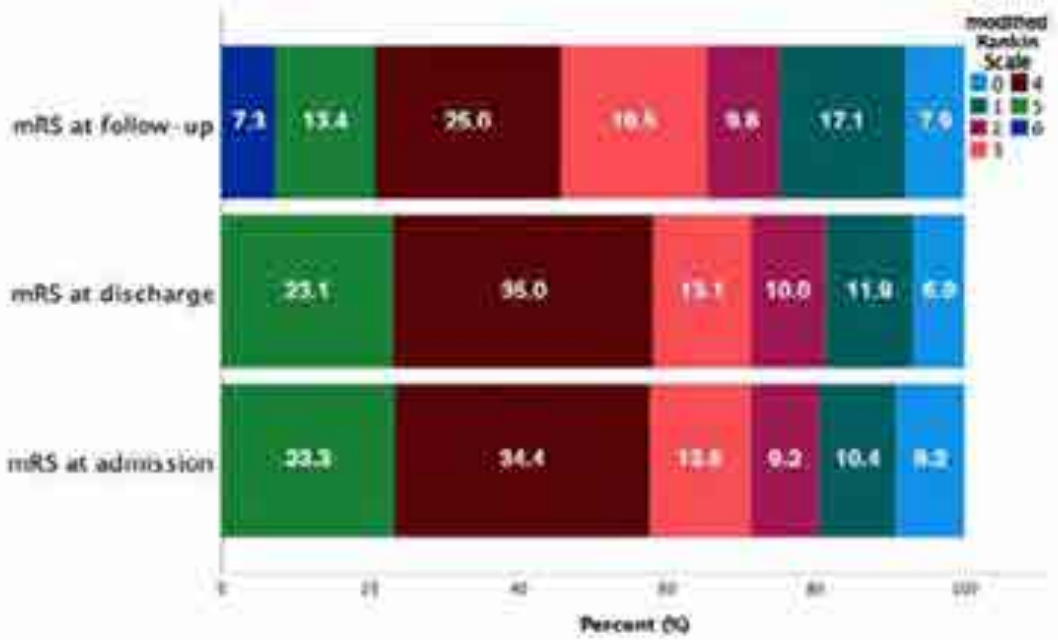

Figure 1: The modified Rankin scale (mRS) at hospital admission for cranioplasty (CP)surgery, discharge and at the follow-up (mean follow-up 938 days). 0 – no symptoms, 1, no significant disability, 2 – slight disability, 3 – moderate disability, 4 moderately severe disability, 5- severe disability 6 - dead

V242

Komplikationen nach Schädeldachplastik - Eine retrospektive, Single-Center Auswertung autologer, PMMA und CAD Implantate

Complications of cranioplasty – A retrospective, single-center evaluation of autologous, PMMA and CAD implants

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Objective

Cranioplasty after craniectomy is a common neurosurgical procedure, however complication rates are often underestimated due to surgical field and commonly severe neurological sequelae of the patients. We have evaluated the surgery related complication rates after cranioplasty using different implants including autologous bone, polymethylmethacrylate (PMMA) and calcium-phosphate titanium (Ca-P) as well as polyaryletherketone (PEEK) based CAD implants

Methods

A retrospective, descriptive, observational single-center study was performed at our institution including 150 patients who underwent cranioplasty between 2016 and 2021. Only primary cranioplasty after decompressive craniectomy or tumor surgery were included. Besides the type of cranioplasty, age, surgery related complications, time of surgery and anticoagulation were analyzed.

Results

Out of 150 patients, decompressive craniectomy (82%, 123) was the most common procedure. Infection was found in 10,7% (16/150) patients as the most often surgery-related complication. PEEK implants were mostly affected (20%, 6/30), followed by autologous bone (13,5%, 5/37) and PMMA (6.8%, 5/73). No infection was diagnosed after Ca-P cranioplasty (0/8). Explantation was performed in 26 cases (17.3%) and besides infection a postoperative epidural hematoma was the typical cause. Median surgical time was 118 minutes. Longer surgical time as well as use of anticoagulation therapy were not significantly related to higher infection rates (p=0.456, p=0.168 respectively). Hydrocephalus and shunt prior the cranioplasty were noted in 30% (45) and interestingly, hydrocephalus was not significantly associated with surgical related complications (p=0.103).

Conclusion

Based on our results, cranioplasty is still related to a relatively high number of infections and further complications. Materials used for the implantation seem to have a relevant effect on postoperative infections since surgical time, anticoagulation therapy and hydrocephalus did not show a statistically significant effect on postoperative complications in our study. PEEK implants seem to possess a higher risk of postoperative infections. Newer, more biocompatible implants such as Ca-P titanium mesh might be beneficial. Further prospective studies are needed to comprehensively evaluate different materials in terms of postoperative patient outcome.

Komplikationen und Trauma/*Complications and trauma*

V243

Der Einfluss von Antikoagulanzieneinnahme auf das chirurgische Ergebnis chronischer Subduralhämatome. Eine monozentrische Studie mit Analyse von 300 durch Nadeltrepanation behandelter Fälle

The effect of antithrombotic drugs on the surgical outcome of chronic subdural hematoma. A monocentric study with an analysis of 300 cases receiving twist drill craniostomy (TDC)

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Objective

Chronic subdural hematoma (cSDH) is considered to be one of the most common diseases in neurosurgical practice. Several authors reported a higher risk of cSDH recurrence with the use of antithrombotic drugs (ATDs), other authors however did not find any effect of ATDs on the surgical outcome. We retrospectively analysed the role of ATDs on the surgical outcome after treatment cSDH by twist drill craniostomy (TDC)

Methods

All patients operated by TDC between December 2016 to December 2019 were enrolled and analysed. Clinical course, outcome and complications were studied. Patients were divided into two groups: group 1 without any ATDs, group 2 with at least one ATD. The last group included patients with anticoagulants (ACs) and patients with antiplatlet drugs (APs). Clinical assessment included the Markwalder score at the admission and discharge. The maximal thickness of hematoma was measured on admission and discharge. Treatment success was defined as improvement of the clinical and radiological findings. Any readmission with necessity for recurrent operation, or conversion to the use of secondary surgical procedures following the initial admission were considered as treatment failure.

Results

A total of 300 patients were included. Male to female ratio was 2.6:1. Age ranged from 32 to 100 years (median 79). Hematomas were in 44,7 % left-sided, 40,7 % right-sided and by 14,6 % bilateral. TDC and fractionated hematoma evacuation was performed up to 7 times during one hospital stay. Hematoma thickness on admission ranged from 5 mm to 40 mm (median of 21). Overall, 58% of the patients presented with neurological deficits on admission. Group 2 included 143 patients (47,3 %), where 24,7 % were on APs, 21,6 % an ACs and 1 % on both drugs. Statistical analysis showed a significantly higher number of atraumatic cSDH in group 2 (p=0.039), the incidence of neurological deficits on admission increased significantly with ATDs (p= 0,004). There was no difference between the 2 groups concerning the number of TDC necessary for treatment. There was a significantly increased mortality rate of 3 % in group 2 (p=0.002).There was no influence of ATDs on treatment success of cSDH treated with TDC (p=0,325).

Conclusion

The use of ATDs had no influence on neurological and radiological outcome in our cohort. Recurrence and revision rates were unaffected by ATDs. A significantly higher mortality rate in patients receiving ATDs is most likely a group effect unrelated to the treatment routines in this cohort.

Komplikationen und Trauma/*Complications and trauma*

V244

Einfluss der postoperativen D-Dimer-Bestimmung und intraoperativen Anwendung der Intermittierenden Pneumatischen Venenkompression (IPK) auf die Entwicklung und den Nachweis perioperativer venöser Thrombembolien bei Kraniotomiepatienten

Influence of postoperative D-Dimere evaluation and intraoperative use of Intermittent pneumatic vein compression (IPC) on detection and development of perioperative venous thromboembolism in craniotomy patients

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Objective

Venous thromboembolism (VTE), which subsumes deep venous thrombosis (DVT) and pulmonary embolism (PE), is a frequent complication in craniotomy patients and associated with increased morbidity and mortality. Duration of surgery has already been identified as risk factor for development of VTE. Further factors like patient positioning and tumor entity have not been studied or are controversially discussed.The determination of D-dimer value with a cut-off at 2ug/ml resulted in a high detection rate of clinically silent DVT in a pilot study of our department. Additionally, the use of intermittent pneumatic venous compression (IPC) drastically reduced the incidence of VTE in a second pilot study. The aim of this work was to investigate our patients with regard to the different methods.

Methods

In the present study, 1387 patients who underwent elective craniotomy between 2011 and 2018 were retrospectively investigated. The staggered use of D-dimer value determination on postoperative day 3 and intraoperative use of IPC resulted in 3 groups: Nor use of IPC, neither postoperative D-dimer value (Group1), no IPC use, but D-dimer value evaluation (Group 2), intraoperative IPC use and D-dimer value evaluation (Group 3). If the D-Dimer value was > 2ug/ml, duplex sonography was performed. Age, sex, tumor entity, duration of surgery, complete or partial tumor resection or biopsy, patient positioning, type of thrombosis, and occurrence of PE were also recorded and analyzed.

Results

In group 1, 1.7% were diagnosed with DVT and 0.5% with PE. With D-Dimer evaluation, 22.2% of the patients were diagnosed with DVT and 5.2% PE (group 2); whereas the number was reduced to 8.1% DVT and 0% PE by using IPC (group 3). Patient positioning, sex, age, or specific tumor subtypes did not correlate with the postoperative development of VTE. However, duration of surgery was significantly linked to the incidence of both VTE and PE. Determination of D-dimer plasma levels on the third postoperative day showed a positive correlation with the numbers of patients who were diagnosed with VTE. Number of VTE was significantly reduced through application of IPC. The increased rate of VTE in group 2 to group 1 might be explained by longer duration of surgery (230min vs 286min).

Conclusion

Intraoperative use of IPC during craniotomy dramatically reduces the risk of VTE. In addition, D-dimer levels should be determined in patients after craniotomy, as this may help to detect DVT early and thereby prevent fatal PE.

Komplikationen und Trauma/*Complications and trauma*

V245

Wundheilungsstörungen in der Neurochirurgie – eine retrospektive Analyse
Wound healing complications in neurosurgery – a retrospective analysis

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Objective

The current study was performed because the subjective impression had occured, that the number of wound revisions after surgery had increased in our department over a period of 2 years for unknown reasons. Therefore, aim of the current study was 1) to analyse the rate of wound revisions, 2) to implement various measures for better wound care in order to decrease the risk for wound revision and 3) to evaluate the result of the implemented measures.

Methods

Wound revision was defined as necessary surgical intervention in case of wound healing problems within 30 days after the initial surgery independent of the underlying cause (e.g. infection, csf-leak, necrosis). The rate of surgical wound revisions was calculated using the electronic patient charts and the documentation of monthly our morbidity and mortality conferences from Jan 2015 until Nov 2020. An interdisciplinary task force consisting of neurosurgeons, anaesthesiologist and nurses discussed various measures to reduce the risk for wound healing disturbances. Measures included complete desinfection of the ward room by room, standardized antiseptic hair washing the night before surgery, standardized administration of perioperative antibiotics in the OR, and a head bandage after cranial surgery for two days. A second analysis was performed after the implementation of the measures covering the time range from Dec 2020 until June 2022.

Results

A total of 12096 neurosurgical interventions between Jan 2015 and June 2022 were analysed. The overall rate of wound revisions before the implementation of the measures (2015 – Nov 2020, n=9554) was 2,5% with a rate of cranial revisions of 1.8%. The rate of cranial revisions had increased from 1.4% in 2016 to 2.2% in 2019 and to 1.8% in 2020. After implementation of the measures the overall rate of wound revisions was reduced to 1.8%. The rate of wound revisions after cranial surgery dropped to 1.1%.

Conclusion

The implementation of various measures discussed by the interdisciplinary team resulted in a reduction of surgical wound revisions. Which of the measures was most the effective cannot be concluded from our data. However, it seems that the increased awareness of the problem might already have been an important factor in this process.

Komplikationen und Trauma/*Complications and trauma*

V246

Der sozio-ökonomische Vorteil der ambulanten Antibiotika-Therapie in der Neurochirurgie
The socio-economic advantage of outpatient antibiotic therapy in neurosurgery

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Objective

Keeping in mind the diagnostic-related group (DRG) system and the nationwide closure of hospital beds, the socio-economic pressure on the health system is increasing. In this study we would like to examine the usefulness of outpatient antibiotic therapy as part of the treatment of neurosurgical infections.

Methods

The aim of this study is to evaluate the usefulness of outpatient antibiotic therapy in neurosurgery. For this purpose, we included all patients who received a peripherally inserted central catheter (PICC line catheter) for intravenous (i.v.) antibiotic therapy between 01/20 and 9/22. Patientswho underwent the three-month follow-up after completion of antibiotic therapy were included. We evaluated the available patient data regarding the socio-economic issues.

Results

In total, we were able to include 80 patients. The distribution of spinal infection to cranial infection was 2:1. The median age was 63 years (SD +/- 14.3). The proportion of female patients was 40%. The mean in hospital stay was 14 days (SD +/- 7 days) for the entire inpatient treatment. The subsequent mean outpatient antibiotic therapy was 70.89 days (SD +/- 25.13 days). The mean outpatient i.v. therapy accounted for 48.55 days (SD +/- 14.49). In total, 3884 hospitals days" worth around € 3.33 million were saved. None of the 80 patients had to be admitted to hospital unscheduled and 4 patients (5%) experienced unexpected complications not related to antibiotic therapy or the PICC-Line delivery system. These complications were all cardio-pulmonary and always related to an underlying cardio-pulmonary disease or pre-existing one.

Conclusion

Outpatient i.v. antibiotic therapy via a PICC line catheter is a safe and good socio-economic alternative.

Gliome Chirurgie/*Glioma surgery*

V247

Einfluss der Resektion auf das Gesamtüberleben bei Multifokalen Glioblastomen – eine multizentrische retrospektive Analyse

Influence of Surgical Resection on Survival in Glioblastoma with Multiple Localizations- a Multi-Center Retrospective Analysis

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Objective

The presence of multiple localizations in glioblastoma is rare and associated with poor prognosis. The presence of a visible junction between enhancing lesions on magnetic resonance imaging (MRI) is defined as multifocal (MF), the absence of a dissemination pathway as multicentric (MC). The aim of this study is to evaluate the impact of reserction and the extent of resection (EOR) on overall survival (OS) in the treatment of glioblastomas with multiple localizations.

Methods

Data collection was performed as a multicenter retrospective analysis at 2 University Hospitals. From Jan 1, 2008, to Dec 31, 2020 patients presenting with IDH wild-type glioblastoma (CNS WHO grade 4) with multiple localizations were included. Demographic data, tumor size, Karnofsky Performance Score (KPS) before and after surgery were analyzed. EOR was measured by FLAIR and contrast-enhanced MRI. Gross total resection (GTR, residual tumor (RTM) < 5%), subtotal resection (STR, RTM < 30%), partial resection (PR, RTM > 30%), and biopsy (RTM > 75%).

Results

117 patients (median age 62 years (18–84 years; 48.7% females) were included. 45 (38.5%) patients had MC lesions, 72 (61.5%) MF. Age did not differ between groups. Median KPS on admission was similar in both subtypes (MF: 70 (40-100), MC: 70 (40-100)). Median OS (MC: 441.6d, SE: 53.2; MF: 391.2d, SE: 81.3) did not differ among MC and MF glioblastomas. GTR was achieved in 37.8% (MC)/36.1% (MF), STR in 40% (MC)/22% (MF), PR in 13% (MC)/8.3% (MF) and biopsy was performed in 9.2% (MC)/33.6% (MF). In MF glioblastoma, GTR (461d, 95CI 224-724; p=0.0001) and STR (317.5d, 95CI 149-783; p=0.0001) significantly increased the median OS compared to PR (334 days, 95CI 57-370) and biopsy (51d, 95CI 38-105). Likewise, OS was increased after GTR (490d, 95CI 195-827; p=0.0272) and STR (416.5d, 95CI 179-677; p=0.0272) in MC glioblastoma, as well. Overall, resection significantly increased OS (510±69.5d) in patients with glioblastoma with multiple localizations compared to biopsy alone (76-+37.24d). KPS did not decrease after GTR/STR compared to biopsy. In multivariate logistic regression analysis EOR and chemotherapy were significant and independent predictors of OS in MC and MF glioblastomas.

Conclusion

These data indicate that GTR and STR positively affects OS in patients with MC and MF glioblastoma. These results argue for a more aggressive stance towards surgical treatment of these tumors with particularly poor prognosis, even when GTR is not within reach before resection.

Gliome Chirurgie/*Glioma surgery*

V248

Ventrikeleröffnung bei Erst- und Rezidivresektion von Glioblastomen - Eine single centre studie
Ventricular opening during primary and recurrent glioblastoma surgery - a single centre study

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Objective

Ventricular opening during primary glioblastoma surgery is contested with differing results regarding impact on patient survival. Little evidence exists regarding its role during surgery of recurrent glioblastoma. Therefore, this study aims to investigate the role of ventricular opening in recurring glioblastoma surgery as well as the achievability of complete resection of enhancing tumour (CRET) via ventricular opening in these cases.

Methods

We reviewed electronic patient records and imaging of all patients having undergone microsurgical tumour resection for IDH wt glioblastoma CNS-WHO 4 at our centre in 2019 and 2020. Demographics, clinical characteristics and radiological features were analysed. Resections status was determined by reviewing imaging and radiology reports of postoperative MRIs conducted within 72h of surgery. Pre- and postoperative neurological status and complications were extracted from patient records.

Results

Between 2019 and 2020, 165 patients received microsurgery for glioblastoma at our centre. Of those, 57 patients underwent opening of the ventricle for tumour resection. Ventricular opening was conducted 46 times during first and 13 times during recurrent glioblastoma surgery with some patients undergoing ventricular opening twice. CRET could be confirmed in 18/46 cases after primary surgery. In 11/28 cases subtotal or partial resection was deliberate. In case of recurrence, CRET could be achieved in 8/12 cases with deliberate partial resection in 3/4 cases with remaining contrast enhancing tumour tissue. The mean age of the recurrent surgery cohort was 53.7 years compared to 64.4 years in the primary surgery cohort. Relevant new persistent neurological deficits occurred in 1/12 patients in the recurrent cohort compared to 2/46 patients in the primary surgery cohort. Postoperative CNS infection occurred in one case after recurrent and 4 cases after primary glioblastoma surgery. In each group, one patient was re-admitted for hydrocephalus treatment with one receiving a VP-shunt and the other receiving best supportive care due to progressive disease.

Conclusion

Ventricular opening should not be withheld when presumed necessary to achieve CRET both in primary and recurrent glioblastoma surgery. So far, we did not detect any contraindication such as increased rate of postoperative neurological deficits or increased shunt dependency in these cases. We are currently expanding the cohort to conduct more in-depth statistical analyses.

Gliome Chirurgie/*Glioma surgery*

V249

Wertigkeit des Resektionsausmaßes bei neu diagnostizierten Glioblastomen: Ergebnisse einer prospektiven kontrollierten Multicenterstudie

Importance of extent of resection for survival in patients with newly diagnosed glioblastoma: Results from a prospective controlled multicenter study

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Objective

The role of the extent of resection in newly diagnosed glioblastoma (GBM) remains a controversial discussion. We aimed to elucidate the impact of residual tumor seen on postoperative MRI based on the volumetric data of a recently finished prospective multicenter study.

Methods

A prospective controlled multicenter trial with two center-specific treatment arms (5-ALA and iMRI) and blinded evaluation was performed. Main inclusion criteria were unifocal completely resectable glioblastomas. Independent blinded review of pre- and post-operative MRI was performed to assess resectability and extent of resection. The primary endpoint was complete resection in early postoperative MRI and volumetric assessment of residual disease. Subgrouping of residual tumor volumes, molecular markers and adjuvant treatment was performed to identify the possible impact on PFS and OS.

Results

314 patients with newly diagnosed glioblastomas were recruited at eleven German centers. 257 patients were evaluated by volumetrics of early postoperative MRI. Perioperative clinical data, as well as adjuvant treatment were comparable between patients. The median preoperative tumor volume was 26.5cm³. A complete resection with 0 cm³ residual disease was achieved in 175 (68%), with ≤0.175cm³ in 205 (80%), with >0.175-0.5 cm³ in 18 (7%), with >0.5-1cm³ in18 (7%) and with >1cm³ in 16 (6%) patients. Complete resections with 0 cm³ resulted in a significantly longer median OS (27.9 versus 19.4 months) and PFS (6.9 versus 3.8 months) compared to incomplete resections, respectively. The volume of any subgroup with residual disease >0cm³ did not influence

PFS or OS significantly in the entire cohort. While in patients with unmethylated MGMT status a significant difference (p=0.008) was seen for OS between patients with and without residual tumor, this was not the case in methylated tumors (p=0.619).

Conclusion

Results of this study reveal the importance of safe total resections with 0 cm^3 residual contrast enhancing tumor in patients with newly diagnosed GBM, especially in patients with unmethylated MGMT promoter status. In patients with methylated MGMT promoter status, small residual tumors might have less impact on survival, likely because of the good treatment effects of temozolomide treatment.

Gliome Chirurgie/*Glioma surgery*

V250

Der Stellenwert der operativen Therapie von diffusen IDH 1/2- Wildtyp Astrozytomen
The role of surgery in IDH 1/2 - wildtype diffuse astrocytomas

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Objective

Isocitrate dehydrogenase (IDH)1/2-wildtype (wt) astrocytomas have high recurrence rates and were classified as CNS WHO grade 4 tumors in the latest WHO classification of 2021. Uncertainty remains regarding clinical impact and decision making - particularly with regard to the role of surgery. The aim of this study is to evaluate the impact of the extent of resection (EOR) of these new CNS grade 4 tumors compared to glioblastoma (GBM) on overall survival (OS).

Methods

Data acquisition was conducted as a multi-center retrospective analysis at 6 university hospitals (2016-2020). Patients with IDH1/2-wt diffuse astrocytoma (CNS WHO grade 2-3) were included in our study. Patients presenting with IDH-wt GBM from one institution served as controls. Primary outcome parameter was OS related to EOR (GTR; <5% residual tumor (RT), subtotal resection (STR; 5-75% RT), and biopsy (> 75% RT).

Results

160 patients with IDH-wt GBM (CNS WHO grade 4), (45.6 % females) and 111 patients with IDH-wt diffuse astrocytoma (CNS WHO grade 2-3), (34.2 % females) were enrolled. The median age was 68 years (37-86 years) in the classic GBM cohort and 59 years (20-87 years) in those with astrocytomas. GTR was achieved more often in patients with GBM: 58.8% compared to those with diffuse astrocytoma 27.9% (p = 0.0001); STR (36.0%, p = 0.0048) and biopsy (36.0%, p = 0.0032) were more often in astrocytomas. The overall survival was 12.7±10.4 months in GBM compared to 18.2±14.8 months in astrocytoma. GTR significantly increased OS in both entities (GBM: 15.3±10.4 months, 95% CI 13.13 – 17.40, p = <0.0001; diffuse astrocytoma: 26.7±17.9 months, 95% CI 20.13 – 33.25, p = <0.0001). Further, also STR significantly increased OS in GBM (11.46±11.03 months, 95% CI 7.55 - 15.37, p = 0.0257) and astrocytoma (18.8±13.54 months, 95% CI 14.47- 23.13, p = 0.0035). ROC analysis identified a residual cut-off tumor volume of >20% in the GBM cohort and >60% in the diffuse astrocytoma cohort to be associated with impaired OS. Multivariate analysis identified age and EOR, but not radio-chemotherapy, as independent predictors of OS in diffuse astrocytomas. MGMT methylation had no impact on OS (p = 0.11).

Conclusion

These data suggests that resection prolongs OS in patients with IDH-wt astrocytomas and is of higher value than radio-chemotherapy. Of note, STR also positively influences OS in these patients. These results underline the importance of surgical resection even if GTR is not achievable.

Gliome Chirurgie/*Glioma surgery*

V251

Prognostischer Stellenwert ausgedehnter Resektionen in IDH-mutierten Lower-Grade-Gliomen: Ergebnisse einer volumetrischen Analyse

Prognostic impact of extended resections in IDH mutant lower-grade diffuse glioma: Results from a volumetric analysis

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Objective

In diffuse glioma, the prognostic impact of resection is still a matter of debate. The outcome benefit of extended resections may be influenced by the tumor"s molecular phenotype. Also, many studies lack objective quantitative assessment of residual tumor volume (RTV). We aimed at analyzing the prognostic benefit of surgery in a molecularly defined cohort of IDH mutant (IDHmut) diffuse astrocytoma and oligodendroglioma WHO grade 2 and 3 ("lower-grade").

Methods

Patients treated at our department were identified retrospectively for whom molecular work-up classified tumors unambiguously as IDHmut diffuse lower-grade glioma and volumetric analysis of RTV was possible. Patient-, tumor- and treatment-related factors including pre- and post-operative MR FLAIR tumor volumes were correlated with progression-free (PFS) and overall (OS) survival by univariate and multivariate analysis. Confounders of resectability were analyzed by multiple linear regression.

Results

206 patients treated over one decade fulfilled inclusion criteria. Mean age was 40.37 (+/-11.38) years. 105 patients suffered from IDHmut astrocytoma WHO grade 2 (n=48) and 3 (n=57) and 101 patients from oligodendroglioma WHO grade 2 (n=61) and 3 (n=40). 185 patients (89.8%) underwent resection as opposed to biopsy. This was associated with prolonged PFS and OS in astrocytoma (p=0.007; p=0.038) and WHO grade 2 tumors (p=0.012; p<0.0001). Adjuvant treatment was administered in 36% and 97% of WHO grade 2 and 3 patients, respectively. In patients undergoing resection, median pre- and post-op tumor volumes did not differ between tumor subtypes but were significantly larger in WHO grade 3 than 2 tumors (pre: 71.3 vs. 28.8 cm3; post: 7.78 vs. 1.98 cm3). Median RTV was 4.6 cm3 in all IDHmut lower-grade gliomas. There was a stepwise improvement of outcome with decreasing RTV (PFS: p=0.0003; OS: p=0.0004; data given for quartiles), with the strongest effect observed for patients with no RTV (median PFS: undefined vs. 58 months; p=0.007). In multivariate analysis, RTV independently predicted OS (p=0.001; HR 1.012) but not PFS. Resectability was only influenced by pre-op FLAIR tumor volume (p<0.0001).

Conclusion

In molecularly defined IDHmut lower-grade glioma, a continuous association of RTV and patient outcome was observed, even at the highest levels of resection. This finding was more pronounced in astrocytoma. Thus, a maximal resection should be strived for whenever safely achievable.

Gliome Chirurgie/*Glioma surgery*

V252

Resektion von Rezidiven intrakranieller Tumoren zur Molekulardiagnostik im Zeitalter der Precision Oncology: Eine Risiko-Nutzen-Analyse

Resection of recurrent intracranial tumors for molecular diagnostics in the age of precision oncology: A risk-benefit analysis

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Objective

Surgery for recurrent intracranial tumors could provide, in addition to cytoreduction, tissue for targeted therapy based on molecular diagnostic analyses. With mostly heavily pretreated patients involved, it is unclear whether the benefits of repeat surgery aiming at molecularly informed treatment outweigh its potential complications.

Methods

Patients receiving surgery for recurrent WHO grade 2, 3, and 4 glial tumors with the goal of tissue sampling for molecular analysis were included in this retrospective analysis. Complication rates (surgical, neurological, and medical) were compared to a cohort including all patients undergoing glioma surgery in 2021. Diagnostic yield of sampled tissue, resulting targeted therapies and post-surgical survival rates were analyzed.

Results

Between 2017 and 2021, a tumor board recommendation for targeted therapy through molecular tissue analysis was made in 143 patients. Of these, 56 patients (38%) underwent repeat surgery (mean age 52.8 years; 34 females). Glioblastoma was the most frequent diagnosis (n=38; 67), followed by other astrocytic (n=10; 18%) and oligodendroglial (n=8; 12%) tumors. 16 cases (28%) comprised IDH-mutant tumors. In most cases, gross total resection was achieved (n=38; 64%). Further surgeries included subtotal resection (n=9; 15%) and open or stereotactic biopsy (n=9; 15%). In 54 cases (96%), tissue was further processed for next-generation sequencing (successful in n=46, 82%), methylation profiling (n=49, 88%), and immunohistochemistry for mTOR phosphorylation (30%, n=17). Targeted therapy was commenced in 15 (27%) of 23 cases (41%) with a recommendation for targeted therapy based on molecular tissue analysis. 6 patients (10%) required revision surgery, including wound revision, revision for CSF fistula and CSF drain implantation (n=2 each). Non-resolving neurological deterioration was documented in 5 cases (9%). PFS and OS after repeat surgery were 150 and 366 days, respectively. When comparing patients undergoing glioma surgery in 2021 (n=266), patients with repeat surgery for molecular diagnostics showed higher revision rates (10% vs 4%; p=0.04).

Conclusion

Surgery for recurrent intracranial tumors aiming at molecularly informed treatment could provide valuable information for targeted therapy under a marginally increased risk of postoperative complications and with satisfactory postoperative survival rates and could therefore complement a multi-modal therapy approach for such patients.

Abb. 1

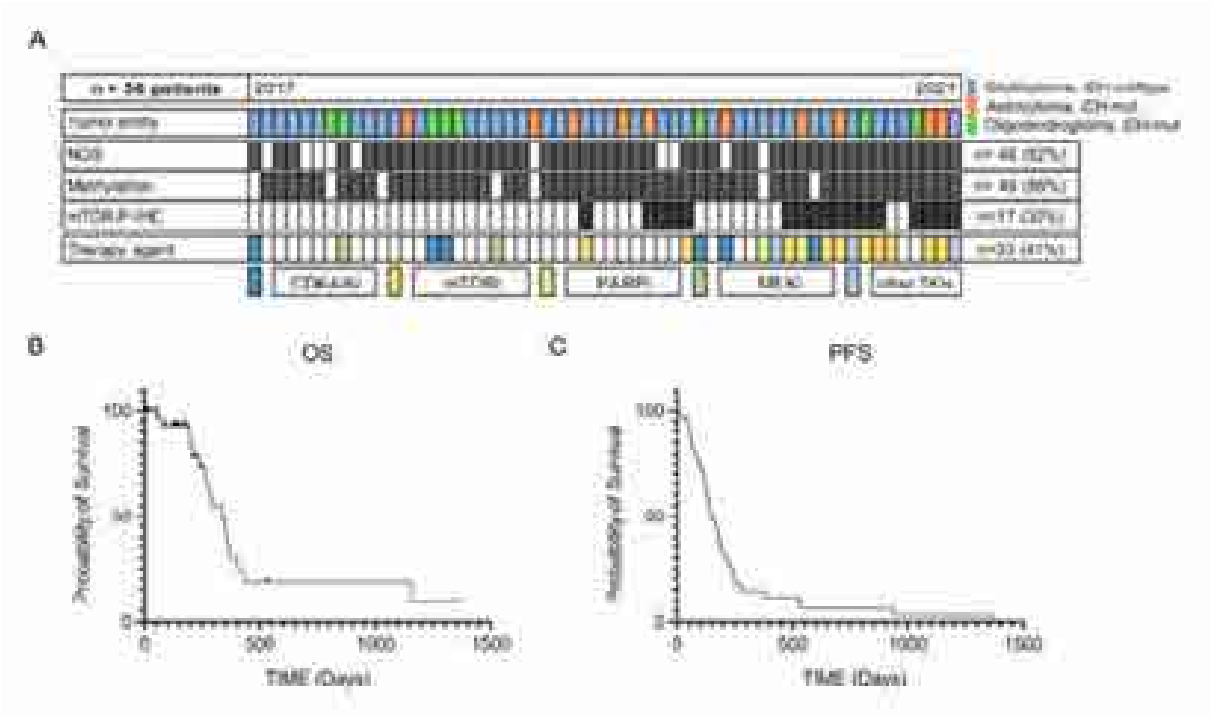
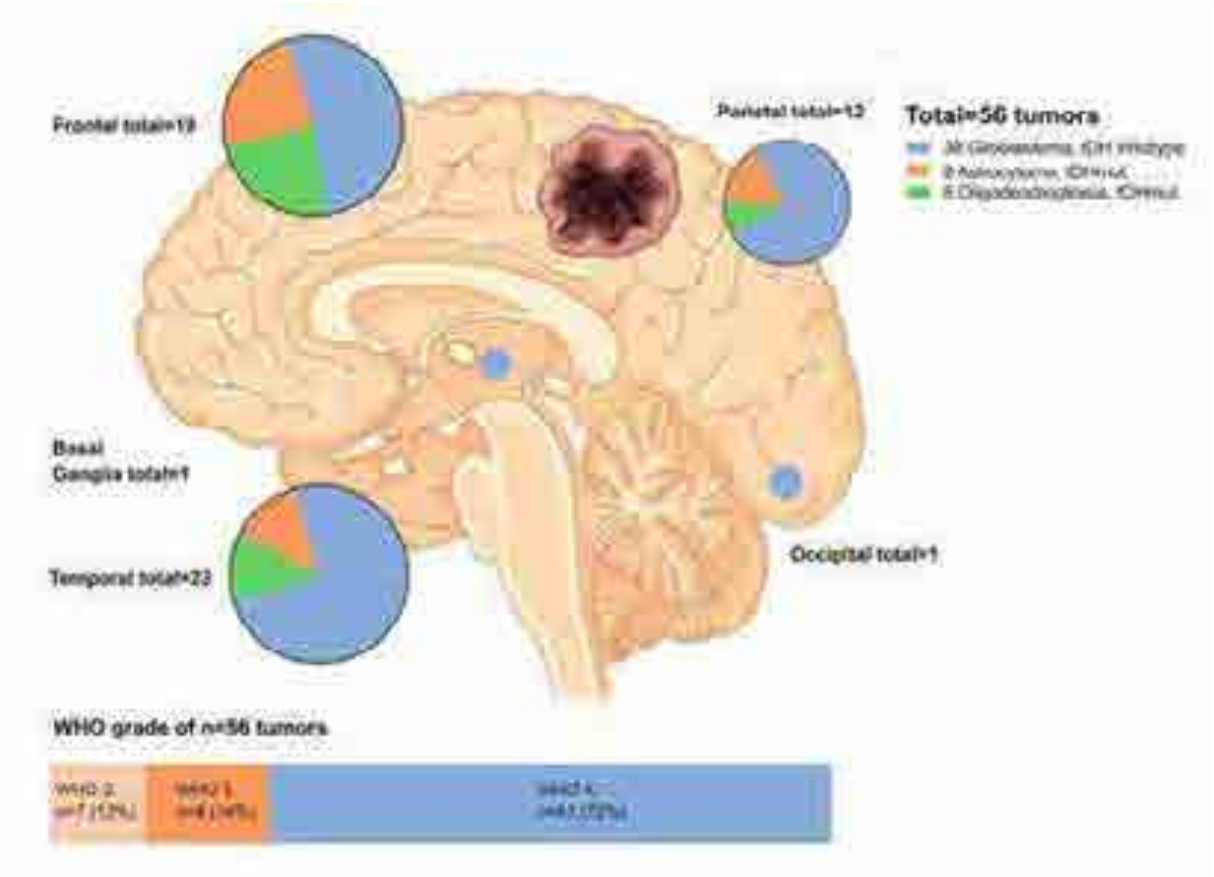


Abb. 2


Frontal total=19
Parietal total=12
Total=56 tumors
Basal Ganglia total=1
Occipital total=1
Temporal total=23
WHO grade of n=56 tumors

Gliome Chirurgie/*Glioma surgery*

V253

Operative Therapie potentiell spracheloquent lokalisierter Tumoren: Retrospektive Ableitung von Indikatoren für die Empfehlung einer Wachkraniotomie mit Sprachmonitoring.

Surgery of potentially language-relevant localized tumors: Retrospective compilation of indicators for the recommendation of awake craniotomy with speech monitoring

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Objective

Awake craniotomy with speech monitoring is the gold standard for surgery of language-relevant localized tumors. However, some patients consider awake craniotomy to be anxiety-laden. We supplemented anamnestic, clinical and image morphological information of the tumor with preoperatively navigated transcranial magnetic stimulation (nTMS) for the counselling of patients eligible for intraoperative language mapping and awake craniotomy. We analyzed patients retrospectively regarding indicators relevant to the decision of performing tumor resection with intraoperative speech monitoring via awake craniotomy.

Methods

Monocentric retrospective analysis of 78 patients (2017-2022) with potentially language-relevant localized tumors (71 glial tumors, 7 metastases). All patients received a 3D isovoxel T1w GD cMRI / Flair / DWI (fiber tract imaging in 50 patients) and standardized nTMS language mapping preoperatively. Aphasia was graded using the Aphasia Severity Rating Score (ASR: no aphasia: 4, mild aphasia: 3, moderate aphasia: 2, severe aphasia: 1 or 0). The tumor localization was determined by using a brain atlas (mainly affected gyrus) and the volume was calculated after segmentation (BrainLab 4.0). Speech errors during nTMS mapping with a distance of less than 10 mm from the tumor edge were defined as language-relevant peritumoral points. Language predominance was assessed using the Edinburgh Handedness Inventory and nTMS language mapping. 40 patients underwent ITN surgery, while 38 patients underwent awake craniotomy with speech monitoring. Standard MRI was performed 24h after surgery.

Results

All 38 patients who underwent awake craniotomy were speech dominant on the left side and had an ASR score of 3-4 (no or mild aphasia (nTMS baseline>60%)). Main tumor locations were the left gyrus frontalis medius, gyrus frontalis inferior, gyrus temporalis superior or supramarginal angular gyrus (91.8%). This differed significantly from the ITN group (p

Conclusion

In addition to anatomical tumor location and individual speech dominance, the degree of pre-existing aphasia (ASR 3-4), the presence of at least one positive nTMS speech point near the tumor, and the tumor volume were indicators for recommending tumor resection with intraoperative speech monitoring and awake craniotomy.

Gliome Chirurgie/*Glioma surgery*

V254

Intraoperatives 3T-fMRT für Brain-Mapping und Neuronavigation mithilfe passiver sensomotorischer Stimuli unter Vollnarkose

Passive sensorimotor intraoperative functional 3T MRI for brain mapping and neuronavigation under general anesthesia

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Objective

Functional MRI (fMRI) is widely accepted as a reliable tool for brain mapping due to its high spatial resolution, which is particularly useful for neuronavigation. Previous studies have shown that results of passive motor fMRI during anesthesia are relevant and helpful for identification of the primary motor and sensory cortex. Here we demonstrate our first experience in using intraoperative 3T fMRI (ifMRI) under general anesthesia for on-site brain mapping using passive sensorimotor stimuli.

Methods

8 patients underwent resection of glioma involving the primary sensorimotor cortex with guidance using intraoperative imaging, neuronavigation and electrophysiological neuromonitoring. Pre- and postoperative 3T fMRI was performed using a block design (finger tapping, ankle motion) motor paradigm (BOLD Sequence, TR=1000ms, voxel size 2.5x2.5x2.5mm). In addition, intraoperative 3T MRI using structural T1 and T2-weighted sequences as well as ifMRI (BOLD Sequence, TR=2000 - 4000ms, voxel size 3x3x3mm) using passive sensorimotor stimuli under general anesthesia were performed before and after gross resection. The acquired data was correlated and validated by intraoperative motor cortex stimulation (MCS) and presurgical planning fMRI data.

Results

Passive intraoperative sensorimotor ifMRI showed unequivocal activations centered in the primary sensory and motor cortices during preoperative scanning under general anesthesia. After gross tumor resection, activations consistent with sensory activations in the appropriate and expected anatomical regions could be detected. MCS validated the motor foci defined by ifMRI imaging in all 8 cases. No complications occurred during ifMRI passive sensorimotor stimulation.

Conclusion

We present a technique for intraoperative on-site mapping of the sensorimotor cortices for intraoperative neuronavigation using passive sensorimotor stimuli in an 3T ifMRI setting, which can be performed safely, fast and on patients, who otherwise would not be able to perform fMRI tasks sufficiently. Further studies on validity considering intraoperative distortion artifacts and systematic postoperative functional outcomes are needed.

Gliome Chirurgie/*Glioma surgery*

V255

Altersabhängiger Einfluss einer konkomitanten Radiochemotherapie und MGMT-Promotormethylierung auf PFS und OS bei Patient*Innen mit IDH-Wildtyp-Glioblastom: the real-life data.

Age-dependent impact of concomitant radio-chemotherapy and MGMT promotor methylation on PFS and OS in patients with IDH wild-type glioblastoma: the real-life data.

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Objective

Biological but not chronological age plus performance have an impact on decision-making in glioblastoma patients, resulting in the application of concomitant radio-chemotherapy also to a proportion of older patients. We aimed to investigate how progression-free survival (PFS) and overall survival (OS) in older patients with IDH wild-type glioblastoma was influenced by concomitant radio-chemotherapy and MGMT promotor methylation status in the real-life settings.

Methods

273 patients with firstly operated IDH wild-type glioblastoma were retrospectively evaluated. Mean PFS and OS were acquired with Kaplan–Meier processing. The influence variables on PFS and OS was compared using LogRank test and Cox regression analysis.

Results

142 patients (52 %) were older than 65 years and 77 (55 %) of them received concomitant radio-chemotherapy. Mean PFS in the younger cohort (18 – 65 years) was 21.1 months (CI95: 17.1 – 25.0) compared to 13.1 months (CI95: 10.1 – 16.1) in the older group (> 65 years), p = 0.003. In senior patients, the initiation of concomitant radio-chemotherapy was associated with significantly better PFS: 15.3 months (CI95: 11.7 – 18.9) *vs.*7.0 months (CI95: 4.3 – 9.6; p = 0.002). At the same time, the favorable influence on PFS was not related to MGMT promotor methylation status like it was in the younger cohort. Mean estimated OS in the younger group was also longer than in the older cohort: 27.6 months (CI95: 22.0 – 33.1) *vs.*13.6 months (CI95: 10.0 – 17.2) respectively (p < 0.001). In patients older than 65 years, concomitant radio-chemotherapy was related to significantly better OS: 20.0 months (CI95: 14.3 – 26.7) *vs.* 4.9 months (CI95: 3.5 – 6.2), p < 0.001. MGMT promotor methylation was related to a more favorable OS only, if concomitant radio-chemotherapy was initiated.

Conclusion

More than half of glioblastoma cohort was older than 65 years. Even if PFS and OS were shorter than in the younger cohort, concomitant radio-chemotherapy provided a survival advantage. In the real life, MGMT promotor methylation had a positive impact on OS only in case of adjuvant therapy.

SAB Prognosefaktoren/*SAH Prognostic factors*

V256

SHELTER-Score - Subarachnoid Hemorrhage Assoziierter EarLy Brain Injury OuTcomE PRediktion Score
SHELTER-Score - Subarachnoid Hemorrhage Associated EarLy Brain Injury OuTcomE PRediction Score

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Objective

To date, management and research in aneurysmal subarachnoid hemorrhage (aSAH) have focused on the prevention and treatment of vasospasm to prevent poor outcome. However, mortality and morbidity of aSAH have not been significantly changed over the last years. Recent experimental research supports the concept of early brain injury (EBI) as an important event in the pathophysiology of aSAH that significantly influences post-EBI events. With this work, we aim to identify clinical and radiological outcome relevant features occurring in the first 72 hours after hemorrhage to develop a rapid and easy score to predict outcome in ICU setting.

Methods

We included 561 consecutive patients who were admitted to our hospital wih aSAH. We retrospectively analysed 14 potential predictors that occurred within the first 72 hours after haemorrhage in patients with aSAH. The mRS at 6 months, discretised to three levels (0-2: favourable, 3-5: poor, 6: dead), was used as the outcome variable. Univariate ordinal regression was used to rank the predictors by significance. Forward selection and McFadden"s pseudo-R^2 as the optimality criterion was applied to find the optimal set of predictors for multi-variate proportional odds logistic regression. Collinear parameters were excluded Five-fold cross-validation was used to avoid overfitting.

Results

561 patients were included in the analysis which ultimately results in the SHELTER-score of 7 clinical features with varying weights: Age (0-4 points), WFNS (0-2.5 points), Cardiopulmonary resuscitation (2 points), Mydriasis (1-2 points), Midline shift (0.5-1 points), Early deterioration (1 point) and Early ischemia (2 points). McFadden´s pseudo-R^2 = 0.339, AUC for death or disability 0.899 and 0.877 for death. An EBI-score below 5 correlates with a good outcome (favourable, mRS 0-2), 5-6.5 with a poor outcome (disability, mRS 3-5) and ≥ 7 with death (mRS 6).

Conclusion

The SHELTER-score shows excellent performance in predicting the neurological outcome of patients with aSAH. In our opinion, this clearly reflects the great impact of the early pathophysiological processes and the resulting early brain damage on the overall outcome of patients with SAH. Thus, therapy should be intensified in the initial phase after aSAH and patients at risk of a poor outcome can be identified relatively early by the SHELTER-score.

SAB Prognosefaktoren/*SAH Prognostic factors*

V257

Zeitpunkt des Schlaganfalls und Einflussfaktoren auf das schlaganfallfreie Überleben bei Patienten mit aneurysmatischer Subarachnoidalblutung

Stroke timing and determinants of stroke-free survival in patients with aneurysmal subarachnoid hemorrhage

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Objective

Cerebral infarction is a substantial contributor to poor outcome of aneurysmal subarachnoid hemorrhage (SAH). Wherein, the stroke timing might play a particular role for the burden of SAH morbidity and mortality. In this retrospective study, we analyzed the determinants of stroke-free survival after SAH and the role of infract timing for SAH outcome.

Methods

To assess the occurrence and timing of cerebral infarction, consecutive SAH patients treated between 01/2003 and 06/2016 who had at least one follow-up computed tomography scan were included. Different baseline characteristics, medications and adverse events during SAH were recorded. Univariate and multivariate analyses were performed.

Results

Follow-up imaging review of 988 SAH patients included in the final analysis revealed cerebral infarcts in 475 cases (48.1%) documented at the mean day 5.5 post-SAH (range: 0 – 92; stroke within 7 days in 70.9% of the cases). Infarct occurrence was independently associated with the risk of in-hospital mortality ($p<0.0001$) and poor outcome at 6 months post-SAH (mRS>3, $p<0.0001$). In the sub-cohort of SAH individuals with a stroke, the infarct timing showed additional impact on in-hospital mortality (OR=0.91 per-day-increase, $p<0.0001$) and 6 months" poor outcome (OR=0.96 per-day-increase, $p=0.012$). According to the ROC analysis, cerebral infarction occurring within 48 hours post-SAH showed the most significant clinical impact. Of 18 parameters included in the final multivariate Cox regression analysis, the stroke-free survival was independently associated with poor initial clinical condition (WFNS≥4, aHR=1.76, $p<0.0001$), intraventricular hemorrhage (aHR=1.25, $p=0.044$), aneurysm rebleeding (aHR=1.73, $p=0.002$), occurrence of cerebral vasospasm on transcranial Doppler ultra-sonography (aHR=1.38, $p=0.012$), and daily aspirin intake (aHR=0.67, $p=0.002$). Accordingly, 80.8% of SAH individuals with unfavorable baseline characteristics (WFNS≥4+IVH+rebleeding) showed cerebral infarcts in the follow-up (mean day 3.1) – in contrast, only 30% of patients without these baseline characteristics developed infarcts at the mean day 7.1 post-SAH.

Conclusion

Cerebral infarcts occur mostly during the first week after SAH. The earlier infarct occurrence, the stronger is the impact on the outcome of SAH. Initial SAH severity and cerebral vasospasm are the major determinants of stroke-free survival, with aspirin as a potential preventive measure against post-SAH stroke.

SAB Prognosefaktoren/*SAH Prognostic factors*

V258

Das logistische Organfunktionsstörungssystem reflektiert die Schwere der frühen Hirnschädigung und prognostiziert zuverlässig die Komplikationen und Krankenhausmortalität nach einer aneurysmatischen Subarachnoidalblutung

Logistic organ dysfunction system reflects early brain injury severity and reliably predicts complications and in-hospital mortality after aneurysmal subarachnoid hemorrhage

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Objective

Cerebral aneurysm rupture induces not only a neurological dysfunction but also causes a systemic reaction affecting multiple organ functions. Early brain injury (EBI) occurring within the first 72 hours after aneurysm rupture involves a series of pathophysiological mechanisms, that can be reflected by cerebral and extracerebral dysfunctions and complications following aneurysmal subarachnoid hemorrhage (aSAH). The Logistic Organ Dysfunction System (LODS) was developed to capture organ dysfunction in critically ill patients. The aim of this study was to assess, whether LODS allows a reflection of EBI-severity and predicts complications and outcome in aSAH patients.

Methods

A retrospective analysis of a consecutive patient cohort treated with aSAH from 2012 to 2020 was performed. LODS was calculated as previously described including GCS, blood cell counts, hemodynamics, pulmonary, renal, and liver function, as well as coagulation status. EBI-severity was assessed on day 1 after ictus applying a previously described score based on early brain edema, persistent loss of consciousness, and intracranial blood burden. Early need for catecholaminergic support und indication for decompressive hemicraniectomy (DHC), as well as the occurrence of delayed cerebral infarction were documented. Functional outcome was evaluated according to modified Rankin scale (mRS) at 3 months follow-up.

Results

A total of 324 patients (36% male) with a mean age of 55.9±13.6 years were included. The mean LODS score in the cohort was 6.8±2.9 points. Patients needing catecholaminergic support on day 1 (r=0.2, p=0.0004), and patients requiring DHC in the early phase (r=0.2,p=0.0002) exhibited significantly higher LODS scores. Patients with delayed infarctions had significantly higher LODS scores compared to those without infarctions (mean 8 vs 6, p<0.0001). A LODS score was associated with more severe EBI (r=0.55, p<0.0001) and worse functional outcome (r=0.35, p<0.0001). A cutoff value of LODS 7 allowed reliable identification of patients with severe EBI (AUC 0.78, p<0.0001).

Conclusion

Although LODS has been widely used for mortality prediction in critically ill patients, this organ dysfunction score was not applied in context of aSAH so far. In this first analysis in a large consecutive patient cohort with aSAH, LODS showed a reliable reflection of EBI-severity and correlated with complications and functional outcome following aSAH.

SAB Prognosefaktoren/*SAH Prognostic factors*

V259

Vergleich von radiographischen Scores zur Vorhersage von Komplikationen und Ergebnissen bei Subarachnoidalblutungen.

Comparison of radiographic scores for the prediction of complications and outcome of subarachnoid hemorrhage.

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Objective

Aneurysmal subarachnoid hemorrhage (SAH) is characterized by high morbidity and mortality proceeding from the initial severity and following complications during SAH. Various scores were developed to predict these risks. We analyzed the clinical value of different radiographic scores for prognostication of SAH outcome.

Methods

Initial computed tomography scans (≤48h after ictus) of 745 SAH cases treated between 01/2003 and 06/2016 were reviewed for the SEBES, Claassen, BNI, Hijdra, original Graeb and Fisher scales. Primary endpoints were development of delayed cerebral ischemia (DCI), in-hospital mortality and unfavorable outcome (modified Rankin scale score>3) at 6 months after SAH. Secondary endpoints included different complications during SAH. Clinically relevant cut-offs were defined using the receiver operating characteristic (ROC) curves. Radiographic scores with the highest values for the area under the curve (AUC) were included in the final multivariate analysis.

Results

The Hijdra sum score≥15 had the most accurate predictive value and independent associations with all primary endpoints: DCI (AUC=0.678, aOR=2.94, p

Conclusion

Initial radiographic severity of SAH was independently associated with occurrence of different complications during SAH and its final outcome. The Hijdra sum score showed highest diagnostic accuracy and robust predictive value for early detection of risk of DCI, in-hospital mortality and unfavorable outcome after SAH.

SAB Prognosefaktoren/*SAH Prognostic factors*

V260

Der "False Poor Grade"-Patient mit aneurysmatischer SAB; eine Untergruppe von Patienten, die durch den traditionellen WFNS-Score falsch beurteilt wird

The False Poor Grade Aneurysmal SAH Patient; A Subgroup Of Patients Misjudged By The Traditional WFNS Score.

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Objective

The timing of the WFNS survey in aSAH patients is controversial and a later evaluation of the WFNS - after treatment of confounding factors, the so-called rWFNS - could have a better predictive value for patient outcome, which we wanted to testify in this study. Furthermore, we hypothesize that there is a group of patients misjudged by the initial WFNS, which could be identified on the basis of the initial native CT imaging.

Methods

We retrospectively analysed the daily WFNS from day 1 to day 7 after admission and checked its predictive value for the mRS at discharge and 6 months post-bleeding in 535 patients with aSAH. We dichotomized patients with an initial WFNS of IV-V. Patients with improvement (even short-term) of WNFS from IV-V to I-II within the first seven days were classified as "false poor grade" patients. Additionally, we collected radiological parameters and scores from the initial native CT imaging and compared them between "false poor grade" and "real poor grade" patients. Univariate and multivariate regression analyses were carried out to identify predictors for the assignment to the "false poor grade" subgroup.

Results

The later the WFNS is collected, the better is its predictive value for neurologic outcome after aSAH ($p<0.001$). Thirty-nine "false poor grade" patients were identified, showing a significantly better outcome compared to the "real poor grade" patients (N=220) (mRS discharge: 0-2, 56% vs 1%, $p< 0.001$; 3-5: 41% vs 56%, $p= 0.12$; 6: 3% vs 43%, $p< 0.001$). The "real" vs "false poor grade" patients differ significantly regarding numerous radiologic parameters in the initial native CT. The falsely bad patients can be identified with a predictive model based on the FH-score = SEBES + Hijdra Score / 10 + LeRoux score / 7 (sensitivity = 0.95, specificity = 0.85, accuracy = 0.863, and F1 = 0.679). The patient is classified as "false poor grade" if that score is ≤ 4.6 and considered "real poor grade" otherwise.

Conclusion

When the initial WFNS is collected, a subgroup of patients is incorrectly classified as poor grade. This misclassification can be avoided either by later collection of the WNFS (day 3-4), losing its usefulness as an early prognostic predictor, or by adding criteria from the initial native CT imaging such as the Hijdra-, LeRoux- and SEBE-score to the initial WFNS grading. Future studies with an even larger number of patients should verify the identification of "false poor grade" patients via the initial native CT scan.

SAB Prognosefaktoren/*SAH Prognostic factors*

V261

Gebrechlichkeit als zusätzlicher Risikofaktor für schlechtes Outcome nach nicht-aneurysmatischer Subarachnoidalblutung

Increasing frailty diminishes functional outcome in patients with non-aneurysmal subarachnoid hemorrhage: a dual specialized neurovascular center analysis

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Objective

Despite numerous established risk factors, the potential role of frailty on functional outcome in patients with spontaneous, non-aneurysmal subarachnoid hemorrhage (NASAH) remains elusive.

Methods

The study cohort was made up of all consecutive patients aged > 18 years that had been treated for NASAH between 2012 and 2021. The modified frailty index (mFI) was used to determine patient frailty before ictus. Patients were divided into two groups: 1) non-frail (mFI 0-1) and 2) frail (mFI ≥ 2). Functional outcome was assessed 6 months after ictus by means of the modified Rankin Scale (mRS) and classified into favorable (mRS 0-2) and unfavorable (mRS 3-6). In addition, multivariate logistic regression analysis was performed in order to identify independent predictors of unfavorable outcome.

Results

A total of 257 patients with NASAH were identified. 56 of 257 patients with NASAH (22%) were classified as frail (mFI ≥ 2) prior to ictus. 17 of 56 patients (30%) with a mFI ≥ 2 revealed unfavorable outcome at the 6 months follow-up examination compared to 21 of 201 patients (10%) with a mFI of < 2 (p=0.001). Besides to delayed cerebral ischemia (p<0.001) and poor-grade NASAH (Hunt & Hess grade III-IV; p=0.001) as known negative prognostic parameters, multivariable analysis identified frailty (p=0.03) as a further independent and significant risk factor for unfavorable functional outcome at 6 months after NASAH.

Conclusion

The present study indicates pre-ictal frailty as objectified by a mFI of ≥ 2 to constitute an independent risk factor for poor functional outcome in patients with NASAH. Further scientific endeavors might comprehensively reveal the overall impact of frailty on patient counselling and long-term prognostication in NASAH.

SAB Prognosefaktoren/*SAH Prognostic factors*

V262

Einfluss von Gebrechlichkeit und Sarkopenie auf das neurologische Langzeitergebnis bei Patienten mit aneurysmatischer Subarachnoidalblutung.

Influence of frailty and sarcopenia on long-term neurological outcome in patients with aneurysmatic subarachnoid hemorrhage.

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Objective

Although the relationship between sarcopenia and frailty and clinical outcome in neuro-oncology patients is well established, its potential impact in neurovascular diseases, such as spontaneous subarachnoid hemorrhage (SAH) is unclear. Here we aim to investigate the effect of frailty and sarcopenia, as measured by serum sarcopenia markers, temporal muscle thickness (TMT) and area (TMA), on neurological outcome after SAH.

Methods

Data acquisition was conducted as a single center retrospective analysis. All patients with SAH older than 55 years and treated in our department between 2015 to 2020, were included in our study. Beside the assessment of demographic and routine clinical data (including Hunt&Hess (HH) grade), the Clinical Frailty Score (CFS) was used to determine the frailty of each patient. At the time of admission sarcopenia was evaluated by calculating TMT/TMA on computed tomography (CT) scans and measurement of creatinine and albumin as serum biomarkers. Outcome was assessed using the modified Rankin scale and the Glasgow Outcome Score (GOS) at discharge and the mRS at 12 months follow-up.

Results

119 consecutive patients were included in our study. 90 patients (75.6%) were female. The mean age of the patients was 63 years (range 55-87). 78 (65.55%) patients were admitted with a moderate sSAH (Hunt and Hess grade 1-3), 41 (34.45%) with severe SAH (Hunt and Hess grade 4-5). The majority of patients had a Fisher score of 4 (69.50%). Patients with TMA <241 cm3 had a significantly lower TMT (P<0.001). In addition, this group of patients had lower creatinine levels (P=0.03) and albumin levels (P=0.08). Patients with a TMT < 5.5 mm were more frail (Mean CFS=4; P=0.04), had a lower GCS (mean GCS=9; P=0.03) and a higher HH (mean HH=3; P=0.009) at admission. Frailty as indicated by a sarcopenic temporal muscle was significantly associated with higher HH grade (P>0.01) and worse neurological outcome (P=0.04) at discharge. Further, hospitalization was prolonged in this group (23±9.2 vs. 27±9.8 days). Multivariate analysis showed that Hunt and Hess score (p<0.001) and Clinical Frailty Score (p=0.004) were independent predictors of clinical outcome at discharge and at the follow-up.

Conclusion

In this study, frailty and sarcopenia parameters such as TMT and TMA are associated with a more severe SAH grade at admission, with a prolonged hospitalization and a poorer neurological outcome independent from their chronological age.

SAB Prognosefaktoren/*SAH Prognostic factors*

V263

Blutzuckerwerte bei Aufnahme können das Auftreten von Komplikationen sowie den funktionellen Outcome von Patienten mit aneurysmatischer Subarachnoidalblutung vorhersagen

Admission blood glucose level predicts the burden of complications and functional outcome after aneurysmal subarachnoid hemorrhage

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Objective

High admission blood glucose (ABG) level is reported to be associated with poor outcome of different stroke types, including acute aneurysmal subarachnoid hemorrhage (SAH). In this retrospective study, we aimed at analyzing the independent predictive value of ABG for SAH outcome, and identifying adverse events during SAH related to ABG level.

Methods

542 consecutive SAH cases admitted within 24 hours post-SAH between January 2005 and June 2016 were eligible for inclusion. Data on ABG values, initial characteristics of patients and SAH, adverse events during hospital stay, and final outcome were recorded. Primary study endpoints were the occurrence of cerebral infarctions, in-hospital mortality and poor outcome at 6 months after SAH (mRS>3). Secondary endpoints included the development of adverse events during disease.

Results

Mean ABG level was 141.4 mg/dL (range: 62 – 390 mg/dL; ABG >140 mg/dL in 220 (40.6%) cases). ROC analysis showed good diagnostic accuracy for ABG for the prediction of study"s primary outcome endpoints: cerebral infarction (AUC=0.677), in-hospital mortality (AUC=0.743), and unfavorable outcome at 6 months (AUC=0.760), with the clinically relevant cutoff at >140 mg/dL. Pre-existing diabetes (aOR=3.13, p=0.018) and poor initial clinical condition (WFNS=4-5, aOR=2.45, p=0.009) were independently related to ABG > 140 mg/dL. In the final multivariate analysis, ABG >140 mg/dL was associated with the risks of unfavorable outcome (aOR=2.45, p<0.0001), in-hospital mortality (aOR=2.73, p=0.001), and cerebral infarction (aOR=2.04, p=0.001). Moreover, the following adverse events during SAH were independently associated with the ABG > 140 mg/dL: occurrence of intracranial hypertension (need for medical treatment [aOR=2.60, p<0.0001] or decompressive craniectomy [aOR=1.78, p=0.013]) and systemic complications during SAH (any infection [aOR=1.80, p=0.007], pneumonia [aOR=1.91, p=0.011], duration of fever [aUC=1.07, p=0.005], tachycardia [aUC=0.39, p=0.036], and need for mechanical ventilation [aUC=1.77, p=0.002]).

Conclusion

Hyperglycemia is common at the moment of SAH onset and is linked with poor initial clinical condition as well as preexisting diabetes. ABG can be confirmed as a robust outcome predictor in SAH patients, and may be used as valuable marker for certain complications during SAH.

SAB Prognosefaktoren/*SAH Prognostic factors*

V264

Einfluss des ICP auf die frühe Beeinträchtigung des glymphatischen Systems bei experimenteller Subarachnoidalblutung

Role of ICP for early impairment of the glymphatic system in experimental subarachnoid hemorrhage

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Objective

Recent studies have highlighted the role of early glymphatic system impairment as a potential contributor for secondary complications after subarachnoid hemorrhage. The extent to which elevated intracranial pressure (ICP) may influence the glymphatic brain clearing impairment is poorly understood. With this study, we aimed to characterize the role of early ICP dynamics on the brain clearing system during experimental SAH.

Methods

We acquired brain slices from rats in which experimental SAH was induced by the cisterna magna blood injection model using 500 µl of autologous blood after intracisternal injection of 20 µl Alexa 594, a red fluorescent dye. SAH groups differed by mild and severe ICP elevation and were compared with sham animals. Interstitial dye distribution and intensity were analyzed 15, 60 and 240 minutes after SAH induction in three different brain regions: (1) a rostral region at the origin of the anterior commissure, (2) a central region, where the hippocampus runs out laterally, and (3) a posterior region including the cerebellum. Kolmogorov-Smirnov and Mann-Whitney U tests were used for statistical analyses of the fluorescence images.

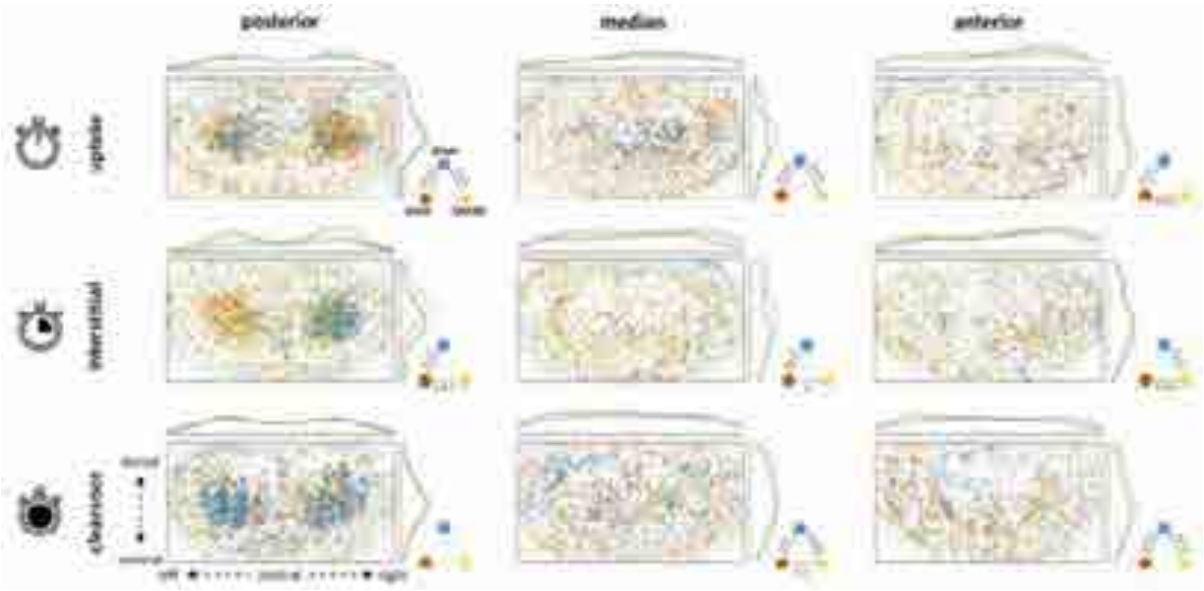
Results

The dye passed the glymphatic pathway and reached cervical lymph nodes. Unrestricted dye clearing was characterized by temporal inflow and outflow in analyzed brain regions. This clearing was significantly altered in terms of dye distribution (all $p<.001$) in an ICP-dependent manner. The differences could not be explained by morphological changes between the SAH1 and SAH30 groups (pericyte count: all $p>.199$; AQP4 polarization: all $p>311$). There was an additional tendency for dye intensity to vary across regions in an ICP-dependent manner.

Conclusion

Our results strongly emphasize the pathophysiological role of ICP dynamics on brain clearing in the acute phase of experimental SAH. Dye distribution is critically impaired depending on the severity of SAH within the first hours after induction. This relationship and the observation of ICP dependence in early brain injury warrant further investigation, taking into account a presumed varying vulnerability of different brain regions.

Abb. 1



Meningeome II/*Meningioma II*

J-SBNC040

Meningeom-Resektionsgrad basierend auf den intraoperativen 5-ALA-Befunden
Meningioma Resection Grade based on 5-ALA Intraoperative Findings

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Objective

Surgery of meningiomas may be curative. Recurrence, however, may occur even after complete tumor resection (Simpson grade I). One possible cause may be remnant tumor cells that are not identified using microscope`s regular white light. Most meningiomas are aminolevulinic acid (5-ALA) positive, and fluorescence-guided resection of these tumors can discover small tumor remnants. In this study we analyze the advantages of using 5-ALA during meningioma surgery and elaborate an adaptation of the Simpson Grading System based on fluorescence intraoperative findings.

Methods

Between January 2018 and December 2022 a total of 93 intracranial meningioma surgeries using 5-ALA were performed. At the end of the surgery, when total resection was supposed under microscope"s white light, final inspection of the surgical field, dura and the bone flap was carried out using a fluorescence filter. Special attention was paid to remnant 5-ALA positive tissue and these were resected when found. Tumors as well as remnant 5-ALA positive tissue were submitted to histological and immunohistochemical studies. Surgical videos and magnetic resonance imaging were analyzed. Based on 5-ALA intraoperative findings a modification of the Simpson Grading System was elaborated.

Results

Remnant 5-ALA positive tissue was identified invading the arachnoid plane, dura, bone or over the brain in 21.5% of the cases after total resection was assumed using the microscope"s regular white light. Histological analysis of the remnant 5-ALA positive tissue that was further resected demonstrated the presence of tumor cells. Almost all tumors were found to be 5-ALA positive, but a distinction of the glowing intensity was observed in different meningiomas.

Conclusion

The use of 5-ALA for meningioma surgery improved total tumor resection in this series. This could possibly reduce the chances of a recurrence in totally removed tumors with additionally 5-ALA free resections. Long-term studies are evidently necessary to evaluate a possible impact of this technique on recurrences and overall survival. So that results in meningioma resection using 5-ALA can be properly evaluated and compared, an adaptation of the Simpson Grading System based on 5-ALA intraoperative findings is presented.

Abb. 1


NEW SIMPSON'S GRADING SYSTEM
IA - Complete removal of tumor, excision of its dural attachment, of any abnormal bone, and 5-ALA free.
I - Complete removal of tumor, excision of its dural attachment, and of any abnormal bone.
IIA - Complete removal of tumor and of its visible extensions, with electrothermy coagulation of dural attachment and 5-ALA free.
II - Complete removal of tumor and of its visible extensions, with electrothermy coagulation of dural attachment.
IIIA - Complete removal of the intradural tumor, without resection/coagulation of dural attachment, or of extradural extensions and 5-ALA free.
III - Complete removal of the intradural tumor, without resection or coagulation of its dural attachment, or alternatively of its extradural extensions.
IV - Partial removal, leaving intradural tumor in situ.
V - Simple decompression, with or without biopsy.

Abb. 2

Meningeome II/*Meningioma II*

J-SBNC041

Die Rolle von 5-ALA in der Chirurgie von Schädelbasis-Meningeomen
The Role of 5-ALA in Surgery of Skull Base Meningiomas

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Objective

In most cases, radical surgery of benign meningiomas is curative. Recurrence, however, may occur even after complete tumor resection. Remnant tumor cells that are not identified by current surgical techniques is a possible cause of tumor recurrence. In meningiomas of the skull base identification of residual tumor may be even more difficult. Most meningiomas enhance aminolevulinic acid (5-ALA), and fluorescence-guided resection using this dye may discover small tumor remnants. The impact of 5-ALA fluorescence-guided surgery on the extent of meningioma resection has not yet been systematically analyzed, especially not in skull base. This study evaluates the possible advantages of using 5-ALA during skull base meningioma surgery and propose an adaptation of the Simpson Grading System based on the presence or not of 5-ALA tumor remnants.

Methods

From a series of 526 patients with brain tumors operated on with fluorescence-guided surgery and 5-ALA between November 2015 and December 2022, 80 patients presented meningiomas including 23 patients with skull base meningiomas. Final inspection was carried out using the BLUE400 microscope filter. Remnant 5-ALA positive tissues were looked for and resected when found. Histological and immunohistochemical studies of the tumors were performed. Based on 5-ALA intraoperative findings a modification of Simpson grading classification was elaborated.

Results

All patients with skull base meningiomas enhanced 5-ALA in this series. Total resection (Simpson's grade 1 and 2) was assumed under the regular microscope xenon white light in 22 cases. Positive 5-ALA tumor remnants were identified in five cases (22.7%). Removal of these residual tumors achieved 5-ALA free resection in 22 patients.

Conclusion

After radical tumor removal in 22 cases under regular white xenon light, five presented residual tumor tissue under the violet–blue excitation light and a BLUE400 filter with the use of 5-ALA. The 5-ALA positive residual tissue was removed. This technique may reduce the chances of recurrence. An adaptation of the Simpson Grading System is proposed to compare recurrences after radical removal of skull base meningiomas using 5-ALA. Long-term studies are necessary to evaluate a possible impact on recurrence and overall survival.

Abb. 1

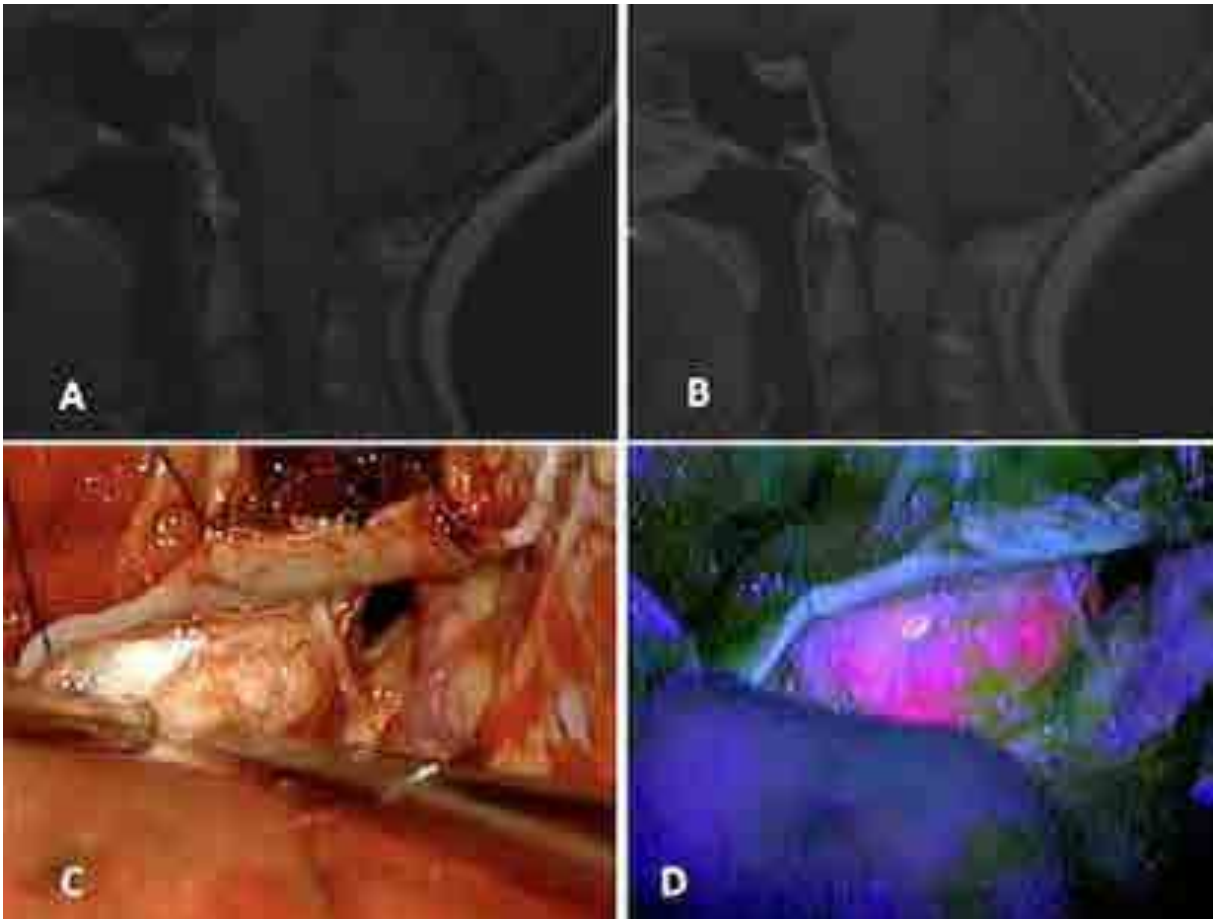
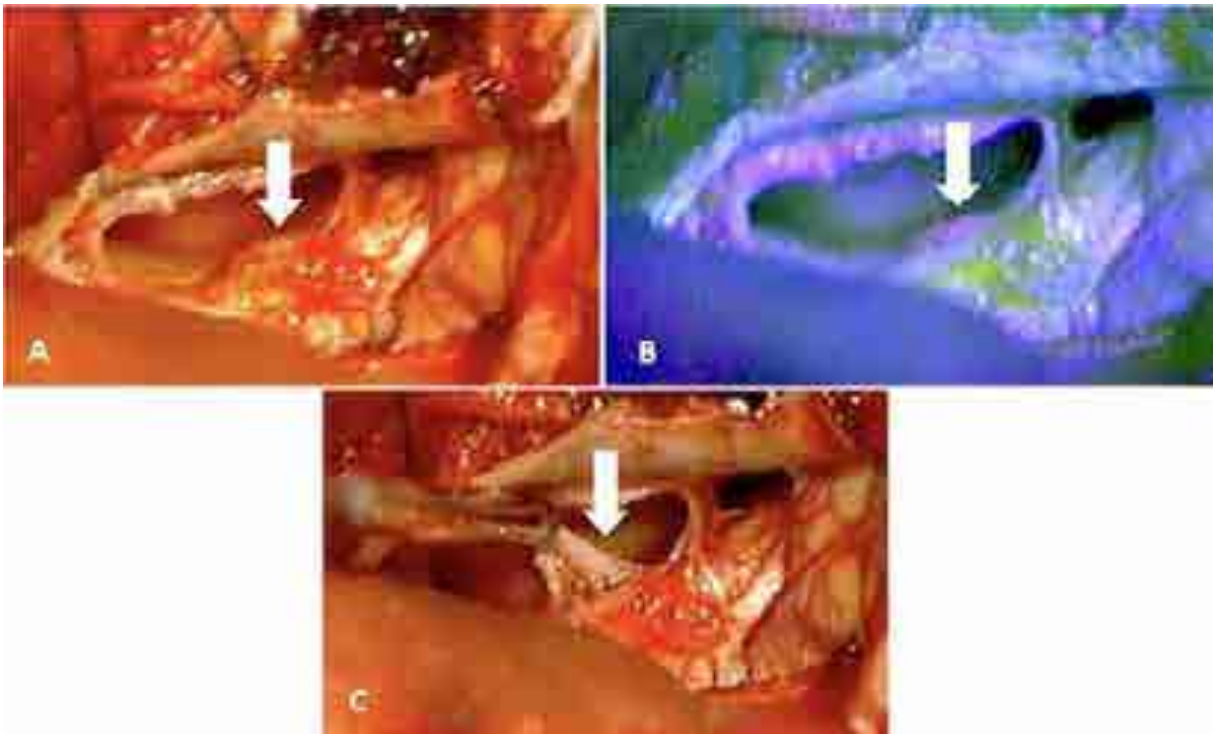


Abb. 2



Meningeome II/*Meningioma II*

V265

Der Effekt von 5- Aminolävulinsäure und Bestrahlung auf humane Meningeomzellen
The effect of 5-Aminolevulinic acid and X-ray irradiation on human meningioma Cells

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Objective

Conventional radiotherapy is recommended as adjuvant therapy for incompletely resected, recurrent, or atypical/anaplastic meningioma. It has been suggested that the application of 5-Aminolevulinic acid (5-ALA) exerts antitumor effects. Here, we studied the effect of 5-ALA administration with X-ray irradiation on human meningioma cells *in vitro*.

Methods

The human meningioma tissues were obtained during surgical interventions of nine patients with benign or atypical meningioma. Meningioma cells were treated with various concentrations of 5-ALA (50-750 µg/ml) with and without X-ray irradiation (2 and 8 Gy) and the cell viability, fluorescence intensity of Protoporphyrin IX (PpIX), apoptosis rate, expressions of various apoptosis-related genes, and generation of reactive oxygen species (ROS) were assessed.

Results

Application of 5-ALA enhanced the expression of PpIX in a dose-dependent manner. Our data indicate that different doses of 5-ALA exert a dose- and time-dependent antitumor effect on human meningioma cells. Furthermore, the evaluation of combined treatment with optimal cytotoxic doses of 5-ALA and various intensities of ionizing irradiation revealed a potent synergistic growth inhibitory effect on human meningioma cells. The co-application of 5-ALA and radiotherapy significantly inhibited the colony formation ability of meningioma cells. Flow cytometry evaluations indicated that this combination therapy markedly enhanced the early apoptosis of meningioma cells compared to the other treatment and control groups. Furthermore, 5-ALA together with irradiation significantly increased the ROS generation. The expression of various apoptotic proteins, including Bax, Bcl-2, and p53, did not show any differences among various groups.

Conclusion

Our findings indicated that the application of 5-ALA efficiently sensitized human meningioma cells to X-ray irradiation.

Meningeome II/*Meningioma II*

V266

Unüberwachtes Lernen an stimulierter Raman-Histologie bei Meningeomen mittels neuronaler Netzwerke
Unsupervised Classification of Stimulated Raman Histology in Meningiomas Using Deep Convolutional Neural Networks

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Objective

Meningiomas are common, most frequently benign intracranial tumors; however, some meningiomas display aggressive growth and relapse. Given the growing focus on personalized medicine and implementation of artificial intelligence in modern neurosurgery, we aimed to develop an intraoperative stratification model based on high-dimensional data acquisition. Here, we curated an atlas of meningioma specimens analyzed by rapid intraoperative stimulated Raman histology (SRH) to explore the morphological diversity across various WHO grades and anatomical locations.

Methods

High-definition SRH of 94 meningiomas was obtained. Furthermore, SRH microscopy as well as the corresponding H&E stainings were processed by an unsupervised learning framework to extract relevant imaging features for classification. For analysis we used a modified SCAN (Semantic Clustering by Adopting Nearest neighbors) algorithm, which advocates a two-step approach in which feature learning (representative learning) and clustering (end-to-end learning) are decoupled. For representative learning, a ResNet architecture was used, followed by an integration of semantically meaningful nearest neighbors as a prior into a learnable approach.

Results

Our unsupervised clustering of SRH images revealed 9 distinct classes characterized by defined morphological patterns such as cellular density, vascularity, necrosis, fiber patterns, spotted cell clusters or artifacts. Although we found that all morphological clusters are present in high and low grade tumors, cellular density was significantly enriched in high grade meningiomas ($p < 0.001$). Comparable unsupervised clustering of the H&E slices displays a markedly lower variance in the latent space of the image class distribution in favor of a higher number of technical artifacts such as blur or embedding artifacts suggesting that SRH images provide enhanced feature information regarding tumor heterogeneity.

Conclusion

Exploration and description of defined morphologies and identification of high-risk patterns will allow to establish intraoperative risk stratification for lower and high-grade meningiomas.

Meningeome II/*Meningioma II*

V267

Erkennung von aggressiven Meningiomen durch markierungsfreie Bildgebung in Kombination mit maschinellem Lernen

Recognition of aggressive meningioma using label-free imaging and machine learning

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Objective

Most meningioma are benign tumors, however, a subgroup exhibits an aggressive clinical course. Those need to be identified as soon as possible in the clinical workflow to adapt therapy accordingly. As label-free imaging visualizes tissue morphochemistry it was investigated as a candidate intraoperative diagnostic technique.

Methods

Specimens obtained from 119 meningioma patients (WHO 1 n=40; WHO 2 n=38; WHO3 n=41) were included in the study. CARS (coherent anti-Stokes Raman scattering), AF (two photon exited autofluorescence) and SHG (second harmonic generation) signals were acquired from unstained cryosections using two different protocols: i) Acquisition time of 200 ms and 1 µm lateral resolution (fast low quality imaging) and ii) acquisition time of 3 s, 0.25 µm lateral resolution and four times averaging (slow high quality imaging), resulting in a dataset of 17561 images each. Texture analysis was performed and different strategies of machine learning were evaluated to develop a classifier discerning meningioma WHO grade 1, 2 and 3 using the training set (8832 images of 60 specimens).

Results

Linear discriminant analysis provided more stable results when transferred to the independent test set (8729 images) than support vector machine, neuronal network and boosted tree strategies. It was, therefore, chosen for comparison of experimental approaches. Analysis of single modalities resulted in correct classification of 57.8%, 70.0% and 56.3% of the images of the test set for CARS, AF and SHG, respectively. Improved probabilities for class assignment were obtained by exploiting all three modalities combined and 73 % of images and accordingly 84% (50/59) of specimens of the test set were assigned to the correct WHO grade. Employing slow high quality imaging slightly improved the classification accuracy on the image level to 75% but did not result in better classification of specimens.

Conclusion

Combined CARS-AF-SHG imaging in conjunction with machine learning has the potential to provide information on the WHO grade of meningioma. The study strongly suggests that information of multiple positions is essential for correct classification of tissue. Importantly, high resolution imaging is not necessary, thus enabling fast image acquisition in the intraoperative setting. As the technique is fast, label-free and can be applied damage-free, it might be applied intraoperatively using fiber based systems.

Meningeome II/*Meningioma II*

V268

Einfluss der Formunregelmäßigkeit bei medialen Keilbeinflügelmeningeomen auf neue postoperative neurologische Defizite und das progressionsfreie Überleben

Impact of shape irregularity in medial sphenoid wing meningiomas on postoperative new-onset neurological deficits and progression-free survival

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Objective

Medial sphenoid wing meningiomas (MSWM) represent a challenging anatomical group among skull base meningiomas regarding function preserving surgery and long-term tumor control. Shape irregularity is suggested to be associated with the histopathology. Aim of the present study is to assess the influence of tumor shape on postoperative functioning, progression-free survival, and neuropathology.

Methods

We included patients operated on primary MSWM (WHO grade 1&2) in our center from 2010 to 2021. The retrospective study included 74 patients (65% women, median age 59 years). MR-images of MSWMs were evaluated regarding bone invasion, calcification, cavernous sinus invasion, meningioma shape, and meningioma volume (semi-automatic). Furthermore, demographics, extent of resection, and neuropathological proliferation analysis were also considered regarding the clinical endpoints (new neurological deficits, progression-free survival).

Results

Irregular MSWM shape was identified in 31 patients (41.9%). Eleven (14.9%) patients developed new postoperative neurological deficit. Eight of the eleven new neurological deficits were found in the irregularly shaped MSWMs. Multivariable analysis revealed that irregular MSWM shape is significantly associated with new neurological deficits (OR: 5.75, 95%CI: 1.15-28.63, p = 0.033). Patients with an irregularly shaped MSWM had a mean time to MSWM progression of 97.0 months, whereas those with a regularly shaped MSWM had a mean PFS of 132.1 months (log-rank test: p = 0.007). Multivariable Cox regression analysis revealed irregular MSWM shape as an independent predictor of shortened time to progression (HR:8.0, 95%CI: 1.04-62.10, p = 0.046). Fifteen patients with an irregularly shaped MSWM (15/31) had an increased MIB-1 index (≥5%), and nine patients with a regularly shaped MSWM had an increased MIB-1 index, respectively (p = 0.023). Multivariable regression analysis showed that irregular MSWM shape is independently associated with an increased MIB-1 labeling index reflecting highly proliferative tumors (OR: 7.59, 95% CI: 2.04-28.25, p = 0.003).

Conclusion

Irregular MSWM shape is independently associated with an increased risk of new postoperative neurological deficits, and shortened time to tumor progression. Irregular MSWM shape might be caused by highly proliferative tumors with an increased MIB-1 index.

Meningeome II/*Meningioma II*

V269

Die Rolle von p16 Immunohistochemie als prognostischer Biomarker in Meningeomen.
The role of p16 immunohistochemistry as a prognostic biomarker in meningiomas.

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Objective

Despite best clinical management many patients suffering from meningioma experience tumor recurrence. During the last decades efforts have been made to improve the prognostic stratification regarding meningioma recurrence. In many other tumor entities, loss of p16 is associated with tumor progression. Evaluation of p16 staining for routine diagnostics and prognostic significance to identify meningiomas at risk for recurrence is of clinical interest.

Methods

In this retrospective single-institutional study the immunohistochemical staining for p16 was analyzed in 397 paraffin-embedded meningioma samples. The distribution and association with tumor grading, clinical data and progression-free survival according to follow-up MRI were assessed.

Results

Of 397 meningioma samples 69 tumors were immunopositive for p16 (17.3%). Significantly higher frequencies of p16 expression were observed in meningiomas with higher WHO CNS grade (p=0.001), in recurrent tumors (p<0.0001), male patients (p=0.0121) and tumors of spinal location (p=0.0031). Univariate analysis revealed a higher rate of tumor recurrence in meningiomas with p16 immunopositivity (p=0.0321) and an unfavorable progression-free survival in the Kaplan-Meier analysis (p=0.0223). But p16 remained a non-significant factor in the multivariate analysis, where CNS WHO grade age, tumor recurrence, resection status and adjuvant RT were significant independent factors regarding tumor recurrence.

Conclusion

The presumed prognostic impact of p16 is mostly attributed to the confounding clinical factors WHO CNS grade, recurrent tumor status, age, extent of resection and adjuvant RT. P16 immunohistochemistry in meningioma samples without further molecular data does not allow for tumor risk stratification.

Meningeome II/*Meningioma II*

V270

Expressionsprofilanalyse der langen, nicht kodierenden Antisense-RNA LBX2-AS1 als prognostischer Marker bei atypischem Meningeom

Expression profile analysis of antisense long non-coding RNA LBX2-AS1 as a prognostic marker in Atypical Meningioma

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Objective

Meningiomas (MGMs) are the most common intracranial primary tumors of the central nervous system. Nearly 80% of meningiomas are benign WHO°I, 10–15% are atypical (WHO°II), and only 2–5% are anaplastic WHO°III. Increasing evidence has shown that long non-coding RNAs (lncRNAs) are important prognostic biomarkers and epigenetic regulators with critical roles in cancer initiation and progression. Previous studies including ours have identified the prognostic role of LBX2-AS1 lncRNAs in different cancer models and brain vascular malformations. However, it"s expression and clinical prognostic value in atypical meningioma (AMs) patients remains unexplored. The aim of this study is to identify the expression of lncRNA, LBX2-AS1 in AMs by qRT-PCR gene expression analysis. Further, we intend to identify the expression of LBX2-AS1 in AMs with relation to clinic-pathogical features, such as peritumoral edema, tumor recurrence, Ki67 and sex.

Methods

Total RNA isolation and quality control from 16 AMs and 5 healthy control tissues were performed. Briefly, LBX2-AS1 expression was performed by real-time quantitative reverse transcription PCR (qRT-PCR) using 40 ng of total RNA and a TaqMan™ Gene Expression Assay (Life Technologies, Germany), according to the manufacturer's guidelines. The housekeeping gene glyceraldehyde-3-phosphate dehydrogenase (Gapdh) was used as internal control for normalizing real-time qRT-PCR data. The fold change in expression of the LBX2-AS1 gene in AMs versus control tissues was calculated using the $2^{-\Delta\Delta Ct}$ method upon normalization to the Gapdh housekeeping gene. All assays were performed in triplicates

Results

We observed a robust > 15-fold higher expression of LBX2-AS1 in AMs compared to the controls ($p>0.001$) by qRT-PCR method (Fig). Further, our gene expression results showed a positive correlation of LBX2-AS1 in AMs both with and without peritumoral edema, tumor recurrence, Ki67 and sex

Conclusion

Our results provide here the first evidence that LBX2-AS1 is strongly up-regulated in AMs and showed a positive correlation with peritumoral edema, tumor recurrence, Ki67 and sex. We believe that such higher expression may contribute to the development of peritumoral edema, recurrence and tumor cell proliferation in patients with AMs. Future studies in larger patient cohorts may validate the above findings and reveal its significance as a prognostic biomarker for early clinical diagnosis and risk stratification

Meningeome II/*Meningioma II*

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Verhalten eines innovativen Somatostatin Rezeptor Typ 2 (SSTR II) zielgerichteten Nahinfrarotfluoreszenzfarbstoff in einem neuen präklinischen Meningeom Modell.

Performance of a Novel Somatostatin Receptor Type 2 (SSTR II)-Targeted Near Infrared (NIR)-Fluorescent Probe in a New Suitable Preclinical Meningioma Model

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Objective

We aim to develop a highly specific and sensitive optical method for intraoperative meningioma imaging to enable tumor visualization and improve the resection completeness by targeting the reliably overexpressed somatostatin receptor type 2 (SSTR2). Suitable preclinical meningioma models to test SSTR2 targeting probes are lacking. We have previously shown the proof-of-principle in a wildtype high grade orthotopic meningioma xenograft model. To determine the full potential, we aim to develop a highly SSTR2 expressing meningioma model and test the performance of our probe in a preclinical scenario in vivo.

Methods

We already presented our first data about our probe that consists of a somatostatin analogue (TATE) linked to a new developed dye (sNIR) demonstrating its optical properties and specificity in physiologically SSTR2 expressing organs. Now, meningioma IOMM-Lee cells were transfected by lentivirus to overexpress the SSTR2. Wildtype and SSTR2+ cell lines were used in cell uptake assays and were ectopically and intracranially implanted in mice to perform fluorescence guided surgery. As negative controls a scrambled probe analogue and Octreotide for blocking were used. The SSTR2 expression was evaluated by immunohistochemistry (IHC) ex vivo.

Results

The SSTR2+ IOMM-Lee cells show a significant higher uptake of TATE-sNIR compared to the wildtype cells and controls. In the ectopic meningioma model, a significantly increased uptake of the probe in the SSTR2+ tumors compared to low expressing wildtype tumors was observed. In the orthotopic meningioma model, the tumor-to-brain-ratio was extraordinarily high after TATE-sNIR injection (28.7; SD 13.7; n = 5) and significantly decreased after injection of scrambled TATE-sNIR (4.8, SD 2.0; n = 3) and the Octreotide blocking (11.1, SD 2.4; n = 3). The IHC proofs the overexpression of SSTR2.

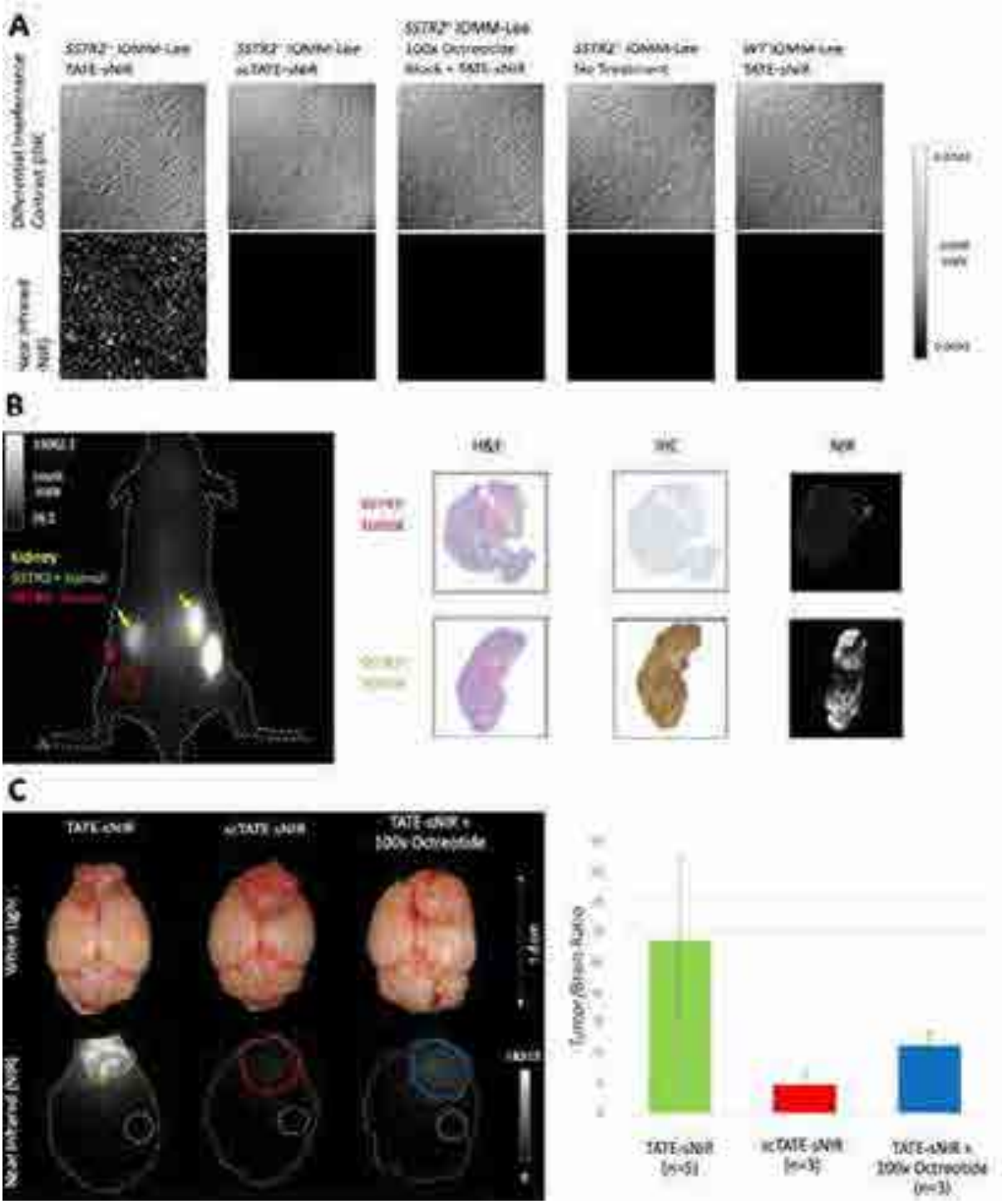
Figure A Increased uptake of TATE-sNIR in SSTR2+ cells compared to controls. **B** High fluorescence in SSTR2+ subcutaneous tumor vs. wildtype tumor and corresponding IHC proofing the matching expression. **C** Specific uptake of TATE-sNIR in intracranial meningioma compared to controls.

Conclusion

Our results demonstrate that our SSTR2-overexpressing meningioma mouse model is feasible to mimic the high SSTR2 expression level in human meningioma. Our newly developed probe is capable of specifically targeting the

SSTR2 in vitro and in vivo. The high tumor-to-brain-ratio potentially enables fluorescent guided meningioma surgery even with micro doses in the future.

Abb. 1



Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

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Management von Vestibularisschwannomen: DEr Einfluss der kraniellen Hirnnervendefizite auf die Lebensqualität

Management of Vestibular Schwannoma: Impact of cranial nerve deficits on the QoL

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Objective

This prospective study aimed to evaluate the impact of cranial nerve deficits on the quality of life (QOL) before and after vestibular schwannoma surgery.

Methods

In this prospective study, 115 patients (51 males, mean age 52y) with retro-sigmoid surgery between 2016 and 2021 were investigated clinically 1-2 days before and 1 week, 3 months, and 1 year after surgery. Gustatory sense was examined with standardized taste solutions, lacrimation by the Schirmer I test, facial function was graded by House-Brackmann-Classification; auditory function and tumor extension were graded by the related Hannover Classifications. QOL was examined with the SF36 and the Penn Acoustic Neuroma Quality-Of-Life (PANQOL) questionnaire, consisting of 7 domains. Composite Score as sum score of all domains could be calculated (max. 100, min 0). Correlations were analysed by a regression model.

Results

Seven cases with small (T1/2), 64 cases with medium (T3A in 34 cases; T3B in 30 cases), and 44 cases with large (T4A in 18 cases; T4B in 26 cases) tumors were included. The *Composite Score of the PANQOL* decreased from an average of 68.8 points before to 62.5 points after surgery and rose to 65.4 points after 1 year. The *SF36 mental health subscore* developed from 40.9 points before surgery to 42.3 points postoperativ to 45.1 points after 1 year. The *SF36 physical health subscore* decreased from 50.4 points before to 33.8 points after surgery to 43.4 points after 1 year. Only the gustatory impairment showed a significant impact on the SF36 physical health subscore ($p=0.03$). After 3 months, facial impairment ($p=0.01$) and dizziness ($p<0.01$) showed a significant impact on the PANQOL sum score and dizziness ($p<0.01$) and tumor extension ($p=0,02$) on the SF36 physical health subscore. At 3 months, dizziness ($p<0.01$) reached significance for the SF36 mental health subscore. After 1 year, taste deficit ($p=0.04$) was significant for the PANQOL sum score, tear dysfunction ($p=0.03$) was significant for the SF36 physical subscore and none of the cranial nerves affected the SF36 mental subscore significantly.

Conclusion

QOL decreases substantially early after surgery. At 3 months, in the recovery period, the facial impairment had the highest impact on the patients, and one year after surgery, when recovery is mostly complete, only the tumor extension had a significant impact on the physical health score. Also less obvious deficits should be concerned cause of their impact on QOL especially in the first year after surgery.

Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

J-SBNC042

Intrakanalikuläre Akustikusneurinome: Operationsergebnis in Bezug auf Tumor- und Hirnnervenposition im inneren Gehörgang

Intracanalicular vestibular schwannomas: surgical outcome related to tumor position and cranial nerves within the internal auditory canal

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Objective

Evaluate if the pattern of displacement of the nerves in the internal auditory canal (IAC) in intracanalicular Vestibular Schwannomas (Hannover T1 VS) has any effect on cochlear and facial nerve outcomes and propose a subdivision of small VS based on it.

Methods

From January 1993 to November 2021, 695 patients with VS were operated. Patients with sporadic T1 VS were retrospectively selected. All cases underwent resection via retrosigmoid transmeatal approach with intraoperative monitoring. Cases where nerves were displaced anteriorly were classified as T1A, and when the vestibular nerves were displaced posteriorly and the facial and cochlear nerves were displaced anteriorly were classified as T1B. Postoperative hearing was assessed with audiogram on postoperative week 12, and facial nerve function was evaluated using the House Brackmann (HB) scale at 6 months from surgery.

Results

Forty-four patients were included. Mean age was 46 years old, and 30 patients were women. Thirty-five cases presented as T1A, and 9 as T1B. Both facial and cochlear nerves were anatomically preserved and gross total resection was achieved in all cases. All patients had normal facial nerve function before surgery and 32 patients had useful hearing, 10 had non-useful hearing, and 2 patients had no hearing (table 1). All patients with T1A VS had normal facial nerve function postoperatively (HB 1), whereas in T1B VS six patients had HB 1, two had HB 2 and one had HB 3. Thirty-three of the 35 patients with T1A VS achieved the same or better hearing status after surgery, compared with 2 of the 9 cases in T1B tumors (table 2).Three patients developed postoperative CSF leak that was successfully treated. No other surgical complications or mortality occurred in this series.

Conclusion

When the tumor lies between the nerves (T1B), the risk of HB grade 2 and 3 increases 24 times. This configuration also implied a significantly higher risk of worsening of hearing status after surgery, wich may be related to the fact that the tumor is in direct contact with the cochlear and facial nerve, whereas in T1A the fascicles of the vestibular nerves serve as a barrier between the tumor and facial and cochlear nerves.

Abb. 1

Table 1

	T1a		T1b	
n	35		9	
House-Brackmann Grade	Facial Nerve Function			
	Preoperative	Postoperative	Preoperative	Postoperative
1	35	35	9	6
2	0	0	0	2
3	0	0	0	1
	Cochlear Nerve Function			
Useful	27	28	5	2
Non-Useful	6	3	4	2
No Hearing	2	4	0	5

Abb. 2

Table 2

	T1a	T1b	p-value
	Facial Nerve Function		
Normal (HB 1)	35	6	0.006
Abnormal (Hb >1)	0	3	
	Cochlear Nerve Function		
Useful	28	2	0.0009
Non-serviceable	7	7	

Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

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Multimodales Hör-Monitoring in der Kleinhirn-Brückenwinkel-Chirurgie
Multi-modality monitoring of auditory function in cerebellopontine angle surgery

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Objective

Monitoring of auditory brainstem responses (ABR), as a far-field technique, bears critical limitations during vestibular schwannoma (VS) surgery. This study evaluates the application of additional near-field techniques.

Methods

Multi-modality monitoring was offered to patients with a very high interest in hearing conserving surgery, independent of pre-surgical hearing quality or tumor sizes. Registration was performed by conventional ABR with needle electrodes at A1, A2 and Cz, near-field recording either by additional placement of a ball electrode for an extra-tympanic electrocochleography (ECochG) or at the eighth nerve entry zone (D-ABR). Evaluation was based on a scoring system (Class 1: normal ABR, 2: latency delay, 3: wave III loss, 4: only wave I or V present, 5: no waves) and correlated with auditory function by Gardner Robertson (GR) Classification.

Results

Analysis could be performed in 107 VS operations. Hearing preservation was achieved in 45 patients (42%), with GR Class I in 10, GR II in 16, GR III in 16 and GR IV in 3 patients. All were accompanied by conventional ABR, 69 by additional ECochG, 46 by D-ABR. In 50 cases, ECochG enabled visualization not only of component I, but also of components II to V. Preoperative ABR, D-ABR and ECochG classes show a positive correlation with preoperative hearing classes. Postoperative ECochG was less reliable than ABR/ D-ABR in predicting postoperative hearing quality: 23 patients with postoperative deafness had a preserved cochlea potential (Class 4) in ECochG. Analysis of ABR and ECochG classes identified a strong positive correlation ($P<0.01$, Kendall-Tau-b preop 0.835, postop 0.734) especially for classes 1 to 3, where wave V is still present ($P<0.01$ Kendall-Tau-b preop 0.741, postop 1.000); here, both methods behaved almost in a linear correlation. ECochG and D-ABR provide recordings at 10 to 100 times higher amplitudes, with new information on the functional status within 5 to 10 seconds. Technical limits were related to the individual anatomy, such as narrow external auditory canals or extensive tumor formation.

Conclusion

Different to previous applications, ECochG may provide information beyond the control of cochlea function. Both nearfield techniques deliver larger and faster responses of all components and are especially useful during direct dissection at the tumor-nerve-border, inside the meatus and at the brainstem enabling a more flexible adaptation of the microsurgical manoeuvers.

Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

J-SBNC043

Akustisch evozierte Potentialle Störungen und Korrelation mit den Manövern des Chirurgen bei der Akustikusneurinom-Chirurgie

Brainstem Auditory Evoked Potential Disturbances and the Correlation with Surgeon"s Maneuvers during Vestibular Schwannoma Surgery

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Objective

Functional preservation of nerves is a main goal in vestibular schwannoma surgery. Intraoperative monitoring with brainstem auditory evoked potentials (BAEP) is an important tool used to help the neurosurgeon during tumor resection. It shows the function of auditory pathway but it presents some delay to acknowledge changes in waveforms after functional impairment. The objective of this study is to identify surgeon"s maneuvers during surgery of vestibular schwannomas that are associated with disturbances of the BAEP.

Methods

Between August 2017 and August 2022 we analyzed 36 cases of patients that were operated on vestibular schwannomas by a single surgeon, had totally or partially preserved hearing function preoperatively and presented a deterioration of the BAEP waves during surgery. Intraoperative BAEP monitorizations and microscope videos were recorded in synchronization. Microscope-video sections between initial changes in BAEP-waveforms and 2 minutes before this happened were analyzed and special attention was paid during drilling of the internal auditory canal, to surgeon"s types of movements during tumor resection, irrigation and use or not of papaverine when BAEP were affected.

Results

The first BAEP deterioration in this selected group of patients occurred on average 63 minutes (range 30 – 175 minutes) after the begin of the surgery with the microscope. Recovery of the waveforms (when it happened), presented on average 158 seconds (range 9 – 419 seconds) after the first BAEP decline. The analysis of these 36 specific cases allowed the recognition of critical surgical steps that were more frequently related with a worsening of the BAEP. The surgical maneuver that was mostly related to a decrease of the amplitude of the BAEP was medial traction of the tumor in the direction of the brainstem during resection. Lateral traction of the tumor to the internal auditory canal and drilling of the internal auditory canal where also related to BAEP deterioration.

Conclusion

Analyses of this specific population of patients allowed us to determine which maneuvers were most associated to BAEP alterations. Understanding these surgical steps and the risk associated with auditory waves and eventual hearing loss may possibly improve surgical outcomes. Most BAEP waves recovered within 5 minutes after the first deterioration. Prolonged decreases in BAEP seems to be related with poor recovery chances.

Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

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Auditorisches Mittelhirnimplantat (AMI): Konzept und Ergebnisse der klinischen Studie des zweischenkligen AMIs

Auditory midbrain implant (AMI): concept and results from the 2-shank clinical trial

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Objective

The auditory midbrain implant (AMI) stimulates the central nucleus of the inferior colliculus and is used for hearing rehabilitation in patients with neural deafness. This novel implant, used in 2 clinical trials of this research group, is considered as an alternative to the auditorybrainstem implant (ABI). The exact positioning of the AMI electrode is relevant for the hearing outcome and represents a surgical challenge.The aim of the study is to optimize the implantation of electrodes in the midbrain via acombined lateral suboccipital (LSO) and supracerebellar infratentorial (SIT) approach for thetwo-shank electrodes.

Methods

We performed an overall of twelve AMI surgeries in patients with neurofibromatosis 2 between 2006 and 2021. In all patients, a medially extended LSO approach was chosen for tumor removal and the SIT route for implantation of the AMI. Placement of the electrodes was based on preliminary animal and cadaveric work of our research group. Intraoperative orientation for definitive implantation of the electrodes was performed using a combination of anatomical landmarks, graph paper and neuronavigation. Postoperatively, a CT scan was performed to verify the exact location of the electrodes.

Results

No complications occurred intraoperatively or immediately postoperatively. In particular, there were no new neurological deficits and no cerebrospinal fluid fistula. Five patients were treated with a single-leg and seven with a double-leg electrode. The 3D analysis of the postoperative CT examinations showed that all electrodes (n=19) were placed in the inferior colliculus region. The exacttrajectory of the electrodes in relation to the angle in the axial and sagittal plane varied. The targets for this, 40° to the midline in the axial plane and 90° to an imaginary line between the dorsal surface of the superior and inferior colliculus in the sagittal plane, were increasingly well achieved as the study progressed. To date, none of the patients has experienced dislocation/migration of an electrode. In all patients, the AMI resulted in hearing benefits. In the best performers there is a good pitch mapping and speech perception.

Conclusion

The AMI concept has been shown to be feasible and safe in clinical practice. The exact placement of the electrodes is technically challenging. In this series of 12 operations, a learning curve is already evident in terms of localization results. These results encourage to further develop the AMI.

Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

V277

Management von Vestibularisschwannomen: Der Einfluss der Intermedius-Störung
Management of Vestibular Schwannoma: The impact of an intermediate nerve disturbance

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Objective

So far, studies on vestibular schwannomas (VS) rarely address the intermediate nerve. The aim of this prospective study was to investigate the frequency and the extent of clinical intermediate nerve affection and its relation to quality of life (QoL).

Methods

From December 2016 to September 2021, 115 VS patients (51 men, Mage 52.3 years) were included in this study and underwent tumor removal via the retrosigmoid approach. Detailed neurological examination included standardized testing of taste and tear secretion before, first week, and 3 months after surgery (FU1), after 1 (FU2) and 2 (FU3) years postoperatively. The Short Form 36 (SF36) and the Penn Acoustic Neuroma Quality of Life (PANQL) were used to collect QoL data.

Results

There was a significant increase in lacrimal dysfunction ($p < 0.001$) and taste dysfunction ($p < 0.001$) in the first postoperative week. New dysfunctions were documented in 32 patients for taste and in 39 patients for tear secretion and persisted over the course of two years. Predictive markers for postoperative intermediate dysfunction were preoperative taste dysfunction ($p = 0.005$), tumor extension ($p = 0.028$), and tumor location on the left ($p = 0.02$). A positive correlation between facial nerve paresis and an intermediate disorder could be established, the percentage probability of a pathological test increases with increasing House-Brackmann (HB) degree (Tear test: 41% pathological with HB 1, 85% with HB 6; Taste test: 29% pathological with HB1, 80% in HB6). Postoperatively, the total PANQL score and the results of the taste test correlated significantly ($p = 0.027$). Looking at the individual dimensions in the PANQL regression model, a significant correlation of a pathological taste test and the dimensions "Facial Symptoms" ($p = 0.028$), "Balance" ($p = 0.026$), Hearing ($p = 0.021$) and "Pain" ($p = 0.003$) could be evaluated. The physical sum scale of the SF36 also showed a significant correlation with the taste test results postoperatively ($p = 0.009$). In the further course (FU2 and FU3), these close correlations between QoL and intermediate dysfunction were not persistent.

Conclusion

A large part of the study cohort developed a postoperative intermediate nerve disorder, which hardly regresses over time. The impact on QoL appears highest early on and diminishes already after 1 to 6 months. Thus, intermediate nerve dysfunction should be part of our consultation.

Vestibularisschwannome IV Lebensqualität und Hörfunktion/*Vestibular schwannomas IV QoL and auditory function*

V278

Anosmie nach Operation an der hinteren Schädelgrube in der halbsitzenden Lagerung
Anosmia following posterior fossa surgery in the semisitting position

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Objective

To assess the incidence of anosmia after posterior fossa surgery in the semisitting position and analyze risk factors.

Methods

From January 2019 till December 2022 73 patients operated in the semisitting position for posterior fossa lesions were enrolled in this prospective study. The patients` olfaction was tested pre- and postoperatively via the Burghart sniffin` sticks©. Demographic patients` data, type of surgical approach and tumor size were registered. In all cases on postoperative day 1 a CT scan was performed and the volume of the postoperative pneumatocephalus defined with the Brainlab software©. 33 patients operated for vestibular schwannomas in supine position were examined as control group.

Results

73 patients operated on for vestibular schwannomas (70), cerebellar metastases (1) and petroclival meningiomas (2) were included. 72 were operated via a retrosigmoidal craniotomy, 1 was operated via a median suboccipital craniotomy. 51 were women, 22 men. Their age ranged from 26 to 80 years (mean age 50.7 years). The extent of the postoperative pneumatocephalus ranged from 0.24 cm^3 up to 183.1 cm^3 with a mean of 50.7 cm^3. Of the 73 patients included in this study 2 (2.7 %) experienced a relevant deterioration of their ability to smell. The extent of the postoperative pneumatocephalus in these two patients was relevant with 161 cm^3 and 133.2 cm^3. Both patients were female, aged 63 and 68, and both received a retrosigmoidal craniotomy for resection of a vestibular schwannoma. The first patient`s tumor size was 1.9 $cm^3$, the second patient`s tumor size was 1.05 cm^3. No patient in the control group suffered from a postoperative anosmia.

However, the incidence of anosmia following surgery in the semisitting position compared to the one after surgery in the supine position failed to be statistically significant (x^2=0.88) presumably due to low patient numbers.

Conclusion

Postoperative anosmia is a possible and clinically relevant complication after surgery in the semisitting position. Traction of the olfactory nerve filaments is the hypothesized mechanism. Further studies will be needed to investigate on co-factors and how to avoid this problem.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V279

Wirksamkeit und Sicherheit der tiefen Hirnstimulation bei chronisch-refraktären Gesichtsschmerzsyndromen: Eine IPD-basierte Metaanalyse

Short-term efficacy and safety of deep brain stimulation for chronic facial pain: An individual-patient data (IPD) meta-analysis

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Objective

Despite available, advanced pharmacological and behavioural therapies, refractory chronic facial pain of different origin still poses a therapeutic challenge. To assess the safety and efficacy of DBS for facial pain.

Methods

We underwent an Individual Patient Data (IPD) meta-analysis according to the PRISMA framework using a mixed effects model and performing searches on PubMed, Embase and Cochrane Library covering the years 2000-2022. Primary endpoint was changes in pain intensity (visual analogue scale; VAS) and secondary outcome included correlations and regression analysis were performed to identify predictive markers (age, duration of pain, frequency, amplitude, intensity, contact configuration, DBS target).

Results

Seven trials consisting of 54 / 77 patients (70%) screened met the inclusion criteria (mean age: 54 ± 14 years; male 49% / female 33%; facial pain origins: post-stroke 32%; post-surgical 22%; 16% trigeminal; 12% post-infection; DBS targets: thalamic nuclei (CmPf;VPM,VPL) 40% / PVG/PAG 31% / combined DBS - CmPf;VPM,VPL + PVVG/PAG 19%). DBS significantly declined VAS after 3 months ($p = 0.001$) (Figure 1) with no superiority of thalamic or brainstem DBS targets [PAG/PVG versus VPL/VPM/CmPf: $p = 0.42$]; [PAG/PVG versus others: $p = 0.74$]; [(VPL/VPM/CmPf versus others: $p = 0.48$] (Figure 2). Correlation assessment demonstrated no relationship between DBS response and age ($r = -0.001$; $p = 0.997$), contact configuration ($r= 0.04$; $p = 0.452$), stimulation intensity ($r = 0.03$; $p = 0.887$), frequency ($r = 0.08$; $p = 0.68$), amplitude ($r = 0.284$; $p = 0.135$) and duration of the underlying pain etiology ($r = -0.172$; $p = 0.373$). Incidence of adverse events (AE) were for infection / lead fracture 19%, stimulation-induced side effects 7% and 3 deaths (unrelated to DBS / cancer progression / second stroke).

Conclusion

Current published data indicates that DBS (thalamic and PVG/PAG) effectively suppresses facial pain at short term, thus long-term data are sparse. However, this may not limit the value of uncontrolled cohort studies reporting sustained DBS responsiveness. Therefore, the authors advocate to consider non-invasive as well as less invasive neuromodulation prior to invasive deep brain stimulation.

Abb. 1

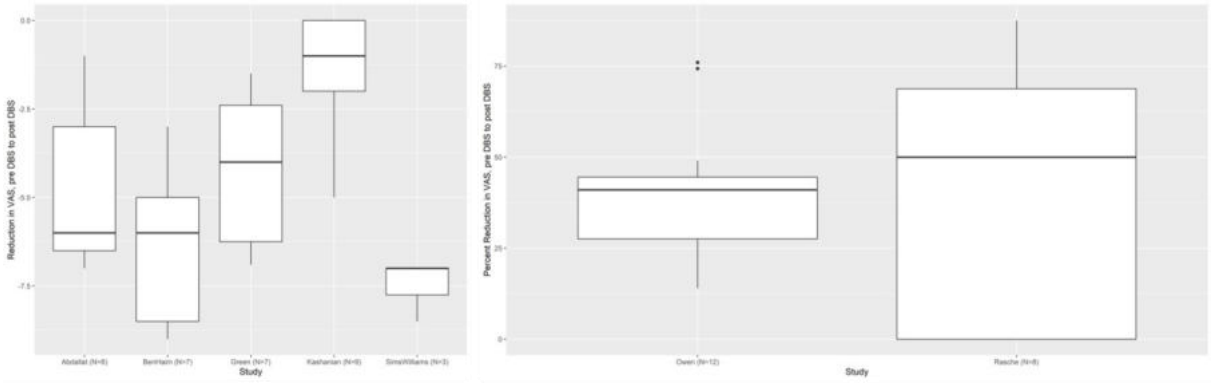
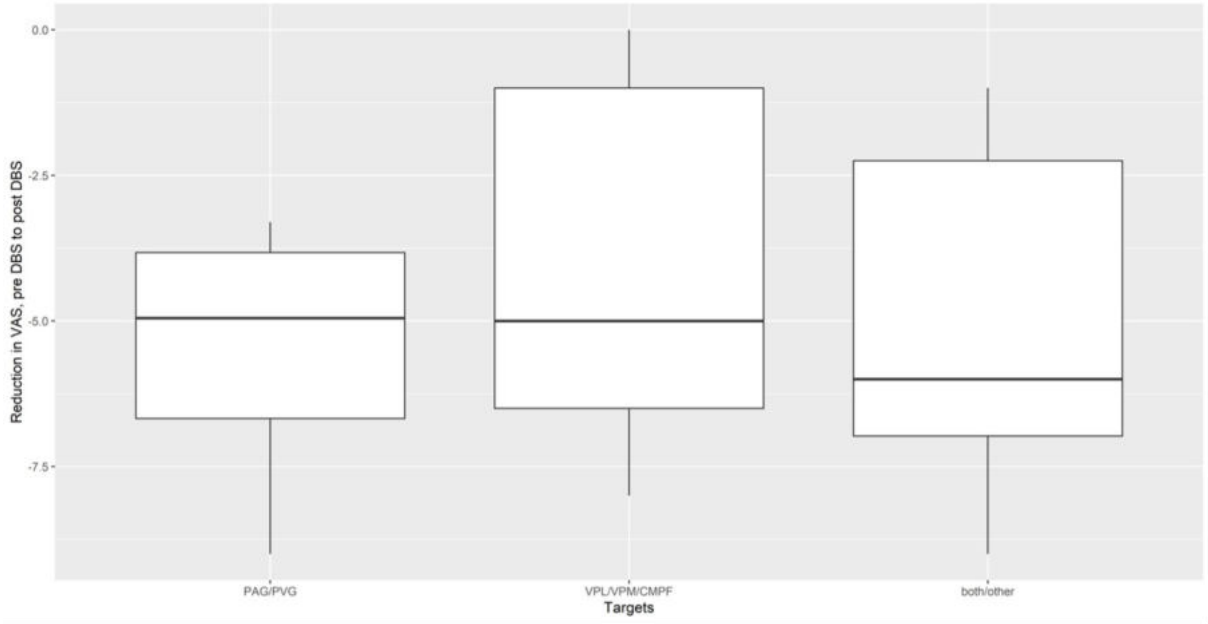

Reduction in VAS, pre DBS to post DBS
Study
Percent Reduction in VAS, pre DBS to post DBS
Study

Abb. 2


0.0
-2.5
-5.0
-7.5
Reduction in VAS, pre DBS to post DBS
PAG/PVG
VPL/VPM/CMPF
both/other
Targets

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V280

Tiefe Hirnstimulation und Depression: Eine Untersuchung der Bahnen, die den subgenualen Gyrus cinguli (BA25) miteinander verbinden.

Deep Brain Stimulation and Depression: A dissection through the pathways that interconnect the Subgenual Cingulate Gyrus (BA25).

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Objective

Deep brain stimulation over the subgenual cingulate gyrus (SCG) (Fig 1 A) is currently proposed as a target for major depressive disorder.

The white matter connections underlying the SCG are still under study and we believe that its knowledge can help us to clarify the fiber network that participates in the mechanism of action of DBS and, in turn, contribute to refine the targeting for electrode placement.

The objective of this study is to carry out a deep investigation of the anatomic connections of the SCG region by presenting a tractography study and the second and most extensive cadaveric study of the anatomical connections of this region.

Methods

Tractographies were performed by using DSI Studio software on a template of 1065 healthy human brains. A one-ROI approach was used, thus a spherical ROI was placed on the ventromedial frontal cortex. The different tracts were observed in a three-dimensional plane. The results were compared with cadaveric dissections performed in 12 healthy human brain hemispheres according to the Klingler technique.

Results

In our study, we found seven main connections (Figs 1-2): 1- Fibers of the cingulum, originating at the level of the SCG and terminating at the medial aspect of the fronto-parietal lobe (Ci). 2- Fibers of the uncinate fasciculus, connecting the orbitofrontal with the anterior temporal region (UC). 3- Fibers from the forceps minor connecting both frontal lobes (FM). 4- Fronto-striatal fibers (F-St). 5- Fibers running more laterally, converging onto the ventral striatum (Accumbofrontal Fasciculus - AF). 6- Fibers connecting both amígdalas running through the forceps minor (Amg). 7- Fibers of the deeper portion of the IFOF.

Conclusion

The SCG presented a large number of white matter connections to the limbic system, the prefrontal area, and mesotemporal areas. In this study we described 3 consistent white matter bundles that were not taken into account in previous studies that could be useful to improve the electrode implantation.These findings can help to explain the role of the SCG in DBS for psychiatric disorders.

Abb. 1

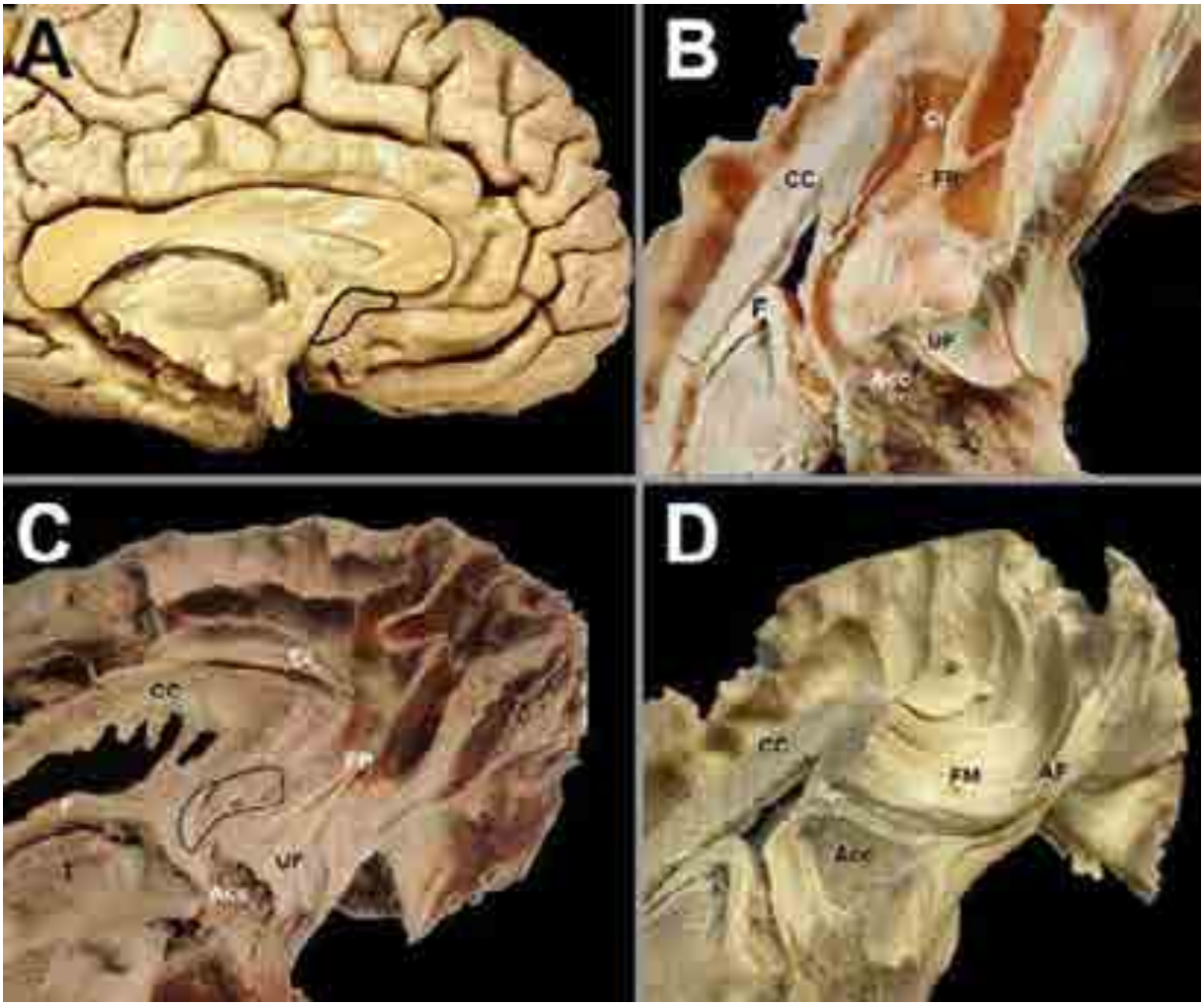
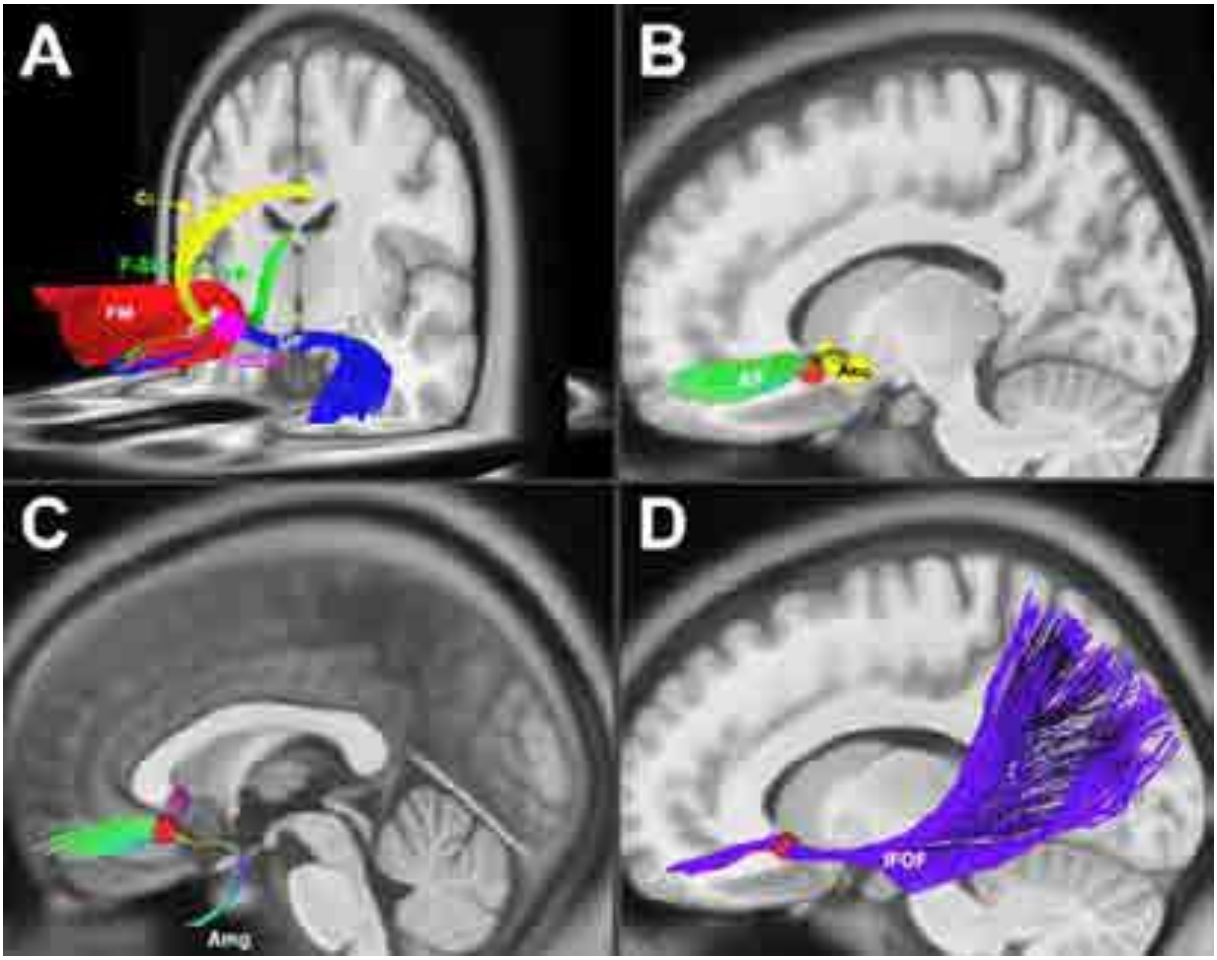


Abb. 2



Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V281

Intraoperative Mikroelektroden-Aufnahmen zur anatomischen Lokalisation in Tiefen Hirnstimulation bei Patienten mit Zwangserkrankung

Intraoperative microelectrode recordings to estimate anatomical location in deep brain stimulation for obsessive-compulsive disorder

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Objective

Deep brain stimulation (DBS) is an established therapy for movement disorders and for psychiatric patients with therapy resistant conditions, such as obsessive-compulsive disorder (OCD). Optimal targeting of the stimulation electrode during surgery is essential to improve function in these patients. Therefore, real-time monitoring of microelectrode recordings (MER) and local field potential (LFP) activity has evolved as a beneficial tool to monitor electrode location in DBS surgery. In this study, we aim to investigate the utility of intraoperatively recorded LFP activity during DBS surgery targeting the nucleus accumbens and anterior limb of the internal capsule (NAcc/ALIC) in OCD patients.

Methods

We intraoperatively recorded LFPs in 10 OCD patients while traversing the surgically planned trajectory during DBS surgery. For each advancement step of one millimeter along the surgically planned trajectory, approx. 60 seconds of raw data were recorded. All patients received bilateral electrodes in the NAcc/ALIC. DBS leads were localized using the Lead-DBS software based on the preoperative MRI and the postoperative CT. All recording sites were projected onto a common MNI space and were overlapped with subcortical atlas structures.

Results

Our results indicate frequency-specific changes in LFPs while traversing the surgically planned trajectory towards target point in the NAcc. With each advancement step towards target point, activity in the low beta-band decreases, while oscillatory activity within the low and high gamma-band increases. This observation holds true for left hemispheric trajectories, however, could not be replicated in right hemispheric trajectories.

Conclusion

Our study is a first step towards the implementation of real-time monitoring of MER and LFP recordings in DBS surgery for OCD. We here present results that indicate frequency-specific changes in white and gray matter oscillatory activity that might help to increase implantation accuracy in the future.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V282

Welche Faserverbindungen werden bei der tiefen Hirnstimulation bei Zwangsstörungen stimuliert?
Which are the fiber tracts stimulated by deep brain stimulation for obsessive compulsive disorders?

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[2]Universität Regensburg, Klinik für Psychiatrie, Regensburg, Deutschland

Objective

In our center we aim at the bed nucleus of the stria terminalis (BNST) in deep brain stimulation for obsessive compulsive disorders (OCD). The aim of this study was to evaluate which fiber tracts are stimulated, in addition to the target, by the implanted electrode contacts.

Methods

In 11 consecutive patients with obsessive compulsive disorders 88 electrode contacts were investigated. Tractography was executed on individual diffusion weighted images with 64 gradient directions on a 3T scanner and the patients under general anesthesia. Each of the electrode contacts was defined as a specific seed volume and the resulting fiber tracts were determined.

Results

All of the 88 electrode contacts were connected to fibers passing through the anterior limb of the internal capsule. 94% of the contacts were associated with the medial forebrain bundle and 69% with the stria terminalis. Overall, 21 cortical and subcortical structures were found to be connected to the electrode contacts in various degrees.

Conclusion

The name of the target used in deep brain stimulation suggests that clinical effects are mediated, at least mainly, by stimulation of that target. However, it seems most likely, that additional subcortical structures may influence these effects significantly. To what extent has to be explored in further studies.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V283

Hochfrequente (10 kHz) Rückenmarkstimulation in Patienten mit Failed Back Surgery Syndrom und bei anderen Syndromen mit chronisch-neuropathischen Schmerzen: Ergebnisse von 6-jähriger Erfahrung

6-year results of high-frequency (10 kHz) spinal cord stimulation in failed back surgery syndrome and other conditions involving chronic neuropathic pain

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Objective

To assess the response and complication rate of spinal cord stimulation (SCS) with high-frequency (HF 10 kHz/HFX) stimulation in patients with chronic neuropathic pain due to failed back surgery syndrome (FBSS) in comparison to other chronic neuropathic pain syndromes (real-world data).

Methods

In this observational, descriptive, retrospective study we analyzed patients, who underwent HF SCS at 10 kHz (HFX) in the last 6 years in our clinic. Patients with a minimum of 12-months documented follow-up were included. Two groups were formed: first group included patients with FBSS, while in the second group were patients with other conditions involving chronic neuropathic pain, such as postherpetic neuralgia, phantom limb pain etc. A clinical response to SCS was defined in having 50% or more pain relief. General complications such as wound infection, lead migration, as well pocket pain were analyzed and compared to recently published studies.

Results

A total of 111 patients received HFX SCS. Of 85 patients with FBSS, 62 (73 %) patients reported 50 % or more pain improvement at twelve months. We have observed a sustained clinical improvement for up to four years. In the second group the responder rate was 50 % (13 of 26). Patients suffering from peripheral neuropathic pain and central pain have shown a substantial improvement. However, clinical conditions, such as phantom limb pain, postherpetic neuralgia have been more resistant to HFX stimulation.

Overall complication rate was 16,2 %. 11 patients (9.9 %) had a wound infection, 2 patients (1.8 %) developed pocket pain, whereas 5 patients (4.5 %) had a lead migration, 2 of them due to trauma.

Conclusion

Our results demonstrate comparable results of HFX SCS regarding patients with FBSS, as compared to recently published studies. It also highlights variable response rates in different clinical conditions. This underlines the necessity to develop more sophisticated neurostimulation paradigms, potentially combining HFX with other forms of low-frequency stimulation.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V284

Vergleichststudie mehrerer Anbieter in der SCS - ein RCT
Multivendor trial in spinal cord stimulation – a randomized clinical trial

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[2]Heinrich-Heine-Universität Düsseldorf, Sektion Stereotaktische und Funktionelle Neurochirurgie, Düsseldorf, Deutschland

Objective

The development of different waveforms and various spinal cord stimulation (SCS) systems increases the options for patients with chronic neuropathic pain. However, the choice for the used stimulation system is commonly made on an arbitrary basis. We therefore prospectively explored the influence of different providers during the temporary trial phase of SCS in a randomized clinical trial.

Methods

30 Patients with the indication for an SCS trial were included in the study. After implantation of a test lead, subjects were tested in a randomized order with two external pulse generators (EPG) of two different device manufacturers (A and B). Test leads from company A, the connection with the EPG from company B was made with an adapter. Tonic stimulation was used for two days with the first EPG. After that, stimulation was switched to burst stimulation for the following five days. There was a washout period of two days and then the second EPG was tested with burst stimulation only for another five days. After the trial, the test lead was removed and, if medically indicated, the entire system of the provider whose stimulator produced the best pain relief is implanted. A prospective data collection of these patients takes place in the following 6 months. During the different study phases, pain intensity and perception of pain were assed with visual analog scale (VAS), PainDETECT and Pain Castastrophizing Scale (PCS).

Results

Persistent spinal pain syndrome (type II) was the most frequent pain etiology, all the subjects had PainDETECT scores over 12 indicating neuropathic pain. Mean pain intensity at the baseline was 6.6 and achieved 6.4 after five days with burst stimulation from company B and 5.4 after burst stimulation from company A. Reduction in PCS was similar between the two groups – from 31.9 to 24.3 points with company B and to 23.3 points with company A. The tonic stimulation phase, which was done with the system of a single company for each patient, elicited 4.8% pain relief with B and 16.0% with A.

Conclusion

The choice of stimulator shows to have no influence over pain reduction (non-inferior). Both types of Burst stimulation were superior in terms of pain relief, however no difference was found among companies A and B.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V285

Klinische Ergebnisse mit einer neuen schnell wirkenden Subwahrnehmungstherapie SCS für chronische Schmerzen: Eine europäische Beobachtungsstudie

Clinical Outcomes Using a New Fast-Acting Sub-Perception Therapy SCS for Chronic Pain: A European Observational Study

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Objective

Traditional Spinal Cord Stimulation (SCS) modalities that achieve sub-perception analgesia (e.g., ~ 1-10 kHz, burstDR) require patients to often wait hours or even days until pain relief is fully realized. A recent study however has demonstrated that quicker analgesic onset is possible using a new sub-threshold-based SCS modality called Fast-Acting Sub-Perception Therapy (FAST). As such, we sought to assess outcomes in patients using FAST-SCS for chronic pain in a European-based, multicenter, observational study.

Methods

This is an international, multicenter, observational case-series of patients permanently implanted with a FAST-enabled SCS system (Boston Scientific) to treat chronic pain as part of an ongoing assessment of real-world outcomes of SCS for chronic pain based on retrospective chart review (Clinicaltrials.gov identifier: NCT01550575). All analyzed patients are programmed using novel FAST (i.e., biphasic-symmetric waveform at 90 Hz; pulse width: 160-260 µs). Numeric Rating Scale (NRS) scores and Percent Pain relief (PPR) are being collected.

Results

To date, 71-patients have been assessed out to a mean follow-up duration of 465±375 days. Baseline mean NRS pain score in this current cohort was determined to be 7.8±1.4. A 5.1±2.6-point improvement ($p<0.0001$) in overall pain was reported at mean last follow-up (n=71). Assessment

Conclusion

A sub-perception SCS methodology that allows for near immediate pain relief following activation represents an advancement that may further improve the outcomes and experience of patients who desire SCS without paresthesia for relief of their chronic pain.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V286

Verbesserte Schmerzergebnisse und Therapielanglebigkeit nach der Rettung mit neuartigen SCS-Systemen: Europäische Erfahrungen

Improved Pain Outcomes and Therapy Longevity After Salvage Using Novel SCS Systems: European Experience

P. Rigoard[1], R. Bougeard[2], J. E. Llopis Calatayud[3], S. Raoul[4], G. Matis[5], H. Belaid[6], J. Vesper[7], Y. Pei[8], R. Jain[8]

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Objective

Providing various waveforms and programming options can facilitate more customized delivery of analgesic neurostimulation to chronic pain patients implanted with a Spinal Cord Stimulation (SCS) device. However, technologies that offer such optimization capabilities are not accessible to long-term implanted patients using older devices, some of whom may experience loss or attenuation in therapeutic efficacy over time. These patients therefore may elect to undergo a "conversion" to a different SCS system that possesses these capabilities to gain access to these new technologies. The ability to connect a new Implantable Pulse Generator (IPG) to existing leads with adapters can provide a simple solution for these patients, thus preventing the need for explantation. Here, we present real-world clinical outcomes of previously-implanted SCS patients with optimized programming who were then converted to an SCS System using an adaptor to existing leads.

Methods

This is a real-world, multicenter retrospective study of patients who were previously implanted with an SCS system (commercially-available device) who went on to convert to a new device (Boston Scientific) capable of multiple modality stimulation and/or combination therapy via an applicable device adaptor and new IPG. Pain relief and other associated outcomes using both the previously-implanted SCS system and the newly connected device IPG are being collected.

Results

Fifty-one patients have been assessed to date. Average age of those evaluated is 57-years with a mean baseline NRS score of 7.7 ± 2.0 (prior to using new system) and were previously implanted for a duration of an average of 8.4 ± 3.6 years. In patients for whom the conversion was performed to "rescue" sub-optimal outcomes with the previous system (N=47), a mean 3.5-point improvement with the current system was noted at last follow-up (3.1 years post-implant, 7.0 ⇒ 3.6, $p<0.0001$). Sixty-nine percent of the patients assessed (N=35) indicated that they sought better pain relief as their primary motivation in seeking to undergo a conversion to a new SCS device, followed by the need to access multiple programs (35%) and/or to get coverage of new areas of pain (31%).

Conclusion

Study results from this multicenter, observational case-series suggest that patients who have lost efficacy over time may benefit from conversion to an advanced IPG capable of engaging multiple mechanisms using an adaptor connected to existing leads.

Funktionelle Neurochirurgie II SCS und DBS/*Functional Neurosurgery SCS and DBS*

V287

FAST-Testung bei Patienten mit persistierendem chronischem Schmerzsyndrom und Evaluation der Rückenmarkstimulation - erste Ergebnisse der intraoperativen On-Table-Testung

FAST-testing in patients with persistend chronic pain syndrome and spinal cord stimulation evaluation – first results of on-table testing

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Objective

Spinal cord stimulation is an established therapy for patients with chronic pain where conservative treatment fails. Patients suitable for spinal cord stimulation usually undergo a trial period of several days or weeks after lead positioning and externalization of the cable extensions resulting in two surgeries. Additionally, extensions may be a source of infection. Different types of stimulations were introduced over the years with the fast-acting sub-perception therapy as the newest invention. Most current studies show significant pain reduction within 11 minutes with FAST stimulation. The aim of the current work was to evaluate the feasibility of on-table FAST-testing to predict a positive response to spinal cord stimulation.

Methods

All patients from May 2021 – January 2023 were identified undergoing on-table FAST testing. Pain level was documented using the NPR scale before and after 15 minutes of on-table FAST stimulation. All patients underwent the normal testing routine with cable externalization and multi-day out-of-hospital testing. The correlation of pain reduction on NPR scale and the implantation rate was evaluated.

Results

23 patients were identified. In all patients FAST testing showed a decrease in NPR scale, in 21 patients the NPR scale score halved (91.3%). Mean pain reduction on NPR scale was 5.0 points. In 22 patients (95.7%) a neurostimulator was implanted after positive multi-day out-of-hospital testing.

Conclusion

First experiences with on-table testing with FAST show a strong correlation with intraoperative response and response to the trial. This indicates the possibility to use intraoperative testing with FAST instead of a long and unpleasant trial period to determine the response of patients to spinal cord stimulation. This could be the first step to enable a guideline conform all-in-one implantation after only 15 minutes of intraoperative testing.

Periphere Nerven/*Peripheral Nerves*

V288

Kortikale Repräsentation der N. Accessorius-innervierten Muskeln: räumlich-funktionale Bestimmung durch navigierte Transkranielle Magnetstimulation

Cortical representation of muscles innervated by the accessory nerve: spatio-functional assessment by navigated transcranial magnetic stimulation

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Objective

Iatrogenic injury is a frequent origin of accessory nerve lesion, which may cause major disability due to a loss of function in the trapezius muscle (TRAP) and/or the sternocleidomastoid muscle (SCM). The spatio-functional cortical representation of these muscles in relation to other upper extremity and face muscles have recently been under debate. Navigated transcranial magnetic stimulation (nTMS) may be a valuable tool to quantify aspects of cortical motor reorganization and support decision making for timing of reconstructive surgery in nerval injury. To set a baseline, our study aims to delineate the spatio-functional cortical representation of muscles innervated by the accessory nerve in healthy subjects.

Methods

Ethics approval for this study was granted by local authorities (EA4/033/21). NTMS mapping of the motor cortex in 30 hemispheres from 15 healthy subjects was performed for the SCM, TRAP, deltoid (DEL), biceps (BBM), first dorsal interosseus (FDI) and zygomatic major (ZYG) muscles. The resting motor threshold (RMT), latency and amplitude, the center of gravity (CoG), the distance to the lateral sulcus (LS), motor area (area), the recruitment curve (RC) and the cortical silent period (CSP) were examined.

Results

Within the motor cortex, the CoG of the SCM was located between the CoG of the face (ZYG) and the CoG of the hand (FDI). The CoG of the TRAP was located superiorly to the CoG of the hand and closer to the midline. Distances to the lateral sulcus differed significantly (TRAP 55.5±6.7, SCM 35.4±12.9 mm, $p<0.001$). The SCM had a significantly larger cortical representation area than the TRAP (mean: 754±447 vs. 434±246 mm^2; $p=0.007$). The RMT (in V/m) of the SCM and TRAP were 113.0±23.1 and 97.4±23.7. No significant differences in the latency, amplitude or parameters of the RC were noted.

Conclusion

This study shows the feasibility of nTMS to describe the detailed spatio-functional representation of the TRAP and SCM within the precentral gyrus according to the homuncular organization of the motor cortex. It allows for comparison to four other locally and functionally related muscles. Our data contributes to the discussion on spatial representation of neck and trunk muscles and may serve as a baseline for future studies in patients with accessory nerve injuries.

Periphere Nerven/*Peripheral Nerves*

V289

Postoperative, Gesundheits-bezogene Lebensqualität und Auswirkungen auf den Arbeitsstatus bei Patienten mit neurogenem Thoracic-outlet-Syndrom

Health related quality of life and impact on work status in patients surgically treated for neurogenic thoracic outlet syndrome

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Objective

Compression of the neurovascular bundle at the thoracic outlet with sensorimotor symptoms is referred to as neurogenic thoracic outlet syndrome (nTOS). The impact of microsurgical decompressive surgery via the supraclavicular approach under neuromonitoring has never been characterized in terms of health-related quality of life (QoL), and impact on individual work status.

Methods

A validated questionnaire was sent to 17 surgically treated patients with nTOS between 2012 und 2022 Data is presented as median and [IQR].

Results

The questionnaire was sent back by 76,5% of patients with a median age of 37 [31;45] years. Symptoms were present 3 years [2;8] before surgery. 11 patients were female, median age was 35 [29;42]. Before surgery, 41% of patients were absent of work, 17% were retired. Follow-up (FU) was accomplished at a median of 1,7 years [0,95;3,45] after surgery. 85% of patients reported a benefit from surgery. Pre-surgical VAS improved from 8 [8;8,4] to 4 [3;6] at FU ($p<0.001$). At FU, 23 % of patients were retired; 0 % due to nTOS. 61 % of patients returned back to work. Preoperative health related QoL on a scale from 0 to 100 was rated with a median of 65 [42;80] and was significantly improved at FU with a median of 85 [75;95] ($p<0.001$). Median dimensional values (1- no problems to 5 – not able to perform tasks) for mobility/self-care/activity/pain/ and anxiety improved from 2/3/4/3/3 to 2/2/2/2/1, respectively.

Conclusion

A substantial number of patients had a benefit from surgery and QoL improvement. *However, the median individual health related QoL in surgically treated patients with nTOS is still lower than the national average.*

Periphere Nerven/*Peripheral Nerves*

V290

Kann ein ergotherapeutisches Hausübungsprogramm die allgemeine Handkraft nach Karpaltunnel- oder Kubitaltunneloperation verbessern?

Does a self performed ergotherapeutic home training improve grip strength in patients after carpaltunnel or cubitaltunnel surgery?

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Objective

A loss of hand function due to intermittend or permanent paraesthesia and/or to weakness in the thenar respectively hypothenar muscles is characteristic for patients with Carpal tunnel syndrome (CTS) and Cubitaltunnel syndrome (CuTS) and the reason to indicate surgery. Ergotherapeutic prescriptions are not written out as a standard although in cases with severe loss of muscle function. Often it is pretty time involving to patients to make it to an ergotherapist at regular intervals after surgery, particularly as car driving might be difficult.

Methods

This is a prospective examination. 13 people with CTS or CuTS surgery received a home training program which was designed by an ergo therapist together and a neurosurgeon. It included 12 exercises for the thumb abduction and –flexion, sensory training and an instruction to scar massage. The program was handed out two weeks after surgery, proper wound healing provided. The patients were said to perform the exercises 10 minutes a day and document it in a diary. Overall grip strength with a dynamometer as well as motoric and sensoric tests were raised preoperatively and 6 weeks after surgery. The non affected hands were used as "control-group".

Results

In December 2022 patient collective includes 5 man and 8 woman. 11 presented with CTS, 2 with CuTS. 7 patients had muscle weakness <4/5 before surgery, 6 presented with sensoric symptoms only. Age ranged from 27 to 80 years. Average grip strength in the affected hand was 24,6kg. 10 patients told that they had performed the exercises daily, 3 said that they did not, resulting in a complicance of 70%. 6 weeks after surgery the grip strength of the operated hand improved with 2,73 kg in average. There was a minimal increase of grip strength in the non-affected hands of 0,5kg in average. Paresis and sensible deficits were less in both groups.

Conclusion

An ergotherapeutic self performed home training is accepted by a majority of patients with nerve compression syndroms. It helps to improve grip strength as a marker of overall hand function. Motor and sensible deficits regress after surgery independently of a training.

Periphere Nerven/*Peripheral Nerves*

V291

Arbeitsstatus und Rückkehr zur Arbeit in einer Kohorte sporadischer gutartiger peripherer Nerventumoren aus dem deutschen Register für periphere Nerventumoren

Work status and return to work in a cohort of sporadic benign peripheral nerve tumor lesions from the german peripheral nerve tumor registry

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Objective

Benign peripheral nerve tumors are rare lesions. Information about the effect of tumor symptoms and surgery on the individual work status of affected patients, especially without any genetic comorbidities, is scarce. Therefore, we analyzed a subgroup of patients without any clinical signs for genetic diseases, such as schwannomatosis or neurofibromatosis, from the peripheral nerve tumor (PNT) registry.

Methods

A questionnaire was send to previously operated patients with a tumorous benign PNT. Only patients without obvious clinical signs of a genetic diseases, like schwannomatosis or neurofibromatosis, were included. Ethical approval was granted by local authorities of the coordinating center (EA4/058/17) and local commitees. Data is presented in % of patients that answered to the questionnaire or median and [interquartile range].

Results

A hundred and thirty patients with sporadic benign PNTs responded to the questionnaire. The median age in our patient cohort was 49 years [38;57] and 56% of patients were male. Schwannoma was the most common histopathological diagnosis (71.5%) and neurofibroma 2nd most common (14.6%). Less common diagnoses were desmoid tumors, hemangioma, lymphangioma, and hybrid tumors. Preoperative sensory deficits were present in 35% of patients and motor deficits in 21%. After surgery, motor deficits were present in 26.2% and sensory deficits in 49.2%, respectively. At a median follow-up of 39 months [24;60], motor deficits resolved in 8% and sensory deficits resolved in 12%. 75.8% of patients had been part of the active work force prior to surgery. 52% of had worked full time and 5% had been retired. Before surgery, 10.1% of patients had been absent from work due to PNT symptoms. For a median of 4 [1;6] days, patients were absent from work to undergo surgery. After surgery, 69.8% returned back to work in the same manner they had worked before. 8.1 % modified their work status after surgery.

Conclusion

In sporadic benign PNTs, absence from work was noted in only a small percentage of patients. Most patients returned back to work after surgery. Factors that may influence individual work status may be timing of surgery, neurological outcome, or comorbidities.

Periphere Nerven/*Peripheral Nerves*

V292

Motorische Ersatzplastiken zur Korrektur des Fallfußes
Tendon transfers procedures for correction of drop foot

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Objective

Drop foot is associated with a significant restriction in quality of life. One of the most common reasons is isolated injury to the common peroneal nerve, e.g. due to fractures of the lower leg. Conservative options are limited to physical therapy, joint orthoses, and functional electrical stimulation. However, functional recovery is often poor and patients are unable to ambulate without orthosis. If primary nerve repair provides unsatisfactory results, tendon transfers can be considered for correction of drop foot. Hereby, we report our experience with tendon transfers for correction of drop foot in the past five years.

Methods

We performed a retrospective chart review to identify patients treated with a tendon transfer procedure because of drop foot. The etiology of drop foot, as well as patients` age, duration of hospital stay, follow-up time and muscle strength according to Medical Research Council Scale pre- and postoperatively were acquired.

Results

Between 2017 and 2022, 17 patients (12 male, 5 female) underwent tendon transfers for correction of drop foot. The mean age was 36.3 years (range: 9-75 years). The duration of the hospital stay was in 3.7 days on average (range: 2 to 10 days). The mean follow-up time was 10.4 months (range: 2 to 35 months). All patients achieved at least strength grade 3 postoperatively while preoperative strength grades ranged between M0 (16/17, 94.1 %) and M2 (1/17, 5.9 %). Six patients (6/17, 35.3%) underwent revision surgery due to insufficient strength of the initial tendon transfer. After revision almost all patients (17/18, 94,4%) achieved plantigrade foot position without the need for orthotic devices. In one case, the patient achieved strength grade M4, but an orthosis was still needed due to occupational requirements. In four cases (4/17, 23.5%, 2 males, 2 females), hyperinversion in the talotarsal joint was noticeable during dorsiflexion in the talocalcaneal joint.

Conclusion

Tendon transfer procedures, such as the stirrup-plasty or the isolated tibialis posterior tendon transfer, serve as a reliable technique for correction of drop foot. In most cases, postoperative results are good to excellent. The risk of postoperative hyperinversion in the talotarsal joint must be taken into account when planning the operation. Possible solutions include centralization of the tibialis anterior tendon or performance of a stirrup-plasty also in case of preserved peroneus longus muscle function.

Periphere Nerven/*Peripheral Nerves*

V293

Ein Update des multizentrischen peripheren Nerventumorregisters
A highly anticipated Update from the multicentric Peripheral Nerve Tumor Registry (PNTR)

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Objective

The establishment of the multicentric Peripheral Nerve Tumor Registry (PNTR) in 2015 allows for systematic analysis of patients with benign, malignant, and other rarer tumor entities associated with peripheral nerves. So far, no multicentric data on peripheral nerve tumors exist in Europe.

Methods

The PNTR was divided into a retrospective (2014-2016) and prospective (since 2017) study arm. Patient characteristics (age, sex) as well as disease (affected nerve, tumor location, histopathology), surgical treatment (type of treatment, pre-and postoperative symptoms), radiological imaging, diagnosis of neurofibromatosis (NF), and long-term follow-up data were analyzed.

Results

In total data from 189 surgical treated patients were analyzed. 56 % of patients were male and 44 % were female. The average age was 49 years. The most affected neural structure was the plexus brachialis with 31 patients. The most common histopathologies were schwannoma (n=120) followed by neurofibroma (n=33) and perineurioma (n=13). Whereas malignant peripheral nerve sheath tumors (MPNST) occurred in 7 cases (n=7) and hybrid tumors in four (n=4). Other rare entities were single represented. Upper extremity was affected in 103 cases whereby lower extremity was involved in 86 cases. Patients were treated by complete tumor resection in 85 %, biopsy in 9 %, and partial tumor removal in 6 %. In 6 % patients were initially treated with biopsy at a non-specialized center which led to motor and sensory deficits prior to surgery at the participating centers. Prevailing preoperative symptoms were pain during stress in 76 % and rest pain in 29 %. Motor deficits occurred preoperatively in 22 %, and sensory deficits in 40 %. After surgery patients benefited from highly reduced pain, only in 34 % of patients pain was still present. Postoperatively motor deficits increased slightly to 30 %, from which were non-permanent in 8 %. Sensory deficits occurred in 51 %, of which were non-permanent in 12 %. In our cohort we didn"t have any wound healing disorders, in 2 patients there was a minor secondary bleeding which was treated conservatively.

Conclusion

Especially in the domain of pain patients did benefit excellently from surgery. The natural history of malignant peripheral nerve tumors can explain the slightly increased postoperative symptoms including sensory and motor deficits. In future analyses, life quality and the ability to return to work in patients with peripheral nerve tumors will be analyzed.

Periphere Nerven/*Peripheral Nerves*

J-SBNC044

Nerventransfer bei Läsionen vom Erb-Typ bei geburtshilflicher Brachialparese: Ergebnisse in 90 operierten Fällen
Nerve transfer in Erb-type lesions in obstetric brachial palsy: results in 90 operated cases

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Objective

Obstetric brachial palsy (OBP) occurs in 1 to 4 cases per 1,000 births, and the Erb-type injury is the most common. About 30% will present motor sequelae that may require surgical treatment. More recently, the use of nerve transfers has been a surgical option.

The authors describe their experience with nerve transfer surgeries, evaluating complications and outcomes.

Methods

The author operated 90 patients with brachial plexus injury between 2011 and 2021.

Patients underwent fascicular transfers from the ulnar nerve to the musculocutaneous nerve and from the accessory nerve to the suprascapular nerve with the aim of improving elbow flexion and shoulder abduction function.

Medical records were reviewed to assess the characteristics and complications presented. The time to the surgery, the type of the nerve transfer, complications and the degree of functional recovery according to the classification Active Movement Scale (AMS) were analyzed after one year of postoperative.

Results

The mean age was 10 months at the time of surgery.

In 86% of cases we obtained improvement in elbow flexion function for at least AMS 5. Shoulder abduction improved in 64% of patients and external rotation in 37%. The mean surgical time was 110 minutes.

Initial complications occurred in 7 cases and were skin dehiscence. No major complications.

Conclusion

The use of nerves in nerve transfers in OBP is an effective and safe technique. In our experience could be the major option to treat Erb palsy.

Periphere Nerven/*Peripheral Nerves*

V294

Traumatische periphere Nervenläsionen der oberen Extremitäten bei Kindern: exzellente Ergebnisse nach frühzeitiger sonographischer/elektrophysiologischer Diagnostik und operativer Therapie

Traumatic upper extremity nerve lesions in children: excellent outcome following early sonographic / electrophysiological diagnostics and surgical intervention

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Objective

To evaluate clinical outcome, sonographic and electrophysiological findings of pediatric patients with upper extremity peripheral nerve injuries and describe operative vs. conservative treatment.

Methods

From our pediatric neurosurgery database all patients <18 years with traumatic peripheral nerve injury of the upper extremities / brachial plexus, except obstetrical brachial plexus injury, were included. Clinical, intraoperative, sonographic and electrophysiological findings were evaluated.

Results

Cohort: Of 72 patients 68.1% were male. Mean age was 8.2 (±4.1) years. The most frequent cause of injury was humerus fracture (63%), followed by cut (11%), forearm fracture (8%) and plexus strain (7 %). Affected were ulnar (50%), radial (21%) and median nerve (21%), partial or complete plexus (7%). 50% received electrophysiological and 67% neurosonographic work-up at initial presentation. 49% of patients had surgery (neurolysis n=15, sural transplant n=12, epineurectomy n=3, removal of compressing bone/metal n=3, end-to-end anastomosis n=2) whereas 51% were managed conservatively. Choice of treatment was significantly associated to sonographic findings (χ^2, p>0.001). Median interval of surgery was 19 (range 0-92) weeks after trauma.

Outcome: Mean follow-up (FU) was 14.2 (±17.3) months. Operated patients had a significantly worse initial status (χ^2, p=0.032) but showed no difference at last FU. At that time 98.5% of all patients showed clear clinical improvement. 4 patients were lost to FU. 78% initially presented with high-grade pareses and/or refractory pain, which was - despite improvement - still existent in 10 (18%), whereas 46% recovered fully. Patients with good motor recovery were significantly younger than those without (7.5±3.7 vs. 11.4±5.0 years). Only 1 operated patient showed no improvement at 13 months.

Conclusion

We demonstrate in pediatric patients with peripheral nerve injuries an excellent functional recovery compared to the adult population in both, the conservatively and the operatively treated group. Neurosonography plays a more important role than NLG/EMG in decision making, since it provides high-resolution imaging information about the grade of compression, on internal scarring or nerve discontinuity, that enables an early operative revision that contributes to good results. Recovery furthermore seems the better the younger children are.

Periphere Nerven/*Peripheral Nerves*

V295

Nervenläsionen nach suprakondylären Humerusfrakturen im Kindesalter: funktionelles Outcome nach operativer und konservativer Behandlung

Peripheral nerve lesions after supracondylar fractures of the humerus in children: Functional outcome after surgery and conservative management

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Objective

Supracondylar fractures are the most common elbow fractures in children. Reported incidence of associated nerve injuries is up to 15%. Traumatic and iatrogenic lesions (caused during K-wire fixation) mainly affect the ulnar nerve. Regeneration in peripheral nerve lesions is considered much better in children compared to adults. The aim of the current study was to highlight clinical scenarios of excellent nerve regeneration after conservative management in children initially presenting with almost severe paresis and to demonstrate postoperative outcome.

Methods

We retrospectively analysed clinical records of pediatric nerve injuries associated with supracondylar fractures, referred to our peripheral nerve surgery[GA1] unit between 2008 and 2020. Children who underwent surgical nerve repair or conservative treatment due to rapid clinical improvement during follow-up were included. All patients underwent multidisciplinary follow-up.

Results

48 patients (22 female) diagnosed for peripheral nerve lesion (21% iatrogenic) after supracondylar fracture of the humerus were included in the study. All patients obtained K-wire fixation due to severe displacement of the fracture. Mean age was 7 years (range 2-12 years) in all children. Presenting symptoms consisted in severe motor deficits, loss of sensitivity (42, 87.5%) and pain (6, 12.5%). The vast majority suffered isolated lesions of the ulnar nerve (23, 47.9%) followed by isolated lesions of the radial (8, 16.7%) and median nerve (6,12.5%), respectively. 26 children received surgical neurolysis due to lack of neurological improvement. Additionally, anterior subcutaneous transposition (15), autologous reconstruction with sural grafting (8) or split repair (1) was done. Postoperatively all children experienced significant restitution of motor deficits. Despite similar high grade motor deficits at initial presentation 22 patients were treated conservatively due to early spontaneous recovery during follow-up. In both treatment groups no severe complications occurred. Median follow-up was 213 days (range 54-3140 days).

Conclusion

The results of the present study demonstrate a favourable functional outcome after surgical nerve repair of traumatic lesions in children with a low rate of complications. However, children with comparable severe motor deficits at initial presentation have a surprisingly high chance for spontaneous improvement and complete restitution without surgery. Therefore, the indication for surgery should be made carefully.

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V296

Pränatale Neurochirurgie: erste Erfahrungen eines neu eingerichteten multidisziplinären Zentrums für den laparotomiegestützten fetoskopischen dreischichtigen Verschluss der Spina bifida

Prenatal neurosurgery: first experiences of a new established multidisciplinary center for laparotomy-assisted fetoscopic 3-layer spina bifida repair

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Objective

Deficits in Spina bifida aperta (SBA) patients are not solely explained by incomplete neurulation, but also by the prolonged exposure of neural tissue to the intrauterine environment, leakage of CSF and a consecutive suction gradient. Prenatal therapy, initially developed as an open technique including laparotomy and hysterotomy, is known to reduce the risk of shunt dependency and improves motor function, as shown by the Management of Myelomeningocele Study (MOMS). This requires a C-section and is associated with lower gestational age (GA) at birth, which led to various modifications. We report our experience of a 3-layer SBA repair in a fetoscopic hybrid technique with exteriorized uterus.

Methods

The method has been offered since 1/2021 for patients matching the MOMS inclusion criteria. First cases were carried out under guidance of an experienced fetoscopic surgeon in 7/2021. For the procedure, a laparotomy is performed, the uterus exteriorized, and 3 ports established. After fetoscopic mobilization of the placode, a bovine dural patch is placed, followed by the closure of muscular and skin layers (Fig. 1).

Results

Since 7/2021 12 patients underwent fetoscopic SBA repair in the hybrid technique. Mean operation time was 356 min.; GA was 25.1 weeks at surgery, and 36.6 weeks at delivery (1 patient is still pregnant). Anatomic level was between T12 and S2, functional level between L5 and S1. Fetal ventriculomegaly was present in 8 cases, 5 of which were severe (≥ 15mm), mean intrauterine ventricle width was 12.2 mm (right), 13.2 mm (left). In 5 cases relaxing incisions were necessary to complete closure. In 6 of 11 born children VP shunting was necessary within 6 months. Due to CSF leakage, 1 case underwent minor revision and in 1 case a skin flap was used to cover the defect. 7 of 11 children had to be delivered by C-section for obstetric indications.

Conclusion

Laparatomy-assisted, fetoscopic SBA repair was successfully implemented. Our data suggest that prematurity is not a main problem and c-section not mandatory. The rate of VP shunt dependency is in line with previous publications. Long-term follow-up will show whether the hybrid technique is superior to the open approach for fetal surgery and/or standard postnatal therapy.

Abb. 1


a
b

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V297

Funktionelles Outcome nach Durchtrennung des Fatty Filum im Kindesalter
Functional outcome after fatty filum sectioning in children

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Objective

One minor variant of occult spinal dysraphism comprise a thickened fatty filum (FF) in children. The underlying abnormal tension of the spinal cord can lead to various clinical symptoms such as motor deficits, urological disturbances, and pain, despite relative discrete radiomorphological signs on MR images. The aim of the current study was to highlight clinical scenarios rectifying microsurgical detethering in children diagnosed for FF, and to demonstrate postoperative outcome.

Methods

We retrospectively analysed clinical records of pediatric patients who underwent microsurgical filum sectioning for FF at the Section of Pediatric Neurosurgery in Ulm between 2019 and 2022. All children underwent microsurgical detethering under intraoperative electrophysiological monitoring and had multidisciplinary follow-up.

Results

33 patients (11 female) diagnosed for FF were included in the study. The cohort included 4 caudal regression- & 5 VACTERL -syndromes and 7 children with developmental delay due to syndromic disease. Mean age at surgery was 5.3 years (range 0.5–14 years). Presenting symptoms consisted in bladder (24, 73%) or bowel dysfunction (17, 52%), motor deficits (7, 21%), foot deformities (8, 24%) and pain (6, 18%; leg & back pain). In addition to a T1-hyperintense filum, MR images showed syrinx in 10 and scoliosis in 6 patients.

Postoperatively, bladder dysfunction improved in 9/24 (37.5%), bowel problems in 6/17 (35.3%), motor deficits in 5/7 (71.4%), pain in 6/6 (100%), and foot deformities in 1/8 (12.5%) patients. One patient got a re-tethering due to worsening of symptoms 3 years after initial surgery. Apart from one superficial wound infection no complications occurred. Mean follow-up was 1.2 years.

Conclusion

The results of the present study demonstrate a surprisingly high chance for improvement of pain, bladder and motor deficits in a rather diverse cohort of patients after fatty filum sectioning. The complication rate is low. Thus, the indication for filum sectioning should always be considered in patients with typical symptoms of tethered cord.

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V298

Neurologisches und urologisches Outcome nach Detethering bei Kindern mit kaudalem Regressionssyndrom

Neurological and urological outcome after detethering in children with caudal regression syndrome

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Objective

The caudal regression syndrome (CRS) comprises a spectrum of anomalies, which includes sacrococcygeal, anorectal and urogenital malformations as well as spinal dysraphism. Malformations like VACTERL (vertebra defect, anorectal malformations, cardial defects, tracheoesophageal fistula, renal anomalies, limb abnormalities) and OEIS (omphalocele, exstrophy, imperforate anus, spinal defects) are often associated with CRS. The challenge in these children is to discern whether a bladder or bowel dysfunction is related to the malformed organ itself or whether spinal cord tethering causes additional neurological impairment. Under this aspect we want to present our experience in a single-center case series.

Methods

We retrospectively reviewed all cases treated at our institution since 2018. Neurological as well as urological examinations were performed in all patients. In children with a morphologically suspected tethered cord on MR and clinical symptoms, microsurgical release was offered.

Results

Twenty-three patients with CRS (13 boys, 10 girls; mean age 4.2 years) were included. Follow-up time was twenty-six months on average. Seven patients had anorectal malformations (5 with VACTERL). Six children had combined anorectal and urogenital malformations, three patients had isolated urological abnormalities and five patients had an isolated sacral malformation. A fatty filum was detected on MR in 12 children (52,7%), five a conus lipoma (21,74%) and four a tight filum (17,39 %). A low-lying conus was evident in 15 (65,22%), an abrupt cord termination in three, and a syrinx in eight cases (34,78%). So far, 17 children underwent microsurgical detethering under intraoperative electrophysiological monitoring. There were no complications or neurological worsening postoperatively. Eleven children (64,71%) showed an improvement of motor function. Seven out of 10 patients (70%) had urodynamic improvement or even a normal bladder function, and obstipation was improved in 4 of 12 patients (33.3%) after detethering.

Conclusion

The incidence of patients with CRS and clinical signs of tethered cord syndrome is most likely underestimated. We recommend spinal MR diagnostics in all patients with CRS and microsurgical spinal cord release if an additional neurogenic component is very likely.

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V299

Langzeitverläufe bei operierten Kindern mit offener Spina bifida, die das Erwachsenenalter erreichten
Long-term outcome in surgically treated children with open spina bifida, that reached adulthood

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Objective

The number of patients with open spina bifida reaching adulthood increased in the last decades as a result of improvement in medical care. The majority of publications about spina bifida treat children, so just a little is known about adult patients and their problems.The purpose of this study was to investigate the occurance of medical issues, living conditions and participation in social life of adult patients.

Methods

Patients with surgically treated open spina bifida and a minimum age of 18 years could participate in this cross-sectional study. A structured and self-designed questionnaire was used. A letter with information about the study was sent to neurosurgical departments, self-help groups and institutions for people with disabilities, to provide information to members and patients. Patients could contact the clinic to participate, if interested.

Results

In total 120 patients participated (61,7% female, 36,7% male, 1,7% various, range of age 18-66 years, mean age 35,2 ± 11,0 years). The study population showed a high prevalance of medical issues (bladder incontinence 85,8%, hydrocephalus 72,5%, pressure ulcers 71,7%, overweight 60,8%, Tethered cord syndrome 42,5%, epileptic seizures 16,7%). 60,8% of the study population is not able to walk without assistive devices, one third cannot take care of their household and only 27,5% are working in a full-time job. In general, patients with lumbo-sacral or sacral spina bifida are more often able to walk without assistive device, can take care of themselves or live independently than patients with lumbal or thoracic spina bifida

Conclusion

This study demonstrates the complex set of medical, physical and social difficulties in adult patients with spina bifida.Transition from pediatric to adult medical care is challenging. Multidisciplinary medical centers for adult patients are missing although medical care in a multidisciplinary team with systematic follow-up is necessary to prevent secondary impairments and hospitalization in these patients. Further research in adults with spina bifida is required to investigate the needs of these patients and to improve medical care.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V300

Erste Erfahrungen mit intraoperativer molekularpathologischer Klassifizierung von diffusen Gliomen des adulten Typs mittels stimulierter Raman Streuungsmikroskopie und künstlicher Intelligenz

First Experiences with Rapid Intraoperative Molecular Pathological Classification of Adult-type Diffuse Gliomas based on Label-free Stimulated Raman Scattering Microscopy and Artificial Intelligence

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Objective

Molecular pathological classification of adult-type diffuse glioma enables individual treatment strategies and improves patient care. Current standard molecular pathological methods are time- and resource intense limiting their influence on surgical resection strategy. Stimulated Raman Histology (SRH) is a novel label-free chemical imaging method of fresh unprocessed specimen that can be potentially used for AI-based molecular image analysis. We opted to test its diagnostic potential for the molecular classification of gliomas.

Methods

An AI-based multimodal SRH image analysis tool for intraoperative molecular classification of adult-type diffuse gliomas was developed and trained on an external SRH data set consisting of 373 gliomas [1]. We tested the model for validity in a prospective observational clinical study. 3 mm3 large fresh, unprocessed specimen were collected intraoperatively and squeezed on a glass slide for SRH image generation. A supervised patch-based contrastive learning model for visual representation and a genetic embedding encoder model were merged into a transformer model for multi-label prediction of isocitrate dehydrogenase-1/2 mutation (IDH), 1p19q chromosome co-deletion (1p19q-codel) and ATRX mutation. The accuracy of the model prediction was determined by the final neuropathological diagnosis set as ground truth.

Results

We analyzed the model performance in 21 glioma patients comprising 14 IDH wildtype glioblastoma, two 1p19q-codel IDH-mutant oligodendroglioma, four IDH-mutant astrocytoma, and one IDH wildtype H3K27M mutant diffuse midline glioma. The model correctly predicted all molecular defined subgroup entities achieving a diagnostic accuracy of 100% for the IDH mutation, 95% for the 1p19q-codel, and 90% for the ATRX loss mutation resulting in an overall diagnostic accuracy of 95% for the correct molecular classification of the glioma SRH images within 90 seconds.

Conclusion

Our study shows that rapid AI-based molecular SRH image analysis for adult-type diffuse glioma is feasible and shows promising results to reliably predict the key genetic alterations in adult-type diffuse glioma. This novel near-realtime intraoperatively applicable method may facilitate the influence of observer-independent rapid molecular diagnostics on surgical glioma resection strategy in the future.

1. Hollon TC, Jiang C, et al. AI-based molecular classification of diffuse gliomas using rapid, label-free optical imaging Nat Med. 2023, in press.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V301

Korrelierte stimulierte Raman Histologie und Protoporphyrin IX Fluoreszenzmikroskopie im Glioblastom
Correlated Stimulated Raman Histology and Protoporphyrin IX Fluorescence imaging in Glioblastoma

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Objective

Fluorescence guided glioblastoma resection is widely used to improve the extent of resection . Intraoperative ex-vivo Stimulated Raman Histology (SRH) and correlated 2-photon fluorescence imaging enables novel perspectives of histo- and molecular feedback during brain tumor surgeries. The objective of this study is to describe the heterogeneity of SRH, 5-ALA mediated protoporphyrin IX (PpIX)-fluorescence and auto-fluorescence (AF) in glioblastoma. The goal is to investigate the tumor biology and its microenvironment and to enable precise intraoperative interpretation of SRH.

Methods

Correlated PpIX fluorescence and SRH imaging (Invenio Imaging) was performed in 92 cases of primary and recurrent IDH-wildtype glioblastoma. For 2-P-fluorescence imaging the tissue was excited with a fixed wavelength of 790 nm and two emission bands matching the emission peaks of PpIX (640 nm) and tissue auto-fluorescence (591 nm) were detected. Image features were summarized in the latent space of a deep autoencoder. The reduced image information was clustered to uncover unique morphological patterns.

Results

Unsupervised clustering revealed 5 distinct SRH clusters reflecting the morphological heterogeneity of glioblastoma. PpIX fluorescence was detected in 58 of 92 cases; there almost exclusively in samples from tumor core (97.5 %). The PpIX fluorescence ranged from exclusive labeling of individual cells and fibers (putative axons) to a ubiquitous diffuse labeling. There was no significant difference in the timing after 5-ALA administration (30 mg/kg) and occurrence of cell-specific vs. diffuse PpIX fluorescence (337 vs. 345 min, p=0.69). At a single-cell level PpIX was expressed in small cells with regular shape nuclei and darker vesicle-rich cytoplasm (likely myloid cells) and in myelinated axon (likely oligodendrocytes). In contrast to vital tumor, samples of necrosis, healthy white matter and neocortex showed a high auto-fluorescence signal.

Conclusion

The correlated SRH and 2-P imaging (PpXI, AF) provides complementary imaging information that improves the intraoperative interpretation of glioblastoma tissue. The distribution of 5-ALA mediated fluorescence is broad ranging from cell specific to ubiquitous diffuse labeling of tumor tissue. Surprisingly, at a cellular level PpIX is enriched in putative macrophages and oligodendrocytes warranting further molecular investigations of the cell-specific mechanisms of 5-ALA metabolism.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V302

Reliabilitätsanalyse der Vorhersage einer histopathologischen Diagnose durch ein neuronales Netzwerk auf Basis von Stimulierter Raman Histologie an frischen und gefrorenen Tumorproben

Reliability of histopathological diagnosis prediction by a convolutional neural network using Stimulated Raman Histology comparing fresh and frozen tissue samples

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Objective

Recently, a novel label-free optical imaging method for rapid intraoperative analysis of fresh tissue samples called Stimulated Raman histology (SRH) has been introduced. The analysis of SRH images using Convolutional Neural Networks (CNN) revealed promising results to predict the histopathological diagnosis of the main classes of neurooncological tumors.[1] Due to the lower number of rare tumors a valid prediction of these entities is limited. To develop reliable analysis tools larger amounts of data are needed that can be acquired using frozen tumor samples from e.g. research tissue banks. Up to now, there is no data available for analysis of previously frozen samples using SRH. The aim of this study was to perform a reliability analysis of CNN based entity prediction using SRH images comparing fresh and frozen samples of the same specimen.

Methods

In a monocentric prospective study SRH images of intraoperative tissue samples of 20 patients undergoing brain or spine tumor resection were obtained using a fiber-laser-based stimulated Raman scattering microscope. Prediction of histopathological diagnosis was performed using an established CNN.[1] The prepared tumor slide and an additional tumor sample were frozen at -80°C. After thawn both samples were re-scanned and CNN analysis was performed. Reliability was analyzed using Cronbach"s alpha (Cα) and Pearson correlation coefficient (PCC).

Results

The mean interval between the first scan and the re-scan of the frozen specimens was 56±47days. In 17 of 20 cases (85%) the CNN predicted the highest probability value for the same diagnosis in the fresh sample, the frozen crush preparation and frozen tumor sample. The internal consistency and test-retest reliability was high (Ca 0.857, PCC 0.76, $p<0.01$).

Conclusion

CNN based diagnosis prediction using SRH images seems to be reliable in fresh and frozen tumor samples, enabling the integration of frozen tumor tissue bank samples to potentially improve the reliability of CNN prediction tools, for rare entities in particular. Further differentiating analyses of critical and physically fragile tumor entities are currently under investigation.

1Hollon TC, Pandian B, Adapa AR et al. (2020) Near real-time intraoperative brain tumor diagnosis using stimulated Raman histology and deep neural networks. Nat Med 26:52–58.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V303

Leistung eines neuronalen Netzwerks mithilfe von stimulierter Raman-Histologie für die intraoperative Vorhersage von extra-axialen Hirntumoren

Performance of a Convolutional Neural Network Based on Label-free Stimulated Raman Histology for Intraoperative Prediction of Extra-axial Brain Tumors

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Objective

In oncological neurosurgery the definite differentiation between meningioma and extra-axial brain metastasis on MRI or intraoperative macroscopy is frequently uncertain. Conventional rapid histopathological microscopic review is time-consuming to influence the surgical strategy intraoperatively. This study aims to evaluate the performance of a fiberlaser-based Raman microscope to acquire stimulated Raman histology (SRH) images with a subsequent convolutional neuronal network (CNN) analysis to differentiate extra-axial brain tumors in near real-time.

Methods

In a prospective observational clinical study, small unlabeled tumor samples (1-3 mm^3) were squashed flat onto a slide, SRH images were acquired on random areas (2x2 mm) under the same conditions by a dual wavelength laser (790nm and 1020nm) for excitation. By combining two Raman shift wavenumbers and by image calculation a virtual hematoxylin-eosin (HE) like image is created. The established CNN for tumor prediction in less than a minute (1) was used for further analysis and major probability was estimated to be the diagnosis by the CNN which was compared to the final histopathological diagnosis.

Results

We analyzed the CNN results of 580 corresponding SRH images out of 94 patients with intracranial tumors (39 patients with meningioma/metastasis) that underwent resection at our center. Regarding the sensitivity and specificity, the ROC-AUC of the CNN for meningioma was outstanding with 0.961 (95% CI, 0.946-0976) and excellent for metastases with 0.826 (95% CI, 0.789-0.862). 73% of the metastasis and 93% of the meningioma SRH images were diagnosed correctly by the CNN related to the histopathological diagnosis. The most common false diagnosis for metastases were meningiomas (9%) and for meningiomas schwannomas (5.4%), respectively.

Figure 1 A CNN prediction for meningioma/metastasis SRH images. **B** ROC-Curve of the CNN for prediction of meningiomas/metastases.

Conclusion

Our data validate that extra-axial brain tumors can be well differentiated by the SRH based CNN algorithm within a few minutes intraoperatively providing a potential alternative pathway to conventional rapid histopathological review. The CNN is not trained enough on rare primaries like e.g. sarcomas and neuroendocrine tumors and to account for rare extra-axial entities like hemangiopericytoma more data acquisition is needed to further improve the accuracy.

1. Hollon TC et al., Nat Med 2020

Abb. 1

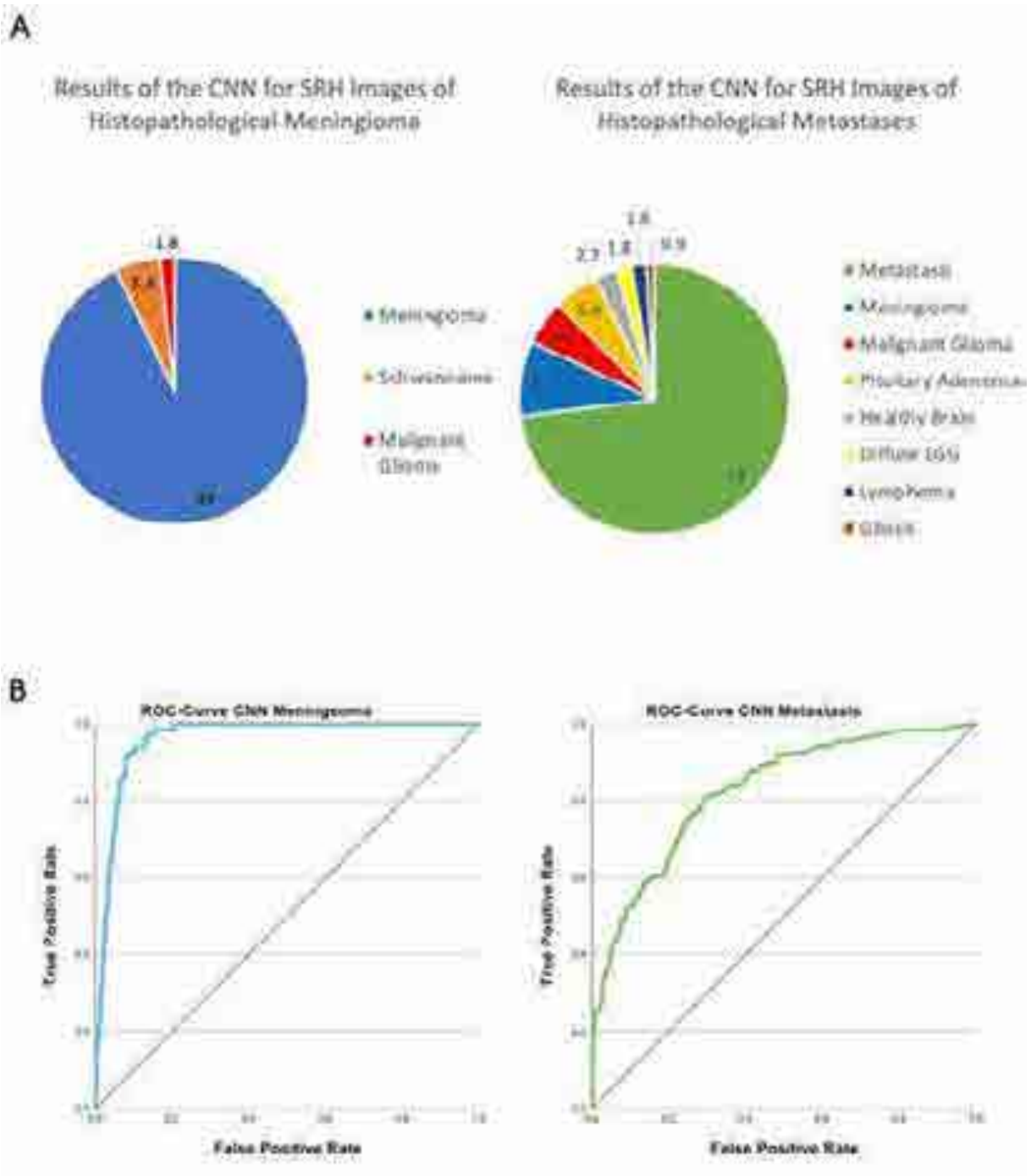

Abb. 2

Tumor Entity	Patients	SRH Images	from CNN correctly diagnosed SRH Images	from CNN misdiagnosed SRH Images
Meningioma	13	56	52	4
CNS WHO I	11	48	45	3
Atypical CNS WHO II	2	8	7	1
Brain Metastasis	26	111	81	30
Colorectal Adenocarcinoma	1	4	1	3
Gastroesophageal Adenocarcinoma	1	3	3	0
Cervix Carcinoma	2	8	8	0
Kidney Cell Carcinoma	1	3	3	0
Mammary Carcinoma	1	3	3	0
Multiple Myeloma	1	6	1	5
Pulmonary Adenocarcinoma	7	30	25	5
Large Cell Neuroendocrine Tumor	1	6	1	5
Small Cell Lung Carcinoma	1	3	0	3
Squamous Epithelial Carcinoma	2	7	7	0
Salivary Duct Carcinoma	1	3	3	0
Sarcoma	1	4	0	4
Melanoma	3	9	6	3
Undifferentiated Cancer of unknown primary (CUP)	3	20	18	2

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V304

Optimierung der Umgebungslichtbedingungen für *in-situ* Raman Spektroskopie
Optimizing ambient light conditions for in-situ Raman spectroscopy

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Objective

Raman spectroscopy is a label-free technique to acquire a biochemical fingerprint within seconds and therefore capable of *in-situ* brain tumor delineation. However, Raman shift is a low energy phenomenon that requires sensitive detectors affected by ambient light. Hence, we used an experimental operating room (EOR) to capture various light sources with our Raman system to improve the understanding on their impact on spectral quality.

Methods

The EOR setting comprised Raman measurements i) under varying ceiling light (CL) and ii) using optical devices e.g. navigation system, exoscope camera, monitors. Raman spectra were obtained with and without manual probe coverage, respectively. Raman spectra of formalin-fixed tissue (e.g. human glioma, human meningioma, rat brain) were acquired with a fiber-optic Raman probe with an excitation wavelength of 785 nm and acquisition time of 2 s. The different components of the tissue Raman signal (dark current, background, auto fluorescence and Raman signature) were analyzed separately. Spectral intensity was calculated as area under the curve of the raw signal after subtraction of dark current and spectral noise was estimated as the standard deviation in flat-line corrected Raman spectra.

Results

In total, 1309 Raman spectra were obtained. Spectral noise correlated with spectral intensity (R2=0.96). CL and optical devices impacted the background, with CL affecting the entire spectral range while optical devices exhibited a spectrally structured effect. CL level was correlated with background intensity (R2=0.99) decreasing to 1.4% comparing full CL (850 lx) to CL switched off (3 lx). Manual probe coverage reduced background intensity at maximal CL to 12.9% ($p<0.001$), with diminishing effect at lower CL levels. Interestingly, the intensity of tissue auto fluorescence varied among tissue types. However, it was always higher than background intensity even at maximal CL (rat brain 6.7-fold, meningioma 1.7-fold).

Conclusion

Tissue auto fluorescence accounts for the largest portion of spectral intensity and thus mainly determines the amount of spectral noise. This implies that CL has a negligible impact on spectral quality. However, optical devices might produce spectrally structured background signals that cannot be compensated by spectral preprocessing. When establishing intraoperative Raman spectroscopy, we suggest to scan the OR for such devices and acquire Raman measurements at moderate CL level for best spectral quality and patient safety.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V305

Spectro-Genomics durch Integration von ortsaufgelöster Transkriptomik und Raman-Streuungsmikroskopie
Spectro-genomics through integration of spatially resolved transcriptomics and Raman scattering microscopy

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Objective

Spatially resolved multiomic technologies provided insights into the topographical architecture of glioblastoma and its microenvironment. Emerging personalized medicine is compelling the deployment of artificial intelligence in modern neurosurgery. Deep generative networks can learn the transfer of various technologies, enabling the prediction of time- and labor-intensive omic methods from rapid histological images. Here, we aim to integrate rapid and meaningful histomorphical images of intraoperative Raman scattering microscopy with spatially resolved transcriptomics to assign molecular significance to the histological phenotype.

Methods

Stimulated Raman scattering (SRS) of 10 patients was performed using a dual-wavelength picosecond fiber laser source with a fixed wavelength pump beam at 790 nm and a Stokes beam tunable from 1010 nm to 1040 nm. SRS is detected in transmission mode with a large area photodiode (PD). A high-frequency lock-in detection at 10MHz was used to achieve high detection sensitivity. We image the sample sequentially at 2845cm-1 and at 2940cm-1 integrated into a pseudo-color scheme that mimics traditional H&E staining. After intra-operative SRS imaging was completed, the same specimens were transferred and processed by our routine pipeline for spatial transcriptomics (stRNA-seq) using the 10X Visium technology and sequenced at a depth of 100k reads per spot. Analysis was performed by the in-house software SPATA2.

Results

Cell type deconvolution of stRNA-seq and immunostainings revealed a significant overlap with the clusters found in the SRS images. Areas prior defined as reactive immune (high tumor cell density and markers of macrophage infiltration), showed significant enrichment of SRS class cellular-dense (padj<0.001). Highly hypoxia-adopted signatures on the other hand revealed enrichment of SRS class 1 'necrosis/apoptosis' and class 'vascular-high'. Through data integration, the SRS class 'dense fiber network' was found to be consisting of two distinct subclasses, one within hypoxia environments, in which the fibers represent swollen neurons/dendrites, and the other within areas enriched for AC/OPC signatures which most likely represents the tumor-cell network with its microtube architecture.

Conclusion

The integration of both technologies provided insights into morphological-transcriptional dependencies and thus the application opens a new perspective for intraoperative use and represents an important step toward intraoperative molecular diagnostics.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V306

Intraoperative Schnellschnittdiagnostik von pädiatrischen Hirntumoren mittels stimulierter Raman-Streuungsmikroskopie und künstlicher Intelligenz

Fast Intraoperative Diagnosis of Pediatric-type Brain Tumors using Label-free Stimulated Raman Scattering Microscopy and Artificial Intelligence

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Objective

Rapid intraoperative neuropathological diagnosis is essential to facilitate individual surgical treatment of pediatric-type CNS tumors. Stimulated Raman Histology (SRH) is a novel label-free intraoperative imaging method of fresh unprocessed specimen to provide digital H&E-like images, suitable for artificial intelligence (AI) based image analysis [1,2]. As data is scarce we opted to test the validity of AI-based SRH image analysis tools for pediatric CNS tumors.

Methods

In a prospective observational clinical study, we applied two AI-based frameworks [1,2] onto SRH images of fresh tumor specimen intraoperatively to (1) predict neoplastic versus normal tissue and, in case of tumor to (2) label and classify them in pilocytic astrocytoma, diffuse low-grade glioma, malignant glioma, medulloblastoma or ependymoma. The final neuropathological diagnosis served as ground truth for inter-rater reliability. Patients with diagnoses not covered by those classifiers had to be excluded from the 2nd analysis. Adult patients were included if a pediatric-type tumor was suspected.

Results

We analyzed preliminary data of 79 SRH images of 39 patients with 22 varying pediatric-type diagnoses. Intracranial diagnostic accuracy for the occurrence of tumor was strong with 89.7% (35/39) on patient- and 93.7% (74/79) on a sample-level. Hereafter, the second AI model evaluated 46 intracranial SRH images of 21 patients. Correct diagnosis resp. entity group predictions were achieved in 71.4% (15/21, k =0.417) on patient- and 56.5% (26/46, k =0.368) on sample-level.

Conclusion

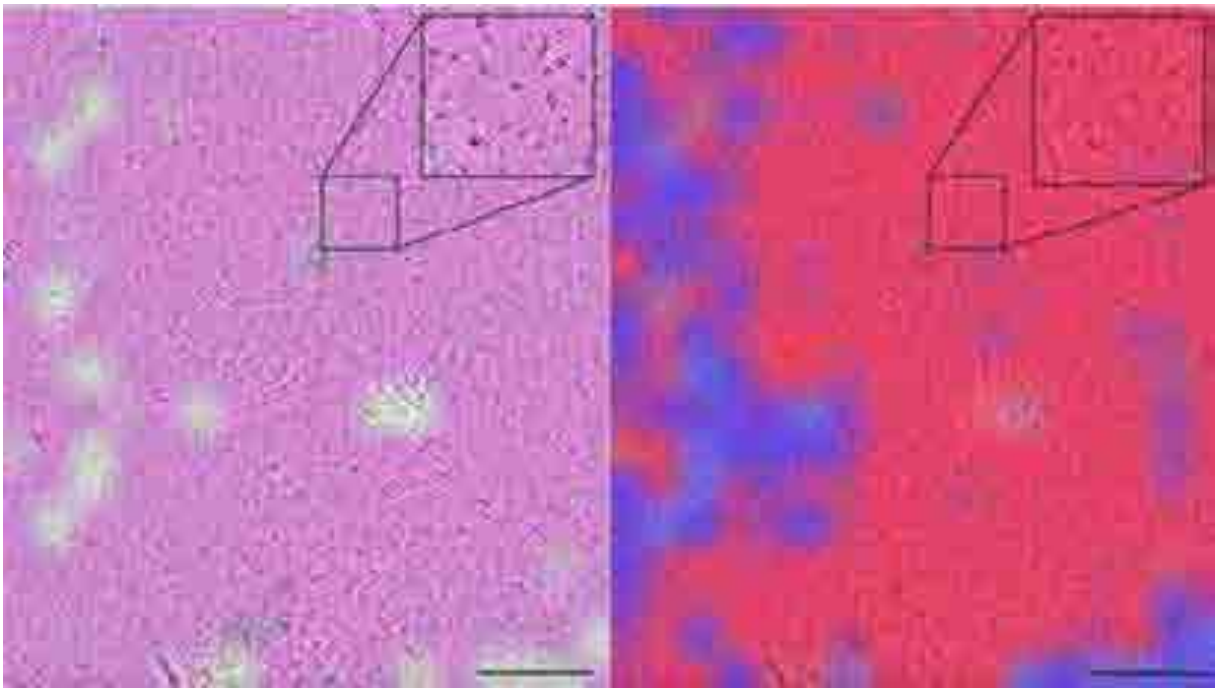
The Raman imaging-based AI models reliably identify pediatric brain tumor tissue intraoperatively within a few minutes and show promising results to predict the diagnosis resp. entity group. Based on our preliminary results, the small number of samples needs to be increased for AI algorithm training to improve diagnostic accuracy.

Fig. 1. An illustrative SRH image of a pilocytic astrocytoma sample on the left. The corresponding second AI model heatmap could correctly identify morphological features (colored in red) and low-quality areas (purple) within the sample.

1. Hollon TC et al. Near real-time intraoperative brain tumor diagnosis using stimulated Raman histology and deep neural networks. Nat Med. 2020;26:52–8.

2. Reinecke D et al. Novel rapid intraoperative qualitative tumor detection by a residual convolutional neural network using label-free stimulated Raman scattering microscopy. Acta Neuropathol Commun. 2022;10:109.

Abb. 1



Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V307

Hyperspektrale Bildgebung in malignen Gliomen: ein ex-vivo Vergleich mit konventioneller Fluoreszenzmikroskopie zur Biopsiebewertung

Hyperspectral imaging in malignant glioma: an ex vivo comparison with conventional fluorescence microscopy for biopsy diagnosis

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Objective

Hyperspectral imaging is a valuable tool for Protoporphyrin IX (PpIX) visualization during 5-aminolevulinic acid (ALA)-mediated fluorescence-guided resection (FGR). The specific contribution of PpIX to overall fluorescence is calculated by spectral decomposition. The number of false positive and negative fluorescence and, thus, tumor identifications declines. This study compares tissue evaluation using the hyperspectral technique with conventional surgical fluorescence microscopy. Meanwhile, fundamental assumptions in algorithms for hyperspectral signal evaluation were reviewed.

Methods

Two hundred forty biopsies obtained during FGR of high-grade malignant glioma (HGG) were analyzed using two different devices: a commercial surgical microscope (KINEVO 900, Carl Zeiss Meditec (CZM)) and an OPMI pico microscope modified in collaboration with CZM for hyperspectral imaging. Experienced neurosurgeons assessed the observed fluorescence quality in the surgical microscope. Afterward, PpIX contribution was measured with hyperspectral imaging. Neuropathological assessment of biopsies was the reference method for diagnosis.

Results

Hyperspectrally measured PpIX contribution significantly differed between groups according to neuropathological classification ($p < .001$). Meanwhile, PpIX contribution positively correlated with fluorescence quality in the surgical microscope. Using receiver operating characteristic analysis to compare both methods for diagnosing a tumor biopsy, the hyperspectral method was superior to visual fluorescence estimation (AUC = 0.845 ± 0.024, CI95% 0.798 – 0.893 *vs.* AUC = 0.710 ± 0.035, CI95% 0.642 – 0.778; $p < .001$). Additionally, pH strongly influenced the calculated PpIX contribution from hyperspectral imaging and fluorescence intensity in the surgical microscope (Figure 1).

Conclusion

FGR is a valuable tool widely applied in HGG surgery as it maximizes the extent of resection. Hyperspectral imaging is more sensitive in diagnosing tumorous tissue than surgical microscopy in biopsies obtained during FGR with ALA. Thus, any instrumentation and data processing improvement will ultimately benefit the patient. We demonstrated the usefulness of hyperspectral imaging and indicated the need to further develop the technique for clinical application.

Abb. 1

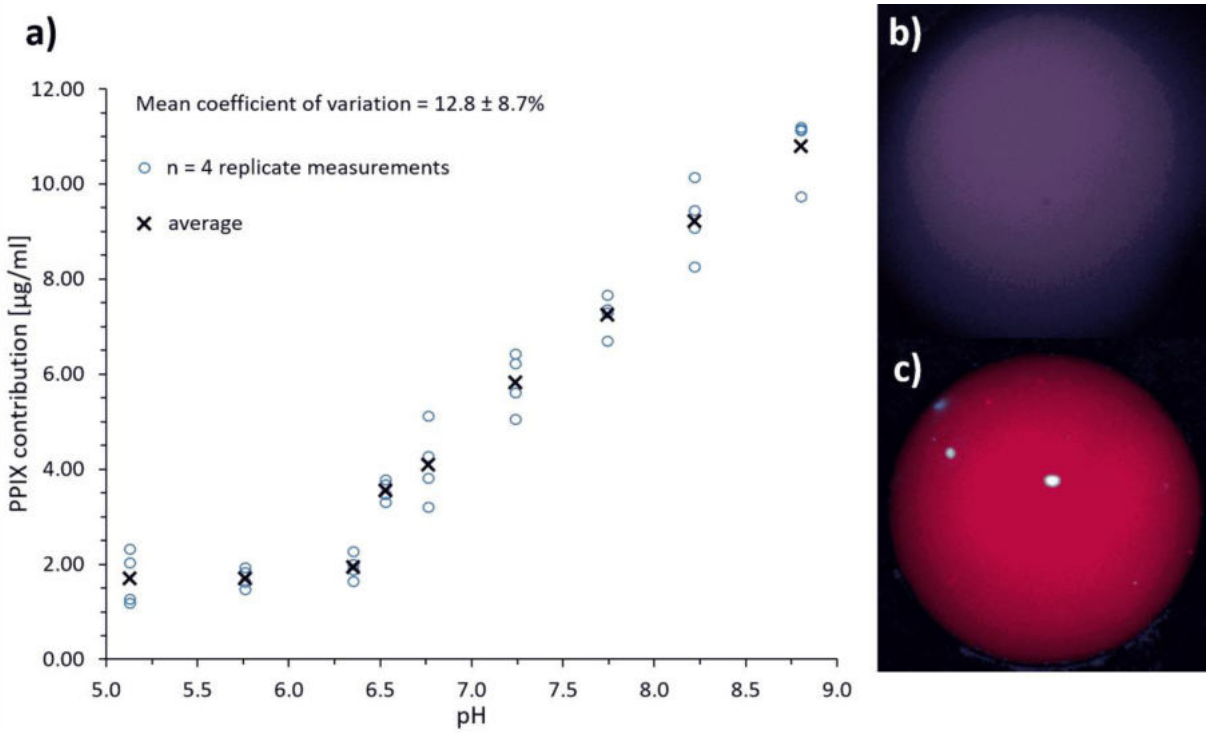

Figure 1: Influence of pH adjustment in tissues with fixed PpIX concentration. A) hyperspectrally calculated PpIX contribution. B) visual PpIX fluorescence at pH 5 and c) pH 9.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V308

Gliom Klassifikationen mit 7T Spektroskopischer Bildgebung
Classifying Gliomas with 7T MR Spectroscopic Imaging

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Objective

The WHO's 2021 classification system for grading tumors is based on molecular properties, such as IDH mutation, which can be useful in determining personalized treatment approaches and patient outcomes. However, current methods for detecting and classifying tumors have both benefits and drawbacks. 7T MRSI aims to address these issues by creating a non-invasive method for molecular tumor classification based on the evaluation of altered tumor metabolism. The current study aims to optimize statistical approaches for more accurate non-invasive tumor classification.

Methods

36 glioma patients received a 15-minute MRSI measurement using a 7T scanner. The scans were post-processed and quantified using an in-house pipeline and LCModel, and a neuroradiologist manually segmented the tumors. Metabolic ratio maps were calculated and specific cutoff values were applied to limit evaluation to metabolic hotspot regions. Random Forest regression and support vector machine models were used for grade and IDH mutation classification, and recursive feature elimination and cross-validation were used to improve statistical significance. ROC curves were plotted and AUC values were calculated to compare diagnostic accuracy.

Results

Diagnostic accuracy for RF and SVM-based IDH mutation detection yielded AUC of 0.86 and grade classification AUCs 0.99. The highest AUC values were obtained using 3-6 selected features for the RF training model. The most important features for IDH classification were Glu, Gln, GSH, and tCho, while Ins, Gly, GSH, and tCho were most important for grade evaluation.

Conclusion

The most important features for IDH classification and tumor grading were similar to those identified in larger studies. The sample size for this study is small and further recruitment is ongoing to expand the data pool. The classification was based on manual tumor segmentation, which could be automated in the future. Further research is needed to confirm the findings of this study and to establish 7T MRSI as a reliable method for glioma classification.

Abb. 1

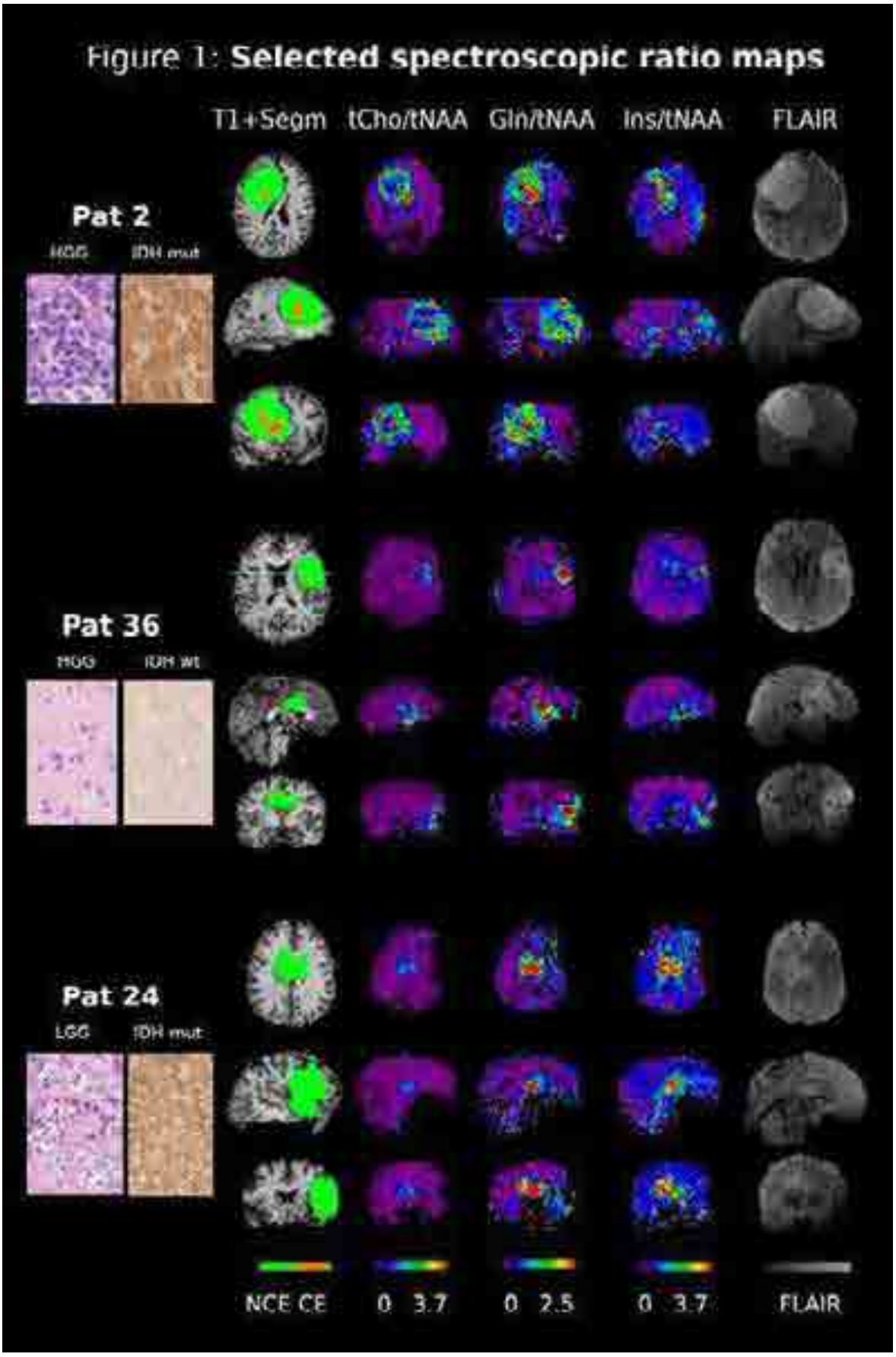
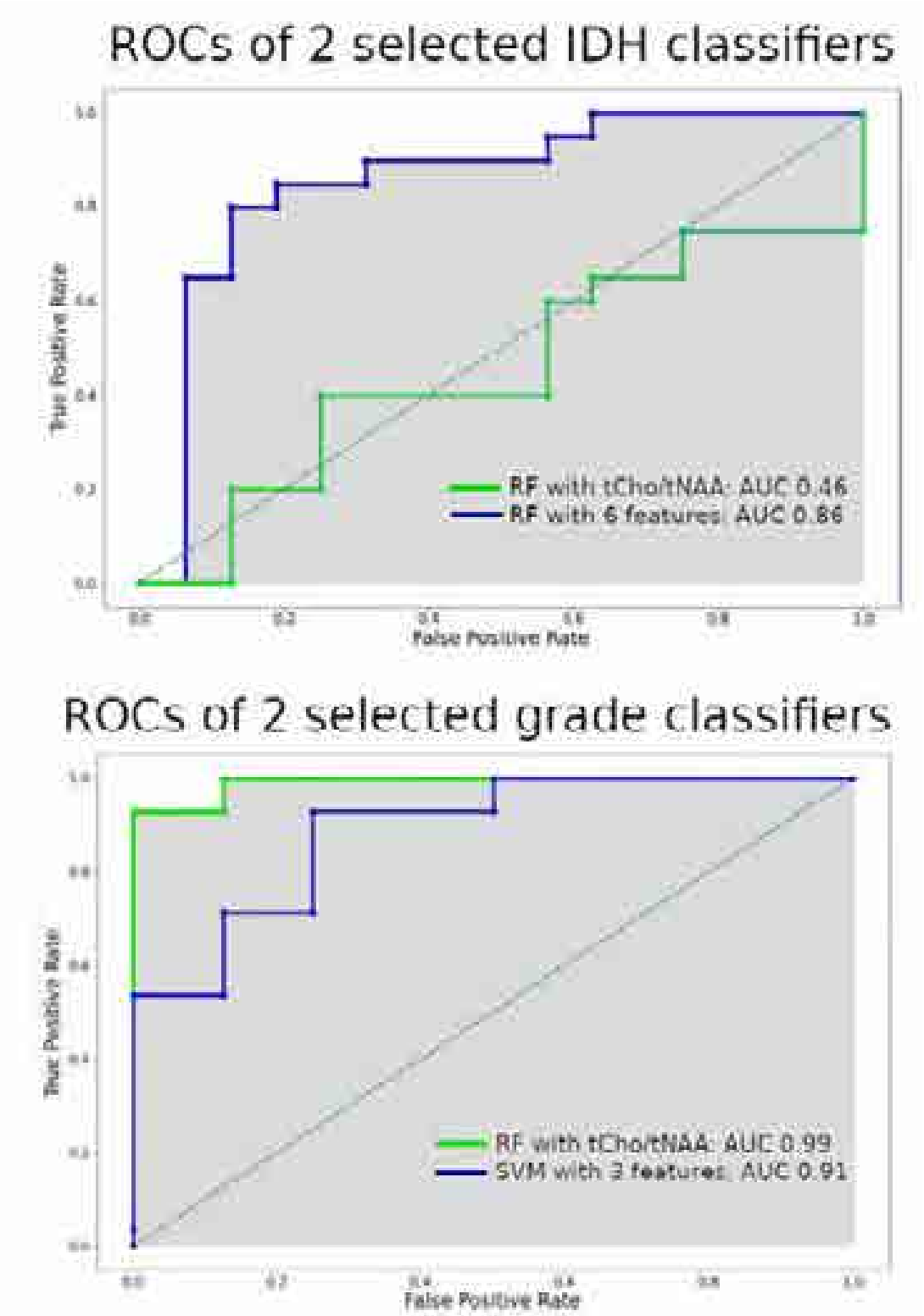


Figure 1: Selected spectroscopic ratio maps
T1+Segm
tCho/tNAA
Gln/tNAA
Ins/tNAA
FLAIR
Pat 2
HGG
IDH mut
Pat 36
HGG
IDH wt
Pat 24
LGG
IDH mut
NCE CE
0 3.7
0 2.5
0 3.7
FLAIR

Abb. 2


ROCs of 2 selected IDH classifiers
True Positive Rate
False Positive Rate
RF with tCho/tNAA: AUC 0.46
RF with 6 features: AUC 0.86
ROCs of 2 selected grade classifiers
True Positive Rate
False Positive Rate
RF with tCho/tNAA: AUC 0.99
SVM with 3 features: AUC 0.91

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V309

Automatisierte Texturanalyse in OCT-B-Scans zur Erkennung von GBM
Automated texture analysis in OCT B scans for GBM detection

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Objective

Maximum safe resection in glioblastoma (GBM) surgery is associated with longer patient survival. However, current intraoperative imaging methods to detect tumor remnants all have their limitations. Optical coherence tomography (OCT) has been used as an experimental imaging technique to detect GBM. Most OCT studies so far rely on extraction of the attenuation coefficient for tumor detection or structural analysis with sophisticated machine learning approaches. However, these approaches might not be suitable for intraoperative use. Here, we evaluate the diagnostic value of automatic morphological analysis in OCT B scans for the differentiation of GBM and healthy tissue.

Methods

Fresh tissue samples collected during microsurgical operations were scanned using a commercial OCT system. Samples were fixed in formaline and underwent histopathological evaluation thereafter. Histopathological evaluation included quantification of tissue content within each sample. 16 samples containing > 95% vital glioblastoma tissue and 20 samples containing > 98% healthy tissue were included in the study. OCT B-scans were preprocessed by segmentation, flattening and averaging, followed by a texture feature extraction according to Haralick yielding the contrast. The texture features were optimized with respect to structure dimensions offering the best discrimination of tissue types. A linear discriminant analysis with a k-fold cross validation was used to classify images into tumorous or healthy tissue and to estimate prediction performance of the model.

Results

Our approach can classify between tumor and healthy tissue with a sensitivity of 87.5% and a specificity of 85%. The best classification could be obtained for the contrast extracted from dimensions in the range of 100 µm. Moreover, we could show that the same approach can differentiate between tumor and white matter more easily than between tumor and grey matter.

Conclusion

Automatic morphological analysis of OCT B scans can differentiate between GBM tissue samples and healthy brain tissue without the need of computing optical parameters such as attenuation coefficient. Using a linear discriminant analysis for tissue classification proved to be robust and might be computationally less demanding than AI approaches and could therefore be implemented into an intraoperative setting more easily.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

V310

"Multiplexed single-cell imaging" zur Charakterisierung von Melanom-Hirnmetastasen unter therapeutischem Einfluss

Multiplexed single-cell imaging to characterize melanoma brain metastases under therapeutic pressure

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Objective

The introduction of novel systemic therapies targeting melanoma driver mutations or immune-checkpoint inhibitors (ICI) have led to a significantly prolonged survival in metastatic melanoma but unfortunately only in a subsets of melanoma brain metastases (MBM) patients. To this regard, the tumor microenvironment (TME) plays a crucial role in therapy success or failure and harbors great potential in predicting ICI responses and explaining treatment failures. To comprehensively characterize the TME of MBM under various therapeutic conditions we used a single-cell imaging technique to explore cell type abundances and spatial interactions and correlate them to clinical features.

Methods

43 resected human MBM specimen of which 27 were ICI naïve with postoperative ICI and 16 with a progress under ICI therapy were included. Samples were co-stained with immunofluorescence (IF) and a 40-plex metal-conjugated antibody panel. Tumor/immune cell regions were selected based on IF images and subsequent tissue ablation was performed using an imaging mass cytometer. Deep-learning based single-cell segmentation and computational downstream analysis was performed and derived characteristics were correlated with clinical features and outcomes.

Results

Single-cell phenotyping of more than 1.1 million distinct cells revealed besides tumor cells all major immune and stroma cell types with various lymphoid and myeloid subsets. Differential abundance analysis showed significantly more CD4+, CD8+, DP and regulatory T, NK and plasma cell infiltrates in ICI-naïve tumors which showed intracranial response upon postoperative ICI therapy. In contrast, ICI non-responder samples were linked to higher frequencies of neutrophil infiltrates with distinct subtype compositions. Furthermore, MBM samples from patients which underwent preoperative radiotherapy showed increased neutrophil and macrophage subpopulation frequencies. Spatial single-cell analysis revealed cellular neighborhoods, cellular interactions as well as vascular milieus which showed strong correlation with ICI response and survival outcomes.

Conclusion

The usability of archived tissue together with a state-of-the-art single-cell imaging method allows the comprehensive mapping of the MBM single-cell TME landscape and revealed distinct cell types and spatial features which were significantly correlated with ICI response/failure or upfront radiotherapy.

Rapid Communication Raman-Histologie and Spektroskopie/*Rapid communication Raman histology and spectroscopy*

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V313

Verlauf und Stellenwert von Interleukin-6 im Liquor bei Patienten mit aneurysmatischer Subarachnoidalblutung

The course and value of interleukin-6 in cerebrospinal fluid in patients with aneurysmal subarachnoid hemorrhage

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Objective

Neuroinflammatory response to aneurysmal subarachnoid hemorrhage (SAH) might play a crucial role in the further course of a disease. Interleukin-6 (IL6) is an inflammatory marker which showed some associations with SAH outcome in previous studies. We aimed at analyzing the course of IL6 in cerebrospinal fluid (CSF) during SAH and its relation to complications and the outcome of SAH.

Methods

Included were consecutive SAH patients with regular CSF IL6 measurements treated between 01/2005 and 06/2016. IL6 values were recorded and analyzed in 72-hours-intervals for the period of three weeks after SAH (d1-3, d4-6, d7-9, d10-12, d13-15, d16-18, and d19-21 post-SAH). Primary study endpoints were the occurrence of delayed cerebral infarction (DCI) on follow-up computed tomography scans, in-hospital mortality and unfavorable outcome at 6 months after SAH defined as mRS>3. Adverse events during SAH were also recorded and analyzed as secondary study endpoints.

Results

There was an initial increase of the cohort"s median CSF IL6 from 1467 pg/mL on d1-3 to 3121 pg/mL on d4-6, with further gradual decrease over the remaining time (from 2768.3 on d7-9 to 503 pg/mL on d19-21). In a univariate analysis, IL6 values on d1-3 and d4-6 showed associations with in-hospital mortality and unfavorable outcome, whereas DCI was related to IL6 values on d4-6. According to a ROC analysis, clinically relevant cutoffs were defined for IL6 on d1-3 (>2000 pg/mL) and d4-6 (>2500 pg/mL). In a multivariate analysis, IL6>2000 pg/mL on d1-3 was independently associated with in-hospital mortality (aOR=2.67, p=0.009) and unfavorable outcome (aOR=2.30, p=0.006). In turn, IL6>2500 pg/mL on d4-6 was independently associated with in-hospital mortality (aOR=2.28, p=0.017) and DCI (aOR=1.64, p=0.044). SAH individuals with angiographic vasospasm showed marked elevation of IL6 from d1-3 to d4-6 (+1770.5 pg/mL vs -21 pg/mL, p=0.02). Finally, IL6 values on d1-3 were associated to the risk of intracranial hypertension, and at a later course to the risk of bacterial meningitis.

Conclusion

Our data confirm the substantial impact of neuroinflammation on SAH outcome. CSF IL6 values measured during the first week after SAH present the most valuable predictors of the further course of the disease.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V314

Assoziation von NETosis-Biomarkern mit verzögerter zerebraler Ischämie nach aneurysmatischer Subarachnoidalblutung

Association of biomarkers of NETosis with delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage

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Objective

Proinflammatory and prothrombotic processes following aneurysmal subarachnoid hemorrhage have been associated with the development of delayed cerebral ischemia (DCI). Platelets appear critical for the crosstalk of these processes. Platelet derived high-mobility-group-box-1 (HMGB1) stimulates neutrophils to release net-like chromatin structures termed neutrophil extracellular traps (NETs). The enzymes protein-arginine deiminase type-4 (PAD4), DNase1 and myeloperoxidase (MPO), the citrullinated histone H3 (H3-Cit) and cell-free DNA (cfDNA) have been identified as markers of NETosis (NET-release). The presence, role and interplay of the NETosis-biomarkers in aSAH patients have not yet been elucidated.

Methods

A post-hoc analysis of a prospective, blinded, single-center biomarker observational study to investigate the role of HMGB1 was performed. The biomarkers of NETosis H3-Cit, PAD4, cf-DNA and DNAse1 were assessed in patient serum obtained on admission and day 4. The association of these biomarkers with the occurrence of DCI and clinical vasospasm (CVS) was analyzed. New infarction on CT after day 1 was defined as DCI whereas CVS was defined as a composite variable of a delayed ischemic neurological deficits and/or pathologic transcranial doppler results corroborated by vascular imaging.

Results

One hundred consecutive non-traumatic spontaneous SAH patients were assessed. In 83/100 (83%) aSAH was confirmed by angiography. Five patients (5/83) died <48h not allowing for DCI assessment. In all serum samples on admission and day 4, H3-Cit, PAD4, cf-DNA and DNAse1 were detected. In all patients, H3-Cit levels significantly decreased from admission to day 4 (p=0.003-0.017). In contrast, in all patients, cf-DNA levels significantly increased from admission to day 4 (p<0.001). No differences were observed among patients who did or did not develop DCI or CVS. The PAD4 levels were similar among all subgroups and remained stable from admission to day 4 (p=ns). DNase1 levels significantly decreased from admission to day 4 in those patients who developed DCI (p=0.028) but not in the non-DCI, CVS or non-CVS subgroups.

Conclusion

Biomarkers of NETosis have been identified in all aSAH patients. This exploratory analysis demonstrated differential dynamics of these biomarkers in the setting of DCI and CVS. Thus, further exploration of NETosis in aSAH with larger datasets is warranted.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V315

Neurodegenerative Marker im Liquor nach aneurysmatischer SAB: eine Kohortenstudie und Vergleich mit einer geschlechts- und alterskorrelierter Kontrollgruppe

Evaluation of neurodegenerative CSF markers in sex- and age-matched cohorts with and without aneurysmal subarachnoid hemorrhage

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Objective

Patients, who survive an aneurysmal subarachnoid hemorrhage (aSAH), regularly suffer from severe cognitive impairment and lack of resilience. There is evidence that neurodegeneration is a pronounced phenomenon after aSAH, which may influence neuropsychological outcome. Here, we present data on neurodegenerative markers (cerebrospinal fluid –CSF- samples) in a sex- and age-matched cohort of aSAH patients compared to patients without an acute cerebrovascular pathology in order to point out specific patterns after aSAH.

Methods

CSF samples two cohorts were compared (sex- and age-matched) for neurodegenerative markers (via immunoassays): 17 patients after aSAH (at days 4 and 10 after aSAH; SAH group) and 17 patients after aortic aneurysm (control group) were analyzed. Statistical evaluation (using GraphPad Prism 9.4.1) took place applying Mann-Whitney-U and Kruskal-Wallis testing due to non-normal distributed data.

Results

Age did not differ significantly between the groups (p=0.07). Each group contained 14 female and three male persons. The CSF levels of established neurodegenerative markers such as total TAU, Amyloid beta 1-40 and Amyloid beta 1-42 differed significantly (each $p<0.0001$; Mann-Whitney U test) between the SAH (both at day 4 and 10) and the control group. The level of phosphorylated TAU (pT181) showed no differences at day 4 (p=0.519; Mann-Whitney U test), but a pronounced difference at day 10 after aSAH compared to the control samples (p=0.0008; Mann-Whitney U test).The results showed higher Tau and lower Amyloid levels in the SAH group, consistent with a neurodegenerative burden. Further, levels of TDP43, a protein linked with neurodegeneration (e.g. in the context of CTE or ALS) were significantly higher in the SAH group (both at day 4 and 10; $p<0.0001$ and p=0.0003; Mann-Whitney U test).

Conclusion

Various neurodegenerative markers are elevated in CSF samples from patients after aSAH compared to a sex- and age-matched control group. The accumulation of pathological proteins such as phosphorylated TAU may contribute to the development of neurocognitive deficits after aSAH. Further, these proteins may serve as biomarkers for cognitive outcome. However, the results have to be evaluated in larger cohorts and newer and less commonly applied markers such as TDP43 have to be checked for plausibility.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V316

Exzessive Freisetzung von endogenem *Neuropeptid Y* ins Serum nach cerebrovaskulärer Manipulation
Cerebrovascular manipulation induces an excessive release of endogenous neuropeptide Y into serum

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Objective

The vaso- and psychoactive endogenous Neuropeptide Y (NPY) has repeatedly shown to be excessively released after subarachnoid hemorrhage and in numerous psychiatric disorders. NPY is stored in sympathetic perivascular nerve fibers around cerebral arteries and in free nerve endings in the *dura mater.* This prospective, controlled study was designed to analyze the impact of microsurgical and endovascular manipulation of the cerebral vasculature versus cranio- and durotomy alone on the serum levels of NPY.

Methods

52 consecutive patients (f:m=25:27; mean age 54.0 years) were prospectively enrolled: The vascular group underwent repair for unruptured intracranial aneurysms (UIA) of the anterior circulation [endovascular aneurysm occlusion (EV) n=13; microsurgical clipping (MS) n= 17]; in the non-vascular group, 13 patients received microsurgical resection of a small-sized, supratentorial convexity meningioma (CM), and 9 patients with surgically treated degenerative lumbar spine disease (LD) served as control. Plasma was drawn 1) before treatment, 2) periprocedurally, 3) 6 hours postprocedurally, 4) 72 hours postprocedurally, and 5) at the 6-week follow-up (FU) to determine NPY levels via competitive enzyme immunoassay.

Results

The serum concentrations of NPY ranged significantly higher in the vascular than in the non-vascular group ($p<0.001$) with a slight decrease in both groups 6 hours postprocedurally, followed by a gradual increase above baseline levels until FU. Perioperatively, the NPY levels moderately decreased in the MS and in the CM group, respectively, whereas, in the EV group, an upregulation of the NPY concentrations was detected periinterventionally. The highest NPY concentrations were measured in the EV subgroup at the time points 2, 4, and 5, reaching a climax at FU.

Conclusion

Our study reveals a first insight into the short-term dynamics of the serum levels of endogenous NPY in neurosurgical and endovascular procedures, respectively: Direct manipulation within but also next to the major cerebral arteries induces an excessive release of NPY into serum. Our findings raise the interesting question of the potential capacity of NPY in modulating the psycho-behavioral outcome of neurovascular patients.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V317

Serumkonzentrationsgesteuerte intravenöse Magnesium Sulfat-Gabe für Neuroprotektion in Patienten mit aneurysmaler Subarachnoidalblutung: Eine monozentrische retrospektive 12-Jahres Evaluation

Serum concentration guided intravenous magnesium sulfate administration for neuroprotection in patients with aneurysmal subarachnoid hemorrhage: Retrospective evaluation of a 12-year single center experience

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Objective

Cerebral vasospasm and delayed cerebral infarction (DCI) remain a major cause of morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (aSAH). Traditionally, oral nimodipine has been administered as prophylactic treatment.

The benefits of continuous intravenous magnesium sulfate as alternative treatment remain controversial, and most previous studies only examined its benefits only as adjunctive treatment to the traditional nimodipine.

Methods

We retrospectively analyzed medical records of patients treated for aSAH with intravenous magnesium sulfate between 2010 and 2021.

We routinely aimed for a serum magnesium concentration of 2.0-2.5mmol/l between post-hemorrhage day 3 and 12. The patients were separated in three groups based on their average serum magnesium concentration (magnesium >2.0mmol/l, reduced magnesium 1.1-1.9mmol/l, and no magnesium). Additionally, we assessed rates of angiographic vasospasm, and DCI defined as cerebral infarction not related to aneurysm treatment and occurring after day 3 post-hemorrhage as well as Hunt & Hess score on admission. Clinical outcome at discharge and the last recorded follow-up was evaluated using the modified Rankin Scale (mRS), categorized in good (0-3) and poor outcome (4-5).

Results

A total of 548 patients had sufficient records and were included in this analysis. Hereof, radiological evidence of DCI could be found in 23.0% (n=126) of patients. The rate for DCI was significantly lower if patients" average serum magnesium was higher than 2.0mmol/l (magnesium: 18.8%, n=85; reduced magnesium: 38.3%, n=23; no magnesium: 51.4%, n=18; p<0.001). Also, at their last recorded follow-up, patients in the group with a higher serum magnesium concentration had significantly better outcome per their mRS scores (good outcome: magnesium: 64.7%, n=293; reduced magnesium: 50.0%, n=30; no magnesium: 34.3%, n=12; p<0.001).

Conclusion

Our 12-year experience indicates that if titrated to a serum concentration of 2.0-2.5mmol/l, magnesium sulfate is a safe and effective neuroprotective agent in aSAH patients. Compared to patients with serum concentration below 2.0mmol/l, we observed lower rates of delayed cerebral infarction and higher rates of favorable functional outcome.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V319

Reduktion des sekundären Hirnschäden im Mausmodell der intrazerebralen Blutung durch Agatroban

Systemic Administration of Argatroban Reduces Secondary Brain Damage in a Mouse Model of Intracerebral Hemorrhage

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Objective

Spontaneous intracerebral hemorrhage (ICH) is a leading cause of disability and mortality. Perihematomal thrombin plays a pivotal role in edema formation and neuronal death. It is hypothesized that direct thrombin inhibitors (DTI; Argatroban) mitigate secondary injury after ICH. Here we analyze the effects of systemic Argatroban treatment on neuronal injury and outcome in an ICH mouse model.

Methods

A stereotactic ICH model using C57BL/6 mice by injection of 30 µl autologous blood into the right basal ganglia was established. Animals were randomized to 4 groups (hematoma (7/7 mice) and sham operated animals with and without DTI (3/3 mice)). Intra-operative monitoring included intracranial pressure (ICP), cerebral blood flow (CBF) and blood pressure (BP) measurement. Argatroban (9mg/kg bodyweight) was injected 1 hour after surgery. Neuroscore and Rotarod testing were performed to detect neurological deficits. Mice were euthanized 24h and 72h after ICH. Immunohistochemistry and PCR for thrombin and prothrombin were used to evaluate parenchymal damage.

Results

The ICP increased during ICH induction with peak values of 54.0+-10 mmHg and returned to baseline values within 30 min in the hematoma group and remained at 8.1+-0.6 mmHg in sham operated animals. CBF dropped to 32.0%+-8.1% of baseline in hematoma- and remained unaltered in sham animals. Perilesional thrombin expression increased by 4.24+-0.50-fold ($p<0.05$) 24h after ICH. Prothrombin expression was significantly lower in DTI treated animals (2.0+-0.5 vs. 4.7+-1.8-fold; $p=0.0001$). Perihematomal NeuN immunoreactivity decreased in animals injected with DTI (3.79+-1.34-fold, 34.4+-0.21% area ($p=0.001$)) and those injected with saline (4.32+-2.26-fold, 31.8+-0.11 % area ($p=0.001$)). After 72h, mice receiving the DTI showed significantly lower neuronal loss, compared to mock injected animals (56+-19.2% area vs 107+-24.5%; $p=0.0013$). GFAP expression was increased in animals receiving the DTI 72h after ICH (0.99+-0.55% area vs 1.88+-0.83%; $p<0.005$). Both groups performed similar using the rotarod performance test (saline: 92.5+-5s; DTI: 95+-3s; $p<0.0001$). Likewise, no disparities were detected using the neuroscore.

Conclusion

Systemic administration of Argatroban starting 1h after ICH significantly reduced prothrombin expression and neuronal damage after ICH. At the same time, GFAP expression increased indicating developing astrogliosis as potential protective mechanism to restrict the extent of neuronal damage.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V320

19F MR Imaging in der experimentellen Subarachnoidalblutung
19F Magnetic Resonance Imaging in Experimental Subarachnoid Hemorrhage

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Objective

Subarachnoid hemorrhage (SAH) caused by rupture of an intracranial aneurysm is a devastating disease associated with neuroinflammation. Previous evidence has shown that nanoemulsions prepared from perfluoro-5-crown-15-ether (PFCE) preferably label inflammatory cells, clearing the nanoparticles from circulation by phagocytosis. Thus, we aimed to visualize neuroinflammation using PFCE, in order to track the immune cell activation after SAH in vivo.

Methods

A filament perforation surgery was performed to induce SAH in C57BL/6 mice, and Sham operation was done for the matching control groups (n=20). Following surgery, mice received an intravenous injection of the PFCE nanoemulsion (150 µL, 40% v/v). Accumulation of ^{19}F particles was visualized at different time points *in vivo* by ^{1}H/^{19}F 7T magnetic resonance imaging. Morphologically corresponding ^{1}H and ^{19}F scans were warped to the Allen brain atlas and a custom subarachnoid space (SAS) atlas. Immunofluorescence (IF) staining for nuclei (DAPI), arachnoid cells (AKAP12/SSeCKS), microglia and macrophages (Iba1) and common leukocyte antigen (CD45) was performed to elucidate the histological location of PFCEs using their rhodamine labelling.

Results

Comparing integrated SNR in both groups, ^{1}H/^{19}F MRI revealed an accumulation of intravenously injected PFCEs in the ipsilateral SAS and adjacent parenchyma following SAH (Sham vs. SAH: 277.93 ±113.43 vs. 50,406.81 ±18,989.14; p=0.004). Furthermore, VOI-based evaluation showed increased ^{19}F signal in the hypothalamus and basal brain parenchyma directly bordering the perforated vessel. Group differences regarding leptomeningeal infiltration of PFCEs into the superior parts of the SAS were observed (integrated SNR in Sham vs. SAH: 10,019.50 ±4,545.08 vs. 22,832.64 ±2,949.39; p=0.008). IF and confocal imaging verified the accumulation of PFCEs in the above-mentioned areas (Sham vs. SAH: 0.09×10^{-3} $\pm0.02\times10^{-3}$ µm^2 PFCE/µm^2 SAS vs. 28.86×10^{-3} $\pm12.58\times10^{-3}$ µm^2 PFCE/µm^{2}SAS; p=0.048), and visualized colocalization and spatial affinity to microglia and other phagocytic cells like macrophages after subarachnoid hemorrhage.

Conclusion

PFCE nanoemulsions generate positive ^{19}F MRI contrast imaging of SAH-associated inflammation, making use of matching anatomic ^{1}H and highly specific ^{19}F images. Moreover, the detection of leptomeningeal PFCEs might give further insights into the lymphatic drainage following SAH, enabling monitoring of the immune cell activation and blood clearance after SAH.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V321

Die Rolle von extrazellulärer RNA für die Immunzellaktivierung nach der experimentellen Subarachnoidalblutung
Extracellular RNA drives the immune cell activation after experimental subarachnoid hemorrhage

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Objective

Subarachnoid hemorrhage (SAH) is a life-threatening type of stroke caused by bleeding into the subarachnoid space (SAS). Microglia (MG) accumulation and neuronal cell death after experimental SAH contribute to secondary brain injury. Here, we assess the potential of extracellular RNA (exRNA) to elicit this intra-parenchymal immune response after an extra-parenchymal insult.

Methods

A filament perforation model was used to induce SAH in male C57Bl/6 mice, while sham operation was performed for the control group. Animals received intravenous injections of RNase A to antagonize endogenous exRNA; NaCl was used for the control group. At day 1, 7 and 14, mice were sacrificed (n=6/subgroup; ntotal=72). The SAS was visualized by processing brain samples with the cryotome with the intact skull still attached at the base of the brain and thus preserving the subarachnoid compartment. Immunofluorescence staining was performed to characterize exRNA, microglia and vessel characteristics.

Results

In the acute stage of SAH, exRNA increased significantly in the SAS on the first postoperative day (Sham vs. SAH: 1,1* vs. 74,8*10³µm² eRNA/mm² tissue, p=0,01), and treatment with RNase 1 reduced eRNA quantity in SAH animals to control levels (SAH vs. SAH+RNase: 74,8* vs. 1,9*10³µm² eRNA/mm² tissue, p=0,01). MG density increased in SAH peaking on day 7 (Sham vs. SAH: 3% vs. 6.5%, p=0.04), and treatment with RNase1 significantly lowered MG density (6.5% vs. 2.4%, p=0.01). Furthermore, MG homed to the perivascular niche as demonstrated by co-staining of Iba-1 and cd31 (Sham vs. SAH: 14% vs. 32%, p=0.008). Administration of RNase1 abrogated this MG-perivascular association (SAH vs. SAH+RNase1: 32% vs. 16%, p=0.002), as well as association with astrocytes. Ncounter gene expression profiling with a panel of 770 neuroinflammatory genes showed hierarchical clustering distinguishing Sham and SAH subgroups.

Conclusion

In this SAH model, exRNA is released into SAS, and its accumulation spreads to the parenchyma, paralleled by an increase in MG density and homing to the vascular niche. RNAse1 treatment abrogates eRNA accumulation in SAS and parenchyma, and reduces gene expression associated with inflammatory signature. Inhibition of exRNA may reduce the proinflammatory cascade in SAH and hence, may serve as a potential treatment strategy to address secondary brain injury.

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V322

Der Effekt von humanem Liquor auf die Genexpression in Kardiomyozyten – Analyse von Herz-Hirn Interaktionen nach der Subarachnoidalblutung in einem *in vitro* System

The effect of human CSF on gene expression in cardiomyocytes - analyzing brain-heart interactions in subarachnoid hemorrhage in an in vitro system

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Objective

Subarachnoid hemorrhage (SAH) leads not only to neurological injury but also systemic changes, including cardiac pathologies. The interplay between cardiac dysfunction and cerebral perfusion is poorly understood. Our previous data in a SAH mouse model showed a distinct phenotype with diastolic dysfunction and cardiomyocyte hypertrophy in the chronic phase of SAH which was reversed after RNase treatment. In this study we sought to describe an in vitro system to investigate the distinct effects of cerebrospinal fluid (CSF) from SAH patients on cardiomyocytes in order to further understand the brain-heart axis in SAH.

Methods

CSF samples from patients with aneurysmal SAH (n=12) were collected within the scope of a prospective observational study. Control samples (n=5) were acquired from patients with pseudotumor cerebri or healthy individuals with indication for lumbar puncture to rule out meningitis. Sampling was conducted at two different time points after SAH (week 1, week 2). RNase activity (U/ml) was measured in CSF samples: supernatant was added to poly(c)solution, RNase buffer, and BSA solution and incubated at 37 C° for 15 min. Substrate degradation was determined by measuring the absorbance of the supernatant at 280 nm. For in vitro culture, neonatal rat cardiomyocytes (NRCMs) were cultured in DMEM medium and starved for 20 hours. Afterwards, they were treated with CSF of SAH patients (10% in DMEM) for 20 hours (Fig. 1A). Then, NRCM RNA was isolated for PCR analysis of markers associated with heart failure and statistically correlated with RNase activity levels in CSF.

Results

The mRNA expression of heart failure markers ANP (atrial natriuretic peptide) and BNP (brain natriuretic peptide) in cardiomyocytes showed a trend towards increased levels after treatment with CSF from SAH patients (Fig. 1B). Interestingly, the mRNA expression of both ANP and BNP showed a statistically significant correlation with RNase activity levels in human CSF (with p=0.03 for ANP and p=0.0091 for BNP); the higher the RNase activity in CSF of SAH patients, the lower the ANP and BNP expression in cardiomyocytes (Fig. 1C).

Conclusion

We describe a novel in vitro model to investigate the interplay between potential CSF mediators on cardiomyocytes. In this model, we find that gene expression of cardiac injury markers correlates inversely with RNase activity in CSF of SAH patients, suggesting a potential protective role of RNase in reducing cardiac injury after SAH.

Abb. 1

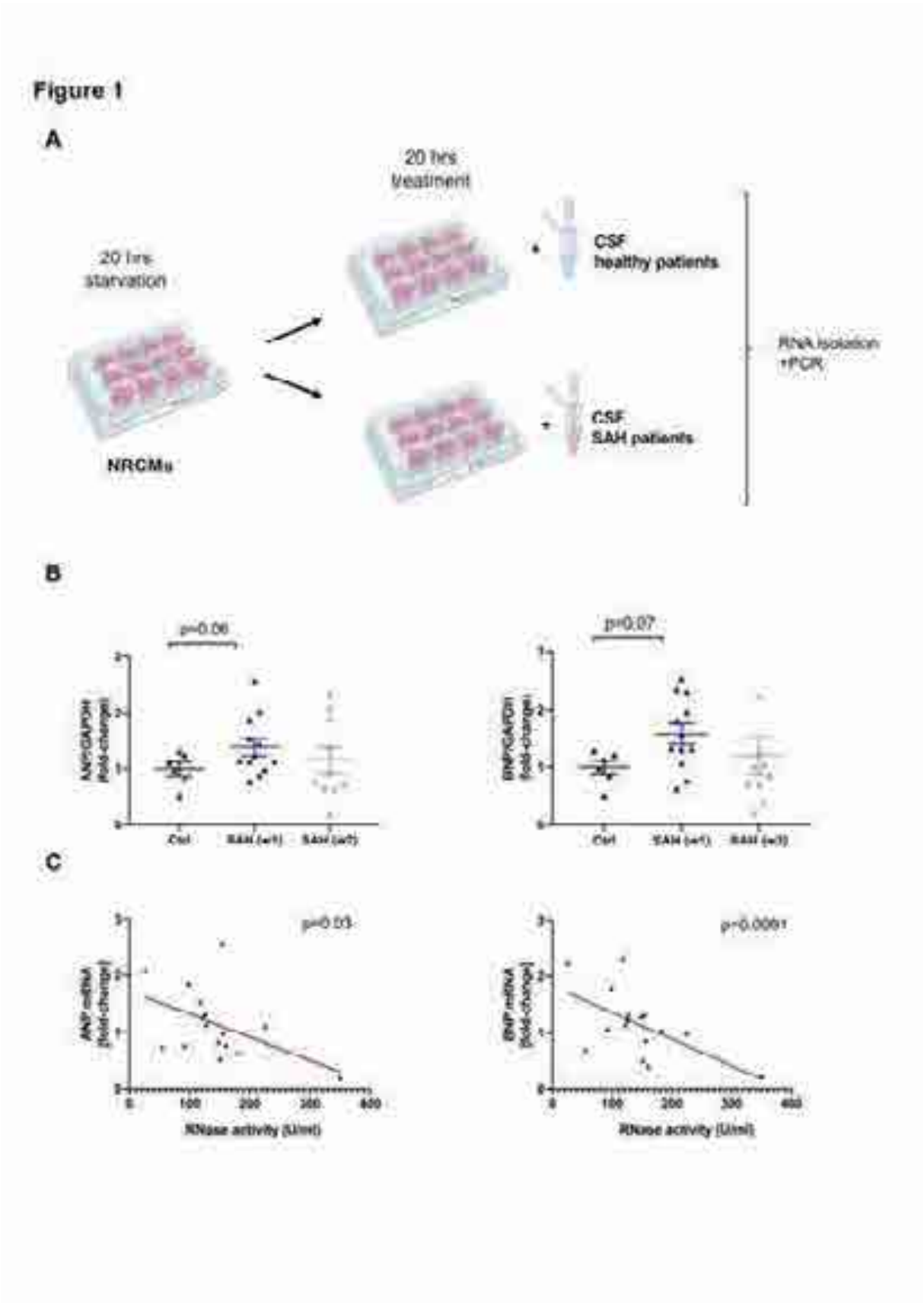
Figure 1
A
20 hrs
treatment
20 hrs
starvation
NRCMs
CSF
healthy patients
CSF
SAH patients
RNA isolation
+PCR
B
p=0.06
p=0.07
Ctrl
SAH (w1)
SAH (w3)
C
p=0.03
p=0.0091
RNase activity (U/ml)

Rapid Communication Pathophysiologie der SAB/*Rapid Communication SAH pathophysiology*

V323

Die Assoziation zwischen der aneurysmatischer Subarachnoidalblutung und dem Vitamin-D-Serumspiegel - eine Analyse der UK Biobank

The association between aneurysmal subarachnoid hemorrhage and vitamin D serum levels – an analysis of the UK Biobank

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Objective

Objective Inflammatory processes play a role in the development and rupture of intracranial aneurysms (IA). At present there is no medical treatment to reduce the risk of rupture of intracranial aneurysms. Vitamin D has anti-inflammatory properties and might therefore reduce the chance of development or rupture of intracranial aneurysms. We aim to compare the vitamin D status of patients with ruptured IA versus the general population using the UK Biobank.

Methods

Methods We included participants from UK Biobank, a prospective population-based cohort study consisting of 502,411 participants and analyzed serum 25-hydroxyvitamin D [25(OH)D] levels between participants with ruptured IA and the general population. Patients with aneurysmal subarachnoid hemorrhage (aSAH) before baseline assessment were excluded.

Results

Results In the general study population, mean age at study recruitment was 56 years; mean serum Vitamin D levels were 48.61 nmol/L with a range from 10 to 340nmol/L. 841 aSAH occurred during follow up. In the aSAH group, mean age was 58 years; mean serum Vitamin D levels were 46.14 nmol/L with a range from 11.3 to 120 nmol/L. 56.12% of aSAH cases had vitamin D insufficiency determined by mean serum Vitamin D levels of of <50 nmol/L compared to 49.4% of the general population. Based on self-assessment at baseline, 5.29% of the general study population reported Vitamin D supplementation, 4.76% reported Vitamin D supplementation in the aSAH group.

Conclusion

Conclusion Shown by this large cohort of the UK Biobank, range and mean Vitamin D levels in participants who have a rupture of an IA were at baseline lower than in the general population and reported a slightly higher proportion of Vitamin D insufficiency. Next research steps are regression analysis and Mendelian randomization and adjustment for other risk factors for IA such as sex, age, hypertension, smoking and family history.

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V324

Anreicherung neuronaler Signaturen im Glioblastom fördert Tumorinfiltration und verringert das Gesamtüberleben

Enrichment of Neuronal-like Traits in Glioblastoma Enhances Invasiveness and Decreases Survival

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Objective

The importance of the interaction between neurons and brain tumor cells as a factor in tumorigenesis has been demonstrated. In this study, we used methylation-based neuronal deconvolution to identify the formation of neuron-tumor networks in *IDH* wild-type GBM.

Methods

We performed deconvolution of bulk DNA methylation data containing a total of 5019 CNS tumors and stratified IDH wild-type GBM according to their deconvolutional neuronal signature into high and low neuronal component groups. Of these groups analyses were performed using differentially methylated genes, RNA sequencing, single-cell transcriptomics, proteomics, resting-state MRI, spatially stereotactic biopsies, MEG, multiplex flow immunoassay of blood serum, and PDX models.

Results

Within GBM subclasses, a lower neuronal phenotype was seen for MES tumors compared to RTK subclasses. Survival analysis of 288 patients revealed shorter OS ($p<0.01$) for GBM with a higher neuronal phenotype. This was externally confirmed in 187 TCGA patients ($p<0.01$) and same applied to 119 PDX models. A survival advantage of GTR or near-GTR compared to partial resection was observed in GBM with low neuronal phenotype ($p<0.01$). Interestingly, the survival benefit of near-GTR was not seen in tumors with a high neuronal phenotype. GBM with a higher neuronal phenotype showed RNA upregulation and DNA hypomethylation of invasive and transsynaptic signaling panels, and neuronal- and synapse-associated GO terms were upregulated. Proteomic analyses confirmed these findings with respect to protein expression. Using single-cell transcriptomics, GBM cells with a high neuronal phenotype exhibited an OPC/NPC-like cell status located in the infiltrating tumor zone. Consistent with these findings, spatially resolved tissue samples showed higher neuronal phenotype in biopsies

of the tumor margin. Using resting-state MRI, a higher functional connectivity (HFC) correlated with a higher neuronal phenotype. By MEG, we defined tumor regions of HFC and LFC which were consistent with the neuronal phenotype and were found to be receptive to neuronal signals. Neuronal methylation signature could be detected in the plasma of GBM patients, and higher BDNF plasma levels were found of tumors with higher neuronal phenotype, which was associated with worse OS ($p<0.01$).

Conclusion

In summary, the results presented here show that GBM use neuronal mechanisms, thus exhibiting a neuronal phenotype that drives tumor invasiveness, which negatively affects patient outcome

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V325

Generierung cytomegalievirus-spezifischer Effektor-T-Zellen bei Glioblastompatienten
Generation of cytomegalovirus-specific effector T-cells from glioblastoma patients

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Objective

Cytomegalovirus (CMV) is considered as a potential target for immunotherapy of glioblastoma (GBM) as it could be detected in almost 90% of all GBM cells. Therefore, the aim of this study was to generate CMV-specific effector T cells from GBM patients and healthy donors *in-vitro* and characterize them functionally and phenotypically.

Methods

CMV-specific T cells were generated from healthy CMV-seropositive donors and GBM patients by co-culturing $CD4^+$ and $CD8^+$ T cells with autologous CMV pp65 PepTivator-loaded mature dendritic cells (DC) for 14 days. Expression of immune checkpoint (IC) molecules, transcription factors (TF) and intracellular cytokines of the generated T cells was determined by flow cytometry.

Results

Prior to stimulation, T cells from healthy donors and GBM patients expressed very low levels of all IC molecules, and T-bet, EOMES and RORγt were the predominantly expressed TF. After PMA/ionomycin stimulation, T cells mainly expressed TNFα and IFN^{γ}, indicating a T_H1/T_c1 phenotype. Stimulation with CMV pp65 PepTivator alone resulted in no detectable response of the T cells and no differences between the two cohorts were observed.

After co-culturing of T cells with the PepTivator-loaded DC, all IC molecules were upregulated except for PD1, with TIM3 being the most abundantly expressed inhibitory IC molecule on $CD4^+$ and $CD8^+$ T cells. However, T cells from GBM patients lacked the upregulation of the co-stimulatory molecule CD40L, which was significantly higher on $CD4^+$ T cells from healthy donors. Expression of TF switched to an $EOMES^{high}$ /T-$betl^{low}$ phenotype, corresponding with a highly differentiated population. Nevertheless, specific re-stimulation of T cells with PepTivator-loaded DC resulted in the induction of IFNγ only in $CD4^+$ and $CD8^+$ T cells of healthy donors, which was absent in the patient-derived cells, whereas TNFα was present in T cells of both cohorts.

Conclusion

Effector T cells generated by co-culturing T cells with autologous CMV pp65 PepTivator-loaded mature DC exhibited a T_H1/T_c1 phenotype, with high expression of immune checkpoint molecules and EOMES. However, in GBM patient-derived $CD4^+$ T cells induction of CD40L was low and associated with an absent induction of IFNγ expression by $CD4^+$ and $CD8^+$ T cells upon specific re-stimulation, implying a dysfunctional CMV response in GBM patients after *in-vitro* stimulation with dendritic cells.

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V327

CMV-Infektion bei Glioblastom – Onkomodulation durch Veränderungen der Gliom-Immunlandschaft
CMV infection in glioblastoma - Oncomodulation through changes to the glioma immune landscape

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Objective

In glioblastoma unchecked tumor development occurs through mechanisms of immune evasion and suppression. The Cytomegalovirus (CMV) is implicated in tumor development and progression, its genome encodes numerous proteins to evade the immune response. Here, CMV specific changes of the immune landscape in Glioblastoma are characterized in a murine model *in vitro* and *in vivo*.

Methods

GL261Luc2 murine gliobastoma cells were infected with mCMVD157. qRT-PCR and RNAseq was performed to assess viral replication and differential gene expression in Gl261fluc *in vitro*. MHC-I/II expression levels were analysed using flowcytometry and immune fluorescence staining. Tumor immune composition was analysed in mCMV+ and naive mice *in vivo*.

Results

After infection of Gl261fluc mouse glioblastoma cells with mCMV D157 with MOI 1, intracellular viral copy numbers increased from 24 hours (8.0x10e5 -+2.3x10e5) up to 96 hours (3.9x10e7-+3.4x10e6, p<0.0001) after infection. Replication was highest within the first 48 hours and markedly declined there after infection. Viral copy numbers in the supernatant increased similarily from 24 hours (4.5x10e4) to 48 hours (3.9x10e5, p=0.0002) and 96 hours (1.1x10e6, p<0.0001) (MOI 1). RNAseq revealed a total of 2711 differentially expressed genes after mCMV infection (p<0.005; n=3) with an overlap of 1108 genes between mouse and human tumor cell lines. Of particular interest was the downregulation of MHC-I associated genes H2-Q1-10 and Tap1 (8.13log2, p<0.005). Following mCMV infection MHC-I expression is reduced by approximately 60% (p<0.0001). Immediate early genes (IE-1) are detected in the brain in mCMV+ animals, not in mCMV naïve. IE-1 expression doubled until day 10 post infection (p<0.0061) and increased up to 3-fold at day 21 (95% CI 6.7e-006-1.32e-005, p<0.0002). mCMV+ mice had a significantly shorter survival depending on initial tumor size (p<0.001). In t-distributed stochastic neighbor embedding (tSNE) plot of tumor immune infiltrates from mCMV+ mice were characterized by B cell infiltrates and low levels of NK cell infiltration compared to naive animals.

Conclusion

CMV enters early latency in glioblastoma cells with only short periods of lytic replication. Lasting transcriptome changes include inflammation signatures and MHC I/II downregulation. In vivo, mCMV infection leads to intratumoral viral spread and immune changes towards B- cell infiltration and loss of NK cells with consecutive accelerated growth and shortened survival.

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V328

5-Aminolevulinsäure Metabolismus ist spezifisch in aktivierten Makrophagen des Tumormikromilieus angereichert

5-Aminolevulinic acid metabolism is enriched in activated macrophages of the tumor microenvironment

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Objective

Fluorescence guided surgery is widely used to improve the extent of resection in brain tumor surgery. 5-aminolevulinic acid (5-ALA), the most widely used fluorophore in glioma surgery, is thought to be selectively metabolized into protoporphyrin IX (PpIX) in tumor cells. Here, we integrated intraoperative two-photon microscopy with spatially resolved metabolomics and transcriptomics to decipher the heterogeneity of PpIX distribution and 5-aminolevulinic acid metabolism at cellular level.

Methods

PpIX two photon-fluorescence is generated by a dual-wavelength picosecond fibre laser source with a fixed wavelength at 790 nm. A 700 nm long-pass dichroic mirror was used to deflect the fluorescence signal toward a dual-channel detector. Two emission bands are chosen to match the PpIX peak (640 nm) and the auto-fluorescence signal (591 nm) emitted from molecules such as lipofuscin, NADH, and elastin. Intraoperative tissue specimens were stored in OCT and processed by our routine pipeline for spatial transcriptomics (stRNA-seq) using the 10X Visium technology, sequenced on a NextSeq550 at a depth of 100k reads per spot and processed by SPATA2.

Results

PpIX 2-P fluorescence imaging of 85 cases of glioblastoma resections revealed distinct patterns PpIX fluorescence patterns ranging from ubiquitous diffuse low-intensity accumulation to cell specific metabolism. Surprisingly, the cells specifically marked by PpIX, had histological features of myeloid rather than tumor cells. The further integration of spatially resolved transcriptomics demonstrated a cell type specific metabolism of 5-ALA in activated immunosuppressive macrophages. This finding was supported by the analysis of an external cohort of 6 spatially resolved multi-omic (metabolomic, MALDI) and transcriptomic datasets, confirming an exclusive upregulation of 5-ALA metabolism in macrophages.

Conclusion

The current results question the exclusivity of 5-aminolevulinic acid metabolism in tumors. On the contrary, PpIX appears to be spatially abundant within the tumor, albeit primarily in activated myeloid cells.

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V329

Menschliches präklinisches Glioblastommodell: Ein Zieltherapieansatz für Patienten mit BRAF-Mutation

Human Preclinical Glioblastoma model: A Target Therapy Approach for BRAF mutant Patient

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Objective

Glioblastoma (GBM) is the most common primary malignant tumors in central nervous system, with median post-diagnosis survival of <15 months. The incredible heterogeneity exhibited by GBM highlights its incurable nature. Referring to specific mutations of the GBM, 40% of GBM"s harbor *EGFR* alterations, whereas *BRAF* alterations are rare (1-2%). The *BRAF* mutation is reported to regulate cell proliferation and apoptosis based on the *BRAF/MEK*pathway. Since, the mechanisms within *BRAF* mutated GBM remain unclear, here we present a novel personalized human GBM model of evaluate the efficacy of various BRAF target therapies.

Methods

Discarded non-neoplastic cortical tissue from a *BRAF* - GBM was sectioned and inoculated with patient self-derived BRAF+ GBM cells, establishing an *ex vivo* human *BRAF*+ GBM model. Tumor growth was live tracked over the culture period (10days), with and without clinically approved BRAF and MEK inhibitors and vitality of the sections was quantified using imaging modalities.

Results

Tumor growth quantification revealed a significant reduction (p=0.001) of tumor volume upon combined treatment with a MEK inhibitor (Trametinib, 5nM) and a new generation BRAF inhibitor (Vemurafenib, 10nM) compared to a standard treatment of MEK inhibitor (Trametinib, 5nM) and an old generation BRAF inhibitor (Dabrafenib, 10nM). Immunohistochemistry based quantification also revealed no toxic effect of the drug on the microenvironment validated using NeuN (for Neurons) and GFAP/IBA (for glial cells) antibodies. Further, there is a significant reduction (p=0.005) of pERK and pAKT [PDOS1] expression on the sections with the combination therapies (Trametinib+ Vemurafenib) compared to monotherapies and standard combinations.

Conclusion

Our findings show that targeted therapy could be beneficial for patients with glioblastoma harboring BRAF mutation, and establishment of human based personalized model would be useful to investigate the influence of different chemotherapies on the immunosuppressive tumor microenvironment.

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V330

Multiplex-Phänotypisierung extrazellulärer Vesikel zur Analyse potenzieller Biomarker bei Glioblastom-Patienten
Multiplex phenotyping of extracellular vesicles for analysis of potential biomarkers in glioblastoma patients

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Objective

Extracellular vesicles (EVs) carry biological information from their cell of origin that is useful for non-invasive detection of tumor biomarkers and disease monitoring. In glioblastoma (GBM), blood circulating EVs are elevated and carry GBM-associated proteins. However, it is still challenging to analyze tumor derived EVs for translational purposes. Here, we used imaging flow cytometry (IFCM) as a robust strategy to perform phenotyping of EVs with GBM related surface markers in human plasma.

Methods

EVs were isolated via differential ultracentrifugation from plasma of (a) 40 GBM patients, pre- and post-surgery, (b) 11matched GBM relapses and (c) 12 healthy donors (HD). EV sizes and concentrations were evaluated by NTA. EV markers (CD9,CD63 and CD81) together with glioma-related markers (integrin beta-1 [ITGB1], tenascin C [TNC], Profilin-1 [PFN1], CD44,GPNMB, SPARC, HLA-II or CD133) were analyzed by IFCM. EV percentages and objects/mL plasma were compared among the groups and correlated with clinical parameters.

Results

CD9 was the predominant tetraspanin in all groups (15-96%), while CD63 had the lowest levels (0-33%) and the strongestdecrease in GBM patients after surgery (fold change [FC]=-5.4, $p<0.01$). Among the glioma-related markers, ITGB1 and TNC displayed the most significant differences between the analyzed groups, especially the double positives ITGB1+/CD63+and TNC+/CD63+, which decreased in patients after tumor removal (FC=-3.5 and -12, respectively; $p<0.001$). Meanwhile,ITGB1+/CD9+and TNC+/CD9+EVs exhibited the highest levels in GBM when compared to HD subjects (FC=8.6 and 17.4;$p<0.001$) and upon tumor recurrence (FC=3.7 and 10.9, respectively; $p<0.01$).

Conclusion

We identified EV surface antigens with potential clinical utility as GBM biomarkers. Among them, we highlight ITGB1 and TNC as the most promising markers.

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V331

Vielfalt der zellulären Kommunikation beim Glioblastom
Diversity of cellular communication in glioblastoma

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Objective

The dynamic nature of the transcriptionally diverse states exhibited within glioblastoma (GB) points to the possibility of the role of intercellular tumor signaling aiding in this dynamic switch. In this study, we aim to explore the diversity of transcellular signaling and investigate correlations between transcriptional dynamics and functional signaling.

Methods

Electrophysiological characterization of GB was carried out using planar microelectrodes and Ca2+ imaging, in either 2D cell culture or in our novel human cortical GBM model (H2H platform). Exposure to physiologically relevant conditions was carried out to identify specific signaling cells of interest and capture the signaling response to alterations in environmental conditions. Transcriptional dynamics and plasticity were examined by means of scRNA-sequencing following CRISPR based perturbation of genes involved in the generation of functional synapses.

Results

Electrophysiological profiles of multiple primary GB cell lines revealed characteristics of scale-free networks, confirmed in both 2D culture as well as a human neocortical GBM model. When GBM was cultured in a "in-vivo" like environment, basal activity was significantly different, owing to interactions with elements within the neuronal environment. Cellular signaling was directly correlated to changes in the environment, like hypoxia or glutamatergic activation, and total inhibition of electrical signaling was achieved by the usage of synaptic inhibitors. Single-cell RNA sequencing revealed that synaptogenesis plays a crucial role in the lineage states present in GB. CRISPR based perturbation of these genes resulted in alterations in cellular morphology and decreased cellular connectivity, with loss of scale free features, and loss of developmental lineages, leading to significant alteration of GB response to the environmental stress.

Conclusion

Our findings highlight the role of electrical signaling in glioblastoma. Cellular stressors induce intercellular signaling, leading to transcriptional adaptation suggesting that intercellular signaling may act as a mechanism for dynamic transcriptional state adaptation.

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V332

Entwicklung eines silikonbasierten, 3-dimensionalen Gerüsts zur Übertragung von Hirntumorzellen in Modellorganismen

Development of a silicone-based, 3-dimensional scaffold to transfer brain tumor cells into model organisms

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Objective

In the commonly used 2-dimensional cell culture approaches of human brain tumor cells, many tumor-associated processes cannot be investigated, and cells behave differently than in their natural environment. The aim of our study was to culture a three-dimensional tumor within a silicone-based, biocompatible scaffold for the transfer into model organisms.

Methods

To represent cells from distinct brain tumor entities, BenMen1 and IOMM-Lee (Meningioma), A-172 and U-87 MG (Glioblastoma) were used. To optimize the surface condition of silicone for each entity the scaffold was treated with different coatings: gelatine, poly-D-lysin (PDL) and vitronectin (Vtn). To evaluate the impact of the silicone scaffold material and its coatings on the tumor cell vitality, cell growth, metabolic activity (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay), proliferation rate (bromodeoxyuridine (BrdU) assay) and fluorescence staining for tumor entity specific marker were performed after incubation for 7 days under standard cell culture conditions. Finally, silicone structures of laboratory grade were compared to silicone structures of medical standard grade approved for human applications as mentioned above.

Results

We could successfully culture all cell-lines on silicone matrices. However, only the meningioma cell-line IOMM-Lee recovered at yield comparable to cell culture plates (97%). In Ben-Men-1 cells, contact to silicone did significantly reduce the cell vitality ($p=0.044$). No significant difference could be found in glioblastoma cell-lines. The observed deficiencies in cell yield of cultures on pure silicone matrix could be overcome by coating the matrix with Vtn (Ben-Men-1: $p=0.010$; U-87 MG: $p=0.006$). Vtn coating did not influence the metabolism or DNA synthesis rate of the cell-lines. Altogether, there was no difference if either standard silicone of laboratory grade or medical grade was used.

Conclusion

Brain tumor cell cultures can be successfully grown on silicone scaffolds in vitro. This could enable transfer of 3D brain tumor cell cultures into model organisms in future.

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V333

Die Rolle von Histon-Methylierungsstatus und Osteonectin bezüglich des invasiven Wachstums und der Prognose von Hypophysenadenomen

The role of histone methylation status and osteonectin on invasion and prognosis in pituitary adenomas

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Objective

Pituitary adenomas are one of the most common intracranial tumors and are usually benign. However, pituitary adenomas tend to show invasive growth and some of them show aggressive behavior with resistance to standard therapies. It is therefore of clinical importance to identify such cases in order to adjust the further clinical management. A prognostic impact of alterations of the histone trimethylation of H3K have been described and osteonectin has been identified as a marker of invasive growth in several other tumor entities.

Methods

We analyzed tumor tissue samples of 927 pituitary adenomas, resected between October 2004 and April 2018 in the authors" institution. Tissue microarrays were constructed and immunohistochemical staining for H3K27me3, H3K36me3 and osteonectin was done and a semiquantitative scoring system applied. Immunohistochemical expression of MIB-1 was quantified digitally using representative images of routine stainings. Clinical data including recurrence-free survival according to radiographic follow-up images was collected. Invasive tumor growth was assessed retrospectively based on surgical reports.

Results

The rate of invasive growth according to surgical reports was 42.61% (395 of 927 cases). The overall recurrence rate was 20.14% (175 of 869 cases with available follow-up data) with a mean follow-up of 2.64 years, ranging from 0.06 to 15.20 years. A MIB-1 expression ³0.6% was associated with a higher rate of invasive growth and a shorter recurrence-free survival in the univariate (p=0.0320 and p=0.0135, respectively) and the multivariate analysis (p=0.0222, odds ratio=1.44 and p=0.0408, hazards ratio=1.58, respectively). Loss of H3K27me3 showed a higher rate of invasive growth in the univariate and the multivariate analysis (p=0.0312 and p=0.0305, odds ratio=2.68, respectively). There was no significant impact of H3K36me3 or osteonectin regarding invasive growth and recurrence-free survival.

Conclusion

MIB-1 expression and loss of H3K27me3 were independent markers for invasive tumor growth but only MIB-1 showed an independent prognostic impact.

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V334

multizentrische Genomanalyse von 62 Meningeomen des Foramen magnum zeigt unterschiedliche mutationsspezifische Tumormerkmale

Multicenter genomic analysis of 62 foramen magnum meningiomas demonstrates mutation-specific distinct tumor features

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Objective

Foramen magnum (FM) meningiomas are surgically challenging tumors that are associated with high morbidity and mortality. We sought to investigate the anatomical distribution of clinically actionable mutations in FM meningioma and further clinical characteristics that correlate with their mutational profile.

Methods

Next-generation sequencing covering all meningioma-relevant genes including *AKT1, KLF4, NF2, POLR2A, PIK3CA, SMO and TRAF7* hot spot mutations was performed in 62 FM meningiomas, gathered from three international institutions. In addition, tumor and patients characteristic including age, sex, radiological features and tumor location were retrospectively collected and evaluated.

Results

Our cohort comprised 46 female and 16 male patients. At least one known driver mutation was detected in 58 patients (93.5%). *TRAF7* mutations represented the most commonly detected alteration (n= 26, 41.9%), followed by *AKT1 (E17K)* mutations (n= 19, 30.6%). Both alterations were significantly associated with an anterolateral tumor location in relation to the brainstem (p= 0.0078). Moreover, tumors harboring one of both mutations showed a meningiothelial histology in 89.3%. Further common mutations in FM meningiomas were *POLR2A* mutations (n= 9, 14.4%), *KLF4*mutations (n= 7, 11.6%) and *PIK3CA* mutations in two cases (3.2%). All aforementioned mutations occurred exclusively in female patients, but with no significant correlation with an anterolateral tumor origin. In contrast, *NF2*mutations occurred in 11 cases (17.7%) with predominantly posterior tumor location. Finally, intratumoral calcification was present in eight tumors and was not associated with a certain mutation.

Conclusion

Genotyping of FM meningiomas may enable a better understanding of tumor features and guide their surgical resection. A large subset of foramen magnum meningiomas harbor *AKT1 (E17K)* mutations and are therefore potentially amenable to adjuvant targeted medical therapy in cases with tumor remnants.

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V335

Methylierung und micro-RNA Expression in primären und rekurrenten Glioblastomen
Methylation and micro-RNA expression in primary and recurrent Glioblastoma

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Objective

Epigenetic tumor characteristics are in focus for glioblastoma prognosis. This raises the question if these characteristics are stable expressed during the progression of the disease and if potential temporal instability might influence their prognostic value.

Methods

A total of 44 patients suffering from glioblastoma who were treated for their primary and relapse tumor were included in the study. Tumor specimens from their initial and recurrent tumor resection were subjected to evaluation of *MGMT*, *p15* and *p16* methylation status. MiRNA-21, -24, -26a and -181d expression was evaluated as well. The stability of these epigenetic markers during the progression of the disease were correlated with further clinical data. A Cancer Genome Atlas (TCGA) dataset of 224 glioblastoma patients was used as an independent cohort to validate the results.

Results

In all examined epigenetic markers instability was observed. *MGMT* methylation changed in 29.5% of patients, *p15* methylation changed in 31.8%, *p16* methylation changed in 34.1% of cases. MiRNA expression in corresponding initial and relapse tumor specimens varied considerably in general, while individual cases presented with a stable expression. Patients with a decreased expression of miRNA-21 in the recurrent tumor showed a significantly longer overall survival. These results are supported by the data from TCGA indicating similar results.

Conclusion

Epigenetic characteristics may change during the course of glioblastoma disease. This may influence the prognostic value of derived molecular markers.

Rapid Communication Tumor und Epilepsie/*Rapid communications Tumor and epilepsy*

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Die Rolle von Epilepsie bei älteren Patient:innen mit Glioblastomen: Eine Österreichsiche multizentrische Analyse

The role of epilepsy in elderly patients with Glioblastoma: An Austrian multicenter analysis

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Objective

Higher age is a significant predictor of poor outcome in glioblastoma multiforme (GBM) patients. The impact of epilepsy in GBM patients on outcome parameters is poorly defined. Furthermore, persisting epilepsy significantly influences the patients" quality of life (QoL). This study aims at specifically evaluating the impact of epilepsy in elderly GBM patients.

Methods

Two Austrian academic neurosurgical centers retrospectively analyzed all elderly (≥65 years) GBM patients with de-novo tumors, who underwent surgery between 09/2006 and 07/2021. Epidemiological, histopathological and survival data were gained from patients" electronic charts. Tumor volume was assessed using standardized software.

Results

391 patients (55%males, 45%females) with a median age at surgery of 73 years (IqR 68.5-77.5) were analyzed. The mean predicted OS was 12.4 months (CI95% 10.9-14.0). Median preoperative Modified Rankin Scale (mRS) was 2 (IqR 1-3). Mean follow-up was 10.4 months (CI95% 9.1-11.6). Median tumor volume amounted to 26.47cm3 (IqR 12.65-43.49).

95/391 patients (24%) suffered from preoperative epilepsy. 17 (4,3%) patients still suffered from epilepsy after tumor resection. Eight patients developed new postoperative seizures, and four patients (1.0%) showed a worsening of already preoperatively diagnosed seizures. Major surgery-associated neurological complications included new motor deficits in 29 (7%) and new aphasia in 16 (4%) patients.

Patients with lower tumor volumes experienced significantly more often seizures compared to patients with larger tumors, p<0.001.

Logistic regression showed patients with seizures had significantly lower mRS (p=0.032) and less frequently occipital tumor location (p=0.018). Postoperative epilepsy resulted in significantly prolonged hospitalization after the surgery (p=0.009).

Survival did not correlate with preoperative epilepsy (p>0.05). However, Cox regression revealed that multifocal tumor location (HR=1.777, p=0.025) as well as thalamic involvement (HR=11.121, p=0.030) negatively influenced OS. Furthermore, surgery-associated complications shortened OS significantly (HR=1.945, p=0.025).

Conclusion

Even though epilepsy was not found to directly impact survival in elderly GBM patients, we found that surgery and AED led to epilepsy freedom in a significant proportion of our patient cohort, thereby potentially leading to improved QoL. Greatest focus should be set on avoiding any surgery-associated deficits, since these severely influence the OS.

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Pharmakologische Neuromodulation Neuronaler Netzwerke im menschlichen Gehirn – Ein innovative Methode in Epileptogenese-Forschung und Cancer Neuroscience

Pharmacological Neuromodulation of Human Brain Neuronal Networks – A novel Approach to Epileptogenesis and Cancer Neuroscience

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Objective

Cancer neuroscience is an emerging field aiming to explain interactions between neurons and brain cancer. Epilepsy represents an impactful clinical hallmark of this interaction as seizures are the effect of synchronized and unsynchronized neuronal activity. The role of neuromodulators in these synchronization and desynchronization events in human brain slices are rarely investigated on a micro- to millimeter order of magnitude. Here, we show how neuromodulators influence neuronal network activity in human brain slice cultures aiming to provide novel insights into epileptogenesis and neuronal crosstalk.

Methods

We cultured human brain slices from entrance tissue of tumor and epilepsy surgeries using human CSF. MEA recordings (n=24) from 5 slice cultures were performed in three conditions (controls n=10, 30µM norepinephrine [NE] n=8, 30µM acetylcholine [AC] n=6). Action potentials ('spikes') were identified using a threshold-based approach and neuronal networks were defined as timely-shared spiking activity. We used graph theory to measure and compare network properties upon neuromodulation in two selected slices. The Kruskal-Wallis test and the Dwass-Steel-Crichtlow-Fligner for pairwise comparisons (p

Results

The mean firing rate was 7.94 Hz for controls, 7.47 Hz for AC and 19.9 Hz for NE treated slices. Mean length of single channel bursts was 44 ms and increased in both modulated groups, with 116 ms for AC and 115 ms for NE. However, inspection of temporal and spatial spike distribution between slices revealed a striking difference in the activity patterns after neuromodulation. NE increased synchronized network activity, while AC disrupted existing spiking network patterns and resulted in disseminated unsynchronized activity. Network changes were quantified using the mean degree of centrality (DC) – a graph theoretical metric for connectedness of network nodes. Mean DC was increased by NE from 0.278 to 0.389, while AC decreased DC from 0.058 to 0.026.

Conclusion

Here, we were able to use neuromodulation to investigate neuronal activity patterns in human brain slice cultures. Both, NE, and AC show distinct forms of modulating neuronal activity patterns, suggesting an important role for network homeostasis. Considering the significance of neuronal network activation in the emergence of seizures or brain tumor behavior, we provide experimental background to explore novel therapeutic approaches in epilepsy and cancer neuroscience.

Abb. 1

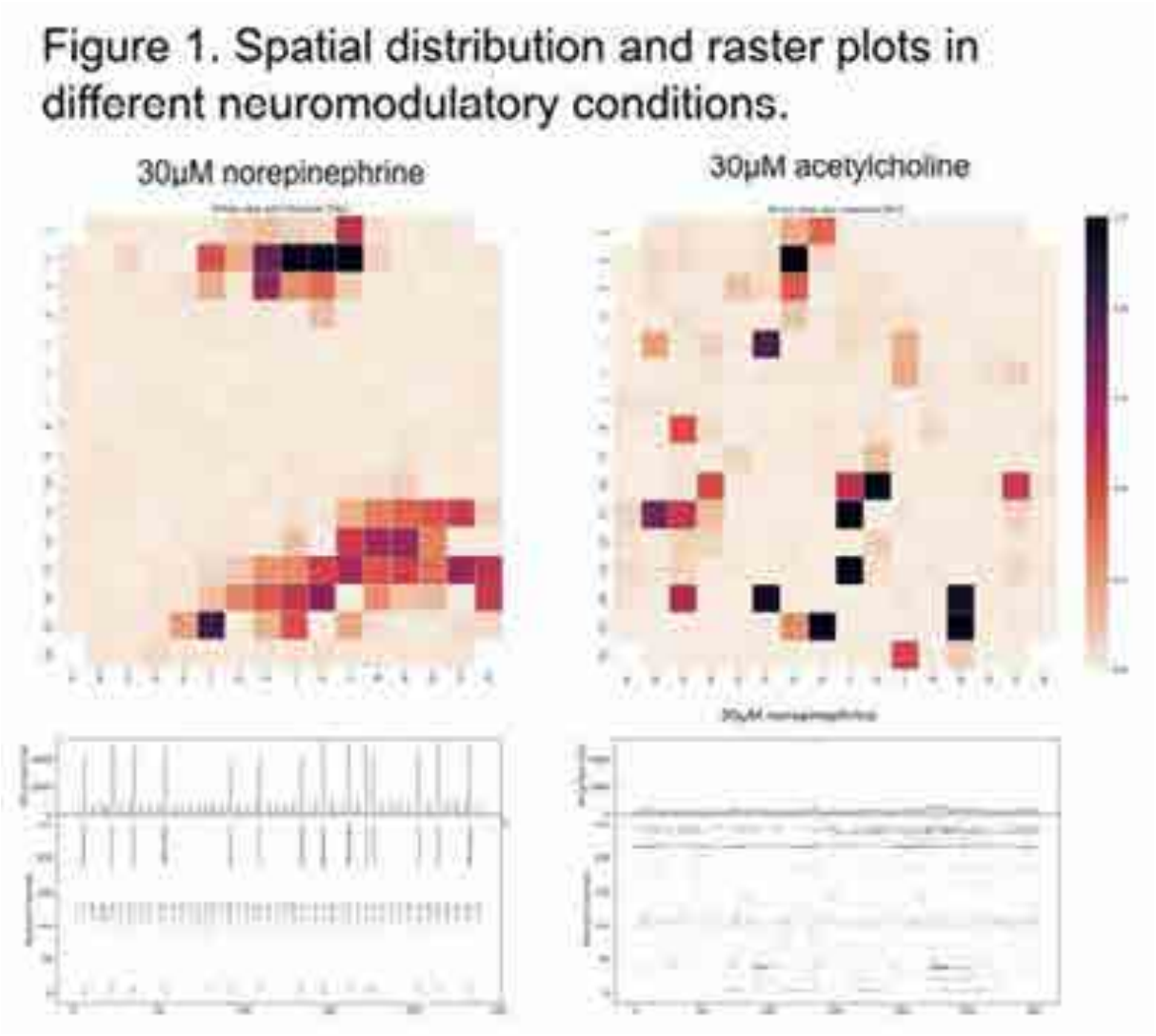
Figure 1. Spatial distribution and raster plots in different neuromodulatory conditions.
30µM norepinephrine
30µM acetylcholine

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Anatomiegestützte Resektionen bei paralimbischen Tumoren der temporomesio-insulären Region – eine Kombination epilepsie- und tumorchirurgischer Konzepte

Anatomy guided resections for paralimbic tumors in the temporomesial-insular region - combining tumor and epilepsy surgery concepts

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Objective

Tumors in the temporomesial region quite often also grow into the insula and vice versa. Surgery carries substantial risks and epilepsy control is a major concern

Methods

We retrospectively studied all 158 intrinsic brain tumors involving the temporomesial region with variable extension into the insula and other paralimbic areas operated by 3 tumor and epilepsy surgeons (TK: 2013-2022, AG: 2017-2022, MS: 2016-2022) at the authors" institution. We employed a surgical strategy addressing anatomical compartments "anatomy guided resection": temporal pole, ant. temporomesial [uncus & hippocampal head], post. temporomesial, insula etc.) defined by specific surgical maneuvers necessary for resecting the respective tumor infiltration rather than a single tumor mass.

.

Results

The study cohort included 38 glioblastomas (GBM, 24.1%), 36 CNS grade II/III gliomas (22.8%) and 74 glioneuronal tumors (46.8%; other: 10 [6.3%]). 78 (49.4%) patients underwent a formal epileptological work-up. Ant. temporal lobectomies (ATL) or variations thereof were perfomed in 140 (88.6%) cases. 38 (24.1%) had insular resections. We recorded 7 (4.5%) CTCAE °III-V neurodeficits >30 days (incl. 4/23 cases with surgery for recurrent tumor). Surgical mortality was 2 (1.3%). 113/158 (71.5%) surgeries included removal of non-tumorous areas of the brain for epilepsy control (extended lesionectomy, ATL, additional amygdalohippocampectomy). 104/116 (89.7%) cases with primary and resectable (no basal ganglia involvement, single lesion) tumors had gross total or supramarginal resections. 78 (49.4%) cases presented with drug-resistant epilepsy (DRE), 46 (29.1%) with seizures but not drug-resistant epilepsy (SZ), and 34 (21.5%) with no preop. seizures (No SZ). Excluding early postoperative seizures <30 days, 86.5% (DRE: 80.5%, SZ 90.0%: No SZ: 96.8%)and 81.1% (DRE: 71.4%, SZ: 90.0%, No SZ: 93.5%) of patients were completely seizure-free (ILAE 1) at 6 and 24 months, respectively. Oncological outcomes were very good, e.g. median overall survival for 30 primary GBM was 27.6 (95% CI: 18.0-37.1) months

Conclusion

Combining tumor and epilepsy surgery concepts for tumors of the temporomesial-insular region was safe and resulted in very good resection and epileptological outcomes. Extensive resections may have translated into superior survival. Patients with brain tumors may benefit from epilepsy surgery strategies even if they are not traditional epilepsy surgery candidates

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MRT-gestützte LASER-induzierte Thermotherapie (LITT): Technische und klinische Erfahrungen in der Behandlung von Epilepsie und Hirntumoren. Eine Single-Center-Anaylse.

MR-guided LASER-induced Thermotherapy (LITT): a single centre clinical experience with LITT in the treatment of epilepsy and cerebral tumours

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Objective

MR-guided LASER-induced Thermotherapy (LITT, Medtronic, Visualase) received the CE mark in 2019. Being one of the first European centres to adopt LITT in the same year, we oversee an overall number of 25 cases focusing on the treatment of epilepsy and brain tumours. This continuously evolving technology demands for very specific technical and procedural requirements. We now share our initial experience with this technology, looking at the clinical effects, its advantages and limitations, potential side effects and organizational issues.

Methods

From April 2019 till to date, we have treated 25 patients (average age: 35 years, 13 females, 12 males) with LITT for epilepsy (18 cases) and brain tumours (7 cases). In a stereotactic fixed frame procedure (Leksell G-frame) we implanted more than one LASER-probe in 14 cases, with an overall implantation of 43 probes. In the 18 epilepsy cases we treated pathologies such sclerosis of the hippocampus and the amygdala, cortical dysplasia, DNET, hypothalamic hamartoma, and status after encephalitis of the temporal lobe. We regularly combined brain-biopsy of the target area with consecutive LITT via the same trajectory. With LITT we predominantly aimed at functional de-connection of the epileptogenic focus. In the patient group of malignant tumours, four patients with pre-radiated metastases and three patients with recurrent glioblastoma were treated. We initiated LITT only if the virtual stereotactic plan covered the tumour-related contrast-enhancement completely employing a maximum of three LASER-probes.

Results

In our series no LITT-related morbidity and mortality was observed. We confirm a precise concordance between the "cell-death-simulation-map" provided by the LITT-system and the postoperative MRI. In all cases with multiple LASER probes the planned extend of ablation was achieved. The surgical results are comparable to open resection, yet with significantly less approach-related destruction. Employing only a single LASER-probe, as done in the initial two cases of selective amygdala-hippocampectomy (AHS), we observed a non-sufficient ablation of the epileptogenic tissue. Thus, in all further AHS-cases we opted for a two-probe approach to cover the hippocampus as well as the amygdala completely.

Conclusion

MR-guided LITT is a safe and very valuable new neurosurgical technique complementing current surgical methods. Yet, the implementation of LITT involves specific procedural complexities.

Rapid Communication Tumor und Epilepsie/*Rapid communications Tumor and epilepsy*

J-SPNC008

MR-guided Laser Interstitial Thermal Therapy (LITT) bei hypothalamischem Hamartom: Erste Erfahrungen eines Zentrums

MR-guided Laser Interstitial Thermal Therapy (LITT) for hypothalamic hamartoma: initial experience of a center

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Objective

Introduction:

Hypothalamic hamartoma (HH) is a rare cause of epilepsy usually associated with drug-resistant gelastic seizures. Many different approaches have been used to treat this lesion, but minimally invasive techniques like MR-guided LITT seem to have better efficacy in epilepsy control and lower complications rates. We report the first experience of the first center in Portugal to perform this type of procedure.

Objectives:

Retrospective analysis of patients undergoing LITT for HH at our institution in the last 3 years. Assess results and complications in this procedure.

Methods

Retrospective analysis of clinical files, imaging studies, planning and surgery records of patients with HH treated with LITT in CHULN between 2019 and 2022.

Results

We included 4 patients diagnosed with HH during infancy, presenting with drug-resistant gelastic epilepsy. They underwent LITT with a total of 5 procedures (1 patient had recurrence of symptoms and had another ablation). There was no difference in gender and their ages were between 2 and 24 years old. All the patients were assessed by the Epilepsy surgical group, composed by neurologists, neurosurgeons and psychiatrists. Two patients had precocious puberty and was also followed by endocrinology.

All cases were operated under general anesthesia, with stereotactic implantation of the laser fiber using Leksell® frame (4) or Neuronavigation System (1). The mean hospitalization time was 4 days and no early complications were registered. All patients had an in-clinic follow-up assessment every 3 months after the ablation. We registered no neurologic or memory deficits. There were no endocrinologic complications. One patient had behavioral alterations prior to surgery that didnn"t improve after the procedure. All the patients had a decrease in the number of seizures after the surgery and 3 of them are free of epileptic seizures for 10, 15 and 18 months.

Conclusion

MR-guided LITT is described as a safe and effective treatment of gelastic seizures related to HH. Our first experience follows what is described in the literature. All the patients had favorable outcome with reduction of epileptic seizures and 75% are free of epilepsy. The complication profile of LITT seems to be superior to previous techniques, with no neurologic or memory deficit and no *Diabetes Insipidus* in our series.

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Klinische und histopathologische Einflussfaktoren auf das Anfallsoutcome nach Gangliogliom Resektionen
Clinical and histopathological factors influencing seizure outcome after ganglioglioma surgery

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Objective

Gangliogliomas (GG) are glioneural tumors causing refractory epilepsy, often early in life. Neurosurgical resection can control or even cure seizures. However, postoperative recurrence of the epileptic seizures can occur. CD34 and BRAF-V600E mutations are well described histopathological markers but their influence on clinical behavior remains debated. We therefore aimed to analyze how these and clinical factors influence seizure outcomes after ganglioglioma surgery.

Methods

We performed a retrospective analysis of patients with histologically diagnosed gangliogliomas and epileptic seizures treated at our center. Seizure outcomes are reported according to the ILAE classification. BRAF-V600E mutation status and CD34 were detected immunohistochemically.

Results

Sixty-one patients, median age 16.1 years (IQR 11.0-28.9), were included in the analysis. The median follow-up time was 5.0 years (IQR 2.4-8.7). The majority of GG, 72.1%, were found in the temporal lobe followed by frontal (11.5%) and parietal (9.8%) localization. One year after surgery, 41 patients (67.2%) had a seizure outcome graded as ILAE class Ia or I. Residual tumor tissue was suspected on MRI in 20 cases (32.8%) and a second operation was performed in 15 patients (24.6%), which ultimately led to 50 patients (82.0%) being seizure free at the last follow-up. Fifty-nine GG were graded as WHO I and two were WHO II. A BRAF-V600E mutation was detected in 29 specimens (47.5%) and 56 specimens were CD34 positive (91.8%). Patients with BRAF had an earlier onset of epilepsy with a median age of 8.3 years vs. 15.2 years in patients, who were BRAF negative (p=0.020). Residual tumor was a strong predictor of early seizure recurrence in a Kaplan Meier analysis (p=0.018). In patients with complete tumor removal, BRAF mutation was a significant factor associated with shorter seizure free survival (p=0.027) but not in patients with residual tumor (p=0.178). We found no influence of BRAF or CD34 on tumor recurrence.

Conclusion

Resection of gangliogliomas can provide seizure control in a high percentage of patients. As previously described complete surgery appears to confer a benefit for patients. BRAF mutation seems to increase the epileptogenicity of gangliogliomas and should be studied further as a predictor of seizure relapse.

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Präparation von humanem kortikalem Zugangsgewebe für translationale Forschung
Surgical Preparation of Human Cortical Access Tissue for Human to Human Translational Research

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Objective

The study of human brain tissue is gaining attention for analyzing (patho)-physiological and molecular mechanisms in health and disease. During neurosurgical procedures, notably brain tumor and epilepsy surgeries, cortical and subcortical access tissue that would typically be destroyed and discarded, may be used for clinical and basic neuroscientific investigations. The objective of this study is to describe the technical aspects of the microdissection and immediate treatment of human cortical access tissue for research, highlighting the measures needed to be taken in the operating theater to ensure standardized and optimal experimental results.

Methods

In multiple rounds of experiments (n= 61) we developed and refined surgical principles for the removal of cortical access tissue. Tissue was immediately immersed in cold carbogenated N-methyl-D-glucamine based artificial cerebrospinal fluid for electrophysiology and electron microscopy or specialized hibernation medium for organotypic slice cultures, respectively.

Results

The surgical principles of brain tissue microdissection were: 1) rapid preparation (40-120s) 2) minimization of mechanical trauma 3) avoidance of cauterization 4) irrigation to maintain visibility and avoid blood clotting 5) retrieval of sample without use of forceps or suction, ideally using a custom-made dissector 6) maintenance of cortical axis during preparation. After a single round of explanation, multiple surgeons adopted the technique to samples with a minimal dimension of 2-20 mm spanning all cortical layers and subcortical white matter. Small samples (5x5x5 mm) were ideal for electrophysiology. Organotypic slice models were cultivated for up to 14 days and were further used for the development of a human glioblastoma invasion model. No adverse events from sample resection were observed.

Conclusion

The technique of microdissection of human cortical access tissue is safe and easily adoptable into the routine of neurosurgical procedures. The standardized and reliable surgical extraction of human brain tissue lays the foundation for horizontal human to human (H2H) translational research on living human brain tissue.

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Erhöhte lokale peritumorale funktionelle Konnektivität steht in Zusammenhang mit der Entwicklung von Krampfanfällen bei Glioblastompatienten

Increased local peritumoral functional connectivity is associated with seizure development in glioblastoma patients

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Objective

More than half of all glioblastoma patients develop epilepsy, which significantly increases the burden of an already devasting oncological disease. Furthermore, increasing scientific evidence suggests that underlying altered neuronal activity may directly regulate the growth of glial malignancies through direct electrochemical synaptic communication, meaning that seizures can play a role in tumor growth. So far, the exploration of local tumor-peritumoral connectivity and their relation to epilepsy have been neglected. Here, we present a novel fMRI-based local biomarker related to the epileptogenic burden in glioblastoma.

Methods

31 treatment-naive glioblastoma patients (mean age: 66.58 ± 10.18 years) were included and underwent resting-state fMRI. Tumor lesions were segmented, and a peritumoral area was defined by dilating the tumor mask by 40 mm while subtracting the contrast-enhancing tumor lesion. While controlling for tumor volume, a novel marker of *local functional connectivity (LFC) synchronization* was analyzed using regional homogeneity defined by the temporal BOLD coherence within a set of a given voxel"s nearest neighbors.

Results

We investigate for the first-time LFC synchronization in the tumor and peritumoral area and found significant differences in the connectivity patterns in patients with and without preoperative epilepsy. Patients with preoperative epilepsy (n=11) showed more densely synchronized local activity (0.06 [CI -0.10, 0.23]) in the peritumoral vicinity than patients without epilepsy (-0.18 [CI -0.28, 0.09]), resulting in a significant difference between groups (t=3.473, p=0.002). In contrast to the peritumoral area, we did not observe a significant group difference in the tumor lesion itself (t=2.053, p=0.05).

Conclusion

Our novel biomarker describing *local* resting-state BOLD coherence suggests that the neural activity in epileptogenic glioblastoma is highly synchronized within its peritumoral vicinity. Our findings provide macroscopic insights into the heterogeneity of neuronal tumor activity. This might add to the development of personalized resection strategies targeting peritumoral hot spots that might influence both epileptogenesis and cancer neuronal integration.

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Antikonvulsive Therapie des *IDH*-Wildtyp Glioblastom basierend auf DNA Methylierungsklassen
Targeted Anticonvulsive Treatment of IDH-Wildtype Glioblastoma based on DNA Methylation Subclasses

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Objective

Seizures occur in one-third of glioblastoma patients, and in another third, seizures develop during the disease. Nevertheless, the choice of antiseizure medication (ASM) remains challenging, and many patients need an increasement of initial dosage or a polytherapy to achieve seizure control. Here, we investigated the efficacy of levetiracetam to achieve seizure control and define therapeutic targets in *RTK I*, *RTK II*, and MES glioblastoma.

Methods

We studied 163 patients with *IDH*-wildtype glioblastoma and DNA methylation was analyzed using the Illumina EPIC array. Differential methylation analysis was performed, examining differentially methylated CpG sites of genes that are therapeutic targets of the most clinically relevant ASM. To further identify RNA expression of these genes, we queried the TCGA database to identify tumors for which DNA methylation and RNA expression were available and vertically integrated both.

Results

Preoperative seizures were observed in 54 (33.1%) patients. Of these, 45 (83.3%) patients were treated with levetiracetam achieving seizure freedom in 51.1%. Subdivision into methylation subclasses revealed seizure freedom in 100% (5/5) of *RTK I* (Figure 1B) and 75.0% (9/12) of MES tumors. In *RTK II*, only 36.7% (11/30) were seizure-free. Additionally, the average daily dose of levetiracetam decreased in patients with *RTK I* and MES tumors during follow-up, whereas in *RTK II* tumors, the dose was increased. We analyzed target receptor genes of levetiracetam (*SV2A*), perampanel (*GRIA*), and benzodiazepines (*GABRR*). RNA expression revealed enrichment of *SV2A* in *RTK I* and MES but not *RTK II* tumors. However, *SV2B* and *SV2C* genes were upregulated in *RTK II*, highlighting its epileptogenic potential. Among the differentially methylated CpG sites of the *SV2A* gene, significant hypomethylation was observed in *RTK I* and MES subclasses, whereas *RTK II* subclass was significantly hypermethylated. Further analysis revealed gene enrichment of *GRIA1*, *GRIA2*, and *GRIA3* in the *RTK II* subclass. These results obtained from RNA expression were reflected in methylation profiling, with CpG sites of *GRIA* genes significantly hypomethylated in the *RTK I* and *RTK II* subclasses.

Conclusion

Our study provides evidence for DNA methylation-based anticonvulsant treatment in glioblastoma patients. According to our findings, levetiracetam achieves satisfactory seizure-free rates in *RTK I* and MES tumors, whereas perampanel may be the optimal ASM choice in *RTK II* tumors.

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Tumorassoziierte Epilepsie im ersten Jahr nach Hirntumoroperation und Fahrverbot
Tumor associated epilepsy and restriction of driving privileges in the first year after brain tumor surgery

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Objective

Primarily in order to prevent seizure related car accidents driving privileges are suspended for 3 months in Germany following brain tumor surgery, and in many cases (i.e. preop. seizures) for ≥12 months. However, the literature contains little pertinent data supporting such policies. The present study was conducted to investigate the postop. seizure incidence in the first year after brain tumor surgery.

Methods

The authors studied the occurrence of postoperative seizures in 523 patients undergoing surgery for a brain tumor (prospective cohort, 09/2021 – 09/2022: 313 & retrospective cohort, 01/2020-12/2020: 210). Relevant clinical data was obtained from the patients" charts and through telephone interviews.

Results

The series included 160 (30.6%) meningiomas, 135 (25.6%) glioblastomas, 111 (21.2%) metastases and 56 (10.7%) other gliomas. 135 (25.8%) of cases presented with seizure(s). Early postoperative seizures (EPS) were documented in 34 (6.5%) patients (1 yr. recurrence rate: 28.6%). At 3 months (excl. EPS) overall 57 (10.9%; prosp. vs. retrospect. cohort: 13.2 vs. 8.1%) patients reported further seizure(s). At 1 yr. the respective figure was 18.4% (prosp. vs. retrospect. cohort: 18.7 vs. 18.2%). 22/173 (12.7%) patients reported de-novo seizures at 1 yr. (incl. 15/166 [9.0%] cases with no preop. and no seizures at 3 months). Statistically significant predictors of seizures at 1 yr. included presentation with seizures ($p<0.001$), an adverse preop. and postop. KPI ($p=0.038$ & $p=0.001$), as well as histology (e.g. meningiomas: 7.5%, metastases: 22.0%, glioblastomas: 38.5%, other gliomas: 18.8%; $p<0.001$). 219/318 assessable patients were not driving >3 months. Reasons included no driver"s license (6.3%), death (7.9%), neurological deficits (38.4%), epilepsy (9.0%), and personal choice (12.9%). 91.3% of glioblastoma patients did not drive >3 months (cf. metastases: 77.8%, other gliomas: 72.4%, meningiomas: 43.8%; $p<0.001$).

Conclusion

A substantial number of patients reported seizures in the first year after brain tumor surgery. This includes a >10% rate of de-novo seizures and many cases presenting >3 months. These figures support restricting driving privileges for 3 months and often longer. Generally higher seizure incidence figures were documented in the prospective cohort. Retrospective studies may underestimate the role of epilepsy in patients after brain tumor surgery. However, epilepsy related issues played only a secondary role among reasons for not driving >3 months.

Rapid Communication Tumor und Epilepsie/*Rapid communications Tumor and epilepsy*

V346

Koexistente extratemporale MRT-Läsionen bei Patienten mit Temporallappen-Epilepsie und Hippocampussklerose haben keinen Einfluss auf das Langzeit-Anfallsoutcome nach Epilepsiechirurgie

Coexistent extratemporal MRI lesions in patients with temporal lobe epilepsy and hippocampal sclerosis do not have impact on long-term seizure outcome after epilepsy surgery

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Objective

About 30% of patients with temporal lobe epilepsy (TLE) develop resistance to antiepileptic medications. Postoperatively, high seizure-free rates can be achieved in patients with mesial TLE caused by unilateral hippocampal sclerosis (uHS). In some candidates, coexisting ipsilateral or contralateral extratemporal lesions (eTL) such as non-specific gliosis or cortical defects are found on pre-surgical MRI. These patients are often thought to have a lower probability of achieving seizure freedom. However, the current data for this subgroup of TLE patients is insufficient. The aim of the study was to evaluate the influence of eTL on long-term seizure outcome in patients with uHS and coexisting eTL compared to patients with uHS as the sole pathology.

Methods

Of the 93 eligible consecutive patients with TLE due to uHS, 88 patients with complete data on long-term follow-up (minimum of 2 years post-surgery) were included. Patients with uHS alone formed group A (n=72), those with an additional eTL on MRI formed group B (n=16). Seizure outcome was classified according to the ILAE classification.

Results

The patient demographics regarding the gender distribution (male 58% vs. female 44%), the mean age at epilepsy-onset (6 years ± 12.6 vs. 15 years ± 15), and the duration of the epilepsy (23.6 years ± 14 vs. 20 years ± 15.7) show no significant difference for groups A and B. Moreover, the mean follow-up (FU) duration was 3.2 years ± 2.4 in group A vs. 4.19 years ± 1.47 in group B and was not significantly different. The uHS in group B was more frequently located in the left hemisphere (87.5% vs. 47.7%, p=0.004). Subsequently, in group A, seizure freedom (ILAE class 1) was observed in 83.3% of the patients in long-term FU, whereas in group B, 75% achieved seizure freedom. There was no significant difference between both groups regarding the seizure outcome.

Conclusion

In this study, we were able to show that the presence of coexisting eTL in MRI in patients with TLE and uHS did not have an influence on the probability of postoperative seizure freedom after epilepsy surgery. These results should be taken into account in the pre-surgical counseling of suitable and carefully selected candidates for resective epilepsy surgery.

Rapid Communication Funktionelle Neurochirurgie III Stimulation von Thalamus und STN/SN/*Rapid communication Functional Neurosurgery III Thalamic & STN/SN stimulation*

V348

Tiefe Hirnstimulation des Nucleus Subthalamicus bei Morbus Parkinson. Vergleich der normalisierten Genauigkeit und klinischen Ergebnissen bei Wachoperation vs Vollnarkose
Awake Versus Asleep Subthalamic Nucleus Deep Brain Stimulation in Parkinsons Disease: Comparison of Normalised Target Accuracy and Clinical Outcomes

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Objective

Traditionally, studies comparing awake and asleep Deep Brain Stimulation (DBS) for estimation of accuracy have measured the deviation of final lead position from the *intended* position, as opposed to the distance from *actual* target location. This allows introduction of bias in accuracy assessment.

Methods

To compare the lead placement accuracy between awake and asleep Subthalamic Nucleus-DBS (STN-DBS) in patients with Parkinson"s Disease (PD), three-dimensional electrode localization and target analysis was used. Then, estimation of accuracy was done by analysing the proportion of electrode contacts residing within the STN and its sub-regions, employing MATLAB™ based *Lead-DBS* and *Lead-Group* toolboxes. Groups were compared for motor and quality-of-life outcomes at one year which were assessed using Unified Parkinson"s Disease Rating scale (UPDRS) and Parkinson"s Disease Questionnaire-39 (PDQ-39) scores, respectively. Additionally, one-year cognitive outcome was compared using a composite cognitive score.

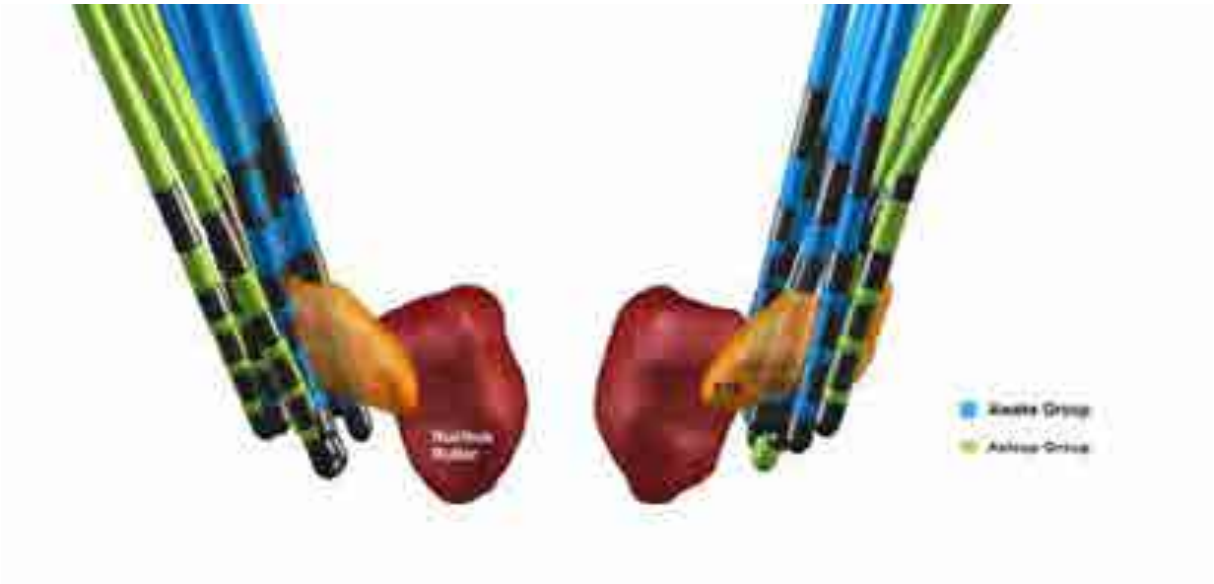
Results

Of the 27 patients analysed, 16 underwent awake while 11 patients underwent asleep DBS. Both awake and asleep groups were noted to have a similar proportion of contacts located within the motor-STN (111/224 (49.55%) versus 91/168 (54.16%); $X2[1, N = 392] = 0.82$; $p = 0.368$. The mean improvement in groups in terms of PDQ-39 and UPDRS scores was not significantly different at one-year follow-up. Awake group had a greater proportion of patients showing significant cognitive decline; however, this difference was not significant (50% vs 12.5%; p=0.093).

Conclusion

Three-dimensional electrode localization with target analysis is a useful strategy for estimating accuracy of lead placement. We observed that intraoperative macrostimulation performed during awake DBS surgery provided no additional benefit in targeting the motor-STN with greater accuracy. Evidently, awake DBS surgery had no meaningfully superior benefit in motor improvement or, quality of life. Additionally, awake group displayed a trend towards worse cognitive outcomes at the end of one year in our patient population.

Abb. 1



Rapid Communication Funktionelle Neurochirurgie III Stimulation von Thalamus und STN/SN/*Rapid communication Functional Neurosurgery III Thalamic & STN/SN stimulation*

V351

SPECTRE imaging - THS Implantation basierend auf individueller MR Konnektivität des Nucleus subthalamicus
SPECTRE imaging - DBS implantation based on individual MR connectivity of the subthalamic nucleus

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Objective

To investigate whether motor improvement after STN-DBS can be associated with individual structural connectivity analyzed by Subject sPEcific brain Connectivity display in the Target REgion (SPECTRE) which is an instance of track weighted imaging (i).

Methods

Patients with Parkinson's disease, that had given informed consent to our DBS Registry were selected for this analysis, if the following was true: (1.) availability of the following: preoperative Med OFF and postoperative follow up Med OFF Stim ON values (12-36 months postOP) of MDS-UPDRS III, preoperative 3T MRI including dMRI, postoperative CCT, stimulation parameters at follow up. (2.) Bilateral volumes of activated tissue (VAT, simulated with Brainlab Guide XT) contained STN (segmented with an inhouse trained convolutional neural network) at a proportion ≥ 0.4. For generation of individual SPECTRE maps limbic/motor/associative (green/blue/red) cortical schemes defined in MNI space are warped to subject space (cf. i) and in a tract weighting approach 500 probabilistic streamlines per voxel are seeded in the VATs to compute their cortical associations (Fig. 1). The overall maximum of the motor connectivity (blue) of both VATs (left/right) is used to predict motor performance. Postoperatively remaining relative motor disability was calculated as the ratio of MDS-UPDRS III follow up values divided by preOP values. A linear regression analysis was calculated to estimate the relation between the variables maximum individual motor connectivity, VAT size and remaining relative motor disability.

Results

30 patients from our DBS-Registry fulfilled the criteria and were included in the analysis. The regression analysis found a significant effect ($F(2, 27) = 4.919$, $p = .015$, $R2 = .27$) where individual connectivity of the VAT with the motor cortex was inversely associated with remaining relative motor disability ($t = -2.95$, $p = 0.006$, Fig. 2) while VAT size was not a significant predictor ($t = 1.73$, $p = .095$). Interestingly, the found association is not significant anymore when including patients where the VATs are farther away from STN (omitting constraint 2). For those, the adjacency to the STN itself becomes a significant predictor.

Conclusion

SPECTRE imaging can explain treatment effects based on connectivity on the single subject level and has the potential to improve image based DBS programming and targeting for DBS implantation.

References:

(i) Reisert M et al. Hum. Brain Mapp. 42, 2309–2321 (2021)

Abb. 1

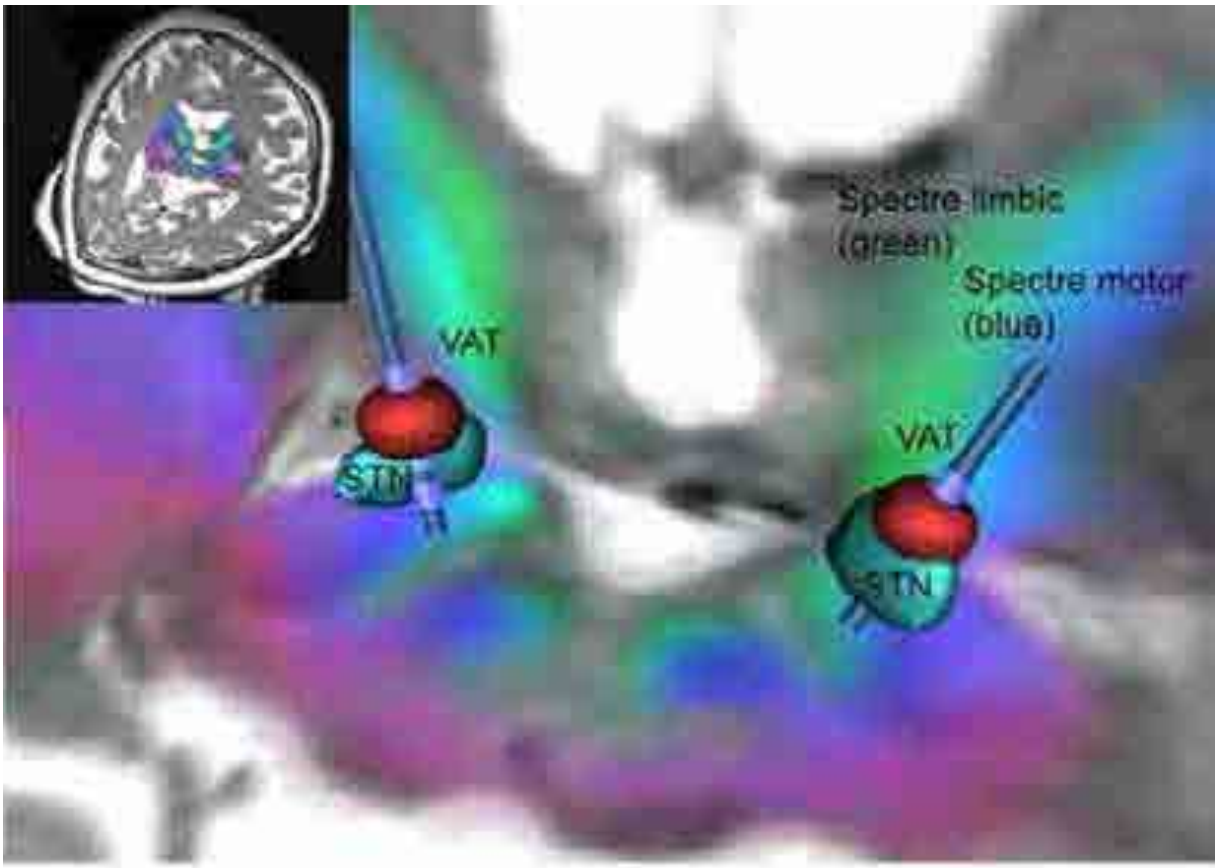

Figure 1: Bilateral VATs addressing the STN in an exemplary patient superimposed on color-coded SPECTRE map of individual midbrain connectivity to the cortex.

Abb. 2

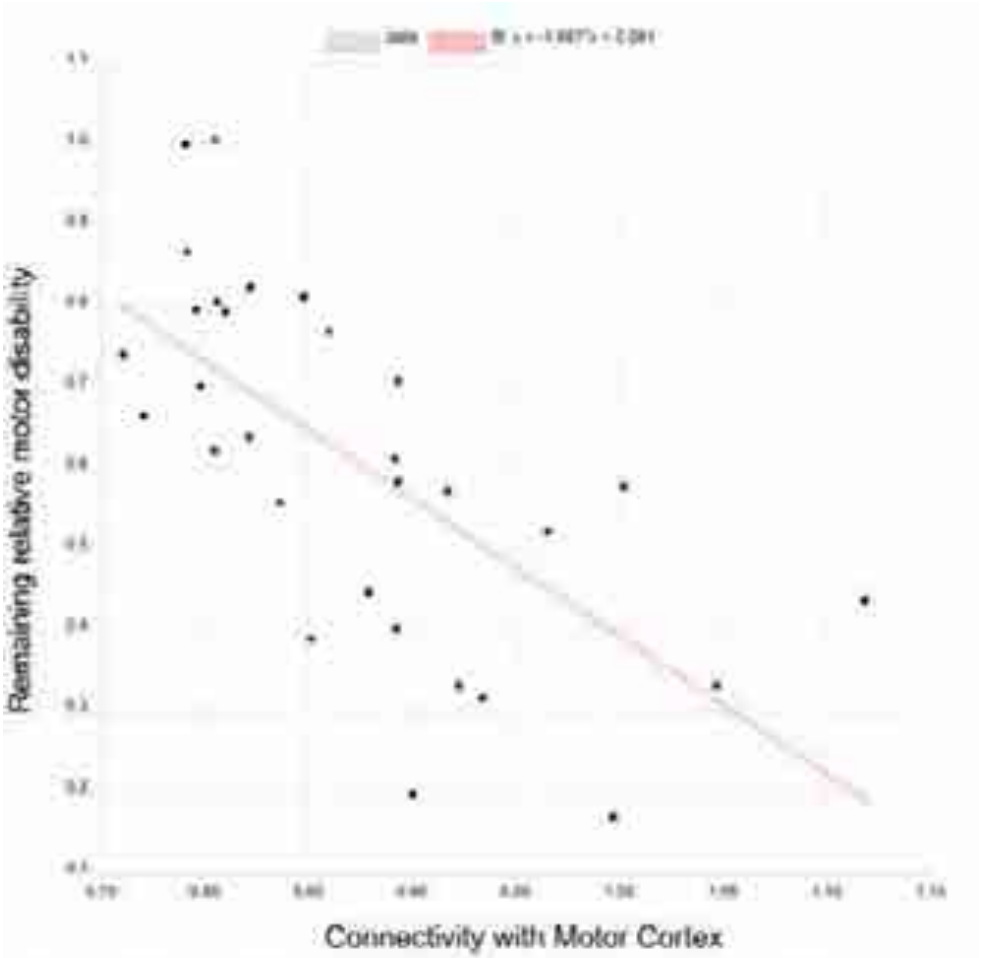

Figure 2: Association of remaining relative motor disability and maximum individual connectivity of both VATs with the motor cortex with each dot representing a patient. Regression line in red.

Rapid Communication Funktionelle Neurochirurgie III Stimulation von Thalamus und STN/SN/*Rapid communication Functional Neurosurgery III Thalamic & STN/SN stimulation*

V354

Ist der Dentato-Rubro-Thalamische Trakt (DRTT) die gemeinsame Struktur in der Vermittlung tremor-reduzierender DBS-Effekte bei Essentiellem Tremor und Morbus Parkinson?

Is the Dentato-Rubro-Thalamic Tract (DRTT) the joint structure mediating tremor reducing DBS effects in Essential Tremor and Parkinson's Disease?

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Objective

Alterations in the functional cerebellar-thalamic-basal ganglia-cortex network have been previously discussed as pathophysiological correlates rather than specific local pathologies for Essential Tremor (ET) as well as Parkinson's Disease (PD). A possible cause for the expression of the three cardinal symptoms of PD could be a partial overlap of different neural circuits within this network. The aim of our study was to evaluate the influence of the Dentato-Rubro-Thalamic Tract (DRTT), representing the main cerebello-thalamic fiber tract, on clinical tremor control derived by DBS in ET and PD.

Methods

Two cohorts of patients with ET (n= 10, 80 electrode contacts) and with PD (n=14, 112 electrode contacts) were independently analyzed. 3T-MR-imaging was performed including DTI-scans with 64 gradient directions with patients under general anesthesia. We used a workflow for probabilistic tractography based on FSL 6.0.3 to depict the course of the crossing and the non-decussating part of the DRTT (ndDRTT/ cDRTT). Distances of electrode contacts to the two parts of the DRTT were measured based on automatically derived distance maps. Results were correlated with clinical tremor control for each electrode pole.

Results

In the ET-cohort, effective contacts regarding control of postural tremor were located significantly closer to both parts of the DRTT than less-effective contacts (cDRTT $p<0.001$, ndDRTT $p<0.05$) in analysis of voltage-steered systems. For intentional tremor, this result could only be retraced for the cDRTT ($p<0.01$). Logistic regression analyses showed stronger correlations between clinical effectiveness and distances to the cDRTT than to the ndDRTT. In the PD-cohort, effective contacts were significantly closer to the c-DRTT compared to less-effective contacts ($p<0.05$). This correlation was also found in logistic regression analysis.

Conclusion

Significant correlations between the tremor reducing effectiveness of electrode contacts and the distance to the cDRTT were found both in ET- and PD-patients. Therefore, the cDRTT could possibly represent a common structure mediating tremor reducing DBS effects regardless of the underlying pathology.

Rapid Communication Funktionelle Neurochirurgie III Stimulation von Thalamus und STN/SN/*Rapid communication Functional Neurosurgery III Thalamic & STN/SN stimulation*

V355

Ein diagnostischer Marker für den verzögerten Wirkverlust nach thalamischer tiefer Hirnstimulation bei essentiellem Tremor

A diagnostic marker for delayed therapy escape after thalamic deep brain stimulation for essential tremor

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[3]Universität Freiburg, Institut für Sport und Sportwissenschaften, Freiburg i. Breisgrau, Deutschland
[4]Universitätsklinikum Freiburg, IT-Abteilung, Neurozentrum, Freiburg i. Breisgrau, Deutschland
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Objective

Delayed therapy escape is a serious yet frequent condition after thalamic deep brain stimulation (DBS) for essential tremor. It is a complex phenomenon and often associated with ataxia that leads to a significant decrease in quality of life. Due to the gradual evolution of the process, early recognition remains difficult. Hence, we aim to identify a diagnostic marker for delayed therapy escape to improve diagnosis and improve patient outcomes.

Methods

31 patients with bilateral thalamic DBS for essential tremor gave informed consent and were included. Tremor, ataxia, and gait were assessed through operationalized and quantitative analyses including video-based motion capture, the Fahn-Tolosa-Marin-Tremor-Rating Scale (FTMTRS), and the Scale for the Assessment and Rating of Ataxia (SARA). Examinations were carried out with activated DBS (ON) and directly after deactivation (OFF). We focused on quantitative tremor analysis of the left arm, as the left hand was usually more affected. If available preOP FTMTRS values were gathered. A higher FTMTRS more than 12 months after surgery compared to the score before DBS implantation indicated delayed therapy escape. To identify potential hallmarks of therapy escape, exploratory correlation analyses were conducted using a Pearson"s product-moment correlation coefficient between quantitative tremor features and clinical scores indicating therapy escape and ataxia. Test validity was assessed by computing receiver operating characteristics (ROC) curves.

Results

PreOP FTMTRS scores were available for 16 patients, among them 5 patients with therapy escape. High values for the ratio of FTMTRS now versus preOP were associated with higher total power of postural tremor at OFF (r = 0.779) and lower tremor frequency at OFF (r = -0.625), both on the left side (Fig. 1). The ratio of these two parameters (Power LOFF/Freq LOFF) yielded the highest pearson"s correlation coefficient (r = 0.791) and an area under the curve of 0.89 in the ROC analysis (p = 0.0149) (Fig2). Further, it correlated with high SARA values (r = 0.694) and decreased step length (r = -0.784) at ON, both signs of ataxia (Fig. 1).

Conclusion

Frequency of postural tremor at OFF on the left side was previously suggested as an indicator of therapy escape (Sajonz et al. 2022). Here a low-frequent and high-power postural tremor at OFF using the ratio of Power LOFF/Freq LOFF was superior for identifying therapy escapers and might be a valuable diagnostic tool in the future.

Abb. 1

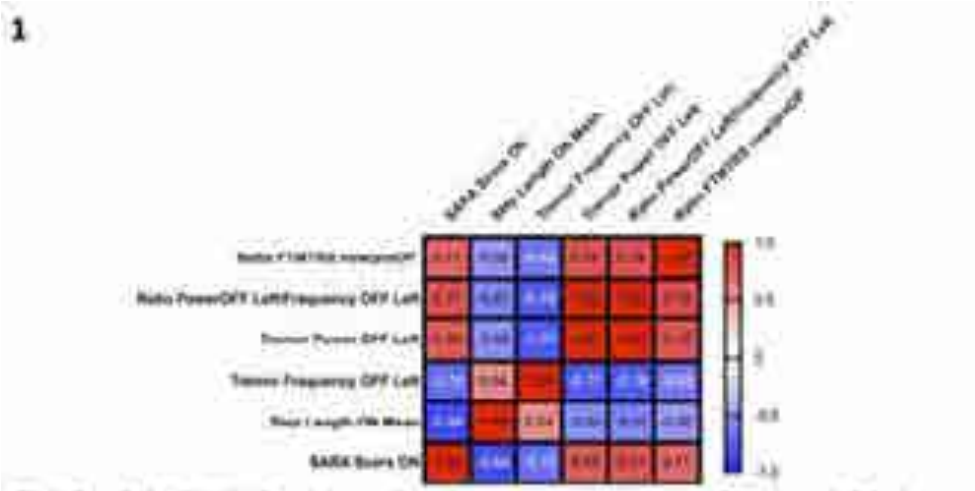

Fig 1. Correlation Matrix. Correlation analyses between quantitative tremor features and clinical scores using a Pearson's product-moment correlation coefficient. Red colour implies positive and blue colour negative correlation.

Abb. 2

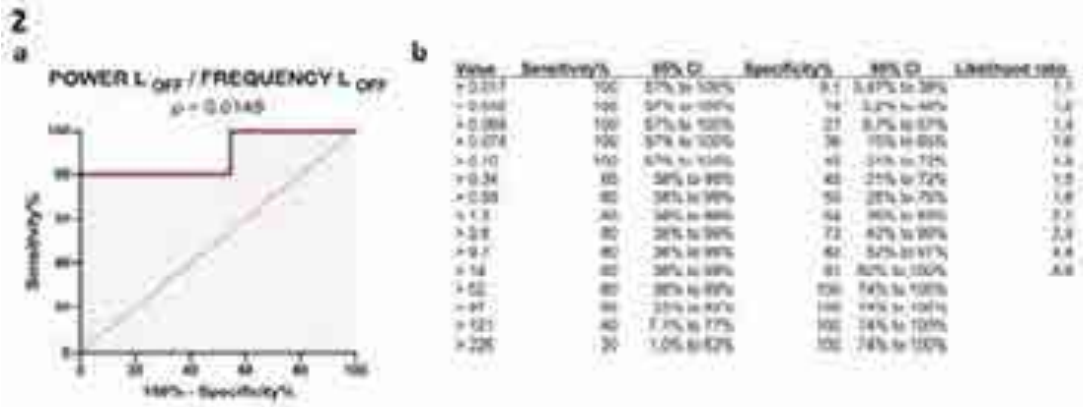

Fig 2. ROC. a ROC curve of ratio between postural tremor power and frequency left at stim OFF to detect therapy escape ($p = 0.0149$). **b** Classification table.

Rapid Communication Funktionelle Neurochirurgie III Stimulation von Thalamus und STN/SN/*Rapid communication Functional Neurosurgery III Thalamic & STN/SN stimulation*

V356

Tiefe Hirnstimulation des Thalamus zur Behandlung des dystonen Kopftremors

Thalamic deep brain stimulation in patients with dystonic head tremor: an observational study

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Objective

Dystonic head tremor (DHT) is a particular manifestation of cervical dystonia which poses several challenges for treatment. Deep brain stimulation (DBS) has evolved as a well established therapy for cervical dystonia for patients, who do not respond sufficiently to pharmacotherapy or botulinum toxin injections. However, for treatment of the tremor component in dystonic head tremor pallidal DBS has shown moderate results. In patients with other forms of tremor, like essential tremor and tremor in Parkinson"s Disease stimulaton of the thalamic ventral intermediate nucleus (Vim) has been applied very successfully. Therefore Vim-DBS was also tried in DHT treatment, but only limited to very few cases. We here report a larger case series with long-term follow-up of chronic bilateral Vim DBS in patients with DHT.

Methods

Data of a consecutive series of 21 patients with DHT, who underwent stereotactic CT-guided bilateral implantation of DBS electrodes into the Vim was analyzed retrospectively. Pre- and postoperative dystonia was assessed using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) and head tremor with the modified Fahn-Tolosa-Marin Tremor Rating Scale (mFTMTRS), which included tremor amplitude and duration of the head tremor.

Results

Patients significantly benefitted from Vim DBS with a mean tremor reduction from 7.95 points preoperatively to 2.35 points ($p > 0.05$) postoperatively in the mFTMTRS. Moreover, the dystonic component of the DHT was markedly improved. The BFMDRS motor score decreased from 16.72 to 9.82 points ($p > 0.05$) as well as the BFMDRS disability score, which decreased from 4.6 preoperatively to 3.2 points ($p > 0.05$) after implantation of DBS. Improvement was sustained after 24 months of chronic DBS.

Conclusion

Vim DBS shows a significant decrease in tremor as well as dystonic symptoms. Long-term follow-up confirms that it is an efficient treatment for DHT. Our results indicate that Vim DBS in DHT might be superior to GPi DBS.

Rapid Communication Funktionelle Neurochirurgie III Stimulation von Thalamus und STN/SN/*Rapid communication Functional Neurosurgery III Thalamic & STN/SN stimulation*

V357

Richtungsabhängige Aufzeichnungen somatosensorisch evozierter Potenziale aus dem sensorischen Thalamus bei chronischen Schmerzpatienten nach Schlaganfall

Directional Recordings of somatosensory evoked potentials from the sensory thalamus in chronic poststroke pain patients

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Objective

The aim of this feasibility study is to investigate the properties of median nerve SSEPs recorded from DBS leads in the sensory thalamus. Furthermore, we attempt to correlate the SSEP amplitudes with stimulation-induced paraesthesia and anatomical lead position.

Methods

Four consecutive patients treated for chronic central post-stroke pain were analyzed. DBS electrodes were placed in the ventrocaudalis nucleus of the thalamus (VC) and median nerve SSEPs were recorded with directional electrodes. We fused the postoperative CT scan with the preoperative MRI and projected the resulting image onto a stereotactic human brain atlas. Early postoperative clinical paraesthesia mapping was performed. Finally, we carried out frequency and time-frequency analyses of the signals.

Results

A directional effect of SSEP amplitudes was observed from thalamic contacts in the VC, with highest amplitudes over electrodes 3 and 6, which did not correlate with the expected sources of SSEPs based on anatomical images. However, the contacts of highest amplitude correlated with the contacts of lowest effect-threshold to induce paraesthesia. The contact of highest amplitude of high frequency components (HFC) did not necessarily correlate with the contact of highest SSEP amplitude.

Conclusion

Our findings provide compelling evidence in support of the somatotopy of the sensory thalamus. To our knowledge, we are the first to observe a directionality in subcortical SSEPs. Directional SSEP recordings might be a promising clinical tool to identify the neurophysiological sweet spot in the sensory thalamus in patients undergoing DBS treatment for pain. The lack of systematic correlation between contacts of highest HFC amplitude and highest SSEP amplitude may be an indicator of different sources. Future study of thalamic SSEP HFC might lead to a better understanding of pain processing in the thalamus.

Abb. 1

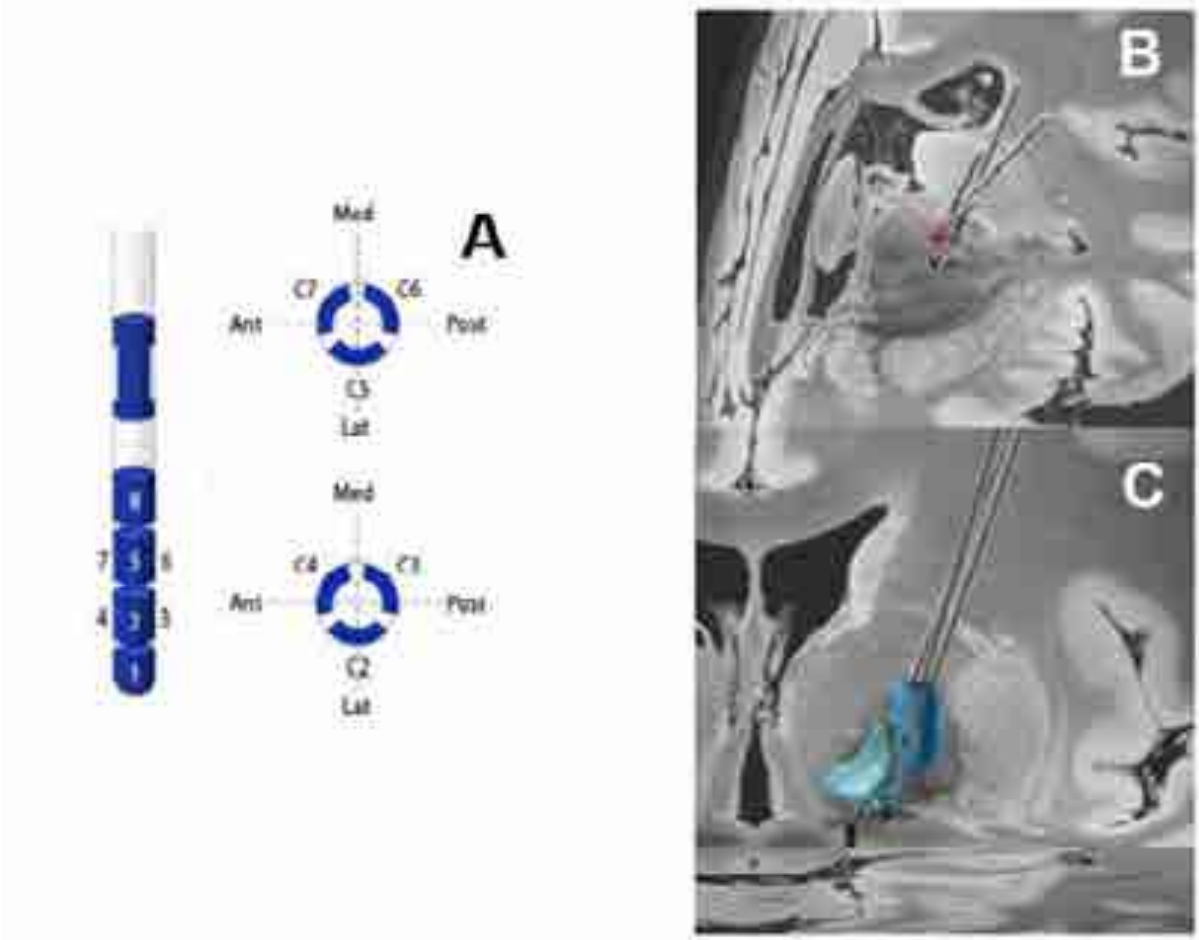

Fig. 1. DBS electrode and location. (**A**) Representation of the DBS directional lead electrode. (**B, C**) Location of the DBS electrodes in the four patients.

Abb. 2

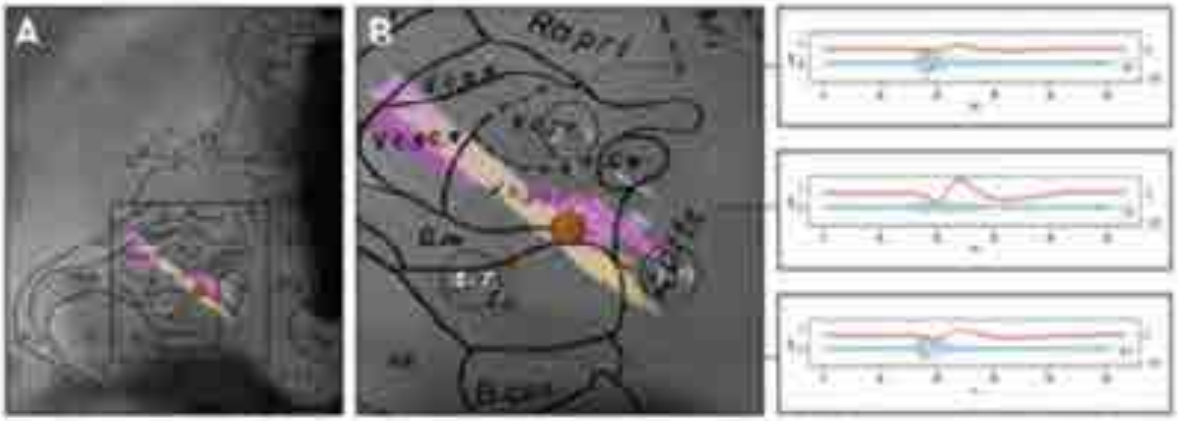

Fig. 2. Directional SSEP amplitude correlated with anatomical images. On the left: fusion of preoperative MRI with postoperative CT projected onto stereotactic human brain atlas. On the right: low frequency component (red), and high frequency component (blue) for the three bipolar montages of one patient.

Rapid Communication Trauma und Infektion/*Rapid communication Trauma and infection*

V358

Analyse des bakteriellen Spektrums eitriger Wirbelsäuleninfektionen und deren Einfluss auf den klinischen Verlauf

Bacterial spectrum analysis of pyogenic spinal infections and its influence on the clinical course

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Objective

To analyze the bacterial spectrum of pyogenic spinal infections (PSI) and to establish a correlation with clinical complications.

Methods

In total, 187 treated patients with PSI and isolated pathogen between 2002 and 2021 were included. The following data were analyzed: bacterial species detected detected in the samples, type of infection, clinical complications, spine localization, length of stay (LOS) in hospital and at the intensive care unit (ICU), relapse, mortality, and source of infection.

Results

Methicillin-susceptible *Staphylococcus aureus* (MSSA, n=100, 53%) was the most commonly isolated pathogen, was significantly frequent associated with meningitis (24% vs. 11%, p=.031) and with PSI in the cervical spine (41% vs. 21%, p=.004), compared with other bacterial species. Moreover, MSSA was more frequently associated with skin infections (41% vs. 16%) and epidural administration (18% vs. 9%, p=.005). Methicillin-resistant *Staphylococcus aureus* (MRSA, n= 5, 2.5%) increased the LOS in hospital (56d vs. 32d) and at the ICU (30d vs. 6d), in comparison with other pathogens. In contrast to other pathogens, coagulase-negative *Staphylococci* (CoNS, n= 20, 11%) was associated with a shorter LOS at the ICU (2d vs. 6d, p=.037), caused no meningitis (0% vs. 20%, p=.027) and less frequent a sepsis (20% vs. 54%, p=.004). CoNS resulted mainly from foreign body infections (12% vs. 4%), spinal screw associated infections (18% vs. 3%), port infections (18% vs. 4%), or late surgical infections (24% vs. 3%, p=.001). *Streptococcus* spp. and *Enterococcus*spp. (n= 31, 17%) caused frequently endocarditis (62% vs. 37%, p=.021) and occurred less frequently in the cervical spine (13% vs. 35%, p=.019). *Enterobacterales* (n= 20, 11%) in PSI occurred frequently in patients with urinary infections (50% vs. 4%, p<.001) and were less common to cause an endocarditis (11% vs. 46%, p=.003). Anaerobic bacteria (n=6, 3%) were identified only by intraoperative specimens. There was no significant difference in relapse and mortality between the subgroups.

Conclusion

Bacterial pathogens detected in PSI patients differ in terms of the source of infection, localization in the spine, and complications. Our data indicates that understanding the clinical complications of each PSI pathogen is important to guide individual patients" treatment.

Rapid Communication Trauma und Infektion/*Rapid communication Trauma and infection*

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Neuartige ambulante Behandlungsstrategie bei spinalen Infektionen – Eine Single-Center-Erfahrung
Novel Outpatient Treatment Strategy for Spinal Infections – A Single-Center Experience

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Objective

Spinal infections are difficult and tedious to treat. The general recommendation of a minimum of 4-to-6-week intravenous (i.v.) antibiotic therapy often is only possible in an in-hospital setting. At our hospital, were able to establish the possibility of outpatient intravenous antibiotic administration.

Methods

The aim of this study was to evaluate the usefulness of outpatient antibiotic therapy in spinal neurosurgery. For this purpose, we included all patients who received a peripherally inserted central catheter (PICC line catheter) for intravenous antibiotic therapy for spinal infections between 01/20 and 9/22. We evaluated the available patient data regarding the infectiological and neurosurgical parameters. All patients received i.v. antibiotics for at least 6 weeks (inpatient and outpatient).

Results

Fifty patients (22 female, 28 male, age (median+/- 1 SD) 65+/-14.18 yrs.) fulfilled the inclusion criteria. . The mean in hospital stay was 19,8 days (SD +/- 8.8 days) for the entire inpatient treatment. Subsequent mean outpatient antibiotic therapy was 70.3 days (SD +/- 18.2 days). Outpatient i.v. therapy accounted for mean 44.7 days (SD +/- 9.2 days). The most common pathogens were Staphylococcus epidermis and methicillin-sensitive Staphylococcus aureus. In 18%, microbiological testing detected no pathogen. 99% of patients showed neither radiographic nor laboratory evidence of spondylodiscitis or intra/extraspinal empyema in the final control. During outpatient therapy, a catheter-associated complication occurred in one patient with substance (heroin) abuse and a soft tissue abscess.

Conclusion

The transfer of prolonged antibiotic therapy for spinal infections to the outpatient area is achieved safely and efficiently using the PICC-Line. Inparticular, we were able to show this for patients of older age.

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Reduzierung tiefer postoperativer Wundinfektionen durch einfach zu implementierende Verfahren zur Infektionsprävention in der Wirbelsäulenchirurgie.

Reducing deep postoperative wound infections with easy-to-implement infection prevention procedures in spinal surgery.

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Objective

The purpose of this study is to investigate the incidence of surgical site infection and wound dehiscence requiring surgical intervention before and after the implementation of a bundle of infection prevention procedures, including wound and disc space irrigation with a modern antiseptic (sodium hypochlorite/hypochlorous acid), change of outer gloves at least every 3 hours and before implant manipulation, covering of implants and instruments when not used, and prolonged wound drainage in complex cases.

Methods

Retrospective review of patients that underwent dorsal spinal surgery for degenerative spinal diseases from 03/2019 to 06/2020 (Group A) and after implementation of new preventive measures from 07/2020 to 10/2021 (Group B). The primary outcome was surgical site infection and wound dehiscence requiring surgical intervention, and more specific, discitis/infectious spondylitis, as well as epifascial and subfascial wound problems. Fisher's exact test was used for statistical analysis.

Results

1001 patients were included, 524 in Group A and 477 in Group B. In both groups 20% instrumented fusions were performed. Overall, rates of surgical site infections and wound dehiscences requiring surgical interventions were not significantly reduced from 2.2% to 1.1% (p=0.21), in the subgroup of instrumented fusions from 6.2% to 2.2% (p=0.17). The incidence of discitis/infectious spondylitis was reduced from 0.5% to 0% (p=0.06). The ratio of discitis/infectious spondylitis to other wound problems was 45% to 55% in Group A, whereas it was 0% to 100% in group B (p=0,12). The ratio of subfascial to epifascial wound problems was 91% to 10% in Group A, whereas it was 20% to 80% in group B (p=0,01). No adverse effects of the antiseptic sodium hypochlorite/hypochlorous acid was observed.

Conclusion

Our results suggest a potential benefit of easily implemented preventive measures in reducing the risk for postoperative discitis/infectious spondylitis and shifting postoperative wound problems toward more benign epifascial complications. We hypothesize that the antiseptic (sodium hypochlorite/hypochlorous acid) considerably reduces potential intraoperative infectious contaminations and warrants further studies as an alternative to widely used local antibiotics that have shown problematic alterations in wound microorganisms.

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Das spinale glymphatische System - eine langzeit (7d) Darstellung der spinalen perivaskulären Räume im Mausmodel.

Spinal glymphatic clearance – a long term (7d) display of spinal perivascular spaces in a mouse model.

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Objective

CNS perivascular circulation - the so called "glymphatic system" is enjoying more and more attention. Its potential to transport and clear metabolites as well as drugs into and from neuronal tissue made it an ideal candidate for research in context of neurodegenerative and neuroinflammatory diseases of the brain. However, spinal cords perivascular clearance pathways and dynamics have not yet been properly characterized. Since acute and chronic spinal cord injuries are at least partially driven by an inflammatory component, there is an intrinsic neurosurgical interest to understand spinal cords perivascular clearance dynamics.

Methods

The fluorescence marker Alexa 594 was surgically injected into the cisterna magna of 40 male C57BL/6 mice. Eight animals were euthanized after 6, 12, 24, 72 and 168h respectively and spinal cords dissected for histological analysis. Axial slices were examined via fluorescence microscopy and analyzed using ImageJ version 2.1.0/1.53c to examine tracer distribution. GraphPad Prism v9.4.1 was used for statistical evaluation.

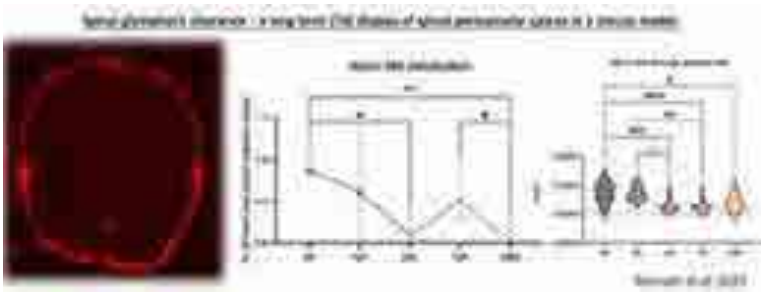
Results

Alexa 594 was found along intramedullary vessels and in the subarachnoid compartment at any given time point. Ordinary one-way ANOVA revealed a significant decrease in stained area of the axial slices over the observed period. A relative decline in stained area comparing 6h (100% ± 63) vs. 24h (15% ± 13;p<.05) 6h vs. 168h (19% ± 32; p<.01) and 72h (80% ± 100) vs 168h (0<.05) as shown by Tukey-test for multiple comparisons, suggests a polynomial function of clearance. The average size of fluorescent particles found within the myelon decreases significantly between 12 and 24h (3.6 ± 1.2x10-5 vs. 1.5 ± 1.1x10-5mm2; p<.05) after intrathecal injection of Alexa 594 displaying a distribution along smaller-caliber vessels.

Conclusion

We demonstrate a mouse model to perform medium to long-term observation of glymphatic circulation as a basis for comparative studies under pathological conditions. To our knowledge this is the first display of perivascular influx and long term circulation from subarachnoid space into the spinal cord and vice versa. Its role in spinal cord injury can be derived from multiple studies of the brains clearance but must be investigated further.

Abb. 1



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Longitudinale *in vivo* Zwei-Photonen Mikroskopie mittels eines implantierten Rückenmarksfensters ist bis zur chronischen Phase möglich nach experimentellem Rückenmarkstrauma in der Maus.

Longitudinal in vivo 2-Photon microscopy via an implanted spinal window chamber is feasible up to the chronic phase following experimental spinal cord injury in the mouse.

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Objective

In vivo microscopy contributes to a deeper understanding of pathophysiology and potential therapies after experimental spinal cord injury (SCI). An implanted spinal window chamber enables longitudinal imaging without the necessity for repeated surgery. Two-photon microscopy (2PM) is used as an advanced technique to image dynamic changes after SCI down to subcellular resolution in the living animal. We present the feasibility of an implanted spinal window chamber for chronic longitudinal *in vivo* 2PM and fluorescence videomicroscopy (IVM) from 1 up to 14 days post SCI in the mouse.

Methods

Adult C57BL/6J and Tg(Thy1-YFP)HJrs transgenic mice underwent low-thoracic (Th11/12) clip-compression SCI or sham-injury, followed by the implantation of a spinal window chamber for *in vivo* microscopy. Longitudinal *in vivo* 2PM (n=10) and IVM (n=4) were performed to image the de- and regeneration of blood vessels and axons at days 1, 3, 7 and 14 in up to 200µm depth. Neurobehavioral assessment (Catwalk®/Basso Mouse Scale) was performed at given time points and was compared to animals (n = 12) without chamber implantation. Histological analysis of tissue integrity and inflammation was performed at every timepoint.

Results

Chronic longitudinal *in vivo* 2PM and IVM was possible up to 14d after both SCI and sham injury and revealed extensive axonal and vascular damage after clip-compression SCI. The implantation of the chamber itself did not result in axonal or vascular changes in sham animals and only slight inflammation was observed. Animals with an implanted spinal window chamber only showed slight temporary differences in neurobehavioral analysis (Basso Mouse Scale 1d: p=0.008, 3d: p=0.05, 7-14d: p>0.05), and no differences in body weight (p>0.05) or histologically assessed spinal cord integrity compared with specimens without chamber implantation.

Conclusion

2PM and IVM after SCI via an implanted spinal window chamber is feasible up to the chronic phase after SCI and allows the comprehensive display of the spinal cord`s neuronal and vascular damage after clip-compression SCI in the living mouse.

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Die partielle Erholung der Integrität der Neurovaskulären Einheit ist assoziiert mit funktioneller Erholung nach experimentellem Rückenmarkstrauma im Mausmodell.

The partial recovery of the integrity of the neurovascular unit is associated with functional recovery after experimental spinal cord injury in the mouse.

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Objective

Spinal cord injury (SCI) is a leading cause of disability. The disruption of the blood-spinal-cord-barrier (BSCB) and the disintegration of the neurovascular unit (NVU) are main contributors to the secondary injury cascade after SCI. Previously, we have shown that neurological recovery after clip-compression SCI starts in the subacute to chronic injury phase and is correlated with the partial restitution of the BSCB. In this study we characterize the posttraumatic restitution of the integrity of the NVU in a mouse model up to 28 days after SCI.

Methods

Adult C57BL/6J mice underwent thoracic (Th6/7) clip-compression SCI (5g, 60s) or sham injury (2-level-laminectomy). Perioperative antibiotics and postoperative pain medication were applied. Neurobehavioral assessment (Catwalk® gait analysis and Basso Mouse Scale with Tally sub-score, n=33) and 7T MRI for tissue morphology analysis were performed at days 1, 3, 7, 14 and 28 post SCI. Immunofluorescent staining was performed to examine the disruption of functionally perfused vasculature (CD31+FITC-Lectin, n=4/group) and the neurovascular unit (NVU) (CD31+Cl5/VeC/Desmin, n=4/group).

Results

Vessel density in the trauma area was severely reduced during the first 3 days after SCI ($p<0.01$) and recovered by days 7-28 ($p>0.05$). FITC-lectin marked functional vessel density however decreased significantly for 14 days after SCI ($p<0.001$) and partially recovered only after 28 days ($p>0.05$). A disintegration of the NVU was seen up to 14 days after SCI through the loss of pericyte coverage ($p<0.05$), with recovery in the chronic phase ($p=0.032$). Tight junctions were significantly reduced in the acute phase 1d ($p=0.003$) after SCI and recovered after 7 days ($p>0.5$). Functional recovery started by days 7-14, with most animals regaining hindlimb function after 28 days.

Conclusion

The partial recovery of the integrity of the NVU and the recovery of functional vessel density over the subacute – chronic phase after SCI correlates with the partial restitution of BSCB integrity and functional recovery which we have previously shown. Further detailed examinations of the regenerative capacities and molecular players involved in the regeneration of the NVU and BSCB are necessary for the development of translational therapies.

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Systemische IL-4 Gabe nach traumatischer Rückenmarksverletzung begünstigt die funktionelle Regeneration durch Immunmodulation im Ratten-modell

Systemic application of IL-4 confers better functional recovery through anti-inflammatory effects after traumatic spinal cord injury in rats.

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Objective

Traumatic spinal cord injury (SCI) elicits local and systemic inflammation, limiting neuro-regeneration and contributing to lifelong disability, which is why tackling systemic stress cascades following SCI could be of interest. Hence, we determined the systemic effect of interleukin-4 (IL-4), an immune-modulator, on functional recovery, systemic inflammation, and local spinal cord regeneration upon its systemic application after SCI.

Methods

120 female Wistar rats were randomized for a laminectomy without (Sham) or with thoracic (Th10) clip compression/contusion SCI (IL-4, Placebo). SCI animals then received IL-4 or placebo intraperitoneally twice daily for 7 days. Function was assessed 3, 7-, 14-, 21- and 28-days post injury (dpi) via the CatWalk XT gait analysis, the BBB (Basso, Beattie, Bresnahan) openfield rating scale and the Gridwalk test (at 28 dpi). Rats were sacrificed at different timepoints (1, 3, 7, 14 and 28 dpi) and immunohistochemistry (IHC) was used to assess neuroinflammation, cellular neurodegeneration, and astrogliosis of explanted and cryosectioned spinal cords. Protein and RNA levels of different cytokines were measured in the serum and peripheral organs via flow cytometry/RT-PCR to assess systemic inflammation

Results

Rats with the IL-4 treatment showed a significantly better recovery of hind limb function, reflected by better BBB scores at 14 and 28 dpi and CatWalk XT gait analysis scores at 14 dpi. At 28 dpi, the IL-4 group demonstrated a lower rate of stepping-errors in the Gridwalk test. Mechanistically, a significantly higher ratio of anti-inflammatory M2- to pro-inflammatory M1-macrophages was observed using IHC in IL-4 treated rats compared to placebo rats 3 and 7 dpi. Furthermore, astrogliosis was significantly reduced with the IL-4 treatment 28 dpi. In terms of systemic inflammation, placebo-treated SCI rats showed significantly higher levels of pro-inflammatory serum cytokines compared to sham rats the acute to subacute post-injury phase, which was effectively suppressed using IL-4 treatment.

Conclusion

Systemic IL-4 application is associated with improved functional recovery after SCI in rats, possibly due to its local and systemic sub-acute immune-modulatory effects. In addition, neuroinflammation and tissue scarring appear to be effectively reduced by the systemic application of IL-4. Further preclinical and ultimately translational studies on IL-4 in the context of SCI should be considered.

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Der zell-spezifische Knockout von endothelialem Ephrin-B2 führt zu aggravierter posttraumatischer Öffnung der Blut-Rückenmarksschranke in der akuten Phase nach experimenteller Rückenmarksschädigung.
Posttraumatic disruption of the blood-spinal-cord-barrier in the acute phase is aggravated by the endothelial cell-specific knock-out of Ephrin-B2 signaling after experimental spinal cord injury.

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Objective

The disruption of the blood-spinal-cord-barrier (BSCB) is a leading pathophysiology in traumatic spinal cord injury (SCI) and its restitution plays a crucial role in spinal cord regeneration. The guidance molecule Ephrin-B2 promotes cell-cell-contacts in the neurovascular unit. However, its specific role in endothelial cells following SCI is unknown. With this study, we characterize the posttraumatic BSCB disruption and restitution dependent on the endothelial cell-specific knock-out (KO) of Ephrin-B2 in a mouse model up to 28d post SCI.

Methods

Adult CDH5-CreERT2-Efnb2$^{lox/lox}$ (KO) and littermate wildtype (WT) mice (m/f, n=94) underwent mid-thoracic (Th6/7) clip-compression SCI via modified aneurysm clip (5g, 60s) or sham-injury (two-level laminectomy). Endothelial cell-specific Ephrin-B2 KO was induced via the promotor CDH5 in a cre-lox-system with consecutive injections of tamoxifen (5d period). Neurobehavioral analysis was performed (n=14) using Catwalk® gait analysis and Basso Mouse Scale at 1, 3, 7, 14 and 28d post SCI. Additionally, *in vivo* 7Tesla-MRI was performed (n=10), and individual specimens were sacrificed for qualitative histological analysis at each time point (LFB+H&E; CD31+Evans-Blue, n=49). BSCB disruption was quantified using Evans-Blue fluorescence assay up to 14d post SCI (Tecan, n=45).

Results

Quantitative assessment of EVB-extravasation displayed a significantly increased BSCB disruption in KO SCI animals compared to WT SCI animals at 1d and 3d but not at 7 and 14d post SCI (1d: p=0,0097, 3d: p=0,0002, 7+14d: p>0.05). Neurobehavioral analyses showed no differences between KO SCI and WT SCI animals, with regaining of some hindlimb function in the course up to 28d post SCI in both groups, without between-group differences (1-28d: p>0.05).

Conclusion

Ephrin-B2 signaling plays a significant role in BSCB maintenance and repair in the acute injury phase, as the posttraumatic BSCB disruption is aggravated by the endothelial cell-specific KO of Ephrin-B2, leading to aggravated secondary injury. Whilst there is no significant difference in functional regeneration, further analysis must be performed to evaluate the regenerative effect and opportunities of the aggravated BSCB disruption.

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Behandlung von traumatischen Wirbelsäulenfrakturen: Vergleich des Ergebnisses des sagittalen Alignments zwischen dorsaler Stabilisierung und ventrodorsalem Ansatz

Treatment of Traumatic Spine Fractures: comparing sagittal alignment outcome between stand-alone posterior Stabilisation vs combined approach

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Objective

Previous studies showed the importance of correcting the deformity resulting from spine fractures, especially through restoring sagittal alignment and vertebral height. We aim to compare the radiological outcomes (sagittal index=SI and loss of vertebral body height=LVBH) for the management of traumatic fractures in the thoracic or lumbar spine between stand-alone posterior stabilisation (group I) and posteroanterior/combined approach (group II).

Methods

In this retrospective single-centre study, we included all patients with traumatic spine fractures (from Th1 to L5) who underwent surgical stabilisation between 01 January 2015 till 31 May 2021. Two clinicians independently examined the imaging and registered SI and LVBH values at baseline, after surgical stabilisation, and at follow-up (at least three months after treatment). The mean values of SI and LVBH among the two clinicians were used. An SI of 0 indicates a perfect sagittal alignment, and absolute values>0 mean an increased malalignment; an LVBH of 1 indicates no loss of vertebral height and values<1 mean an increased loss. A linear mixed-effects regression model was used to compare the SI and LVBH between the groups adjusted to baseline.

Results

Seventy-one patients (42 men) with a median age of 38 years (IQR 28 to 54) and a median follow-up of 4 months (IQR 3 to 17) were included, 32 in group I and 39 in group II. Forty fractures localised in the thoracolumbar junction (in Th12 or L1), 15 in the thoracic spine, and 14 in the lumbar. The regression model showed a better sagittal alignment in group II with an adjusted mean difference for SI of -4.24 (95% CI -7,13 to -1,36; p-value= 0.004) and a better restoration of vertebral body height with an adjusted mean difference for LVBH of 0.11 in the combined approach (95% CI 0,02 to 0,2; p-value= 0.02). There were nine postoperative complications in the whole cohort (4 in group I and 5 in group II).

Conclusion

A combined posteroanterior stabilisation of traumatic spine fractures improves the deformity through better sagittal alignment and increased vertebral body height, with accepted morbidity compared to the stand-alone posterior approach.

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Frakturen der ankylosierten Wirbelsäule - Signifikante Unterschiede bzgl. der Frakturmorphologie zwischen DISH und Spondylitis ankylosans (Morbus Bechterew)

Fractures in ankylosing spinal disorders – Differences in fracture morphology between diffuse idiopathic hyperostosis (DISH) and ankylosing spondylitis (AS)

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Objective

Fractures in ankylosing spinal disorders (ASD) are being diagnosed with increasing frequency. In addition to increasing life expectancy and demographic change, changes in the mobility and activity requirements of older people are discussed as reasons for this. In the literature, hyperextension injuries [HEI] in ASD in particular are often erroneously presented as a single entity.

Methods

In a cohort study, fracture morphology of HEI in ASD was analyzed. Between 01/1997 and 12/2021, 227 thoracolumbar HEI in 202 patients (55 women and 147 men, Ø age 73.1 ± 11.6 years, range 43-93 years) were prospectively recorded and followed up in a standardized fashion. Injury morphology of the anterior column was divided into 3 groups (transosseous, mixed, transdiscal) based on CT scans and supplementary MRI examinations, and that of the posterior column into 2 groups (predominantly osseous or ligamentous). The combination of anterior and posterior column injury categories resulted in six different types of HEI (figure 1). In addition, type of ASD, localization, concomitant injuries, type of care and complications were recorded.

Results

In the past 25 years, more than a tenfold increase in the number of patients with HEV of ankylosing spondylitis has been registered in our hospital (figure 2). 168 (74%) of the 227 HEI occurred in disseminated idiopathic skeletal hyperostosis [DISH] and 33 (15%) in ankylosing spondylitis. 26 (11%) lesions underlay other synostosis/ankylosis. HEV in DISH and ankylosing spondylitis differed significantly in injury morphology. Thus, in the subcollective of ankylosing spondylitis patients, bony injury of the posterior column was present in all cases (33/33), with predominantly (25/33, 76%) transosseous laceration of the anterior column. Pat. with DISH had a mostly incomplete ligamentous lesion of the dorsal structures in the majority (126/168, 75%), with transosseous involvement of the anterior column in 62 cases (37%), mixed involvement in 72 lesions (43%), and purely transdiscal involvement in 34 injuries (20%).

Conclusion

The different injury morphology has consequences for the therapy. While the HEV of the ankylosing spondylitis patients were in all cases highly unstable 2-column injuries, which mostly required long-segment posterior fixation. More than 30% of DISH patients had injuries with only hinge-like instability, which have been successfully treated conservatively.

Abb. 1

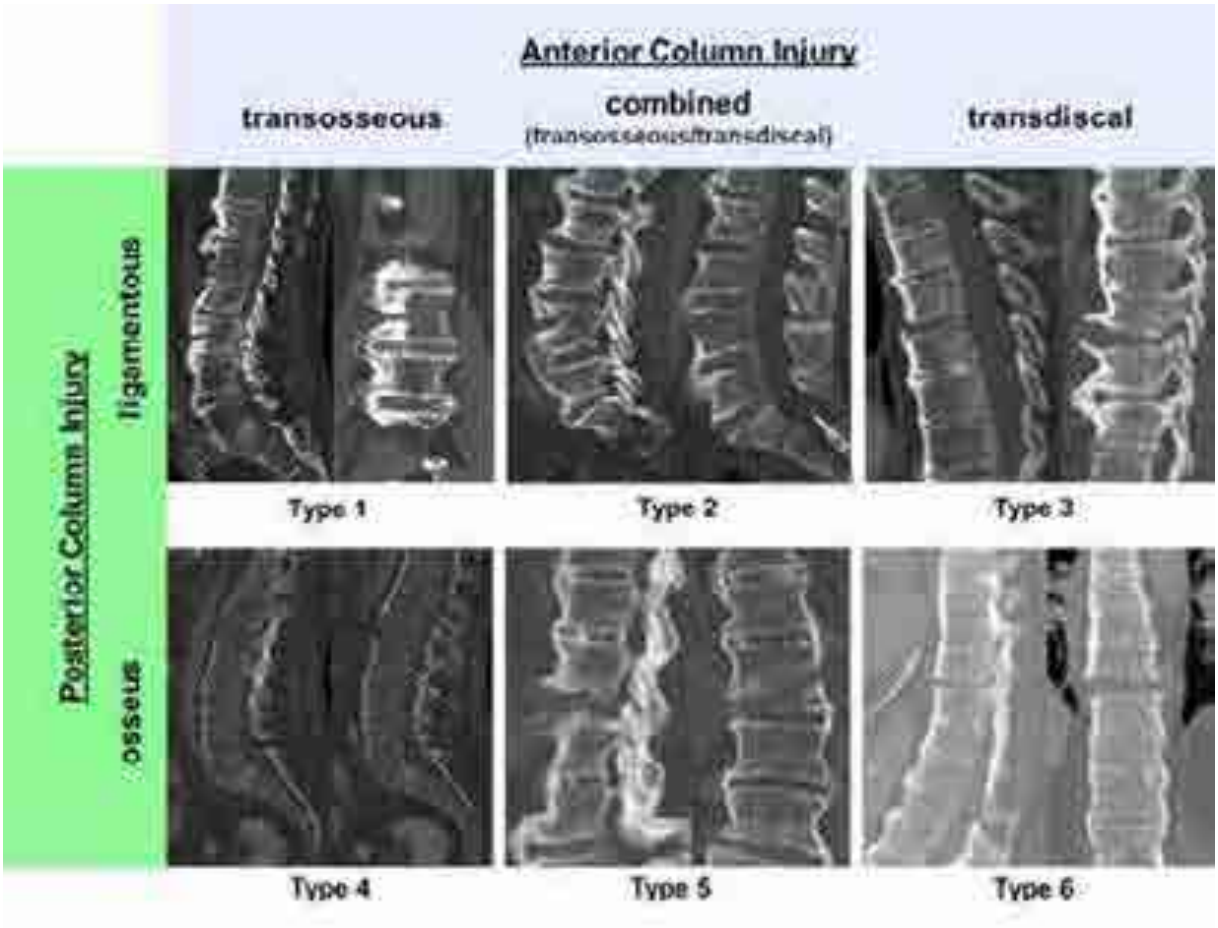
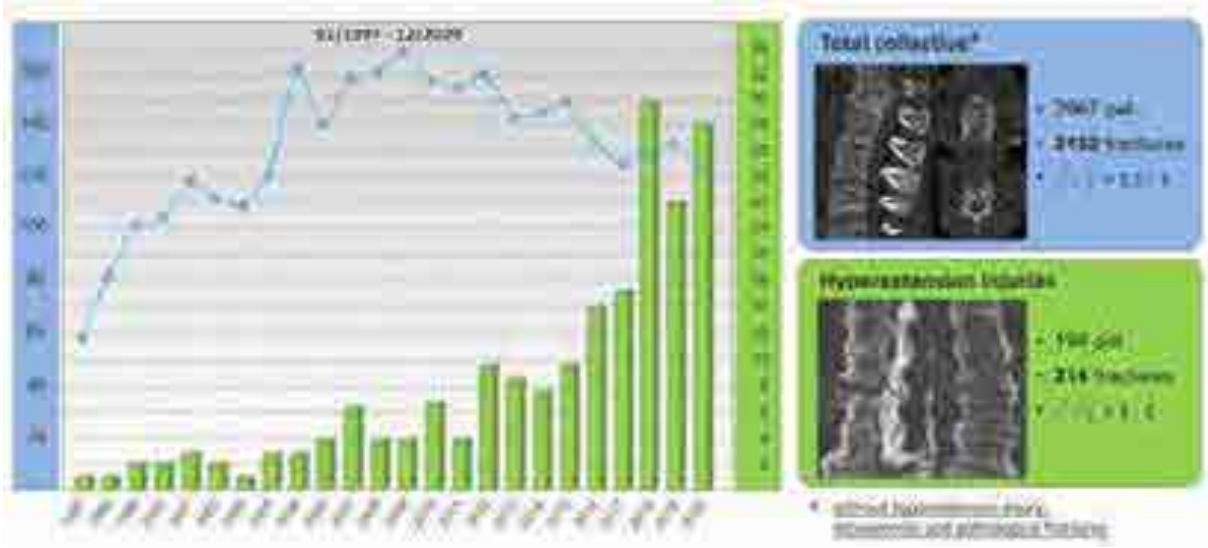

Anterior Column Injury
transosseous
combined
(transosseous/transdiscal)
transdiscal
Posterior Column Injury
ligamentous
osseus
Type 1
Type 2
Type 3
Type 4
Type 5
Type 6

Abb. 2



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Angst als Einflussgröße schlechten funktionellen Outcomes throrakolumbaler Wirbelkörperfrakturen - Ergebnisse der EOFTT-Studie

Adressing anxiety as a tool to provide poor functional outcome in patients with osteoporotic fracture of the spine - results of the EOFTT study

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Objective

Anxiety as an impact factor on the functional outcome of patients with osteoporotic vertebral compression fractures (OVCFs) of the spine has not been addressed in literature so far. But fearfulness and subjective well-being of a patient is known to be an important variable in healing processes. Studies purpose was to analyze, if anxiety has an impact on the functional outcome of patients with OVCF and if the individual fear is influenced during hospitalization.

Methods

The study was built as a prospective, multicentric cohort study, which included patients with OCVF during 2017 until 2020. To measure the functional outcome, mobility was evaluated as well as timed-up-and-go-test (TuG), Barthel-Index, Oswestry-Disability-Index and EQ5D-5L were performed. Additionally, trauma mechanism, analgetic medication and anti-osteoporotic therapy during hospitalization were documented to recognize, whether there is an influence on the measured fear itself. General linear model for repeated measures was used plus post hoc pairwise comparisons were carried out using 95% confidence interval. To measure the individual fear of a patient, the item anxiety/depression of the EQ5D-5L was used.

Results

A review over total data from 518 patients out of 17 different hospitals was made. Thereby, a significant correlation between fracture severity ($r=0.087$, $p=0.0496$) and anxiety could be found. Start of pain medication ($p<0.001$), anti-osteoporotic treatment ($p<0.001$) as well as the initiation of surgical therapy ($p<0.001$) during hospitalization were related to less anxiety. Furthermore, the fearfulness of a patient at discharge was reported

to negatively affect the functional outcome at the individual follow-up: TuG ($p<0.001$), Barthel index ($p<0.001$), ODI ($p<0.001$) and EQ5D-5L ($p<0.001$).

Conclusion

The presence of fear has an impact on the functional outcome after OCVF, which can be easily detected by the item anxiety/depression of EQ5D-5L. This may allow an easy and quick access to screen anxiety and offers the possibility of addressing it to provide poor functional outcome.

Rapid Communication Trauma und Infektion/*Rapid communication Trauma and infection*

V369

Minimalinvasive 3D-navigierte Osteosynthese von Insuffizienzfrakturen des Sakrums: Erfahrungen aus vier Jahren Praxis

Minimally invasive 3D-navigated osteosynthesis of fragility fractures of the sacrum: a single center's experience from four years practice

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Objective

The incidence of osteoporotic fractures of the sacrum is increasing due to the demographic change. With the evolution of computer navigation minimally invasive techniques became available. Aim of this study was to evaluate the surgical outcome and complication profile of minimally invasive computer navigated techniques in the treatment of fractures of the sacrum.

Methods

Records of all consecutive patients receiving minimally invasive computer-navigated osteosynthesis of fractures of the sacral bone between 2018-2021 were analyzed. Medical history, fracture morphology and etiology, clinical status and surgical as well as radiographic data of each patient were retrospectively assessed. Fractures were classified using the Fragility Fractures of the pelvis score (FFP). Patients were grouped according the applied technique: (1.) monoportal iliosacroiliac screws, 2.) biportal bilateral iliosacral screws, 3.) combination of 1.) and 2.)). Endpoints were mobility at discharge and follow up visit, screw loosening and surgical revision rate.

Results

Mean age of the 128 patients included in this study was 81 years. Of the 103 (80.5%) female and 25 (19.5%) male patients 82 (64%) suffered from low and 7 (5.5%) from high energy trauma. Atraumatic fractures were present in 39 (30,5%) cases. Osteoporotic fractures were the main indication (94.5%). All patients suffered from immobilizing pain. Main fracture type was FFP2 (47%) followed by FFP3 (27%) and FFP4 (18%). 48 patients (35,5%) were included in group 1, 33 patients (29,8%) in group 2 and 47 patients (36,7%) in group 3. Overall average incision-suture time was 62min ranging from 30-140min (group 1: 52min (30-91min); group 2: 82min (45-140min); group 3: 62min (35-103min)). Scheduled 1-year follow up appointments were kept by 66.4%. Documented screw loosening occurred in 11 (9.4%) cases (group 1: 7 cases (14.6%); group 2: 2 cases (13.6%); group 3: 2 cases (6.4%)). Compared to preoperative status, mobility at discharge and at follow up was improved in 100% of patients. The overall revision rate was 6.25%.

Conclusion

The different techniques of computer-navigated sacral fracture osteosynthesis presented here have proven to be safe and feasible minimally invasive procedures with an excellent postoperative outcome and a low overall complication rate. Concerning screw loosening during follow up, further investigation is required to identify risk factors.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V371

Versorgungspfade und ärztliche Entscheidungsfindung bei 376 Notfallpatienten (≥ 80 Jahre) mit Schädel-Hirn-Trauma an einer neurochirurgischen Universitätsklinik

Care paths, clinical management and decision making in 376 mild TBI patients over the age of 80 presenting to a neurosurgical emergency department

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Objective

Mild traumatic brain injury (TBI) is an increasing phenomenon, partially associated with neurological impairment and reduced quality of life. Given the current demographic change, assessing possible factors associated with an unfavorable outcome after mTBI in the elderly is becoming increasingly important. We, therefore, aimed to describe the clinical management and outcome of elderly mTBI patients presenting to a neurosurgical emergency department (ED).

Methods

All TBI patients admitted to the ED of neurosurgical maximal care provider were prospectively assessed between April 2021 and December 2022. Demographic and clinical variables were collected and the necessity for neuroimaging, admission to the regular ward or ICU, medical or surgical interventions and the clinical outcome at discharge (mRS) were analyzed.

Results

Over a period of 21 months, 2014 patients were assessed, of which 1867 presented with mTBI (GCS 13-15). For further analysis, only the 376 (20%) mTBI patients aged >80 years (50% male; mean age 86 ± 4,4 years) were included. The most common cause of injury was an incidental fall (n=360; 96%), typically occurring in the home environment. Neurological deficits were rare (n=27; 7%), but 51 patients (14%) suffered from amnesia and 24 (6%) had experienced vomiting. Antithrombotic medication was taken by 69% of patients (n=258). Intracranial pathologies on brain CT imaging were observed in 124 patients (33%). Neurosurgery was deemed necessary in 16 (4%) cases. Interestingly, receiving neurosurgery was more likely for octagenarians than nonagenerians (OR 4,4; 95% CI 0,58-34; p=0,15). Admission to the hospital was deemed necessary in 31% of patients (n=118), from which 27 (23%) were admitted directly to the ICU. The mean length of hospital stay was 4 ± 5 days and 61 (52%) of patients had a mRS of 0 or 1 at discharge. In univariate statistical analysis, no parameters associated with a worse clinical outcome could be identified.

Conclusion

Mild TBI is associated with neuroimaging, medical/surgical interventions, and hospital admission in a substantial number of elderly patients presenting to a neurosurgical maximum care provider. Our findings suggest that the causal injuries might be less "mild" than suspected and should raise awareness for their adequate clinical management.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V372

Prädiktion von klinischem Outcome bei älteren Schädel-Hirn-Trauma (SHT)-Patienten mitehilfe von Machine Learning - eine CENTER-TBI-Studie

Outcome prediction in elderly traumatic brain injury patients using machine learning algorithms - a CENTER-TBI study

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Objective

Traumatic brain injury (TBI) in the elderly, despite being mild in many cases, has become a major cause for morbidity with need for inpatient treatment and post hospitalization care, posing a major challenge for health care systems. We thus aimed to assess predictive parameters for 30-day mortality as well as 6- and 12-month global outcome in a cohort of ≥65-year-old TBI patients, using the CENTER-TBI study database.

Methods

All patients aged ≥65 years in the CENTER-TBI database were included. We conducted two ML algorithms for each of the outcomes (30-day mortality, 6- and 12-month global outcome): one with parameters available on admission only, and one with all information gathered up to day 14 of hospitalization. Unfavorable global outcome was defined as a Glasgow Outcome Scale Extended (GOSE) score of ≤ 4. The models were performed via logistic regression, decision tree, random forest, XGBoost and K-Nearest Neighbors algorithms using the Python software.

Results

We identified 932 TBI patients with a median age of 74 years and a median GCS of 15. incidental falls were the major cause of injury (67.1%) leading to tSAH as the main CT-morphologic pathology (51.3%). Overall, 44.1% of the patients were admitted to an intensive care unit and the 30-day mortality was 34.1%. At 12 months after TBI, an unfavorable outcome was seen in 32.4%. The most relevant predictive parameters for 30-day mortality were compression of basal cisterns on early CT, the Injury Severity Score (ISS) as well as neuroworsening. Systemic comorbidities, basal cistern compression and neuroworsening were strong predictors for unfavorable 6- month outcome - and lastly, total ISS, basal cistern compression and mass lesion on early CT were predictive for unfavorable 12-month outcome. Accuracy of the ML algorithms yielded AUC values of 0.88-0.89 for 30-day mortality, 0.85-0.88 for 6-month and 0.85-0.86 for 12- month outcome. Precision of the models was improved when clinical data up to day 14 was included.

Conclusion

Prediction accuracy in the presented ML approach proved AUCs ranging from 0.85 to 0.89. Although older age has been demonstrated to weaken accuracy of the CRASH and IMPACT predictive models, the current data demonstrates that predictive models specific to the older population are possible - and could thus become useful tools for patient counseling and clinical decision making.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V374

Systematische Charakterisierung von präklinischen Modellen des leichten, mittelschweren und schweren Schädel-Hirn-Traumas mittels Controlled Cortical Impact

Systematic characterization of preclinical models of mild, moderate and severe TBI utilizing controlled cortical impact

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Objective

Despite the desperate need for new treatment options for patients with traumatic brain injury (TBI), the translation of promising preclinical results into clinical practice has been insufficient for decades. This is, in part, due to the fact, that in most clinical trials, randomization depends on a certain trauma severity, while high quality data on the standardization of preclinical methods of, i.e., the trauma induction itself, and, therefore, the trauma intensity, are scarce. Therefore, we evaluated the effect of different adjustable parameters of one of the most utilized preclinical models of TBI, the Controlled Cortical Impact (CCI) model, on trauma intensity, to produce a distinct mild (mCCI), moderate (moCCI) or severe (sCCI) injury.

Methods

A total of 128 wildtype C57Bl/6 mice were subjected to mCCI, moCCI and sCCI using three different sets of parameters (tip diameter/impact depth/velocity of 1mm/1mm/4m/s; 2mm/2mm/6m/s; 3mm/3mm/8m/s, respectively) or to sham surgery (craniotomy only). Structural damage was assessed using Nissl staining at 1, 3, 7 and 28 days post injury (dpi). Functional outcome was assessed using Hole Board, Video Open Field and CatWalkXT gait analysis tests 1, 3, 7, 14 and 28 dpi.

Results

With increasing trauma intensity, 1-day mortality increased from 2.6% after mCCI to 35.0% in the sCCI group. At the same time, lesion volumes also increased with rising trauma intensity throughout the observation period (i.e. 1.8 mm^3, 14.1 mm^3 and 33.8 mm^3 for mTBI, moTBI and sTBI, respectively, 7dpi). In addition, more severely traumatized mice lost significantly more weight, especially within the first week after CCI (i.e., -5.6%, p=0.005 and -7.9%, p=0.001 vs. sham 1 dpi for moCCI and sCCI, respectively). Assessment of functional outcome showed impaired exploration behavior (i.e., 51.2 vs. 29.2 Hole Board explorations, p=0.006 for sham vs. sCCI 1 dpi), reduced motor function (i.e., *average run speed* of 17.4 m/s vs. 22.0 m/s for sTBI and sham 3 dpi, respectively) and pronounced disinhibition especially in the later stages of the observation period (i.e., 277.7s vs. 285.9s spend on the borders of the Open Field, p=0.038 for sham vs. sCCI 14 dpi).

Conclusion

The three evaluated sets of CCI parameters lead to progressive structural and functional damage after trauma induction that resemble the impairments seen in patients with mild, moderate and severe TBI. Therefore, we provide guidance for the choice of CCI parameters appropriate for the respective research question.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V375

Frailty ist assoziiert mit der 30-Tages Mortalität von älteren Patienten mit Schädel-Hirn-Trauma – eine retrospektive Studie an 1104 Patienten

Frailty is associated with 30-day mortality after traumatic brain injury in elderly patients – a retrospective study in 1104 patients

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Objective

Frailty rather than chronological age is a known risk factor for poor outcome in medical conditions requiring hospital admission and intensive care therapy, but there is little evidence of its impact on outcome after TBI. In the present study, we evaluated different frailty scales with regard to feasibility and their effect on outcome and 30-day mortality in elderly TBI patients.

Methods

Clinical notes of all patients ≥ 60 years who presented to our hospital with traumatic brain injury from 01/2010 - 12/2021 were retrospectively analyzed. Four frailty grading scales (Clinical frailty score (CFS), Charleston Comorbidity Index (CCI), Modified 5 (mFI-5)- or 11-item (mFI-11) Frailty Index) were determined for each patient and correlated with clinical outcome parameters.

Results

1104 patients with a median age of 78 years (IQR 72-84) were identified. 14.5% sustained severe TBI, 8.6% moderate, and 76.9% mild TBI. Univariate logistic regression revealed a significant association of age (OR=1.05; p<0.0001), cardiovascular disease (OR=1.66; p=0.02), initial GCS (OR=0.78; p<0.0001), pupil dilation (OR=3.15; p<0.0001), prehospital hypotension < 90 mmHg, (OR=5.18; p=0.002), invasive mechanical ventilation (OR=6.2; p<0.0001), and hospital acquired pneumonia HAP (OR=3.35; p<0.0001) with mortality within 30 days after TBI. Anticoagulant use was not a significant predictor of mortality (OR=1.12; p=0.57). All frailty assessment scales compiled correlated, indicating they all feasibly determine frailty: Spearman correlation revealed correlation coefficients of 0.4473 (95% CI 0.3953 - 0.4964) for mFI-11, 0.4326 (0.3798-0.4825) for mFI-5, and 0.34 (0.28-0.39) for CCI with CFS respectively.Higher scores in Clinical Frailty Scale and Charleston Comorbidity Index (CFS: OR=1.33; p<0.0001; CCI: OR=1.19; p<0.0001), but not the mFI-11 and mFI-5 (OR=3.25; p=0.17; OR=1.05; p=0.65) were significantly associated with 30-day mortality. Multivariate logistic regression revealed CFS (OR=1.66; p=0.034), CCI (OR=1.32; p=0.02), Injury Severity Score (OR=1.14; p<0.0001), and HAP (OR=3.96; p=0.0078) as significant predictors of 30-day mortality after TBI.

Conclusion

Frailty as assessed by CFS and CCI was associated with 30-day mortality in our large cohort of elderly patients with TBI of varying severity. Our data indicates that frailty rather than chronological age may determine outcome in TBI and should be considered when determining treatment strategies in elderly TBI patients.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V376

Das Post Intensive Care Syndrome bei Patientin mit Schädel-Hirntrauma
Post Intensive Care Syndrome in patients sustaining a Traumatic Brain Injury

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Objective

Post Intensive Care Syndrome (PICS) is defined as new or worsening physical, cognitive, or mental impairments following critical illness or treatment in the intensive care unit (ICU). Traumatic Brain Injury (TBI) is widely recognized as a large public health and social problem, often associated with long ICU stays. The scope of PICS in patients suffering from TBI and its specific risk factors have not yet been described. In this study we thus aim to assess the occurrence of PICS and its risk factors in a large, prospectively collected TBI database.

Methods

Patients in the Collaborative European NeuroTrauma Effectiveness Research in TBI (CENTER-TBI) core study treated on an ICU were enrolled. These patients received brain CT imaging and had given their informed consent for study participation within 24 hours after TBI. Their 3-, 6- and 12-month outcome was assessed using the Short Form 36 (SF-36) and the Rivermead Post Concussion Symptoms Questionnaire (RPQ-13). PICS °1 was defined by a change in either the SF-36 physical component score (PCS) ≥ 10 points, the SF-36 mental component score (MCS) ≥ 10 points or any worsening of the RPQ-13 between the 3-, 6- and 12-month follow-up. PICS °2 was defined as a combination of any of those changes. Results were statistically compared between groups (PICS, No-PICS) and correlation analyses of risk factors were performed.

Results

280 TBI patients treated on the ICU with available SF-36 and RPQ-13 questionnaires at 3-, 6- and 12 months were included. 121 (43,2%) Patients developed PICS. Patients with PICS were predominantly male (72%), had a median age of 43 (13 - 84) years and mostly suffered from severe injuries (GCS 3-8 in 39%). Cranial and extracranial surgeries were performed in 27% and 32% of those patients, respectively. In patients with PICS, correlation analysis showed associations between the length of in-hospital stay and worsening of PCS (r=-0,164, p=0,01), MCS (r=-0,145 p=0,01) and RPQ-13 (r=0,167) after 12 months. Similarly, associations between the duration of mechanical ventilation and worsening in PCS (r=-0,146 p=0,01), MCS (r=-0,140 p=0,01) and RPQ-13 (r=0,132 p=0,01) could be observed in those patients.

Conclusion

Our findings shed light on the not well-known occurrence of PICS in TBI patients treated on an ICU. Factors associated with PICS such as the hospital length of stay and the duration of mechanical ventilation should be considered and patients at risk closely monitored.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V373

Radiomics zur Vorhersage einer diffusen axonalen Schädigung (DAI) bei Patienten mit Schädel-Hirn-Trauma
Radiomics for the assessment of diffuse axonal injury (DAI) in patients with traumatic brain injury

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Objective

De- and acceleration traumata can cause diffuse axonal injury (DAI) in 40-75% of patients with traumatic brain injury and is associated with a high risk of long-term morbidity. The diagnosis of DAI on CT is challenging due to the lack of structural abnormalities. To overcome this limitation, MR imaging including diffusion- and susceptibility-weighted sequences is necessary, but not always suitable for instable ICU patients. Therefore, DAI remains underdiagnosed. Radiomics, a method from the field of artificial intelligence, not established in DAI patients yet, offers the opportunity to extract additional information from routine imaging data. The purpose of this work was the evaluation of the feasibility of multimodal radiomics for an improved diagnosis of DAI.

Methods

MR imaging including T2, FLAIR, DWI and SWI/T2* sequences was performed in 42 patients suspicious of DAI due to the clinical state, and a control group (n=44). DAI was diagnosed by an experienced neuroradiologists based on imaging data. To define the target volume, a standardized MRI-based atlas of the predilection areas for DAI was developed. After radiomics feature extraction, a test-retest analysis was performed to identify robust features prior to feature selection. The radiomics model was trained and validated by five-fold cross validation. Diagnostic performance was evaluated using receiver operating characteristic (ROC) analyses.

Results

Radiomics features showed significant differences between patients with DAI and healthy controls, especially in the thalamus, basal ganglia, and corpus callosum. The developed random forest classifier using the radiomics signature, yielded an AUC under the ROC of 0.89, 0.86 und 0.95 in these areas.

Conclusion

MRI based radiomics analysis is feasible for the assessment of DAI with high diagnostic performance. The validity of the model will be evaluated further in an external test data set, and the utility for CT-based radiomics to assess DAI is currently under investigation.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V377

Die Applikation von Interleukin-4 reduziert den Sekundärschaden nach experimentellem Schädel-Hirn-Trauma im Mausmodell

The administration of Interleukin-4 ameliorates secondary brain damage after experimental traumatic brain injury in mice

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Objective

Recent focus of experimental research in traumatic brain injury (TBI) has been directed towards the role of inflammatory processes. It has been shown that activation of the Interleukin-4 (IL-4) pathway ameliorates secondary brain injury; therefore, we assessed the effect of therapeutic application of IL-4 on secondary brain damage after experimental TBI in mice.

Methods

C57/Bl6 wildtype mice were subjected to controlled cortical impact (CCI) injury. IL-4 was administered subcutaneously at a dose of 5mg/kg 15 minutes after trauma induction. Neurological function was assessed using hole board, video open field and CatWalk XT gait analysis tests 24 hours as well as 3, 7, 14 and 28 days post injury (dpi). In addition, contusion volume was determined by Nissl staining. Finally, inflammatory response (quantification of astrogliosis, macrophages, microglia, and M1/M2 microglia polarization) and cellular neuroregeneration (quantification of oligodendrocytes and myelinization) was assessed in the pericontusional area, the contralateral cortex as well as in the ipsi- and contralateral hippocampus by immunofluorescent staining.

Results

IL-4 treatment resulted in reduced contusion volumes especially within the first two weeks after CCI (e.g.,10.9 vs. 6.8 mm³, p=0.02 for control and IL-4 7 dpi). While some parameters of gait and motor function improved with IL-4 treatment (e.g., *difference in max intensity* in the left hindpaw: 1.89 U vs. 6.00 U, p=0.048 for IL-4 and control 3 dpi, respectively), others indicated even slower recovery after IL-4 administration (e.g. *difference in body speed* in the right hindpaw: -5.8 m/s vs. -1.2 m/s, p=0.033 for IL-4 and control 14 dpi, respectively). On the histological level, the local inflammatory response was ameliorated (e.g. 37.8 vs. 57.3 Iba1+ cells/ROI for IL-4 and control 1 dpi, respectively), while proliferation processes were observed more frequently (e.g. 26.9 vs. 12.3 Ki67+ cells/ROI for IL-4 and control 1 dpi, respectively) and apoptosis less frequently (e.g. 40.7 vs. 95.8 TUNEL+ cells/ROI for IL-4 and control 1 dpi, respectively) in the traumatic penumbra especially in the acute phase after IL-4 application.

Conclusion

The administration of IL-4 lead to reduced structural damage and an ameliorated inflammatory response after CCI, while we observed mixed results with regards to functional outcome. Further studies need to evaluate the optimal treatment regimen to fully exploit the neuroprotective potential of IL-4 and aid its clinical translation.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

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Stereotaktische Transplantation von neuroD1/Prox1 Gyrus Dentatus Vorläuferzellen zur Behandlung der Hippocampusschädigung nach Schädel-Hirntrauma im Rattenmodell

Stereotactic transplantation of neuroD1/Prox1 gyrus dentate precursor cells for the treatment of hippocampal damage after Traumatic Brain Injury in a Rat Model

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Objective

Traumatic Brain Injury (TBI) is a devastating disease frequently associated with the impairment of cognitive function. Such deficits might be related to damage of the hippocampus but data on long-term neurocognitive and histopathological changes after hippocampal injury remain scarce. We sought to investigate potential long-term effects of hippocampal transplantation of neuroD1/Prox1 gyrus dentate precursor cells after experimental TBI in a rat model.

Methods

22 male Wistar rats were allocated to either right parietal Controlled Cortical Impact (CCI) with a depth of 3 mm, a contact time of 150 ms and an impact speed of 8 m/sec or sham surgery. At 7 days post injury (dpi) stereotactic transplantation of 6 x 105 gyrus dentate precursor cells expressing neuroD1 and Prox1 or a placebo (PBS) to three distinct areas in the hippocampus were performed. Motor function and behavioral changes were examined via the Rotarod (RR) and Open-Field test (OF) after 1, 3, 7, 14, 21, 28 and 35 dpi. Learning and memory function were tested via the Sacktor"s Active Avoidance test (AAT) 4, 12, 24 and 31 dpi. Histological changes in neuroregeneration, degeneration, microgliosis and neuroinflammation were investigated via immunocytochemistry (ICC) whereas hippocampal atrophy and neuronal loss were examined via Nissl-Staining 35 dpi.

Results

A slight improvement of motor deficits was observed via the RR 14 and 21 dpi only in the stem cell group. A significant decrease of anxiety-like and an increase of exploratory behavior was seen via the OF 14 and 28 dpi with the stemcell compared to the placebo treatment. In the AAT significant worsening of spatial learning and memory was observed 4 dpi in injured CCI animals compared to sham animals. A slight improvement of cognitive function was detected 21 and 28 dpi solely in the stemcell group. CCI led to severe neuronal loss and atrophy of the hippocampus 14 dpi and even more pronounced 28 dpi. Less contusion volume was detected 28 dpi exclusively in the stemcell group. A substantial decrease of neurodegeneration, microgliosis and an increase of neuroregeneration were observed with the cell transplantation.

Conclusion

Our study provides a better understanding of short -but also long-term histopathological and neurobehavioral changes in the hippocampus after experimental TBI. Stereotactic transplantation of neuroD1/Prox1 expressing gyrus dentate precursor cells might be a potential therapeutic approach to improve such long-term sequalae of TBI.

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V379

ICP-Messung mittels transorbitale Sonographie und Bestimmung des Optikus-Nerven-Scheiden-Durchmessers (ONSD) - eine einfach zu erlernende Methode für den untranierten Untersucher

ICP Assessment by transorbital ultrasound measurement of the optic nerve sheath diameter (ONSD) – an easy to learn method for untrained examiners

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Objective

Knowledge about intracranial pressure (ICP) is invaluable in the management of a plethora of neurological pathologies. Measurement of the optic-nerve-sheath-diameter via transorbital ultrasound (US-ONSD) provides a non-invasive surrogate marker for estimation of ICP. ONSD measurement using MRI/CT (MRI/CT-ONSD) provides an alternative if such imaging is available. The aim of this study was to determine and quantify repeatability and observer reliability in comparison of US- to MRI/CT-ONSD in an adult cohort and to investigate whether US-ONSD can be learned easily and reliably by previously untrained persons.

Methods

70 adult individuals (aged 18-87 y, mean 50.3±20.4 y) were investigated. Pathologies were active hydrocephalus (n = 31), pseudotumor cerebri (n = 20), and normal pressure hydrocephalus (n=19). A novice medical student (A.K.) was methodically trained and initially supervised by an experienced investigator (S.R.K.) . Binocular US-ONSD in the axial plane was obtained by the medical student with a 12Hz Linear-array transducer and compared to ONSD taken from MRI (T2-weighted) in 47 patients and from CCT in 23 patients. In 30 random patients, an inter-reliability analysis of US- and MRI-ONSD was made between medical student and expert.

Results

The repeatability of US-ONSD was excellent (Cronbach's α 0.983). Mean US-ONSD was 6.42± 0.31mm , mean MRI-ONSD was 6.34 ±0.27mm.. The correlation between US and MR/CT-OSND was outstanding (r= 0.961, p<0.001). Bland and Altman analysis revealed a minimal mean bias of 0.079 ± 0.17 mm in favor of US-ONSD. Inter-observer reliability between medical student and expert was excellent for both US-ONSD and MRI-ONSD, (Cronbach´s α 0.975 and 0.981, respectively).

Conclusion

These results confirm previous pediatric data regarding high repeatability values, the excellent correlation of US-ONSD to MRI/CT ONSD and a clinically negligible difference between methods. The study furthermore shows that US-ONSD determination if done by a well advised novice is as reliable as in the hands of an expert, at least in compliant adult patients. Therefore US-ONSD has a steep learning curve and great potential to be acquired and spread quickly to all members of a clinical neuro team dealing with patients with raised ICP. For this reasons US-ONSD has become the first-line ICP assessment tool in our department and is applied by all residents.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V380

Studie zu nichtinvasiven ICP-Messung mittels transkraniellem Ultraschall (TTUS) (Akustocerebrographie)

Feasibility study for noninvasive ICP monitoring with transcranial transmission-Ultrasound (TTUS) (acoustocerebrography)

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Objective

The standard ICP monitoring requires the implantation of an intracranial probe. Non-invasive ICP monitoring would be beneficial. We compared standard ICP measurement with non-invasive transcranial transmission-Ultrasound (TTUS) measurements in sheep with normal and induced ICP increase and subsequently in human subjects with different intracranial pathologies.

Methods

TTUS measures the alterations in time of flight (ToF), and thereby the variation in brain elasticity. A pair of ultrasound probes are coupled to the head. First TTUS was performed on an anaesthetized sheep model with normal and increased ICP. Thereafter patients with intracranial pathology and implanted ICP probes underwent the TTUS survey. The TTUS measurement was adjusted with the standard ICP assessment (intracranial probe). We examined three patients with normal-, increased ICP and malignant generalized cerebral edema (lack of brain perfusion), and compared the morphology of the scaled TTUS and ICP curves. Representative curves of each TTUS measurement were analyzed and morphologic features such as pulse widths were compared between the patients.

Results

In the animal experiment, brain pressure-dependent changes could be observed in alterations of TTUS amplitude. By the viscoelastic response of the brain tissue to increased ICP, the ICP Pulse-Curve correlated with the course and morphology of the TTUS Brain-Pulse-Curve ($r>0.8$). Significant changes in morphologic features of the TTUS curve were observed between the three patients: Pulse widths of the TTUS measurement at 30% / 80% of the pulse maximum were significantly lower in the normal ICP patient compared to the increased ICP patient (mean ± standard deviation): 7.0 ± 0.6 / 26.0 ± 1.8 vs. 15.3 ± 1.2 / 45.7 ± 3.1. TTUS measurements in the patient with malignant generalized edema showed comparable pulse widths (8.6 ± 0.8 / 25.8 ± 1.3) to the patient with normal ICP Values. Due to the absence of brain autoregulation in the patient with generalized brain edema, the TTUS Pulse-Curve morphology was equal to the invasive blood pressure curve.

Conclusion

The Brain-Pulse-Curve represented by conventional ICP-Probe, correlated strongly with the TTUS curve. The TTUS is feasible for measuring viscoelastic brain tissue changes. It presents an entirely non-invasive diagnostic tool for measuring intracranial pressure. Thereby the detection and monitoring of certain intracranial pathologies and their time course can be better described.

Rapid Communication SHT und ICP monitoring/*Rapid communication SHT and ICP monitoring*

V381

Transkranieller Transmissionsultraschall ermöglicht einen zuverlässigen nicht-invasiven Ausschluss von erhöhten Hirndrücken in Schädel-Hirn-Trauma Patienten

Transcranial transmission ultrasound allows for reliable non-invasive exclusion of raised intracranial pressure in traumatic brain injury patients

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Objective

Non-invasive measurement of intracranial pressure (ICP) has failed for decades. Non-invasive, transcranial transmission ultrasound (TTUS) measurements provided promising experimental data via brain pulsatility. This study investigates the potential of TTUS in the detection of elevated ICPs via machine learning-based analysis.

Methods

Patients with severe traumatic brain injury (TBI) and invasive ICP monitoring were prospectively enrolled. ICP, arterial blood pressure, heart rate and TTUS measurements were simultaneously recorded in situations with and without elevated ICP. A classification model was implemented based on measurements derived from 9 patients with 387 episodes of increased ICP (>15 mmHg) and 345 episodes of normal ICP (<10 mmHg). The model was validated in a leave-one-subject-out procedure.

Results

25 patients aged 61.6 +/- 17.6 years were enrolled from October 2021 to October 2022. 279 data sets with a mean ICP of 11.3 mmHg (1st quartile 6.1 mmHg; 3rd quartile 14.8 mmHg) were acquired and analyzed. Automated analysis of the TTUS measurements successfully identified increased ICP values >15 mmHg with a sensitivity 100% and a specificity 47%. A negative predictive value of 100% was achieved, the positive predictive value was 14% for the test set.

Conclusion

TTUS can precisely exclude elevated ICP in TBI patients with a negative predictive value of 100%. Despite low specificity, exclusion of raised ICP can already partially replace invasive ICP measurement in intensive care and emergency medicine. Worth mentioning, this is the first automated approach achieving such a highly applicable reliability.

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P001

Ein neuer Score zur Einschätzung des Erfolgs der endoskopischen dritten Ventrikulostomie bei Patienten mit idiopathischer Aquäduktstenose: eine retrospektive monozentrische Studie

A new score to assess success of endoscopic third ventriculostomy in patients with idiopathic aqueduct stenosis: a retrospective single-center study

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Objective

In occlusive hydrocephalus, pressure difference between ventricles and basal cisterns leads to bulging of third ventricular floor and lamina terminalis. Endoscopic third ventriculocisternostomy (ETV) is the standard treatment in these patients. We tried to assess success of ETV depending on those two radiological changes.

Methods

We implemented a simple (**D**amaty) D-score system retrospectively to assess the state of third ventricular floor (bulging +1, straight 0, retracted -1) as well as lamina terminalis in same manner in midsagittal constructive interference in steady state (CISS) MR image. Every patient had a preoperative, direct- and 3 months postoperative score from -2 to +2. We correlated the scores to the clinical course to decide whether the score is reliable in defining success of ETV.

Results

Between 2017-2021, 27 patients with aqueduct stenosis (AS) treated successfully with ETV were included. Mean age was 29.2 ±24.1 years, 66.7% females. There was a marked shift of the score to the left after surgery, noticed through the distribution of the score immediate postoperative and 3-months later. Majority of patients (66.7%) showed (+2) before surgery, 56% scored (0) after surgery, 52% showed further score drop to (-1) 3 months later, **p=.001**. The score was valid for pediatric and adult patients.

Conclusion

D-score describes anatomical changes in third ventricle after ETV and can serve in assessment of MR images to define success of the procedure in patients with AS. This score should be validated for other etiologies before widely using it in assessment of MR imaging following ETV.

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P002

Endoskopische Drittventrikulostomie zur Behandlung eines Hydrocephalus Internus aufgrund einerAusgangobstruktion des vierten Ventrikels: Bericht über zwei Kinder und systematischeLiteraturübersichtsarbeit mit Meta-Analyse

Endoscopic Third Ventriculostomy (ETV) in the Treatment of Hydrocephalus Internus due to a Fourth VentricleOutlet Obstruction (FVOO): Report of Two Children and Systematic Review with Meta-analysis

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Objective

FVOO is a rare cause of hydrocephalus. The last century's standard treatment was a suboccipital craniotomy with magendieoplasty or ventriculoperitoneal shunt. Since the beginning of the 21st century, the ETV has been considered a less invasive alternative. The medical literature lacks reports of FVOO cases, and there is insufficient evidence about ETV's efficacy in treating this condition. We report two cases of FVOO treated with ETV in our department and review published similar cases.

Methods

Clinical and radiological findings of two FVOO cases with outcomes after ETV were presented. Moreover, we conducted a systematic review after protocol registration in PROSPERO (CRD42021281474). Medline and Embase were searched from inception till 31st December 2021. Studies were included if they reported cases of FVOO treated only with EVT. Cases with Chiari malformation, Dandy-Walker malformation, tuberous sclerosis, tumour, or space-occupying lesions were excluded. Two reviewers independently examined title/abstract records in the first stage and full-text publications in the second for eligibility. The primary outcome was the recurrence rate, defined by the need for re-ETV or other invasive treatments. Other outcomes included clinical state at follow-up and mortality. STATA software was used for statistical calculations.

Results

Two cases, a 3-year-old male and 3,5 female, with FVOO, were treated with ETV in our department by the same neurosurgeons in 2012 and 2021. Both cases improved significantly after ETV, and there was no recurrence through the follow-up. Besides the present cases, we found 57 other cases of FVOO treated with ETV reported in 17 studies between 2001 and 2021. The median age was 26 years, with an interquartile range from 2.4 to 59 years, and 56% of cases were females. The recurrence rate was 33% in the whole sample (n=59), and ETV succeeded in treating the condition in 66% of the cases. The mean time to recure was 8±27 months (mean± standard deviation). A ventriculoperitoneal shunt was the treatment of recurrence in 65% and a re-ETV in 35%. At the follow-up (41±29 months), only one case died, and one deteriorated clinically; all other cases improved.

Conclusion

FVOO is a rare cause of hydrocephalus encountered mainly in the first or sixth decades of life. ETV provides the first reasonable treatment. Despite the moderate recurrence rate, the outcomes are favourable.

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P003

Mamillopontine Distanz bei Kindern mit Hydrozephalus triventrikularis, Änderung der Distanz nach endoskopischer dritter Ventrikulozisternostomie und Vergleich mit der mamillopontinen Distanz von erwachsenen Patienten

Mamillopontine distance in children with triventricular hydrocephalus, distance changes after endoscopic third ventriculocisternostomy and comparison with the mamillopontine distance in adult patients

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Objective

Mamillopontine distance (MPD) is a morphometric parameter, which can be influenced in obstructive hydrocephalus. A common type of obstructive hydrocephalus is the triventricular hydrocephalus because of many causes like aqueductal stenosis (AqS), brain tumors and longstanding overt ventriculomegaly in adults (LOVA). Here, we measured the MPD in children with triventricular hydrocephalus (TvH) before and after endoscopic third ventriculocisternostomy (ETV) and we compered with the findings in adult patients.

Methods

We retrospectively measured the MPD in sagittal MRI images from 14 pediatric and 34 adult patients pre- and postoperatively. All patients underwent an ETV because of TvH in our institution between 2012 to 2022. Patients with hydrocephalus caused from meningitis, hemorrhage and tumors with obstruction of the foramen of Monro were excluded.

Results

Our children cohort comprises 14 patients (50% female) with a mean age of 6.8 years (range, 2 months to 17 years). 8 children (57%) were diagnosed with AqS and 6 (43%) with an obstructing tumor. The overall mean MPD was preoperatively 3.6 mm (range, 1.4 to 8.1 mm). The mean MPD for children with AqS (3.4 mm) was shorter than that for children with tumor (3.8 mm). Postoperatively, a greater MPD has been registered. The MPD improvement was in percentage 208% for all children, 229% for children with AqS and 180% for children with tumor. Moreover, the improvement of MPD was in follow up (range, 2 months to 5.5 years) increasing (353%). A tumor biopsy was performed in 50% of the children with tumor. After ETV there were 2 children with hygromas, both had preoperative macrocephaly. The adult patients (n=29, 65% female) had a median MPD of 5.1 mm (range, 0.6 – 9.7 mm). In the subgroup of adults with AqS (n=19) was the median MPD 5.5 mm and in that with tumor (n=10) 4.4 mm. The registered improvement of MPD postoperatively was in adults overall 155%, for the adult patients with AqS 109% and for them with a tumor 242%. Additionally, we found an extra group of adult patients with LOVA (n=5, mean age 63 years), which demonstrated a mean MPD of 7.1 mm (range, 5.6 to 11 mm). The ETV has caused no MPD improvement in this group.

Conclusion

The shorter preoperative MPD and the greater postoperative MPD improvement in children than in adults with triventricular hydrocephalus denotes the need of immediate ETV as well as its high effectiveness in pediatric patients.

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P004

Evaluation von Shuntunabhängigkeit bei Kindern mit Hydrocephalus

Towards a more Structured Approach to Evaluate Suspected Shunt Independency in Children with Hydrocephalus – A Single Center Analysis

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Objective

To identify factors relevant for successful shunt ligation and to develop and present an algorithm for the evaluation of suspected shunt independency in children with hydrocephalus.

Methods

We conducted a retrospective chart review of all patients that received a revision of a peripheral catheter between 2002 and 2022 (OPS-Code 5-024.2). The "index surgery" was defined as a shunt ligature in pediatric patients with hydrocephalus who were suspected to not need further CSF diversion.

Demographic parameters (age, gender, cause of hydrocephalus), clinical parameters (number of revisions, type of shunt and type of valve, signs of CSF flow during surgery) and radigraphic parameters (signs of disconnection, Evans-Index, ventricular volume, Callosa angle) prior to shunt ligation were collected and analyzed.

Results

We identified 27 patients who underwent a shunt ligature between 2002 and 2022 due to suspected shunt independency, those are 9.2% of all 293 pediatric patients with hydrocephalus who received a revision of the peripheral catheter during that time. Of those 27 patients 13 (48.1%) were female and 14 (51.9%) male, the median age at the time of the index operation was 12±4.2 (range 0 – 18).

The etiology of hydrocephalus was aqueduct stenosis in 4 cases, postinfectious in 1 case, posthemorrhagic in 6 cases, tumor in 2 cases, spina bifida in 4 cases and other in 10 cases . All 27 patients had a ventriculoperitoneal shunt. The median time with shunt was 11.78±4.58 years (range 0-18).

The number of shunt revisions prior to shunt ligation was 3.2±2.3 (range 1-8).

Shuntligature was unsuccessful in 44,4% (n=12) cases. Age, time the shunt was implanted, type of valve and type of hydrocephalus did not have a significant influence on outcome.

Conclusion

Shunt ligature is a procedure with a very high failure rate, exposing the child to two unnecessary operations, it is therefor paramount to improve patient selection.

Due to the small number of preselected cases none of the parameters we analyzed so far showed a significant impact on prognosis. Based on our analysis we were able to develop an algorithm which we are planning to evaluated prospectively in a multicenter study.

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P005

Ventil mit verstellbarer Gravitationseinheit der neuesten Generation - Erfahrungen und Schlußfolgerungen aus einem Zentrum für Kinder- und Erwachsenenneurochirurgie

Last Generation adjustable gravitational Valve - Experiences and Conclusions from a Center for child and adult Neurosurgery

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Objective

The development of ventriculoperitoneal/-atrial shunt valves has improved over the years, allowing a physiological drainage of CSF and preventing over-drainage frequently caused by a siphon effect. The objective of this retrospective study was to analyze our first experiences with a new generation valve, consisting of a fixed differential pressure unit (DP/DPU) and an adjustable gravitational unit (GU).

Methods

We retrospectively analyzed the existing data of all patient who received this specific valve, regarding sex, age, diagnosis, prior interventions, prior valve, selected DP and GU-adjustment, complications, revision surgery and improvement of prior over-drainage.

Results

Within 2.5yrs., we implanted 40 valves, 7 of them during primary surgery, 33 during revision surgery, being dysfunction of the preexisting valve the most frequent indication. The etiology of hydrocephalus varied, although post hemorrhagic hydrocephalus was the most common (19/40). Distribution of DPU was 6 (5cmH2O) vs. 33 (10cmH2O) vs. 1 (15cmH2O). Five of the newly implanted valves had to be explanted, 2 due to valve occlusion, the remaining 3 because of over-drainage, suboptimal function and a low-grade infection. Relevant differences were detected between age group 2m.-2yrs. (n=13) and patients older than 2yrs. (n=27, 2-35yrs.). In patients older than 2yrs., we observed very low rates of complications and high satisfaction rates of patients/parents. The younger patients showed higher complication rates and finding the optimal valve setting seemed more demanding.

Conclusion

This specific valve is a promising system that allows a physiological CSF drainage; however, we observed that a DP of 10cmH2O was suitable for the majority of patients, unlike DP 5cmH2O, as recommended by the manufacturer. We recommend instead selecting a DP of 10cmH2O for most patients older than 2yrs.. Regarding age group 2m. – 2yrs., the physician has to decide even more carefully, which valve and pressure setting might be suitable. In this age group, we recognized that an adjustable gravitational valve did not bring great benefit and, on the contrary, complications occurred more frequently. The size of the valve in relation to the delicate skin is also a limiting factor.

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P006

Erste klinische Erfahrung und biomechanische Analyse eines neuartigen schwerkraftunterstützten Ventils (M.blue®) bei pädiatrischen Patienten mit Hydrozephalus: eine retrospektive Studie mit zweijährigem Follow-up

Initial clinical experience and biomechanical analysis of a novel gravity unit assisted valve (M.blue®) in pediatric patients with hydrocephalus: a retrospective study with two years follow-up

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Objective

Overdrainage is a widely reported complication representing common indication for shunt revision. Despite recent advances in valve design, repeated shunt revisions represent burden on health-care systems. To investigate the efficiency of a novel gravity unit assisted programmable valve "M.blue®" in pediatric hydrocephalus using clinical and biomechanical analyses.

Methods

Retrospective single-center study included pediatric patients, who received M.blue® valve between April 2019 and April 2021 . Several clinical and biomechanical parameters were documented including complications and revision rates. Permeability, functional assessment in vertical and horizontal positions and extent of depositions inside valve were analyzed in explanted valves.

Results

Thirty-seven M.blue® valves in 34 pediatric patients with hydrocephalus (mean age 2.82 ± 3.91 years) were included. Twelve valves (32.4%) were explanted during a follow-up period of 27.3 ± 7.9 months. One-year survival rate of 89% and over-all survival rate of 67.6% with a valve survival average of 23.8 ± 9.7 months were observed. Patients with explanted valves (n=12) were significantly younger with 0.91 ± 0.54 years of age in average, **(p= .004)** and showed significantly more adjustments difficulties (**p= .009**). 58.3% of explanted valves showed deposits in more than 75% of the valve surface despite normal CSF findings and were associated with dysfunctional flow rate in vertical, horizontal or both positions.

Conclusion

The novel M.blue® valve with integrated gravity unit is efficient in pediatric hydrocephalus with acceptable survival rate. Deposits inside valves could affect its permeability in different body positions and might lead to dysfunction or difficulties in valve adjustments.

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P007

Von nicht-verstellbaren paediGAV Ventilen zu programmierbaren proGAV/proSA Serienventilen für die Behandlung des pädiatrischen Hydrocephalus im ersten Lebensjahr - Eine technische Single-Center Analyse

From fixed-pressure paediGAV to programmable proGAV/proSA serial valves for pediatric hydrocephalus within the first year of life – A technical single-center analysis

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Objective

Programmable valves have gained increasing popularity in the complex treatment of pediatric hydrocephalus. Over the last decade, adjustable serial valves have gradually replaced fixed-pressure valves in the authors" department. The presented study investigates this development by analyzing shunt and valve-related outcomes for this vulnerable population.

Methods

A retrospective analysis of all shunting procedures between 01/2009 and 01/2021 in children under one year was performed at the authors" single-center institution. Postoperative complications and surgical revisions were set as outcome parameters. Shunt and valve survival rates were evaluated. Statistical analysis compared children who underwent implantation of the programmable serial valves Miethke proGAV/proSA, with those with fixed-pressure Miethke paediGAV systems.

Results

A total of 85 procedures were evaluated. The paediGAV system was implanted in 39 cases, and the proGAV/proSA in 46 cases. The mean follow-up was 247.7 (±140) weeks. Back in 2009 and 2010, paediGAV valves were used exclusively, whereas, in 2019, the use of proGAV/proSA has evolved into the first-line therapy. PaediGAV systems were significantly more often revised ($p<0.05$). The main indication for revision was proximal occlusion, with or without impairment to the valve. Valve- and shunt survival rates of proGAV/proSA were significantly prolonged ($p<0.05$). Surgery-free valve survival of proGAV/proSA was 85% after one year and 63% after six years. There were no overdrainage-related revisions of proGAV/proSA valves.

Conclusion

Favorable shunt and valve survival validate the increasing use of programmable proGAV/proSA serial valves in this delicate population. Potential benefits in postoperative overdrainage treatment should be addressed in prospective multicenter studies.

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P008

Einsatz von Shuntscope in ausgewählten Fällen von pediatrischem Hydrocephalus: Indikationen, neurochirurgische Technik und Resultate

Application of the Shuntscope in selected cases of paediatric hydrocephalus: Indications, Surgical Technique and Results

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Objective

Optimal ventricular catheter implantation in paediatric hydrocephalus can be highly challenging due to a distorted anatomical configuration. Transluminal endoscopy with the Shuntscope has been invented to increase the rate of successful catheter placement. This presentation aims to evaluate ShuntScope- guided technique, achieved intraoperative image quality, related surgical and radiological outcomes in the paediatric population.

Methods

A retrospective analysis of all paediatric patients undergoing ventricular catheter placement using the Shuntscope from 01/2012 – 01/2022 in the author"s department was performed. Demographic, clinical, and radiological data were evaluated. The visualization quality of the intraoperative endoscopy was stratified into the categories; excellent, medium, and poor and compared to the postoperative catheter tip placement. Follow-up evaluation included the surgical revision rate due to proximal catheter occlusion.

Results

A total of 65 Shuntscope-assisted surgeries have been performed on 51 children. The mean age was 5.1 years. The most common underlying pathology was a tumor- or cyst-related hydrocephalus in 51%. Achieved image quality was excellent in 41.5%, medium in 43%, and poor in 15.5%. Ideal catheter placement was achieved in 77%. There were no intraoperative complications associated with the Shuntscope. The revision rate due to proximal occlusion was 4.61% during a mean follow-up period of 39.7 months. No statistical correlation between image grade and accuracy of catheter position was observed (p-value was 0.290).

Conclusion

The Shuntscope can be considered a valuable addition to standard surgical tools in treating of selected cases of paediatric hydrocephalus. Even suboptimal visualization contributes to high rates of correct catheter placement and, thereby, to a favourable clinical outcome.

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P009

Management von Kindern mit Shunt-versorgtem Hydrozephalus und Cochlea Implantat
Management of pediatric patients with CSF shunts and cochlear implants

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Objective

The management of children with CSF shunts which need cochlear implants (CI) can be challenging because of possible interferences between the devices. Here we present our experience with the interdisciplinary management in such scenarios.

Methods

The database of all patients who presented with a diagnosis of hydrocephalus and an implanted CSF shunt was screened for the co-occurrent implantation of a CI. A total of 26 patients were identified. Here we present the two pediatric cases in the lowest age group.

Results

Case 1 was a 22-month-old male baby with posthemorrhagic hydrocephalus due to preterm birth. He had initially a VP shunt which than was replaced by a VA shunt. Case 2 was a 26-month-old male baby, also with posthemorrhagic hydrocephalus due to preterm birth. He had multiple shunt revisions with two ventricular catheters implanted, and two separate shunt valves. Both valves were programmable. Both cases were discussed interdisciplinary and it was decided to change the programmable valves of the shunt to a non-programmable valve choosing an opening pressure according to the last settings of the programmable valve. Three months thereafter the CIs were implanted. In the first case contralateral to the shunt, and in the second case with CIs were implantetd. There were no complications related to both surgeries.

Conclusion

We propose to replace programmable valves for non-programmable valves prior to implantation of CIs in shunt-dependent pediatric hydrocephalus to allow safe management on long-term.

Pädiatrischer Hydrozephalus Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

P010

Abdominelle Liquorzysten als Ursache für abdominelle Dysfunktionen ventrikuloperitonealer Shunts bei Kindern

Abdominal pseudocysts – A cause of peripheral dysfunction in ventriculoperitoneal shunts in children

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Objective

Previous abdominal surgery and peritoneal adhesions in the children´s medical history are apparent and therefore may already focus the practitioners´ attention. However, abdominal pseudocysts are usually only detected in case of clinical symptoms of already present shunt dysfunction.

We analyzed our series of children treated with ventriculoperitoneal shunts for hydrocephalus in our neurosurgical department between 2013-2022 to evaluate the circumstances abdominal cysts have been detected and led to shunt dysfunction as well as to identify risk factors for the development of cysts.

Methods

We conducted a retrospective chart review and identified all pediatric patients treated in our department between 01/2013-12/2022 due to peripheral shunt dysfunction (OPS 5-024.2). We included all patients with abdominal complications demanding shunt revision in the analysis. The patient cohort was analyzed for multiple epidemiological factors, surgical circumstances (e.g., team, shunt devices, duration of surgery), date of shunt implantation, date and cause of complication, underlying symptoms, and diagnostic path.

Results

We initially identified 68 patients requiring revision for peripheral shunt failure. 41 (60.3%) children required revisional surgery of their peripheral shunt device due to abdominal complications. Among these, we found 12 (29.3%) patients presenting with causal peritoneal cysts, 6 (50%) male and 6 (50%) female, respectively. Mean age at presentation for abdominal revision was 10.3years.

Conclusion

As confirmed in our series, abdominal CSF pseudocysts constitute a relevant cause of peripheral shunt dysfunction in pediatric patients. To further explore its present unknown etiology and to prevent clinically apparent shunt dysfunction whenever possible, we suggest to include regular abdominal sonography into the follow-up algorithm.

Pädiatrischer Hydrozephalus Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Hydrocephalus Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

J-SPNC001

Sekundäre Chiari-Malformation mit Syringomyelie aufgrund einer Fehlfunktion eines lumboperitonealen Shunts: ein Fallbericht

Secondary Chiari Malformation with syringomyelia due to malfunction of a lumboperitoneal shunt: a case report

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Objective

Chiari Malformations are complex lesions though to originate during in utero development. Type 1 Chiari Malformation originates when the defect occurs after the second trimester which results in a caudally displaced tonsils. Many treatments have been proposed but posterior fossa decompression with C1 laminectomy with or without duroplasty seems to be the most consensual one. In the literature there are descriptions of secondary Chiari Malformations, usually associated with spinal cord injury, posterior fossa tumours or spontaneous CSF leaks. We present a case where the origin was a lumboperitoneal shunt previously placed that was overdraining.

Methods

Radiological, surgical and physical examination findings of a patient with secondary Chiari Malformation were reviewed.

Results

The patient is a 24 year old female who had a previous diagnosis of pseudotumor cerebri and had been treated with a lumboperitoneal shunt seven years prior. She presented to the emergency room with a bilateral distal paresis of both superior limbs associated with paresthesias. We did brain MRI that showed tonsillar descent associated with cervical syringomyelia which was diagnosed as type 1 Chiari Malformation. This patient's previous MRI showed no evidence of a Chiari Malformation. We assumed that this was caused by a malfunction of the previous shunt and opted to ligate it and place a ventriculoperitoneal shunt. After the procedure the patient gradually improved and has been improving ever since.

Conclusion

Secondary Chiari Malformation is a rare entity but one that should not be ignored. This case shows that, with special attention to the treatment modality. If the correlation between the lumboperitoneal shunt and the acquired Chiari hadn"t been done we may have been inclined to treat this patient as a regular type 1 Chiari Malformation. We treated this patient with ligation of the shunt and placement of a VP shunt with almost complete symptomatic resolution.

Varia/*Mixed topics*

J-SBNC001

Eine seltene Ursache für Ischiasschmerzen: Bösartiger Tumor der peripheren Nerven
A rare cause of sciatic pain: peripheral nerve malignant tumor

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Objective

To review and describe a case of nerve sheath tumor as a rare differential diagnosis of patients with sciatica.

Methods

Case description and systematic literature review in order to establish imaging characteristics of benign and malignant lesions and alert about this possible differential diagnosis.

Results

Male patient, 32 years old, presented with a progressive right sciatic pain associated to paresthesia in the right foot. Initially treated conservatively for sciatica, evolved in two months with hypoaesthesia in lateral aspect of the right leg and right foot plant, trength grade II in anterior tibial and grade IV in gastrocnemius. During the investigation, no presence of lumbar disc herniation or other alterations in the axial column that would justify the condition was observed. A mass was palpable in the right gluteus. The magnetic resonance showed a mass next to the right gluteus, which involved the sciatic nerve, generating edema and compression of the adjacent structures. Surgery for resection of the lesion was performed, requiring amputation of the right sciatic nerve. The anatomopathological evaluation showed that it was an Ewing's sarcoma.

Conclusion

Peripheral nerve sheath tumors responds nearly 12% of the benign and 7-8% of the malignant soft tissue neoplasms. This diagnosis should be suspected in patients with sciatica who present rapid progression of symptoms and neurological deficit despite targeted and optimized treatment. Magnetic resonance imaging (MRI) plays a pivotal role in the identification, characterization, and differentiation of these lesions. The differentiation of benign and malignant nerve sheath tumors is an imaging challenge, hence, a few imaging signs serve as problem-solving tools. Imaging signs, when used in combination, may be helpful in identifying a neurogenic lesion and may, to an extent, differentiate between their benign and malignant counterparts. Ewing's Sarcoma of the sciatic nerve is a rarely reported tumor. Early histological diagnosis should be sought to avoid diagnostic delay.

Abb. 1

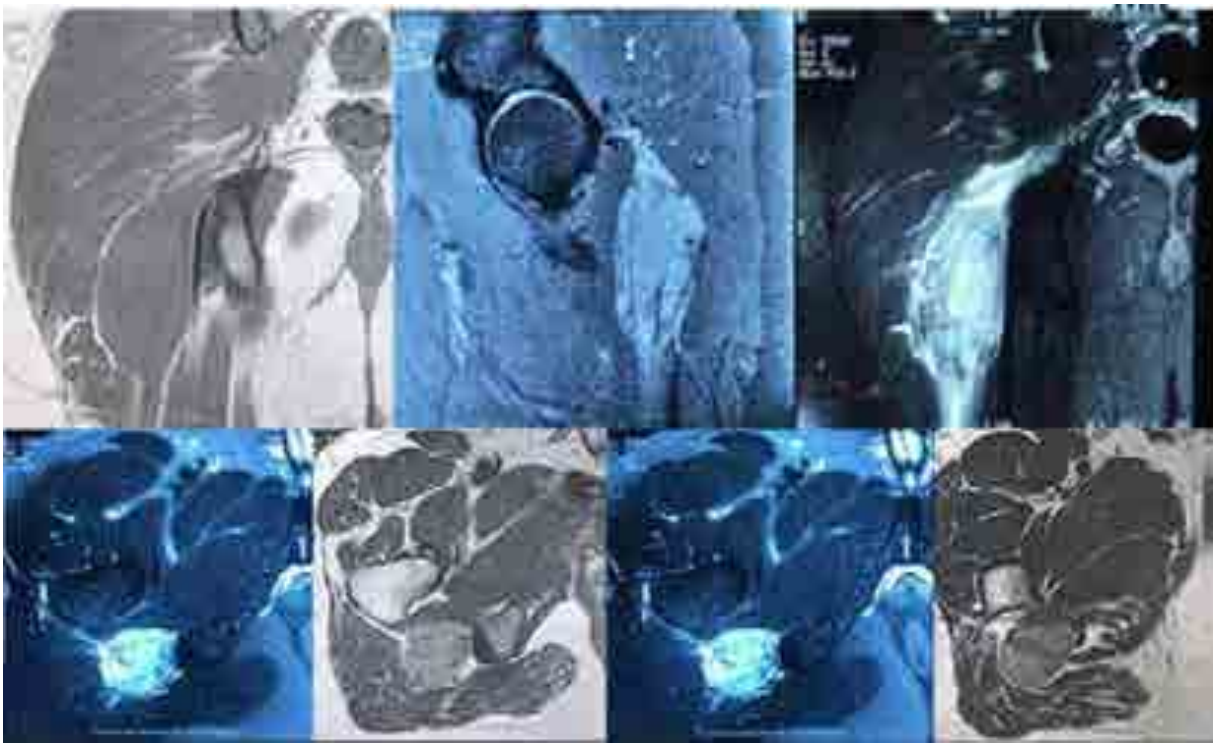
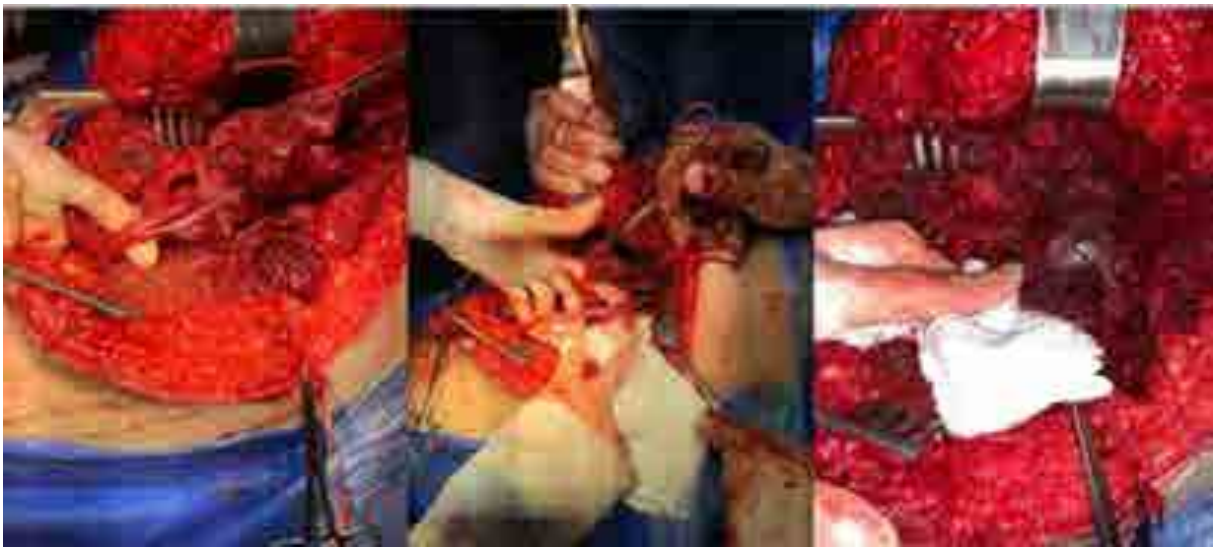


Abb. 2



Varia/*Mixed topics*

P012

Fortschritte bei der Behandlung der entzündlichen, nicht traumatischen atlantoaxialen Subluxation bei Kindern durch eine individuell angepasste Orthese

Advances in management of inflammatory nontraumatic atlantoaxial subluxation in pediatric patients through custom bracing

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Objective

Inflammatory nontraumatic atlantoaxial subluxation is an often-misdiagnosed disease in pediatrics. Torticollis following infection is a typical presentation. Initial treatment with nonsurgical management consists of closed reduction and immobilization. Timing of treatment and grade of immobilization is crucial to avoid further damage and need for secondary surgical fixation. Whereas adequate immobilization was challenging in the past and halo fixators or casts had to be used, custom orthoses based on 3D printing provide new possibilities.

Methods

A retrospective review of pediatric patients with inflammatory nontraumatic atlantoaxial subluxation in our institution was conducted(2010-2022). All patients received diagnostics with X-ray/Ct-Scan and MR. Treatment included either reposition and Halo-Fixation, casting or a customized cervical brace. An additional review of the literature was performed by searching in PubMed, MEDLINE and Embase databases.

Results

Six children (mean 4+- 4y) with Fielding type I-III nontraumatic atlantoaxial subluxation were identified. Two patients were treated with Halo-fixation, one patient with a Minerva cast and three patients with a customized brace. Treatment period was 10-12 weeks with 2 weekly follow ups and a final MRI. Patients were also treated for the underlying infections with antibiotics and/or anti-inflammatory medication. No recurrence and need of surgical fixation were observed. A review of the literature showed no common guidelines on treatment and the use of custom orthoses based on 3D printing has not been reported in this disease yet.

Conclusion

Cervical custom braces based on 3D printinghas are an effective conservative treatment option for inflammatory nontraumatic atlantoaxial subluxation. Guidelines on diagnostics and treatment need to be established to improve management of this disease.

Varia/*Mixed topics*

P013

Ist die spinale Dekompression eine optimale operative Therapieoption für die apophysäre Frakturen im Kindesalter? Fallbericht und Literaturübersicht

Is decompression alone an optimal mode of treatment at children with apophyseal ring fracture? Case Report and Literature Review

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Objective

Fracture of the apophyseal ring is an important but rare disorder. Apophyseal ring fractures typically occur in adolescents and may be related to strenuous sports activities. Multiple treatment options have been described in literature, both conservative and surgical. Removing the compressing fragment can be achieved surgically but is often difficult, as the fracture fragment is usually adherent to the end plates and annulus. We report a case of apophyseal ring fracture for which decompression alone was found to be an effective treatment.

Methods

We report a 10-year-old girl who has L4-Dermatom pain for 3 weeks. She was playing Volleyball at the time she fell. There was nothing remarkable in her body examination. Her MRI indicated an acute fracture of L4 and the left herniated lumbar disc L4/5 . The CT revealed the bone ridge that impinged on the spinal canal at the inferior level of L4. In the next week the patient had the same level of pain and she suffered from a mild foot dorsiflexion. In this moment we decided for the operation. With standard midline incision decompression of stenosis was done with a L4 laminectomy and unilateral deroofing of L5 foramen. Intraoperatively, dura was immobile and adherent to the apophyseal fragment. We removed neither the disc nor the bone fragment. Patient had a significant reduction in pain and improvement in her neurological deficit. Over the years were published studies concerning this disorder. Due to its rarity, there is lack of an agreed treatment strategy. A literature search was performed in electronic database PUBMED. Our search yielded 4 articles. All of them were case reports. The most used surgical options were posterior discectomy simultaneous excision of apophyseal fragments without spine fusion.

Results

Because of methodological shortcomings in publications, it is not possible to definitively conclude what treatment modality is the best. More high-quality clinical studies are needed to draw more confirmable conclusions. In our case, decompression with laminectomy was found to be an effective treatment, leading to a good functional outcome.

Conclusion

Posterior apophyseal ring fracture with a calcified disc adherent to dura is a rare condition which requires not only meticulous decision making for the treatment but also a high index of suspicion for diagnosis by CT and MRI scans. In situations where the dura is adherent, decompression alone without discectomy can be an optimal mode of treatment.

Abb. 1

Figure 1: Mray showing L4/5 disc protusion and CT scan images showing the fracture fragment in sagittal and axial view.

Abb. 2

Year	Author	Treatment
2009	Yen CH et al.	Conservative (2) & Lamina fenestration, nerve roots decompression and discectomy (2)
1998	Peh WC et al.	Lamina fenestration, nerve roots decompression and discectomy (3)
1998	Martinez-Lage JF et al.	Lamina fenestration, nerve roots decompression and discectomy (1)
1990	T. D. BROWNE et al.	Lamina fenestration alone (1)

Table 1: Our literature search (1990-2022) yielded 4 articles (A must be excluded), reporting 9 patients experiencing lumbar fractures. All of them were case reports or case series.

Varia/*Mixed topics*

P014

Langfristige Follow-up nach Dekompression der hinteren Schädelgrube bei Kindern mit Chiari-Malformation Typ I

Long-term follow-up of posterior fossa decompression for children with Chiari malformation type I

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Objective

Posterior fossa decompression is a procedure used to treat symptomatic Chiari malformation type I. The purpose of this study was to analyze and determine the long-term follow-up after posterior fossa decompression in the pediatric setting.

Methods

We describe a series of 10 pediatric patients with Chiari malformation type I, who were treated with posterior fossa decompression with a standard technique consisting in osteoclastic widening of the foramen magnum, laminectomy of C1, opening of the dura, dissection of the arachnoid with opening of the fourth ventricle and duroplasty.

Results

Seven patients were male, 3 were female. Mean age at surgery was 9.7 years (range, 2-16 years). In five patients there was also a syringomyelia. Mean operative time was 167 minutes (range, 130-230). The osseous decompression measured 7.5 cm2 (range, 5-15.6 cm2). All patients were symptomatic (headache, neck pain, dizziness, and ataxia). Early postoperative complications occurred in 2 patients (cerebrospinal fluid leak). All patients had improvement of their preoperative symptoms and of the syringomyelia in MRI scans. The mean follow-up time was 70 months. No patient underwent another surgery during follow-up.

Conclusion

There is an ongoing discussion on the choice of surgical techniques for treatment of Chiari malformation type I. We here show that using a standard technique including dissection of the arachnoid is associated with low postoperative morbidity and provides long term relief of symptoms in children. Nevertheless, multicenter prospective randomized studies are urgently needed to address the question which surgical techniques are the most appropriate.

Varia/*Mixed topics*

P015

Kitesurfing- Unfälle in Verbindung mit cranio-spinalen Verletzungen
Kitesurfing – accidents and association with craniospinal injuries

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Objective

Kitesurfing has gained much popularity over the last 20 years. It is a high impact sport characterized by high speed and big jumps. Despite several safety features, kitesurf injuries can be serious especially with respect to craniospinal injuries. The aim of the study was to identify risk factors and presumed reasons related to local kitesurfing accidents.

Methods

A retrospective study of 18 patients with cranial and spinal injuries, who were consecutively admitted to our institution between 2007 and 2020, was performed. Demografic data, circumstances of the accident, local wind conditions, experience of the kitesurfer, kind of injury, clinical features, operative or conservative therapeutic management, complications and follow up results were analyzed.

Results

The average age of patients was 39,8 years (range 18-64 years) with a male dominance (male/female: 16/2). Six patients were admitted with a mild traumatic brain injury and 3 with a severe brain injury. Surgical decompression due to intracranial mass effects was needed in 2. One patient received an ICP probe for monitoring. Cervical spine injuries were observed in 9 cases. Altogether, 7 vertebral fractures of the thoracic or lumbar spine were found. Complex spinal surgery was required in 4 patients only. Fortunately, no spine injury was combined with a neurological deficit. Besides the craniospinal trauma, additional fractures of the extremities and so on were seen in 12/18 cases.

Non-medical evaluation revealed 2 experienced, 5 advanced and 11 beginning kitesurfers. Thirteen accidents occured on shore. The other 5 kitesurfers sustained injuries as a consequence of a fall and collision with the ground in shallow water or with a breakwater respectively. Maximum wind strength on the day of the event was on average 18m/s, that means 8 beaufort (stormy conditions). None of the athletes used a helmet, only 3 an impact protection vest. During follow up, residual neurological deficits were observed for the patients with severe brain injuries.

Conclusion

Craniospinal injuries due to kitesurfing are rare. In our study, they were allways related to collisions. Mainly, they occured on shore and not on the water, during very stormy conditions and involved mostly non-experienced (88%), non-local (83%) kitesurfers without protection gear. Therefore, the use of protection gear is recommended for the latter community. Especially, the risk of severe brain injury may be minimized by using a helmet.

Varia/*Mixed topics*

P016

Postoperativ prolongierte mechanische Beatmung von chirurgisch versorgten Spondylodiszitis-Patienten: ein Surrogatendpunkt für die frühe postoperative Mortalität

Postoperative prolonged mechanical ventilation in patients with surgically treated pyogenic spondylodiscitis: a surrogate endpoint for early postoperative mortality

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Objective

Surgical procedures with spinal instrumentation constitute a prevalent and occasionally highly indicated treatment modality in patients with pyogenic spondylodiscitis (PSD). However, surgical therapy might be associated with the need of prolonged postoperative intensive care medicine which in turn might impair intended operative benefit.

We analyzed postoperative prolonged mechanical ventilation (PMV) as an indicator variable for such intensive care treatment with regard to potential correlations with mortality in this vulnerable patient cohort.

Methods

Between 2012 and 2018, 177 consecutive patients received stabilization surgery for PSD at the authors" neurosurgical department. PMV was defined as postoperative mechanical ventilation of more than 24 hours. A multivariable analysis was performed to identify independent predictors for 30-day mortality.

Results

23 out of 177 patients (13%) with PSD suffered from postoperative PMV. 30-day mortality rate was 5%. Multivariable analysis identified "spinal empyema" (p=0.007, Odds ratio (OR) 8.1, 95% confidence interval (CI) 1.8-36.8), "CCI > 2" (p=0.04, OR 3.9, 95% CI 1.1-14.8), "early postoperative complications (PSIs)" (p=0.002, OR 14.7, 95% CI 2.6-82.3), "postoperative need for vasopressors" (p=0.04, OR 4.4, 95% CI 1.1-18.0) and "PMV > 24 hrs" (p=0.01, OR 5.9, 95% CI 1.5-22.8) as significant and independent predictors for early postoperative mortality (Nagelkerke"s R2 0.5).

Conclusion

The present study indicates PMV to significantly correlate to elevated early postoperative mortality rates following stabilization surgery for PSD. These results might entail further scientific efforts to investigate PMV as a so far underestimated negative prognostic factor in the surgical treatment of PSD.

Abb. 1

Table: Factors associated with postoperative PMV following stabilization surgery for PSD[1]

	Patients without PMV n=154	Patients with PMV n=23	p-value
Median Age (yrs) *	72 (60-78)	73 (68-77)	0.35
Female sex	62 (40)	6 (26)	0.25
Location of disease			0.03
Cervical	15 (10)	7 (30)	0.01
Thoracic	31 (20)	5 (22)	0.79
Lumbar	98 (64)	9 (39)	0.04
Combined	10 (6)	2 (9)	0.66
Level of disease			< 0.0001
1-2	140 (91)	11 (48)	
> 2	14 (9)	12 (52)	
Associated spinal empyema	45 (29)	14 (61)	0.004
Median CCI	1 (0-3)	3 (1-4)	0.004
Preoperative anticoagulant medication	33 (21)	14 (61)	0.004
Preoperative neurological deficit	39 (25)	11 (48)	0.04
Preoperative systemic inflammation levels			
CRP > 10 mg/L	132 (86)	23 (100)	0.08
WBC > 12 G/L	17 (11)	9 (40)	0.002
Median time of surgery	243 (185-317)	274 (189-393)	0.27
Postoperative need for vasopressors	41 (27)	23 (100)	0.004
Early postoperative complications	24 (16)	9 (39)	0.02
PSIs	9 (6)	5 (22)	0.02
HACs	10 (6)	4 (17)	0.09
Specific SSCs	5 (3)	0 (0)	1.0
30-day mortality	7 (5)	9 (39)	< 0.0001

[1]Values represent the number of patients unless indicated otherwise (%)

CCI, Charlson comorbidity index; CRP, c-reactive protein; HAC, hospital-acquired conditions; IQR, interquartile range; PSIs, patient safety indicators; PSD, pyogenic spondylodiscitis; SSCs, spinal surgery-related complications; WBC, white blood cells; yrs, years; * Median (IQR).

Varia/*Mixed topics*

P017

Das chirurgische Management von spinalen Kavernomen: Resektionsausmaß und Outcome
Surgical management of spinal cavernous malfomations: extent of resection and outcome

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Objective

Spinal cavernous malformations (SCM) are rare intramedullary lesions. This study aims to present the surgical management of SCM in our Department of Neurosurgery in the last 18 years, focusing on the extent of resection and clinical outcome.

Methods

Patients who underwent surgery for SCM from January 2004 to December 2022 were identified by a computer search. Patients were evaluated for initial symptoms, location of SCM, extent of resection, and complications by reviewing patient documents.

Results

In total, 39 patients with SCM were surgically treated in our department in the last 18 years (mean age 48 ± 17 years, 18 male). SCM was located in the thoracic spinal cord in 64.1% of the cases, in the cervical spinal cord in 33.3% and in the medullary cone in 2.6%. Three patients had previously underwent surgeries for SCM in external hospitals. On admission 61.5% of patients presented with spinal ataxia, 56.4% had motor deficits, 82.1% had sensory deficits, and 35.9% bladder and/or bowel dysfunction. Gross total resection was achieved in thirty-seven cases, while subtotal resection was attained in two cases. Postoperative improvement of spinal ataxia, motor deficits, sensory deficits, and bladder/bowel dysfunction was seen in 43.2%, 46.0%, 35.1% and 24.3% of 37 patients with follow-up (mean age 49 ± 17 years, 16 male); worsening in 8.1%, 13.5%, 21.6% and 2.7% (all patients had only slight worsening of symptoms); while stable function was seen in 48.7%, 40.5%, 43.2% and 73.0%. Two patients were lost in follow-up.

Conclusion

Surgical removal is the therapy of choice for SCM and save. In most cases, gross total resection of SCM was achieved without worsening of symptoms in follow-up.

Varia/*Mixed topics*

P018

Ausgebremst: Wie die Tübinger Universität den Neurochirurgen, Neurologen und Anti-Nazi Heinz Köbcke (1895-1969) in der Nachkriegszeit behandelte.

Thwarted: How Tübingen University treated the anti-Nazi neurosurgeon and neurologist Heinz Köbcke (1895-1969) in the post-war period.

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Objective

The life and career of the neurologist, neurosurgeon and Nazi opponent Heinz Köbcke after WW II in Tübingen.

Methods

We evaluated the personnel files of the universities of Tübingen and Munich and Köbcke's legacy in the library of the Ludwig Maximilian University of Munich, his travel reports and neurosurgical publications.

Results

There is hardly any information published on the neurologist and neurosurgeon Heinz Köbcke. Already educated in neurology, internal medicine and general surgery, he spent the years 1933-39 with the world"s most famous neurosurgeons at that time (Olivecrona, Cushing, Dandy, Jefferson, Vincent to name a few) and can be considered as one of the best-trained in the new field of neurosurgery in Germany. But as a political opponent of the Nazi regime and so-called "state enemy" (Nazi Medical leader Leonardo Conti), he was locked out from clinical work when he returned to Germany in 1939. He worked as a medical officer in neurology and psychiatry for the National Insurance Agency. In 1946, he was offered an administrative position as Deputy medical director of the main pension office in Tübingen. In 1948, he habilitated in neurology and worked as an unpaid lecturer in neurology and neurosurgery at Tübingen University, from 1950 as associate professor, still unpaid. The main reasons for the faculty to approve his habilitation were his widespread international connections in a time of scientific isolation of Germany and his influential position as editor of the Deutsche Medizinische Wochenschrift. Nevertheless, he still did not receive a clinical position, and his proposal to establish a modern brain research institute with an operating room was not accepted by the faculty. Instead, the young Werner von Strenge, only trained in military hospitals during the war, headed the neurosurgical ward of the utility hospital and operated on neurosurgical patients, whereas Köbcke had no facilities to treat patients and no income.

Conclusion

The archival documents show how Köbcke was withheld from the opportunity to relaunch his neurosurgical operative work by individual faculty members even after World War II. He finally had to give up neurosurgery and in 1955 accepted a paid position as an adjunct professor of neurology and psychiatry at the Ludwig Maximilian University of Munich.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

J-SPNC002

Späte Zystenbildung nach radiochirurgischer Behandlung von AVM: Fallbericht und kritische Überprüfung
Late cyst formation after radiosurgery for AVM: case report and critical review

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Objective

Stereotactic radiosurgery (SRS) is a frequent treatment option for certain cerebral arteriovenous malformations (AVMs). A greater knowledge of its potential delayed complications is currently being acquired.

Methods

A 58-year-old man who had multiple episodes of cerebral hemorrhage in the context of a left central core AVM with deep venous drainage into the vein of Galen (Spetzler Martin Grade 4) since 2009 had been treated with gamma knife radiosurgery in two separate timepoints. An almost complete obliteration of the AVM was confirmed after treatment and he was making steady progress. Approximately ten years after the first radiosurgery treatment, he presented with severe motor aphasia, Grade 3 right hemiparesis, progressive confusion and memory deficits.

Results

Cerebral imaging revealed cystic degeneration in the AVM periphery and cyst fenestration and posterior cystoperitoneal shunt was proposed. Treatment was not effective and there was progressive cyst enlargement with no clinical improvement. Patient was therefore proposed for surgical mass and cyst excision with an interhemispheric transcallosal intraventricular approach. Postoperative MRI showed complete removal of the nidus. He had an uneventful post-operative course. At 6-month follow-up, our patient experienced remarkable improvement in his speech, power, dexterity and was able to walk autonomously.

Conclusion

Cystic degeneration of AVMs is a possible long-term complication after SRS. Long-term follow-up and data on such patients is crucial, even with complete nidal obliteration.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

P019

Die mikrochirurgische Dekompression der A. vertebralis: Ein interdisziplinärer Therapieansatz bei rezidivierenden Infarkten im hinteren Kreislauf.

Surgical decompression of the vertebral artery: A novel interdisciplinary approach for the treatment of recurrent strokes in the posterior circulation.

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Objective

Thromboembolic strokes caused by mechanical compression of an aberrant course of the VA is a rare phenomenon. Owing to its rarity, there is little experience on the surgical management and outcome of such cases. Here we report a novel interdisciplinary surgical approach for circumferential decompression of the VA in two patients with early-onset strokes of the posterior circulation.

Methods

Diagnostic workup and surgical treatment are described.

Results

We report on two male patients who presented with recurrent early-onset strokes in the posterior circulation at age 36 and at age 28, respectively. While CT-angiography ruled out occlusion or stenosis of extra- and intracranial arteries, it revealed entry of the right VA into the transverse foramen at the C4 level as well as an unusual proximity to the thyroid cartilage. While in the first patient digital substraction angiography (DSA) indicated focal dissection at the very spot where the cartilage and the right VA were closest to each other, dynamic DSA with neck rotation ruled out compression or focal dissection of the VA in the second one. In both cases, further thorough diagnostic workup was inconclusive. Medical treatment failed to prevent further arterio-arterial thromboembolisms. After multidisciplinary discussion, an extrinsic compression at the variant predilection site of the VA was suspected. Therefore a circumferential surgical decompression deemed as the best approach in order to reduce focal mechanical stress on the VA. Following a right sided transverse paramedian skin incision at the level of C5 the superior cornu of the thyroid cartilage was mobilized and resected. After microsurgical dissection of the longus colli and the longus capitis muscles the VA was identified and released from the adjacent structures. Subsequently the anterior tubercle of the transverse process of c5 was resected and flattened with a diamond burr. Intraoperative Doppler was utilized to assess adequate arterial flow after decompression. The postoperative course was uneventful and none of the patients experienced further strokes during a follow-up of 18 and 6 months after the operation.

Conclusion

Our targeted surgical technique at the level of the extrinsic compression is a straightforward approach with excellent results. Circumferential decompression with resection of the anterior portion of the transverse process and the superior cornu of the thyroid cartilage is pivotal in order to avoid treatment failure as previously reported.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

P020

Rate der Volumenveränderung von chronischen Subduralhämatomen nach der Embolisation der Arteria meningea media

Rate of volume change of chronic subdural hematomas after embolization of the middle meningeal artery

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Objective

The objective of this study is to evaluate the rate of volume change of chronic subdural hematomas after the embolization of the middle meningeal artery.

Methods

We retrospectively analyzed the volume change of hematomas dependent on clinical and radiological factors. Volume of the hematoma before embolization and in all follow-up CT scans were measured by software. Rate of volume change was then calculated as follows: rate of volume change (ml/d) = (Volume in ml in the last follow-up CT scan – Volume in ml in the initial CT scan) / time differences between these CT scans in days.

Negative values represent decrease and positive values represent increase of volume.

Possible influencing factors such as the pre-interventional volume, radiological type (modified Nakaguchi Classification), embolic agent and whether the hematoma was operated before embolization or not, were statistically tested. A p-value of < 0.05 was considered significant.

Results

A total of 43 hematomas in 36 patients were treated by embolization. The mean pre-interventional volume was 68,93 ml (SD=29.59, max. 144, min 12). Most hematomas appeared homogenous hypodense (n=14) or trabecular (n=12). Other types included the homogenous iso-dense type (n=5), the homogenous hyperdense type (n=6), the gradation type (n=1) and the laminar type (n=5). The embolic agents used in this study were Onyx (n=21), Squid (n=15) and PHIL (n=7). 18 hematomas were not treated surgically prior to embolization.

Mean volume change of all hematomas was -1.95 ml/d (SD=3.55, max. 7.3, min -15). There was neither an influence of the pre-interventional volume (R^2=0.026, p=0.313), the radiological type (p=0.33) nor the embolic agent (p=0.282). There was no significant difference of the rate of all hematomas within the first month compared to the rate within the whole follow-up period (p=0.071).

However, there was a significant faster volume change in previously surgically treated hematomas (-2.77 ml/d vs. -0.68 ml/d; p=0.046). The rate of responding hematomas without surgery within the first month was faster than the total rate (-1.44 ml/d vs. -0.94 ml/d; p=0.043).

Conclusion

Rate of volume change after embolization of the middle meningeal artery is slow with a mean rate of -1.95 ml/d in all hematomas. Previously surgically treated hematomas regress faster. Studies with a larger patient cohort and with an equal follow-up regime are necessary to confirm our findings.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

J-SBNC003

Kreatininwerte und glomeruläre Filtrationsrate: mögliche Marker für den Verlauf von intrakraniellen Aneurysmen?

Creatinine levels and glomerular filtration rate: possible markers of intracranial aneurysms outcome?

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Objective

To analyze the role of serum creatinine levels as a biomarker of intracranial aneurysm outcomes.

Methods

This is a prospective cohort study with patients who were admitted in the hospital due to Subarachnoid hemorrhage (SAH), between January 2018 and November 2019. Patients of both sexes and ages, with ruptured and unruptured cerebral aneurysm, who were admitted to University of São Paulo (HCFMUSP) between January 2018 and November 2019 were included in the study. One hundred forty-seven patients were followed with serum creatinine at admission and 6 months after the event. Linear and logistic regressions were used to analyze the data. Modified Rankin scale (mRS) was used to assess outcome.

Results

Creatinine level was not directly related to clinical outcome nor aneurysm rupture ($p > 0.05$). However, patients with a glomerular filtration rate (GFR) lower than 72.50 mL·min–1 had an odds ratio (OR) of 3.049 ($p = 0.006$) for worse outcome. Similarly, aneurysm rupture had an OR of 2.957 ($p = 0.014$) for worse outcomes. Stepwise selection model selected 4 variables for outcomes prediction: serum creatinine, sex, hypertension and treatment. Hypertensive patients had, on average, an increase in 0.588 in mRS ($p = 0.022$), while treatment with microsurgery had a decrease in 0.555 ($p = 0.038$).

Conclusion

Models to predict aneurysm outcome are important to take medical decisions that will improve patient's quality of life. This study shows that creatinine was not directly related to mRS 6 months outcome, but might have a role in predictions models as shown by the stepwise selection model approach. Furthermore, GFR can be used to help predict long term outcomes.Patients with GFR lower than 72.5 mLymin-1 had an OR of 3.049 ($p = 0.006$) for worse outcome after 6 months measured by mRS.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

J-SBNC004

Homocysteinspiegel als Risikofaktor für einen ischämischen Schlaganfall: eine systematische Überprüfung und Meta-Analyse

Homocysteine levels as a risk factor for ischemic stroke: a systematic review and meta-analysis

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Objective

Analyze if there's a correlation between higher homocysteine levels and ischemic stroke

Methods

A systematic review was performed at Pubmed and Embase platforms using the keywords "Plasma homocysteine", "Homocysteine", "Hyperhomocysteinemia", and "Ischemic Stroke". All articles published in English up to August 13, 2022 were included. The initial search found 1361, after a thoroughly analysis, 38 studies were selected to compose the final analyzed data, however, only 13 of those reported means and standard deviations for cases and controls, and therefore were used in the meta-analysis. The studies were then categorized into two groups, prospective and retrospective based on the time the blood sample used to assess the homocysteine levels was collected, before or after the stroke event, respectively. Only 7 of the previous studies were prospective studies, the statistical analysis was made by a random-effects inverse-variance weighted meta-analytical approach in order to pool standardized mean differences, with estimation of $\tau 2$ through the DerSimonian-Laird method.

Results

Analyzing only the prospective studies, homocysteine levels were significantly higher in stroke patients (SMD = 1.27, 95% CI 0.49–2.04, p = 0.0013). The heterogeneity between the studies, though, was very high (I2 = 99%). When compared to the retrospective studies similar results were found (SMD = 2.35, 95% CI 0.99–3.70, p = 0.0007) with heterogeneity also very large (I2 = 99%).

Conclusion

This meta-analysis shows that homocysteine levels are higher in patients with ischemic stroke than in controls. Further studies are necessary to evaluate its prognostic value and if it"s a modified risk factor.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

J-SBNC005

Dekompressive Kraniektomie: Operationszeit und Prognose, eine Erfahrung eines einzigen Zentrums in Brasilien im Vergleich zu früheren weltweiten Studien

Decompressive craniectomy: surgical time and prognosis, a single center experience in Brazil compared to previous worldwide trials

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Objective

Evaluate the correlation between surgical time and clinical/functional outcome found at a neurosurgical reference center in Brazil and previous trials

Methods

A retrospective study was conducted using medical records of patients treated at the Neurosurgery service of Hospital da Resaturação (HR), between March 2010 and March 2018. The following variables were gathered and analyzed: age, sex, comorbidities, time from onset of symptoms to arrival at the hospital, time from symptom onset to neurosurgical procedure, laterality of the ischemic event, preoperative Glasgow Coma Scale (GCS), surgery time, intraoperative complications, postoperative complications, length of hospital stay and clinical/functional status after the procedure, evaluated by the modified Rankin Scale and Glasgow Outcome Scale at 6 months and 12 months postoperative. The secondary data for the comparative analysis was composed by four randomized, double-blind, controlled trials chosen by its level of scientific relevance as well as the number of citations in the main studies on the theme.

Results

A total of 263 patients were analyzed, 118 were part of the randomized trials. The clinical outcome was analyzed using the modified Rankin Scale at 6 and 12 months postoperative. The average time of intervention was 28.4h since the beginning of symptoms, 95% of the group who underwent a decompressive craniectomy between 12 and 24 h had a favorable outcome (mRS 2 and 3) after 6 months postoperative. A significantly better outcome was observed at the group operated < 12h at our study when compared with the other trials, our study showing (mRS 2 and 3) in 55 and 70% of the cases in 6 and 12 months respectively, as the trials it ranged from 7 to 47% in 6 months and 6 to 50% in 12 months period. A worse prognosis was observed at the group with the late approach (>24h) as shown at the comparative trials.

Conclusion

A favorable clinical outcome was observed with higher prevalence in the group operated <12h from the beginning of symptoms in our study when compared with the above-mentioned trials. Further studies are necessary to evaluate the variables that contributed to these diverse findings

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

J-SBNC006

Unterschiedliche Risikofaktoren für Kurz- und Langzeitergebnisse bei Patienten mit rupturiertem Aneurysma je nach chirurgischem Ansatz

Different risk factors for short- and long-term outcomes in patients with ruptured aneurysm based on surgical approach

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Objective

To evaluate the risk factors for poor outcomes after microsugical or endovascular treatment of aneurysmal subarachnoid hemorrhage (aSAH).

Methods

Patients with ≥ 18-years of age and aSAH were included, while patients who died within 12 h of admission or lost follow-up were excluded. All participants underwent standardized clinical and radiological assessment on admission and were reassessed at discharge and at 6-months follow-up using the Glasgow Outcome Scale (GOS).

Results

Death at discharge was associated with female gender, anterior communication artery (ACoA) aneurysm location and presence of atherosclerotic plaque in the surgical group, and with age in the endovascular group. Both groups had clinical condition on follow-up associated with mFisher score on admission and hypertension. GOS on follow-up was also associated with presence of atherosclerotic plaque and multiple aneurysms in surgical group, and with age in endovascular group.

Conclusion

Subjects treated surgically are prone to unfavorable outcomes if atherosclerotic plaques and multiple aneurysms are present. In patients with endovascular treatment, age was the main predictor of clinical outcome.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

P021

Intraaneurysmale Kontrastmittelstauung während der intraoperativen digitalen Subtraktionsangiographie: Ein Prädiktor für Thrombose und langfristigen Verschluss eines intrakraniellen Aneurysmarestes nach Clipping?

Intra-aneurysmal contrast agent stasis during intraoperative digital subtraction angiography: A predictor of thrombosis and long-term occlusion of intracranial aneurysm remnant after clipping?

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Objective

Routine use of intraoperative digital subtraction angiography (iDSA) leads to increased detection of intracranial aneurysm (IA) remnants after microsurgical clipping. Spontaneous thrombosis of IA remnants after clipping is considered a rare phenomenon. We analyse iDSA characteristics to find predictors for IA remnant thrombosis.

Methods

Treated aneurysms with intraoperative detection of an IA remnant after clipping were identified and subdivided into remnants undergoing spontaneous thrombosis and remnants with long-term patency and/or remnant growth. Angiographic features of iDSA were analysed and compared between the two groups. In addition, we performed a systematic review of the literature to identify similar cases of spontaneous IA remnant thrombosis.

Results

Out of 22 remnant aneurysms few cases underwent a spontaneous thrombosis and long-term occlusion. In all thrombosed cases (n=4) iDSA revealed stasis of the contrast agent within the IA remnant until the late venous phase (mean 6.75 ± 0.4 sec.). By contrast, in all cases with patent long-term IA remnant (n = 18) iDSA demonstrated early wash-out without stasis of contrast agent. In the literature we found 13 cases with spontaneous regression of an IA remnant.

Conclusion

Spontaneous thrombosis of IA remnants after clipping is a rare phenomenon. Contrast stasis in IA remnants during iDSA seems to predict long-term IA occlusion and therefore clip correction manoeuvres may not be warranted in these cases.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

P022

Chirurgische Behandlung des schweren posterioren reversiblen Enzephalopathie Syndrom mit Beteiligung des Hirnstamms: Systematische Übersicht und illustrativer Fall

Surgical treatment of severe posterior reversible encepha-lopathy syndrome with brainstem involvement: Systematic Review and Illustrative Case

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Objective

Untreated hypertension can lead to severe posterior reversible encephalopathy syndrome (sPRES), that is a reversible intracranial complication. Involvement of posterior fossa structures including brainstem is extremely rare but life threatening condition if not treated properly and timely.

Methods

We searched the MEDLINE electronic database for studies on PRES with brainstem involvement. Hypertensive crisis as a cause of PRES and surgical treatment of PRES were inclusion criteria. We show an insight into a systematically treated case that has this constellation. Finally we show summarize the data in current literature to provide recommendation for this rare devastating condition.

Results

5 reports with a total of 7 patients depicted cases of PRES with brainstem involvement which were treated by posterior fossa decompression. Hypertension and malignant hypertension were common at onset of PRES. 85% of all cases were female and one of these cases was a 3-year-old girl. 71% of patients had an mRS bet-ter than 4 at discharge.

Conclusion

The link between hypertensive emergency and PRES has often been overlooked. A clinically manifest brainstem PRES can be alleviated through posterior fossa decompression so the ischemic and oedematous brain tissue can regenerate without further injury due to mechanical compression.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

P023

Meta-Review über die Einhaltung der Kriterien der Experimental Secondary Ischemia (ESI) in SAB Mausmodellen

Meta-review of compliance with Experimental Secondary Ischemia (ESI) criteria in experimental studies using SAH mouse models

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Objective

Despite over 750 animal research studies addressing Delayed cerebral ischemia (DCI) having been published - some of which yielded very promising results - translation from bench to bedside has failed so far. One reason for the failed translation might be a lack of DCI definition in experimental SAH. In humans, (1) focal neurological impairment or a neurological deterioration, (2) occurring secondarily and not after aneurysm occlusion and (3) cannot be attributed to other causes are key features of the DCI definition by Vergouwen et al (2010). Based on this, a definition for DCI was developed for experimental SAH in mice – called the "experimental secondary ischemia" (ESI).

The aim of this study was to assess to what extent the previously published work on experimental SAH in mice has considered the key features of the aforementioned ESI.

Methods

We performed a professional Embase and PubMed literature research to identify all (1) experimental injection or perforation SAH models (2) in mice, (3) using no transgenic mice, (4) assessing experimental SAH in comparison to either a sham or other control group, (5) published between 01/1999 and 11/2018 and (6) that are in English language. Data on publication date, model and definition on DCI / vasospasms were extracted and analyzed using Prism 9 (GraphPad Prism).

Results

Out of 1454 publications identified by our search strategy, 72 studies met the inclusion criteria. Of the total of 1920 non-transgenic mice in the 72 studies, 836 mice were assigned to control groups without SAH and 1084 were SAH mice without treatment. 44/72 studies (61.1%) induced SAH using perforation and 24/72 (33.3%) used the injection model. 53/72 studies (73.6%) defined neurological impairment and/or deterioration and described the occurrence of general / focal neurological impairment. In 6/72 (8.3%) studies, it was ensured that the neurological deterioration was a secondary event and neither caused by a primary damage following SAH induction nor by anesthesia. 4/72 (5.6%) ruled out other conditions for neurological deterioration. In total, 1/72 studies (1.4 %) met the ESI definition.

Conclusion

Key features of DCI were considered in 5.6% to 73.6% of recent studies analysing experimental SAH in mice. Ensuring that DCI/ESI-related neurological deterioration in experimental SAH is a secondary event and not caused by a primary damage following SAH induction might be essential for a successful translation from bench to bedside.

Vaskuläre Neurochirurgie/*Vascular neurosurgery*

J-SBNC007

Ischämischer Schlaganfall: Kann chronische Migräne ein Risikofaktor sein?
Ischemic stroke: may chronic migraine be a risk factor?

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[6]Escola Superior de Ciências da Saúde, Medicine, Brasilia, Brasilien
[7]Universidade Federal do Piaui, Medicine, Piaui, Brasilien

Objective

To conduct a literature review on the relationship of chronic migraine as a risk factor for ischemic stroke (IS) and to identify the main causes that highlight this association.

Methods

Bibliographic review of scientific articles searched in PubMed, Medline, Embase, Science Direct, The Cochrane Database.

Results

Stroke is responsible for about 100 thousand deaths/year in Brazil and is the leading cause of death and disability in the country, also corresponds to 80% of hospitalizations in the public system. Migraine affects 5 to 25% of women and 2 to 10% of men and can present symptoms similar to those of IS. The incidence of migraine inducing infarction ranges from 0.5 to 1.5% of all IS and 10 to 14% of IS in young patients. The relationship between migraine and IS showed to be more prevalent in women, since chronic migraine was present in 25.4% of patients who had IS. The relative risk of IS was twice as high in people with migraine compared to individuals without migraine. In this context, it was observed that the risk increased in migraine with aura. Symptoms similar to those of a stroke such as hemiparesis, aphasia, amnesia, transient blindness and mental confusion may be present in migraine.

Conclusion

Although the etiology of IS in migraine is still not fully understood, studies recognize that migraine is a risk factor for IS and advocate the importance of early identification of red flags to potentially reduce neurological morbidities. There may be several interactions between migraine and IS that show that it is possible to confuse the symptoms of both diseases by their similarities, therefore, an accurate diagnosis is necessary, and the use of imaging exams is essential to rule out IS.

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Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P024

Analyse der stromalen Tumor-Mikroumgebung in Brustkrebs-Hirnmetastasen mit hoher und niedriger Immuninfiltration

Analysis of the stromal tumor microenvironment of breast cancer brain metastases with high and low immune infiltration

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Objective

Immunotherapy is suggested to be a powerful new treatment approach for many cancer entities with formerly poor outcomes, like breast cancer with brain metastases. Our study aims to identify possible interactions between T cells, the main effector cells of current immunotherapies, and the stromal tumor microenvironment of breast cancer brain metastases.

Methods

Across a clinically annotated cohort of 152 cryopreserved breast cancer brain metastases whole tissue sections and a sub-cohort of the 24 tissues with the highest and lowest T-cell infiltration, multiplexed immunofluorescent imaging and semi-automated quantification of stromal compartments were performed. To detect possible interactions, associations between the number and spatial distribution of the stromal components with the number and spatial distribution of T cells were investigated.

Results

First, we focused on the stromal composition in the sub-cohort with the highest and lowest T cell infiltration. We defined three main stroma compartments: brain parenchyma (GFAP+ astrocytes, NF160 kDa+ neurons, Myelin+/Olig2+ oligodendrocytes), blood vessels (CD31+ endothelial cells, NG2+ pericytes) and extracellular matrix (Collagen I, Collagen IV, Fibronectin, Tenascin C).

There was no significant correlation between the cells from the brain parenchyma subset and immune infiltration.

Concerning vessels, it was striking that 24.24% of all T cells were found within a radius of 10 µm of the nearest endothelial cell, and 98.24% within a radius of 100 µm. Endothelial cells in cases with high T cell infiltration were significantly less covered by pericytes suggesting a lower blood brain barrier function.

Furthermore, vessels were far more likely to be embedded in the matrix-rich tumor stroma than the tumor cell islands ($p<0.001$). Out of all extracellular matrix proteins, Tenascin C was the best predictor of immune infiltration, as high Tenascin C content significantly correlated with high T cell content ($p=0.0353$). This finding was validated in the full cohort of 152 cases.

Conclusion

In our study, we showed that most T cells were within direct reach of blood vessels, and often separated from the tumor islands by a rich layer of extracellular matrix. The finding of a different matrix composition in brain metastases with high and low T cell infiltration suggests that targeting matrix proteins could impact immunotherapeutic treatment responses. Further investigation of the functional mechanisms behind those findings is needed.

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P025

Kombinatorische Analyse für das Monitoring von Glioblastomen mithilfe von Omics-Daten
Combinatorial analysis for GBM monitoring using Omics data

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Objective

Knowledge of individual time-to-recurrence (TTR) of GBM patients is critical to enable life-prolonging repeated surgery. MicroRNAs (miRNAs) are non-coding single-stranded RNA molecules of 21 to 25 nucleotides and related to numerous tumor cell functions in GBM. We envisage the realization of a multi-omics approach integrating miRNAs, EVs, and proteomics to enable a combined rational detection of markers associated with GBM recurrence.

Methods

Pre- and postoperative serum samples from newly diagnosed GBM patients and patients with GBM recurrence were collected from a cohort of 50 patients and subjected to proteomic and radiomic analysis in conjunction with RNASeq analysis. Proteomic analysis was performed on initial GBM and patient matched recurrent GBM samples by LC-MS/MS using a training cohort (retrospective). Protein candidates identified as differentially regulated in rGBM were validated by IHC, qPCR analyses, and ELISA measurements in tumor tissue and in plasma samples.

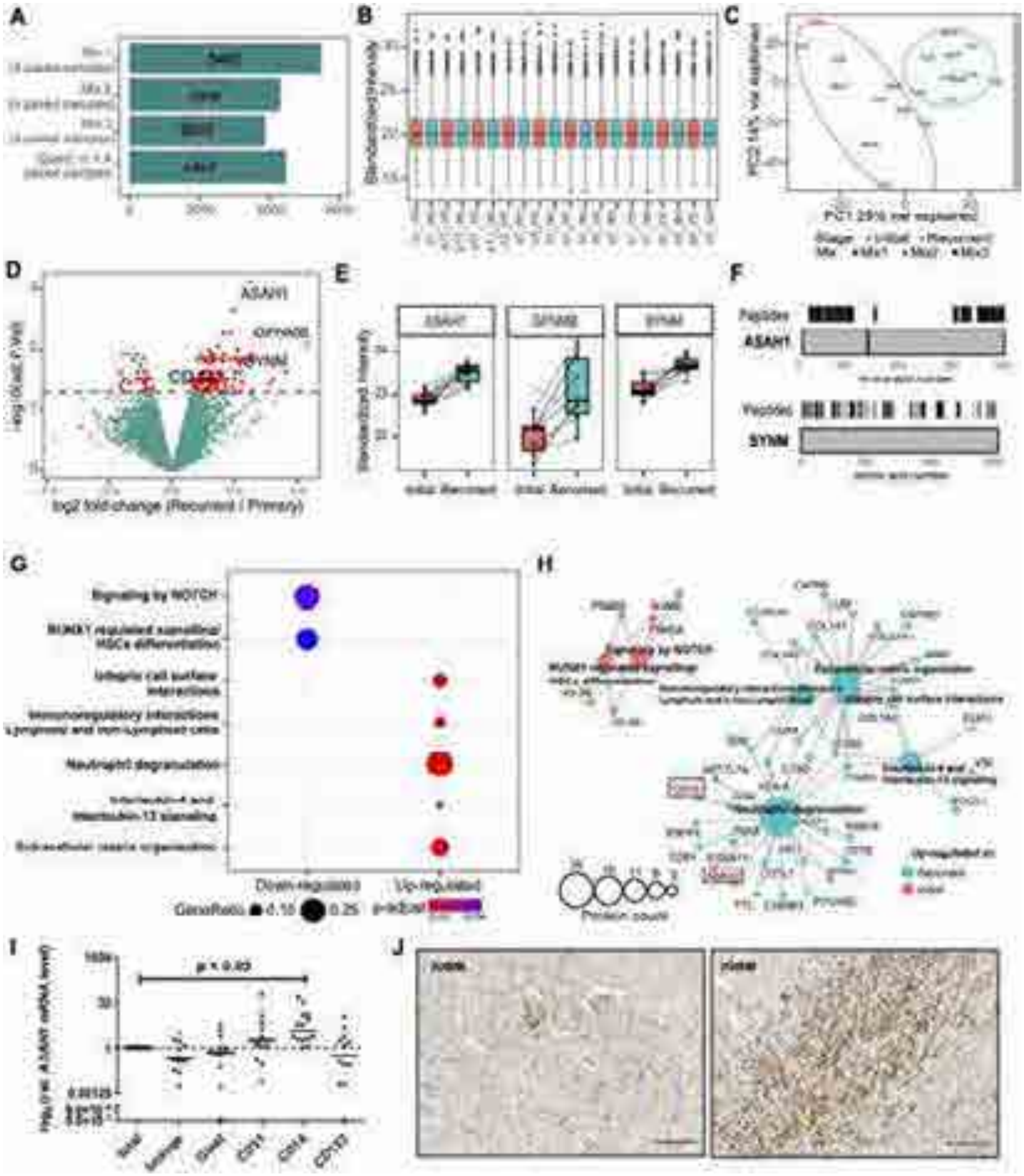
Results

By proteomic analyses, several proteins were identified in normal vs. initial GBM. Among these, we identified the acid ceramidase (ASAH1), the nanofilament protein synemin (SYN), the glycoprotein nonmetastatic melanoma protein B (GPNMB), and, according to a neutrophil signature in recurrent GBM, the metalloprotease MMP-9 as prognostic markers for recurrent GBM. Further analysis revealed that ASAH1 expression is detectable in tumor-associated neutrophils (TANs). All four markers were tested in a prospective GBM patient cohort and showed a significant specificity with an AUC of >90%.

Conclusion

This study proposes a combination of protein analytes in serum samples that could potentially be used to monitor GBM progress and identify recurrence at an early stage in disease progression. In particular, the combination of miRNA and proteins isolated from plasma or from serum EVs has a high potential to be considered as specific GBM prognostic factors.

Abb. 1


A
B
C
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I
J
ASAH1
SYNM
Standardized intensity
log2 fold change (Recurrent / Primary)
Initial Recurrent
Peptides
Signaling by NOTCH
Integrin cell surface interactions
Neutrophil degranulation
Down-regulated
Up-regulated
Protein count
p < 0.05

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P026

Synergistisch Effekte durch kombinierte Therapie von TTFields und Nimodipin bei Gliom-Zellen
Synergistic effects of combining tumor treating fields with nimodipine in glioma cells

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Objective

The non-invasive application of low-intensity alternating electric fields (tumor treating fields, TTFields/TTF) to WHO grade 4 gliomas has been shown to significantly prolong progression-free survival. Calcium channel activation appears to be a mechanism of action of TTFields. Nimodipine as a calcium antagonist has so far found its indication in neurosurgery in the prophylaxis of vasospasm after subarachnoid hemorrhage. Our own preliminary work showed a cell type independent neuroprotective and -regenerative effect in neuronal cells and increased therapy response of cancer cells. Furthermore, there is evidence of improved response of selected cell lines to TTF in combination with other calcium channel inhibitors. Therefore, the aim of our study was to investigate the effect of combination of TFFields and nimodipine in glioma cell lines.

Methods

In this in vitro study, glioma cell lines LN299 (WHO grade 4) and U343 (WHO grade 3) were used. $5x10^4$ cells pre-treated with 20µmol/l nimodipine were exposed to alternating electric fields for 24 and 48h using the Inovitro™ system (Novocure) while maintaining the drug therapy. In each of the experiments, medium was changed with nimodipine application after 24h. Subsequently, cell death was analyzed by cell counting with the Chemotec CellCount and with the sulforhodamine B assay.

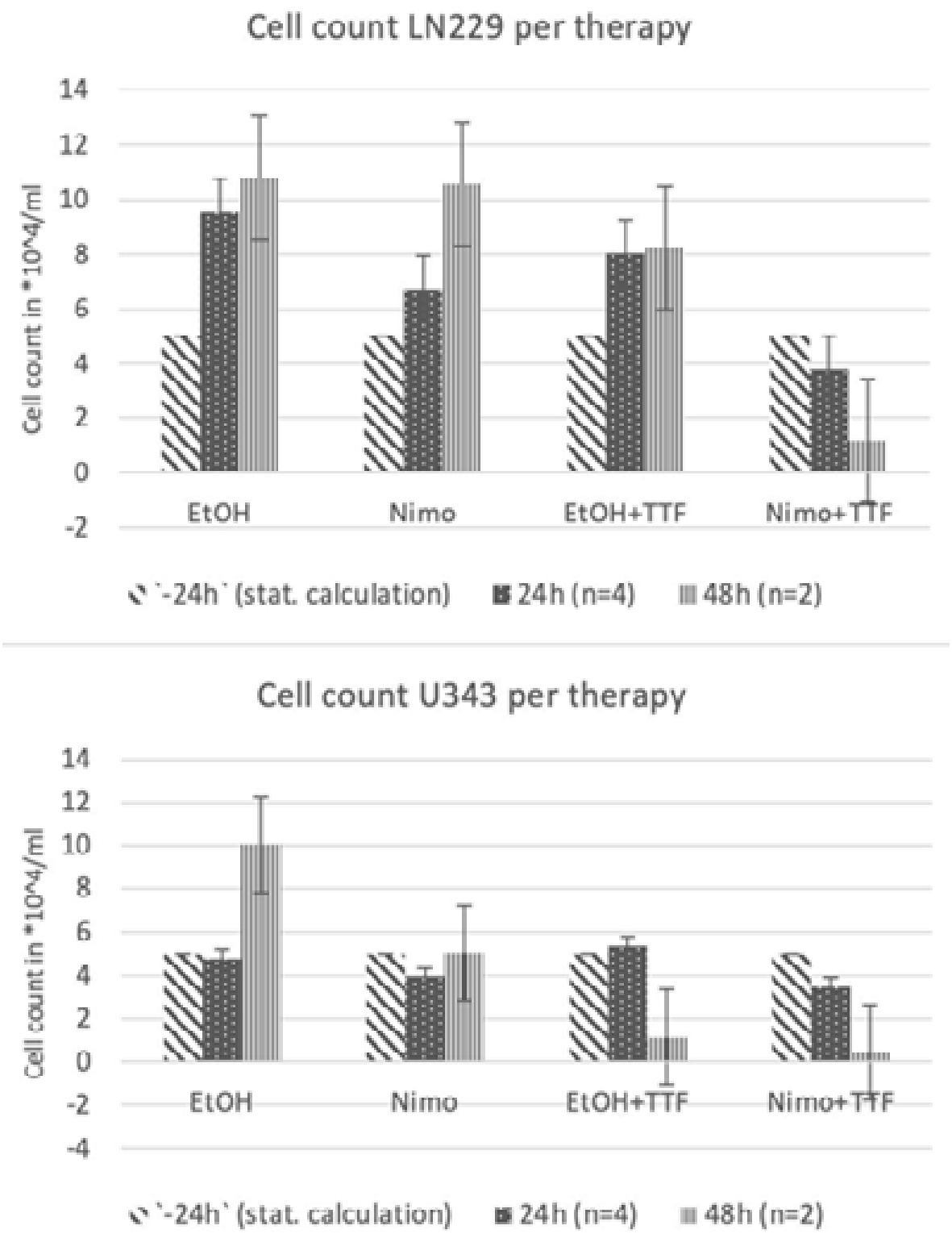
Results

The results showed a 29.3% reduction in cell number (LN229) with nimodipine therapy and 15.8% with TTFields after 24h. A combination of nimodipine and TTF resulted in a 60.4% reduction in the trial, all compared with the control group. For U343, a similar observation was made: -17.6% cells with nimodipine and +12.1% with TTF therapy only, and the largest reduction with combination therapy at -27.5% (nimodipine + TTF). Over the 48-hour period, the values with lower significance are -2% (nimodipine), -23.4% (TTF), and -89% (combination therapy) for cell line LN229 and -50% (nimodipine), -88.9% (TTF), and -95.5% (combination therapy) for U343.

Conclusion

The combination of TTFields and nimodipine administration appears to be superior to TTF therapy alone in terms of cell death. It can be demonstrated by calculation (by multiplying the observed effect for TTF alone with that for nimodipine) that not only is there an additive effect, but the combination of the two forms of therapy has a synergistic effect. This raises hope that therapy with TTFields and nimodipine may have a positive impact on progression-free and overall survival in WHO grades 3 and 4 gliomas.

Abb. 1


Cell count LN229 per therapy
Cell count in *10^4/ml
14
12
10
8
6
4
2
0
-2
EtOH
Nimo
EtOH+TTF
Nimo+TTF
`-24h` (stat. calculation)
24h (n=4)
48h (n=2)
Cell count U343 per therapy
Cell count in *10^4/ml
14
12
10
8
6
4
2
0
-2
-4
EtOH
Nimo
EtOH+TTF
Nimo+TTF
`-24h` (stat. calculation)
24h (n=4)
48h (n=2)

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P027

Die funktionelle und prognostische Rolle des TWEAK Rezeptors FN14 in glioblastoma
A functional and prognostic role for the TWEAK cytokine receptor (Fn14) in glioblastoma

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Objective

Fibroblast growth factor-inducible 14 (Fn14; TNFRSF12A) is a cell surface receptor for the tumor necrosis factor (TNF) family member TNF-like weak inducer of apoptosis (TWEAK). The Fn14 gene is normally expressed at low levels in healthy tissues but expression is significantly increased in GBM and correlates with poor prognosis. A significant role is also ascribed to the soluble form of Fn14 (sFN14) which might be generated by proteolytic cleavage, termed ectodomain shedding. The objective of this study was to evaluate the importance of Fn14 and its release in tumor cells as a contribution to tumor cell motility and to assess soluble FN14 as a potential diagnostic marker in GBM.

Methods

Using protease inhibitors TAPI (Metalloproteases) and DAPT (Gamma-Secretase, GS), the shedding of FN14 was investigated by ELISA in patient-derived GBM cells. A CRISPR/Cas9 knockout of FN14 was generated in the mouse GBM cell line GL261. Cell motility was investigated by scratch and invasion assays in the presence of recombinant TWEAK. Plasma samples from healthy individuals, initial GBM and recurrent GBM tumor patients were collected and subjected to FN14 ELISA measurements.

Results

In primary GBM cells, DAPT inhibited release of sFN14 by 92 % ($p=0.003$) suggesting that soluble FN14 is mainly generated by gamma-secretase activity. Functionally, DAPT reduced GBM cell migration but migration was restored when cells were treated with TWEAK in a dose-dependent manner. In FN14 knockout GBM cells, invasion was inhibited significantly from 42.6 for control vs. 6.1 % for FN14 knockout cells ($p<0.0001$) and TWEAK was not able to restore invasive properties of Fn14 knockout cells indicating that shedding of FN14 plays a pathophysiological role by mediating invasion of GBM cells. Soluble FN14 was also detected in the circulation and showed an increase in plasma from GBM patients compared to healthy control individuals. When comparing plasma levels of sFN14 from initial vs. recurrent GBM patients, an increase of protein levels was observed.

Conclusion

Our data suggest that FN14 and its proteolytic release plays a pathophysiological role in GBM and could be of importance when defining easy access markers for glioblastoma manifestation and recurrence.

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P028

Analyse funktioneller neuroplastischer Veränderungen im sensomotorischen Kortex von Glioblastompatienten in Abhängigkeit vom Tumorwachstumsmuster

Analysis of functional neuroplastic changes in the cortical sensomotor system in relation to different growth patterns of glioblastoma

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Objective

The interpretation of fMRI data in glioblastoma multiforme (GBM) is challenging as these tumors exhibit specific hemodynamic processes which together with malignancy and tumor volume as well as its proximity to eloquent cortex areas may lead to misinterpretations of fMRI signals. The aim of this study was to investigate if different radiologically defined GBM tumor growth patterns may also influence the fMRI signal, activation pattern and functional connectivity differently.

Methods

37 patients (21 male, 16 female, mean age 59.46 years) with GBM located in the sensomotor cortex were included and stratified according to their radiologically defined tumor growth pattern into a group with uniform (U-TGP) and diffuse tumor growth pattern (D-TGP). Functional data were acquired while patients performed motor tasks (movement of hand, foot, and tongue) and were analyzed using Statistical Parametric Mapping (SPM12) with the marsbar, LI and CONN toolboxes. Here, the percent signal change (PSC) and the laterality index (LI) were analyzed, as well as functional connectivity (FC) between 22 ROIs of the Default Mode, Salience, Dorsal Attention, Fronto Parietal, and Sensorimotor network.

Results

When comparing the PSC in sensomotor cortex ROIs, patients with D-TGP showed lower PSC values than patients with U-TGP in most ROIs examined, although these differences were statistically not significant. The comparison of both hemispheres also showed minor but statistically not significant reductions in PSC in the affected hemisphere in both groups. We also found higher LI values in the prognostically less favorable group of patients with D-TGP, although these were also not statistically significant. In FC, only minor differences were found during hand and tongue movement. During foot movement, however, U-TGP patients showed enhanced intra-network connectivity in the Sensorimotor network as well as increased inter-network connectivity between the Sensorimotor network and the ROIs of all other networks.

Conclusion

The results showed that minor and statistically not significant differences between both patient groups with different tumor growth patterns seem to be present on a functional level. Interestingly, the differences in FC were more distinct during foot movement compared to hand and tongue movement, showing an increased intra- and inter-network connectivity of the Sensorimotor network.

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P029

Entwicklung eines Protokolls zur Expansion von NKG2C-positiven NK-Zellen im klinischen Maßstab zur Behandlung des Glioblastoms

Development of large-scale expansion protocol for NKG2C-positive NK cells for treatment of glioblastoma

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Objective

Natural killer (NK) cells have proven as a promising candidate for immunotherapy of tumors. Glioblastoma express elevated levels of HLA-E and therefore block NK cells with expression of the inhibitory NKG2A receptor. Of note, GBM cells also overexpress non-classical HLA-G, which provides a nonameric peptide that, in complex with HLA-E, has the highest affinity for NKG2A described so far. HLA-E-peptide complexes are also recognized by a small NK cell subset expressing the activating NKG2C receptor, preferentially found in HCMV-seropositive donors. The NKG2C+ NK cell subset mostly represent differentiated NK cells with high lytic capacity and is therefore a potential candidate for immunotherapy of GBM. In this project, we aim to establish a large-scale *ex vivo* expansion of functional NKG2C+ NK cells employing bioreactors and using a recently developed PC-3 feeder cell line genetically engineered with IL-2, membrane-bound IL-15, as well as an first generation single chain trimeric HLA-E molecule.

Methods

NK cells from healthy HCMV-seropositive donors were expanded in bottom-gas permeable membrane bioreactors for 11 days using different feeder cell to NK cells ratios. NK cells were characterized for expression of NKG2A/C, activating/inhibitory receptors and for appearance of maturation and exhaustion markers by flow cytometry analysis. The cytotoxicity of NK cells with or without pre-treatment with 50 IU IL-2 towards primary GBM cell lines HT7606 and HT18584 was analyzed using a chrome release assay.

Results

Co-cultivation of NK cells from 14 donors with feeder cells at a ratio of 10:1 resulted in the best mean expansion factor (40-fold ± 13.2 SEM) of total NK cells. Additionally, a selective expansion of NKG2C+ NK cells was achieved resulting in a NK cell product skewed to NKG2C+ cells (day 0: 7.5% ± 3.2% SEM; day 11: 57.9% ± 16.6% SEM). Expanded NK cells from six donors showed a basal cytolytic activity towards two primary GBM cell lines which was significantly boosted by concomitant treatment with IL-2.

Conclusion

We have established a convenient protocol for selective and large-scale expansion of NKG2C+ NK cells, which easily can be shifted to a GMP-compliant process. Our results furthermore demonstrate an efficient cytotoxicity of NKG2C+ NK cells primed with low doses of IL-2 towards primary GBM cells. Further *in vivo* studies are warranted for future translation into the clinics.

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P030

Selektive Anlieferung von Toll-like-Rezeptor 3-Agonisten zur *in situ* Vakzinierung in orthotopen Gliomen
Selective delivery of Toll-like receptor 3 agonists for in situ vaccination in orthotopic gliomas

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Objective

Gliomas represent the most common primary adult brain tumors. Despite multimodal treatment, most gliomas ultimately recur. One promising strategy for the treatment of gliomas is immunotherapy. Yet, several vaccination approaches as well as adoptive transfer of tumor-reactive lymphocytes revealed disappointing responses. Thus far, agonists for toll-like receptors (TLRs) appear promising to reprogram the immunosuppressive environment of gliomas. We developed a selective delivery system for TLR3 agonists designated "Rapid Inducer of Cellular Inflammation and Apoptosis" (RICIA) for treatment of glioma. By employing an anti-EGFRvIII targeting moiety in RICIAs, we sought to treat established intracranial EGFRvIII-positive astrocytoma in immune-competent syngeneic mice.

Methods

For assembly of anti-EGFRvIII RICIA mono-biotinylated EGFRvIII-specific single-chain antibody was produced and conjugated to (neutr)avidin and mono-biotinylated 50bp dsRNA (Riboxxol-biotin; TLR3 agonist). The endosomal localization of anti-EGFRvIII RICIA in murine EGFRvIII-positive SMAvIII cells was examined by confocal laser scanning microscopy (CLSM). Endosomal activation of TLR3 and a consecutive type-I interferon response was analyzed using ELISA. The immunotherapeutic anti-tumor effects of anti-EGFRvIII RICIA were investigated in syngeneic immunocompetent VM/Dk mice. Orthotopically grown ff-Luc-SMAvIII astrocytoma were treated with consecutive intratumoral anti-EGFRvIII RICIA injections and tumor mass was assessed using *in vivo* imaging.

Results

The receptor-specific endocytosis and endosomal localization of anti-EGFRvIII RICIA in EGFRvIII-expressing murine astrocytoma cells (SMAvIII) was confirmed by CLSM. Treatment of SMAvIII cells with anti-EGFRvIII RICIA led to the release of type-I interferon in a dose-dependent manner. Consecutive intratumoral injection of anti-EGFRvIII RICIA led to complete and stable tumor remission in 20 % of mice, a significant total mean regression of tumor mass and prolonged overall survival when compared to controls.

Conclusion

Our results demonstrate the feasibility of RICIAs for targeted delivery of TLR3 agonists to murine glioma. Further investigations are warranted to decipher immunological responses in RICIA-treated glioma.

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P031

Hochdurchsatz -In-vitro-Medikamentenscreening identifiziert neue gezielte Behandlungsmöglichkeiten in Meningiom-Zellkulturmodellen

High-throughput in vitro drug screening identifies novel targeted treatment options in meningioma cell culture models

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Objective

Meningiomas are the most common group of intracranial tumors in results, representing 37% of all primary CNS tumors. Most meningiomas are benign tumors. Approximately 20% of meningiomas show histological features of atypia (CNS WHO grade 2) and are associated with an increased risk of recurrence. Malignant meningiomas (CNS WHO grade 3) are rare and biologically aggressive tumors with an unfavorable prognosis.

Methods

To comprehensively characterize the drug response of meningiomas, we examined the drug response of 273 anticancer drugs using primary tumor cells from 16 patients. We focused on repurposing existing medications and selected only FDA-approved and clinical phase III-IV drugs. To avoid false positive and negative results, all components were dispensed in a 6-7 dilution. After 72 h treatment, cell viability was evaluated by measuring ATP concentration.

Results

As slow-growing tumors, meningiomas were highly resistant to a broad spectrum of anti-cancer drugs, with more than 87% of the tested compounds showing no or very limited effects. Out of the 273 drugs evaluated, 34 compounds showed evidence for treatment responses in primary meningioma cell cultures, including two topoisomerase inhibitors, six tyrosine kinase inhibitors, three JAK/STAT inhibitors, and two proteasome inhibitors. The strongest anti-meningioma effects were found for the proteasome inhibitor ixazomib and the STAT 3 inhibitor homoharrigtonine. There was no significant difference in the drug response between primary cultures derived from CNS WHO grade 1 or 2 tumors. We validated these results in two commercially available meningioma cell lines, i.e. the low-grade meningioma cell line Ben Men 1 and the malignant meningioma cell line IOMM LEE.

Conclusion

Our study provides a set of targeted drugs that showed preclinical evidence for potential efficacy against meningioma cells. Among these, the proteasome inhibitor ixazomib and the STAT 3 inhibitor homoharrigtonine demonstrated the most promising effects. In line with our data, homoharrigtonine has been recently reported as a promising anti-meningioma agent by Jungwirth et al (2022).

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P032

Etablierung eines neuen *ex vivo*-Modells zur Untersuchung von Tumor Treating Fields (TTFields)-Effekten auf die Blut-Hirnschranke

Establishment of a novel ex vivo model for the assessment of Tumor Treating Fields (TTFields) effects on the blood-brain barrier (BBB)

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Objective

Tumor Treating Fields (TTFields) are alternating electric fields of intermediate frequency (100-500 kHz) and low intensity (1-3 V/cm). The use of TTFields at 200 kHz as a treatment modality in combination with adjuvant chemotherapy was reported to increase progression-free survival and overall survival of patients with newly diagnosed glioblastoma. Recently, our group demonstrated that TTFields at lower frequencies could also increase permeability of the blood-brain barrier (BBB) *in vitro* and in murine *in vivo* models. However, for clinical translation it is critical to consider interspecies differences. Since human-derived tissue more faithfully resembles the situation in patients, we have established a protocol for the generation of patient-derived *ex vivo* material such as tumor slices, spheroids and organoids. Here, we aimed to establish an *ex vivo* system composed fully or partially of patient-derived material, which could be used to evaluate TTFields effects on the human BBB.

Methods

Brain microvascular endothelial cells of murine and human origin were seeded onto transwell inserts. After three days, organotypic cerebellar and hippocampal slice cultures were placed on top of the endothelial cells. Various culture media were tested for optimized growth of both endothelial cells and brain slices together. Morphology, growth and survival of the brain slices were assessed by live/dead staining and microscopic visualization. Integrity of the BBB was evaluated by transendothelial electrical resistance (TEER) measurements.

Results

The combination of endothelial cells and brain slices demonstrated optimal growth in a culture medium that combines both culture medium specific for brain slices and culture medium formulated for endothelial cells, in a 1:1 ratio. TEER values using various media did not significantly differ from each other.

Conclusion

We have established a patient-derived human ex vivo model of the BBB, which can be used to study TTFields effects on BBB integrity in a set-up that more closely resembles patients *in situ* situations.

P033

ALDH1A3 erhöht die Tumorzellmobilität und stimuliert die Angiogenese der Endothelzellen durch PAI-1 und IL-8 beim Glioblastom

ALDH1A3 promotes tumor cell mobility and stimulates endothelial cell angiogenesis via PAI-1 and IL-8 in glioblastoma

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Objective

Objective High invasiveness and hyper-angiogenesis are hallmarks of glioblastoma (GBM). ALDH1A3 is classically considered as a stem cell marker. Recently, we found a dominant expression of ALDH1A3 in tumor infiltrative area and in proliferating vessels on tumor section of GBM patients, which is associated with poor prognosis of patients. The present study aimed to investigate the role and underlying mechanism of ALDH1A3 in GBM.

Methods

Methods Overexpression (ox) of ALDH1A3 was achieved by the lentiviral transduction in GBM cell lines. The control cells were transduced with empty vector (ev). Scratch- and transwell invasion assays were carried out in ev/oxGBM cells. Endothelial cells (EC) were cultured in conditioned media from ev/oxGBM cells (ev/oxCM), followed by angiogenesis behavior studies. The effect on GBM cell invasion and on EC angiogenesis were further studied *in vivo* by chorioallantoic membrane (CAM) models. Protein array was performed in ev/oxCM.

Results

Results oxALDH1A3 enhanced GBM cell migration and invasion *in vitro* and *in vivo*. oxCM significantly stimulated EC proliferation, migration, tube formation and sprouting. Treatment of CAM with oxCM largely increased the microvessel density on CAM. Protein array revealed significant upregulation of PAI-1 and IL-8. Treatment with specific inhibitors of PAI-1 or IL-8 reversed the oxCM-evoked EC angiogenesis both *in vitro* and *in vivo*.

Conclusion

Conclusion This study demonstrated the pivotal role of ALDH1A3 in promoting GBM cell mobility and in stimulating EC angiogenesis, consistent with our previous findings in the cohort study. PAI-1 and IL-8 as downstream targets of ALDH1A3 prompts an autocrine and paracrine signaling in GBM cells, which plays crucial roles in stimulating mobility of themselves and in promoting EC angiogenesis. Our findings suggest ALDH1A3/PAI-1/IL-8 as a novel signaling for future therapeutic intervention of GBM.

Neuroonkologie experimentell I/*Experimental Neuro-Oncology I*

P034

Effekte von Riluzol und Dexamethason auf Migration und Migrationsrelevante Marker in U87MG Zellen

Riluzole and dexamethasone effects on Migration and expression of Migration related markers in U87MG cells

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Objective

Dexamethasone (Dex) is a corticosteroid used to control cerebral oedema in patients with glioblastoma multiforme (GBM). Negative effects of Dex treatment have been reported in patients with GBM and in experimental studies. In the present study we used riluzole, an approved drug for amyotrophic lateral sclerosis (ALS), to examine its effect on Dex-induced changes in gene expression and cell migration in GBM cells.

Methods

The U87MG cells were treated with riluzole (25 µM) or/and Dex (1 µM). The expression of the following genes, in relation to the housekeeper ß-Actin, was examined by quantitative PCR: TFPi2, N-Cadherin. Migration was examined using the xCELLigence system. Before the experiment, the cells were pretreated either with 25 µM riluzole or with vehicle for 72 h. The rate of migration was expressed as Cell Index after 5 h co-treatment.

Results

The U87MG cells treated with Dex showed a significant decrease in both TFPi2 and N-Cadherin expression (***$p<0.0005$), where riluzole significantly increased the expression of TFPi2 (*$p<0.05$) and decreased the expression of N-Cadherin (*$p<0.05$). Furthermore, significant increase in migration could be registered in cells treated with Dex (**$p<0.005$), which could be counteracted with a treatment of riluzole (**$p<0.005$).

Conclusion

Here, we showed that Dex has an effect on TFPi2 and N-Cadherin expression. Treatment with riluzole induces TFPi2 gene expression, an important marker for the migration/invasion of GBM. Examining the actual migration *in vitro*, Dex treatment increased cell migration, while a combined treatment of riluzole/Dex decreased the effects of Dex on migration. Nonetheless, the effect of this treatment should be further studied-confirmed by examining additional genes (proteins) as well as in other functional assays e.g. measuring invasion and using more cell lines.

P035

Die Rolle von *ENO1* in Hirntumoren: Überexpression in LGG und positive Korrelation mit dem WHO Grad in Meningeomen

The role of ENO1 in brain tumors: Up-regulated expression in low-grade gliomas and positive correlation with meningioma WHO grade

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Objective

α-Enolase (ENO1) is a glycolytic enzyme involved in the Warburg effect, whereby cancer cells reorganize their metabolic pathway to carry out glycolysis under normoxic and hypoxic conditions. Thus, cancer cells can satisfy their higher need for nutrients. The up-regulation of ENO1 has been detected in several tumor types, including endometrial carcinoma, melanoma, gastric and colorectal cancer. In these tumors, ENO1 may function as prognostic marker. Therefore, it was our interest to determine the expression of ENO1 in braintumors (i.e. glioma, meningioma) and whether chemotherapy alters ENO1 expression.

Methods

Tumor samples and control tissues were obtained during neurosurgery. All tumor samples were grouped according to WHO classification. qPCR and Western blot were used to detect the expression of ENO1 in glioma and meningioma. All assays were carried out in triplicates; ß-actin was used as housekeeping gene. For western blots, all samples were incubated with mouse monoclonal anti-ENO1 followed by secondary horseradish peroxidase-linked anti-mouse antibody, with ß-actin as a loading control. Immunofluorescence (n=33) was performed to determine the presence of ENO1 in tumor and control tissues using primary antibody to ENO1 and anti-Cy3 as secondary antibody.

Results

The expression of *ENO1* mRNA was significantly higher in the control group compared to glioma tissue ($p<0.0001$). ENO1 protein was significantly up-regulated in low-grade gliomas in comparison to high-grade gliomas ($p<0.0001$). ENO1 expression in grade II and III meningioma was enhanced compared to grade I (grade I *vs.* grade II, $p=0.016$; *vs.* grade III, $p=0.0010$). ENO1 expression was also increased in grade III compared to grade II meningioma ($p=0.0363$).

Conclusion

Our findings suggest that ENO1 might be a tumor marker for meningioma progression. Moreover, th effect in gliomas seems to be inverse, as its expression decreases with higher malignancy. Cell culture experiments investigating this effect are ongoing.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P036

Reelin: Ein neuer potentieller Invasionsfaktor bei Glioblastomen
Reelin: A new potential microenvironmental factor contributing to Glioblastoma invasion

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Objective

Glioblastoma (GB) is the most common and lethal primary tumour of the central nervous system (CNS) in adults. Regardless of the aggressive regimen, the prognosis remains poor due to GB highly invasive nature. Targeting the interaction of tumour cells with their microenvironment and the invading single GB cells into the peritumoral area, which inter alia includes the degradation of the extracellular matrix (ECM), is a promising therapeutic approach.

Reelin (Rn), an extracellular matrix glycoprotein, is critical for the modulation of neuronal migration during foetal brain development as it serves as a natural positional signal. Intriguingly, the expression of Rn in GB is associated with increased overall survival.

Thus, this project is designed to investigate whether the natural properties of Rn as a stop signal can be harvested as part of an anti-invasive strategy that reduces the invasive potential of GB cells and turns the malignancy into a more localized and easier to treat disease.

Methods

In the context of an initial feasibility study a model system was investigated, whereby a matrix out of the ECM protein fibronectin (Fn) and Rn was created and the effects of those two components were differentially investigated on established GB cell lines. Hence, an adhesion assay was performed to address the potential effect of Rn on cell adhesion by measuring cell binding to different coatings.

Results

It could be observed that cells adhere quickly to Fn in a cell line independent manner as previously described in literature. Intriguingly, Rn impaired the ability of cells to adhere to Fn-coated surfaces as the addition of Rn blocked the motility promoting properties of Fn. Furthermore, Rn embedded in the Fn matrix has a mechanistic effect on the interaction of GB cells and Fn since the combination of both components lead to an increased number of detached cells.

Conclusion

Our data suggest that Rn is potentially an inhibiting factor in GB motility and as such of potential therapeutic value.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P037

Entwicklung von CAR-T Zellen gegen die Oberflächenantigene TMEM158 und PTPRZ1 für die Behandlung von Glioblastomen

Development of CAR-T cells targeting TMEM158 and PTPRZ1 for treatment of Glioblastoma

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Objective

Chimeric antigen receptor (CAR)-based immunotherapies have shown impressive clinical results for treatment of hematologic cancers, but did not show comparable efficiency in treatment of Glioblastoma (GBM) so far. One major hurdle is the molecular heterogeneity, which necessitates the discovery of novel antigens and combined targeting in a personalized manner. The aims of this study were to analyze overexpression of the recently discovered GBM antigens TMEM158 and PTPRZ1 in GBM patient samples, to develop CAR-T cell therapies against these targets and to evaluate the CAR-T cells´ cytotoxic effects for the first time.

Methods

TMEM158 and PTPRZ1 expression was analyzed based on public databases and in samples of a patient cohort (N=80). CAR-T cells were produced by lentiviral transduction of human peripheral blood mononuclear cells and T-cell stimulation. Cytotoxicity was analyzed against two GBM and a neuroblastoma cell line using a luciferase-based co-culture assay. In vivo function of both CAR-T cell therapies was investigated in a murine xenograft glioblastoma model.

Results

Overexpression of TMEM158 and PTPRZ1 was confirmed in the majority of patient samples and GBM cell lines. Protein expression of TMEM158 was also shown in GBM cell lines. The produced CAR-T cells show cytotoxicity against glioblastoma cell lines but not neuroblastoma cells with low antigen expression. Different mutated versions of the CARs were identified that enhance cytotoxicity against the GBM cell lines in vitro. Additionally, CAR versions were identified that allowed the parallel targeting of integrin αVβ3, a known GBM antigen, by introduction of an RGD motif into the CAR sequence. Mice treated with CAR-T cells against TMEM158 or PTPRZ1 showed strongly prolonged survival and reduction of tumor volume in comparison to mice that received control T cells.

Conclusion

For the first time, CAR-T cell therapies were produced against TMEM158 and PTPRZ1 and their basic function was shown in vitro and in vivo. We thereby confirmed that TMEM158 and PTPRZ1 are suitable targets for CAR-based immunotherapies and broadened the repertoire of antigens that can be targeted for treatment of GBM in the future. In addition, a possible way to target each antigen in combination with integrin αVβ3 was identified, which might help to address the heterogeneity of GBM further.

P038

Der EGFR-Inhibitor Osimertinib reduziert das Überleben von humanen Glioblastomzellen
The EGFR-inhibitor Osimertinib inhibits survival of human glioblastoma cells

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Objective

Tyrosine kinase receptors play a critical role in the proliferation and progression of almost all malignancies. In 83% of glioblastoma the endothelial growth factor receptor (EGFR) is affected by genetic alterations leading to cell proliferation and therapy resistance. The most common EGFR alteration is the EGFRvIII mutation, which is present in about 20% of human glioblastoma. The EGFR-inhibitor osimertinib showed anti-tumor effect in lung cancer patients with cerebral metastasis and is reported to have high affinity for the EGFRvIII variant in in vitro models. This study was performed to investigate, whether Osimertinib has an antiproliferative effect in human glioblastoma cells.

Methods

Immortalized glioblastoma cell lines U87, A172 and U251 were grown to 80% confluence and treated with Osimertinib in concentrations ranging from 3 µM to 7 µM. After 72 hours cell viability was quantified via XTT-assay. Dose-response curves were calculated by probit analysis.

Results

Osimertinib reduced cell survival in all glioblastoma cell lines with a mean ED50 of 6.81 (95%CI: 6.75-6.86) µM and a mean ED95 of 13.4 (95%CI: 13.3-13.5) µM in A172 cell. The mean ED50 in U87 cells was 5.44 (95%CI: 5.4-5.48) µM and the mean ED95 was at 10.6 (95%CI: 10.5-10.7) µM. In U251 cells the ED50 of osimertinib was 7.5 (95%CI: 7.39-7.62) µM and the ED95 was 19 (95%CI: 18.7-19.3) µM. The mean ED50 of all investigated glioblastoma cell lines was 6.37 (95%CI: 6.33-6.4) µM and the mean ED95 was 13.3 (95%CI: 13.2-13.4) µM.

Conclusion

The EGFR-inhibitor osimertinib showed an antiproliferative effect in immortalized glioblastoma cell lines. As EGFR-alterations are frequently prevalent in glioblastoma further investigations on the therapeutic effects of this substance especially in EGFR altered glioma models should be performed.

P039

Aus Glioblastom-Zelllinien abgeleitete Sphäroide als Modellsystem zur schnellen und reproduzierbaren Evaluation von Behandlungsbedingungen in präklinischen Studien

Spheroids derived from glioblastoma cell lines as model system for rapid and reproducible evaluation of treatment conditions in preclinical trials

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Objective

Numerous compounds, that exhibit anti-cancer effects in preclinical studies turn out to be ineffective in clinical trials. This is not least due to models based on 2D cell cultures. Other models, such as slice cultures, despite of great value, are not suitable for large series of experiments, e.g., to test effective concentrations of a compound. Therefore, we investigated which human glioblastoma cell lines are suitable for the establishment of spheroid models, mimicking gradients of nutrients, oxygen, waste and test compounds, and we tested parameters such as initial number of cells and time of cultivation.

Methods

Different amounts of cells from 10 human glioblastoma cell lines were used to establish spheroids in ultra-low attachment plates using DMEM supplemented with 10 % FCS. The sizes of the spheroids and the size of their cores of dead cells were monitored over 7 days using PI staining and microscopy. Finally, the effect of treatment with temozolomide (200 µM) and ionizing irradiation (8 Gy, Xstrahl 200 at 150 kV, 1.4 Gy/min) at day two after spheroid formation was determined 5 days after treatment using Cell Titer Glo for 2D cultures (used for comparison) and Cell Titer Glo 3D for spheroids.

Results

We observed that independent from the initial number of cells, spheroids of cells from the lines LN405, MZ18 and MZ54 did not grow but exhibited a constant loss of size during cultivation. Growth of spheroids from the other lines was dependent on the initial number of cells. Whereas spheroids from U87MG and G55T2 exhibited a constant growth at almost all initial cell numbers (250 to 15,000 cells), growth was observed with initial cell numbers between 250 and 1000 cells using the lines T98G, LN229, 1321N1and U343. Spheroids from U373 exhibited growth only at initial cell numbers below 500. Determining the layer of living cells not stained by Pi around the necrotic core of the spheroids, we estimated that there are mostly 3 to 5 layers of living cells. Treating spheroids from the lines G55T2, U87MG and U343 with temozolomide and x irradiation, we observed, that spheroids were more susceptible to treatment than cells in 2D cell culture in G55T2, which formed the fastest growing spheroids, less in U343 and comparable in U87MG.

Conclusion

Spheroids established from cell lines can be produced comparatively quickly, easily and in large quantities. However, not all cell lines are equally suited and the initial cell number is an important experimental parameter to be carefully considered.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P040

FTY720 (Fingolimod) reduziert die Kolonienbildung und Stoffwechselaktivität von humanen Glioblastomzellen alleine und in Kombinationstherapie mit Temozolomid

FTY720 (Fingolimod) reduces the colony formation and cell viability of human glioblastoma cells in combination with temozolomide

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Objective

FTY720 is used in the treatment of multiple sclerosis. It interferes with numerous signalling pathways connected to lymphocytes and astrocytes. The aim of the study was the investigation of the antiproliferative effect of FTY720 on immortalized and primary human glioblastoma cell lines. Furthermore, post-therapy cell viability of the cells and the association to the EMT-signalling pathway was examined. Additionally, we analysed the EMT-related genes SNAIL1, SNAIL2, STAT3 and VIM.

Methods

U251, two primary human glioblastoma cell cultures and astrocyte cell cultures were plated to 80-90% confluence. FTY720 was administered at a dose of 5 and 10µM alone and in combination with 150µM TMZ for 72 hours. Afterwards cell survival was evaluated by XTT-Assay and automatic cell count. Colony forming assays were used to evaluate the cell viability after the treatment. For the analysis of the EMT-signalling pathway PCR-analysis as well as western blot was used. Statistical analysis was performed using the Kruskal-Wallis- and Mann-Whitney-U Test.

Results

FTY720 had an antiproliferative effect on human glioblastoma cells at 5 and 10µM. Evaluation of cell viability using colony forming assays showed that the fraction of newly built cell colonies from the FTY-treated cells was decreased in comparison to the untreated and TMZ-treated cells. Analyzing the effect of FTY720 on the colony formation of astrocytes, only a minor reduction was detected. The cell survival was significantly stronger decreased if treated with FTY720 10µM compared to TMZ in U251 ($p=0.002$). Combination treatment with FTY720 and TMZ was significantly more effective than TMZ alone in all cell cultures. The combination treatment had a stronger impact than every single treatment on the survival fraction in U251 ($p=0.001$). SNAIL1, SNAIL2, STAT3, and VIM were only slightly decreased in the PCR-analysis.

Conclusion

The combination of FTY720 in micromolar concentration and TMZ in the treatment of glioblastoma cells decreases the colony formation and significantly reduces cell survival compared to treatment with TMZ alone. Despite recent evidence, no influence on the expression of examined EMT genes could be observed, suggesting a different mechanism of action of FTY720.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P041

Erhöht FTY720 die Sensitivität von Temozolomid durch Herabregulation der N-Cadherin Expression in Glioblastomzellen?

Does FTY720 increase sensitivity of Temozolomid due to down-regulation of N-Cadherin expression in glioblastoma cells?

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Objective

Despite the current therapy with temozolomid (TMZ) patients with the diagnosis of glioblastoma multiforme (GBM) have still a short survival time. The aim of this study was to investigate the effect of FTY720 (fingolimod) and TMZ on glioblastoma cells with regard to the Epithelial-Mesenchymal-Transition (EMT). The EMT-transcription genes lead through cell proliferation, invasion and chemoresistance to a malignization of the glioblastoma. FTY720 is an approved immunosuppressant in the treatment of multiple sclerosis and has already shown an antiproliferative effect on immortalized glioblastoma cells.

Methods

Cell lines U87, A172, U251, patient-derived primary GBM cells and astrocytes were treated with either TMZ (150µM), FTY720 at doses of 5 and 10µM, or a combination of TMZ and FTY720.A 72-hour cell cultivation was followed by a determination of cell survival by XTT and Colony-forming-Assay. The correlation between the antiproliferative effect of FTY720 and the gene/protein expression of the transcription factors N-Cadherin, E-Cadherin, ZEB1 and CDK1 was analysed by PCR and Western blot.

Results

In addition to the antiproliferative effect of FTY720 in monotherapy and in combination with TMZ, the Colony-forming-Assay showed a non-significant greater impairment of astrocyte viability with TMZ (mean survival-fraction (SF) 0±0) than with FTY720 (mean SF 82±48. 08). PCR and Western blot showed a non-significant decrease of EMT-promoting transcription factors under FTY720 treatment. The Western blot showed an influence of FTY720 on the N-Cadherin- and CDK1-Expression. FTY720 induces a decrease of the N-Cadherin-expression in the cell lines A172 as well in U87. Furthermore, FTY720 also causes a CDK1-decrease in the cell line A172.

Conclusion

While the EMT signalling pathway was not significantly affected at the gene/protein level, a slight inhibitory effect of FTY720 on EMT could be observed. Furthermore, a decrease in N-cadherin could be detected in some cell lines. Previous studies showed, that reduced N-Cadherin expression is experienced with a better effect of TMZ (Q. Chen et al, 2018). Therefore, not only the proven antiproliferative effect of FTY720, but also the increased sensitivity of TMZ due to down-regulation of N-Cadherin expression by FTY720, is promising for the GBM therapy in the near future and requires further research.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P042

Glykierung führt zu verstärkter Invasion von Glioblastom-Zelllinien
Glycation leads to increased invasion of glioblastoma cell lines

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Objective

Recent studies suggest that diabetes patients are at a significant higher risk of developing cancer. In line with this, glioblastoma (GBM) patients with high serum glucose levels have been linked to poor prognosis. Consequences of elevated glucose levels are irreversible glycation of proteins and formation of advanced glycation end products (AGEs). AGEs affect functions of extracellular matrix (ECM) proteins, signalling pathways and genomic stability, which can trigger the initiation and progression of cancer. As the poor prognosis of GBM is often due to wide tumour cell dissemination and invasion, we examined the impact of glycation on GBM cell invasion and the ECM proteins involved in these mechanisms.

Methods

We analysed the effect of glycation on the cell lines U251, LN229 (both WHO grade 4 GBM), U343 (WHO grade 3, glioma) and human astrocytes (hA), using Methylglyoxal (MGO) as a glycation agent. The cells were cultivated with different MGO concentrations (0-1mmol/l). Subsequently cell viability were examined with XTT assays and microscopy. Invasion, adhesion and chemotactic cell migration were measured with the *Real Time Cell Analyzer (xCelligence)*. Furthermore, ECM proteins were examined on mRNA level using qPCR and E- and N-cadherin on protein level by immunoblotting.

Results

MGO showed cytotoxic effects at a concentration of 1mmol/l but remained viable and morphologically unaffected up to a concentration of 0.3mmol/l in all cell lines. Glycation was increased in a concentration-dependent manner in all cell types after incubation with MGO. Invasion of the malignant cell lines LN229, U251 and U343 increased after glycation. In contrast, invasiveness of the normal hA was reduced with higher MGO concentrations. Chemotactic cell migration and adhesion was not affected by MGO treatment. In addition, glycation led to upregulation of CD44 in all cell lines and increased expression of MMP2 in LN229 and U343.

Conclusion

We could demonstrate that glycation with MGO leads to increased invasion of glioma and GBM cells, resulting in more aggressive cell types. However, chemotactic cell migration and adhesion was not affected. In addition we could show the glycation has cell line specific effects on ECM expression. Upregulation of MMP2 could increase invasion through remodelling and degradation of ECM. Further studies are necessary to examine the prevention of glycation as new potential therapeutic strategies such as MGO-scavengers and Glyoxalase1-activators against glioma and GBM.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P043

Expressionsverhalten von MTH1 in Ependymomen
Expression behaviour of MTH1 in Ependymomas

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Objective

The enzyme MutT homolog 1 (MTH1) prevents the accumulation of reactive oxygen species (ROS) in the cell by sanitizing oxidized gNTP pools. This is an important feature for cancer cells, because ROS leads to DNA damage and thus to cell death. It has already been shown that MTH1 is overexpressed in various types of cancer and different kinds of MTH1 inhibitors for example Crizotinib have already been developed and tested. Ependymomas arise from ependymal cells and account for 5-10% of gliomas. They are located near the ventricles of the brain and therefore often cause disturbances of the cerebrospinal fluid, which leads to increased intracranial pressure. Surgery is still the first-choice therapy, although ependymomas can often only be resected incompletely due to their localisation.

Methods

All tumour samples and control tissues were taken during neurosurgery and were sorted according to WHO-Classification. We performed qPCR and Western Blot to quantify the expression of MTH1 and to be able to compare the expression according to tumour grade, patients" age and gender, localisation and whether it was a primary tumour or a relapse. As housekeeper gene we used ß-actin and all experiments were done in triplets.

Results

MTH1 was expressed at higher levels in the tumour tissue than in the control tissue, both in total and in all subcategories. With regard to the tumour grade, MTH1 was expressed lowest in grade 1 tumours and highest in grade 3 tumours. Furthermore, there was a higher expression in the recurrences compared to the primary tumours. With increasing patient age, a reduced MTH1 expression was observed. Cerebral ependymomas showed higher MTH1 expression than spinal ependymomas, with the lowest expression found in the lumbar spine or thoracolumbar junction and the highest expression in the 4th ventricle or in the lateral ventricles.

Conclusion

As shown in other work for different tumours, MTH1 is also overexpressed in ependymomas, which indicates that it plays an important role in tumour biology, making it an interesting target for tumour or cancer therapies. However, it has also been shown that certain tumour or patient groups seem to be better suited for such therapy projects. In particular, ependymomas with a higher tumour grade, young patients" age, cerebral localisation and tumour recurrences appear to be promising with regard to a response to therapeutic suppression of MTH1.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P044

Expression der MAGUK Proteine DLG4, DLG1, Magi2, Shank1, and Homer1 in Gliomen
Expression study of the MAGUK Proteins DLG4, DLG1, Magi2, Shank1, and Homer1 in glioma

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Objective

To thrive, glioma cells exploit pathways that are active in normal CNS cells, as well as in normal neurotransmitter signaling. In healthy excitatory synapses the postsynaptic submembrane space consists of multiprotein complexes called the postsynaptic density (PSD). The PSD is responsible for the structural organization, the functioning, and the regulation of neuronal signaling. The five MAGUK Proteins DLG4, DLG1, Magi2, Shank1, and Homer1 are part of the healthy PSD complex and play a crucial role not only in NMDA and AMPA receptor signaling. Investigating the role of these MAGUK proteins in glioma biology could bring further insight into which principal neurobiological features, including organization in communicating networks, are recapitulated by tumor cells of different stages in gliomas.

Methods

qPCR was used to determine expression levels of DLG4, DLG1, Magi2, Shank1, and Homer1 in 7 different glioma groups (GII, GIII, primary GBM before and after chemotherapy, secondary glioblastoma recurrence with and without chemotherapy). Western Blot was done for DLG4, DLG1, and Homer1. Immunohistochemical staining of frozen sections, paraffin sections and in vitro cells was performed.

Results

The expression levels of DLG4, DLG1, Magi2, Shank1, and Homer1 were reduced especially in high grade glioma compared to control tissue. A tendency of decreasing protein levels with increasing malignancy is visible for the majority of proteins. In cell culture all proteins were also present. siRNA experiments are ongoing.

Conclusion

The presence of these synaptic proteins in glioma tissue and moreover also primary cell culture could indicate a role in tumor biology and the connection of glioma cells with neuronal tissue.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P045

Einfluss des *Copy Number Variation* - Profils auf die Expression von Tumorstammzellmarkern im Vestibularisschwannom

Impact of copy number variation profile on cancer stem cell marker expression in vestibular schwannoma

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Objective

Vestibular schwannomas (VS) are one of the most common intracranial tumors in adults. Affected patients suffer from unilateral hearing loss, tinnitus, and vertigo. In recent years, extensive research has been performed on the pathogenesis of VS to offer patients a pharmacological therapy as an alternative to surgical removal. An occurrence of cancer stem cells (CSC) has already been demonstrated by increased expression of CSC markers in VS. This indicates a possible presence of CSC in the VS, which could represent a potential drug target. Therefore, our study aimed to detect the copy number variation profile of VS at the genomic level about a gene loss or gain in CSC markers.

Methods

The study included 26 VS equally distributed among the four Koos grades. Patients of legal age with at least one preoperative MRI image used for volumetry were included. Patients with recurrent, irradiated, or hereditary VS were excluded. DNA was extracted from VS samples obtained during surgical excision and was used for genotyping. Copy number variation (CNV) profiles were generated using IGV Viewer. In particular, the gene loss or gain of 11 different CSC markers was investigated.

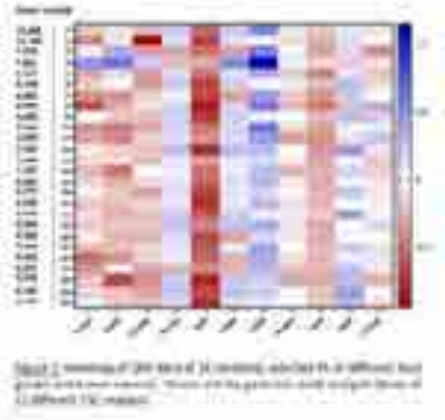
Results

The CNV profiles vary depending on the CSC marker (Figure 1). The VS examined showed a loss of the protooncogene c-myc, which was most evident in larger VS. Similar results can be observed in CNV analysis of CXCR4 and Oct4, which are responsible for maintaining CSC pluripotency. In contrast, for the tumor suppressor gene Klf4, there was a tendency for less gene loss in larger VS but increased gene loss in smaller VS. Larger VS showed more frequent gene gain of the pluripotency factors SOX2 and CD44, whereas smaller tumors showed more frequent gene loss. Increased gene gain in large VS was also seen when CD45 was analyzed. Exclusively for Sall4, there was an elevated gene gain in smaller VS.

Conclusion

On the mRNA level, an increased expression of some CSC markers in the VS could already been detected. In some CSC markers, a gain on the genomic level especially in bigger VS actually seems to lead to increased expression of CSC markers and thus have an impact on the pathogenesis of VS. This is why CSC in VS could represent a potential drug target and thus provide patients with an alternative to surgical removal.

Abb. 1



P046

Glukose-Level beeinflussen die Expression von Sialyltransferasen und die Sialylierung in benignen und malignen Meningeom-Zellen

Glucose levels interfere with the expression of sialyltransferases and sialylation in benign and malignant meningioma cell lines

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Objective

Meningiomas generate like most tumours, energy by using anaerobe glycolysis. This so called Warburg effect consequently leads to a higher amount of the metabolite methylglyoxal (MGO). This metabolite is a side product of glycolysis and known to react with amino groups, thereby building advanced glycation end products (AGEs). It is known that these AGE accumulate in older people, which are formed in the course of glycation. In our previous studies, we could show, that glycation with MGO leads to increased invasive behaviour in benign meningioma cells, whereas we observed opposite effects in malignant meningioma cells. Additionally, glycation led to an alteration in the expression of sialyltransferases (ST), which are directly and indirectly involved in tumour development. Some of these ST may have antitumor properties. On the other hand, malignant tumours often have an altered sialylation (which is caused by the ST), which can serve as a tumour escape mechanism.

Methods

We used a benign meningioma cell line (WHO Grade 1) and a malignant meningioma cell line (WHO Grade 3). Cells were cultured for 24h using different glucose levels: normal (5.5mM), low (3mM) and high (15mM) and were additionally treated with different concentrations of MGO (0.1mM, 0.3mM, 0.6mM, 1mM). We performed an MTT assay to analyse the effect of MGO with different glucose levels on the metabolic activity in both meningioma cell lines. Expression of ST mRNA was measured using qPCR. Furthermore, sialylation and N-acetyl neuraminic acid levels were compared by using HPLC and resorcinol assay.

Results

In the MTT assay, we observed that high glucose levels had a protective effect against MGO in the benign cell line. Sialic acid level were affected by different glucose level and/or more affected by additional MGO treatment. Furthermore, partly opposite changes in the expression of the ST of the benign and malignant cell lines could be observed under varying glucose concentrations. Interestingly, some ST mRNA in the benign cell line were clearly upregulated at low glucose and downregulated at high glucose levels. In benign cells, the ST6GALNAC2 was upregulated at low glucose levels and with additional 0.3mM MGO treatment less increased compared with the normal glucose level.

Conclusion

The results show different effects in both cell lines which may indicate that low blood glucose levels could be protective concerning tumorigenesis while high glucose levels and MGO treatment show opposite effects.

Neuroonkologie experimentell II/*Experimental Neuro-oncology II*

P047

CAR-T-Zellen gegen drei neuartige Antigene zeigen antitumorale Wirkung im *ex vivo*-Modell von Glioblastom-Organoiden aus Patientengewebe

CAR-T cells against three novel antigens show antitumoral efficacy in ex vivo patient derived glioblastoma organoids

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Objective

Glioblastoma (GBM) is the most prevalent malignant brain tumor in adults with limited treatment options. The emerging field of immunotherapies for solid tumors has led to promising experimental and clinical results. However, tumor heterogeneity, antigen escape mechanisms and the complex tumor microenvironment (TME) hinder smooth translation of therapeutics from bench to bedside. Therefore, *ex vivo* models resembling the precise patient conditions are needed. Previous work in our lab has identified three suitable antigens (target 1, 2, 3) with stable expression in primary and recurrent GBM. We assessed the effector functions (proliferation and target cell apoptosis) of three different chimeric antigen receptor (CAR) T cell constructs in GBM patient derived organoids (PDOs).

Methods

We generated PDOs from freshly resected GBM tissue. Subsequently, CAR-T cells against three targets were produced by transduction of peripheral blood mononuclear cells derived T cells of healthy humans. PDOs were separately incubated with the three CAR-T cell variants and untransduced control T cells at an effector to target ratio of 1:4 and fixated after 24 h, 48 h and 72 h to conduct immunofluorescence staining (T cell proliferation: CD4+/Ki67+, target cell apoptosis: target+/CC3+).

Results

We incubated PDOs of four different patients showing different levels of antigen expression in parental tissue. The PDOs exhibited disintegration and loss of circular shape over time, whereas PDOs treated with control T cells maintained their morphology. High fractions of CD4+ CAR-T cells proliferated homogenously in all four PDOs (p-value target 1/2/3: 0.0008/<0.0001/<0.0001). CAR-T cells against target 1 and 2 induced significantly increased apoptosis (p-value target 1/2/3: <0.0001/0.0439/0.1306, non-significant but trending towards more apoptosis in treated PDOs).

Conclusion

By testing CAR-T cells targeting three steadily expressed GBM antigens, we contribute valuable data of preclinical performance and additionally promote lesser-known antigens by proving them as reasonable target antigens in GBM. However, further *ex vivo* models like slice cultures or the lasting implementation of a TME in PDOs are necessary to fully understand CAR-T cell effectiveness. Additionally, approaches like a combination of different CAR-T cell constructs and/or the addition of checkpoint inhibitors should be prioritized as next evaluation steps in both *ex vivo* and *in vivo* models.

Neuroonkologie I/*Neuro-Oncology I*

P048

Untersuchung des Effekts der Hippocampussklerose auf das parietale Gedächtnisnetzwerk
Investigating the Effect of Hippocampal Sclerosis on Parietal Memory Network

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Objective

We aimed to investigate differences in episodic memory networks between patients with temporal lobe epilepsy (TLE) due to hippocampal sclerosis and healthy controls, especially with regards to the parietal memory network (PMN), as well as their relation to neuropsychological memory performance after mesial temporal resection.

Methods

28 healthy subjects as well as 21 patients with TLE (12 left, 9 right) were investigated using a spatial memory fMRI paradigm, which has been shown to activate the PMN. Regions of interest (ROI) were defined based on the group results of the healthy subjects and activations within the predefined ROIs were compared across groups and correlated with post-operative verbal and non-verbal memory scores.

Results

Healthy subjects showed activations within regions belonging to the dorsal visual stream and the PMN as well as the bilateral parahippocampal place area and the bilateral frontal eye field (Fig. 1). Comparison between groups revealed that TLE patients activated significantly less in the left middle occipital gyrus and the right precuneus (Fig. 1). The activation pattern in left TLE patients showed further reductions, mainly in areas belonging to the dorsal visual stream and the PMN within the left hemisphere (Fig. 1). Activations within the left superior parietal lobulus, bilateral posterior middle temporal gyrus, left precuneus, and left frontal eye field correlated significantly with post-operative verbal memory scores, and activations within the left superior parietal lobulus, left posterior middle temporal gyrus, and left precuneus correlated significantly with higher performance in post-operative non-verbal memory scores (Fig. 2).

Conclusion

The PMN is involved in episodic memory encoding. Activations in areas belonging to the PMN and the dorsal visual stream, especially within the left hemisphere, are predictive for a favourable memory outcome after amygdalohippocampectomy.

Figures

Fig. 1: fMRI activations in healthy subjects (p<0.05, FWE corr.) and comparison between healthy subjects and patients with left TLE (LTLE) and right TLE (RTLE); * show statistically significant differences (p<0.05).

Fig. 2: Correlations between activations and postoperative verbal (VLMT) and non-verbal (DCS) memory performance. Grey dots = LTLE patients, black dots = RTLE patients.

Abb. 1

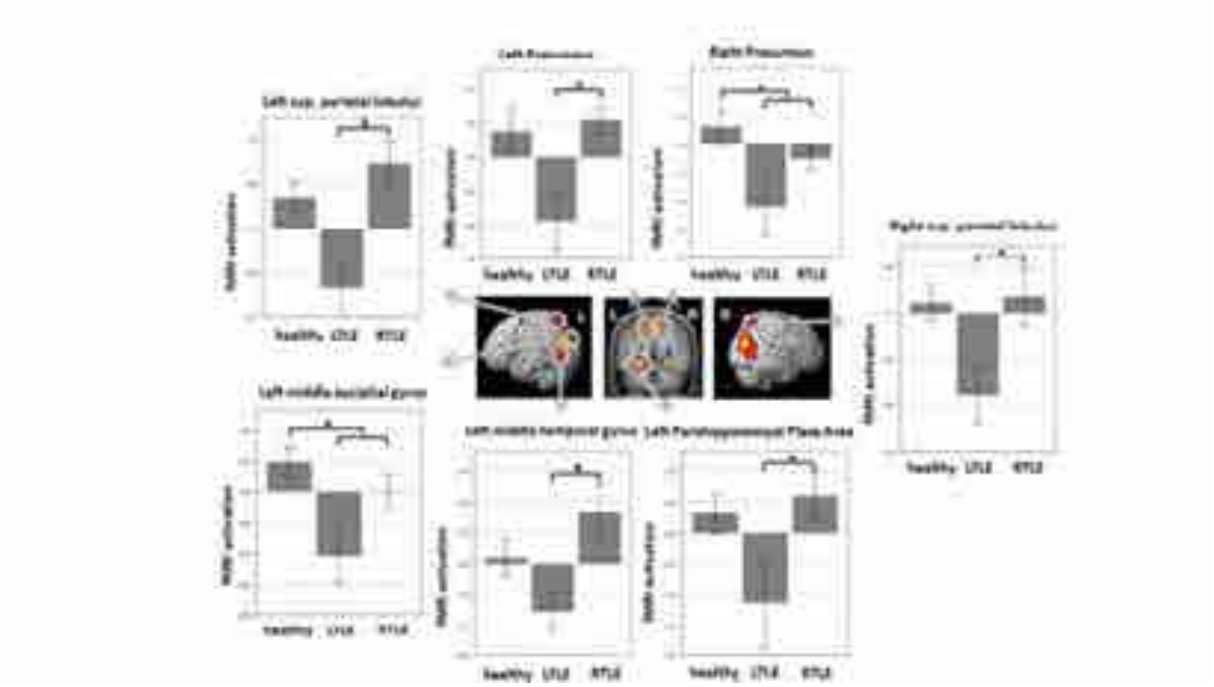
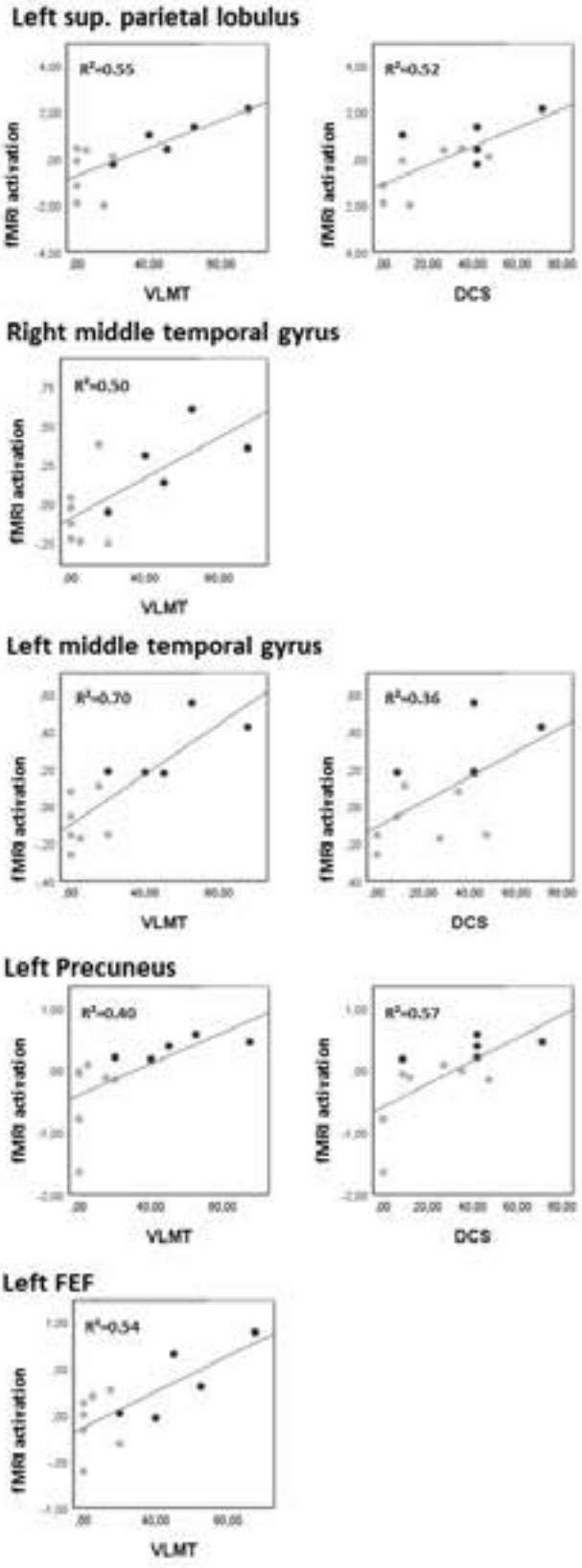


Abb. 2


Left sup. parietal lobulus
R²=0.55
fMRI activation
VLMT
R²=0.52
fMRI activation
DCS
Right middle temporal gyrus
R²=0.50
fMRI activation
VLMT
Left middle temporal gyrus
R²=0.70
fMRI activation
VLMT
R²=0.36
fMRI activation
DCS
Left Precuneus
R²=0.40
fMRI activation
VLMT
R²=0.57
fMRI activation
DCS
Left FEF
R²=0.54
fMRI activation
VLMT

Neuroonkologie I/*Neuro-Oncology I*

J-SPNC003

Frontoparietale Schädelmetastasen eines uterinen Leiomyosarkoms
Frontoparietal skull metastasis from uterine leiomyosarcoma

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Objective

To report a case of an adult female patient with a rapidly-growing frontoparietal skull metastasis from uterine leiomyosarcoma with intradural extension.

Methods

A 51-year-old female was admitted to the emergency department with progressively worsening headaches and rapidly-growing swelling in the right frontoparietal region. The patient had been diagnosed with uterine leiomyosarcoma nine years before and was submitted to excision of lung metastases three years prior to this event. The computed tomography and the magnetic resonance showed a large frontoparietal skull metastasis, measuring 50 x 60 x 45 mm - transverse x posterior-anterior x cephalocaudal axes, with erosion of the bone and both epicranial and intracranial components (including an intradural tumor nodule), being avidly gadolinium-enhancing. The frontoparietal cortex was compressed but seemingly not invaded.

Results

The patient was positioned supine with the head rotated to the left and a right frontoparietal craniectomy (maintaining a 1-cm surgical margin from the normal bone) was performed, with removal of the epicranial and intracranial bulk of tumor. The dura was opened and the intradural component was successfully removed. Intraoperative evaluation of the brain parenchyma showed no signs of pial involvement. The invaded dura was removed with margins and a duroplasty with synthetic dura was done. The skull was reconstructed with a titanium mesh. The postoperative period was uneventful with resolution of the headaches. The patient was discharged 3 days after the surgery. Postoperative computed tomography and magnetic resonance confirmed complete tumor removal and excluded complications. The histologic analysis confirmed the lesion to be a metastasis from uterine leiomyosarcoma. The patient did consolidation radiotherapy two months after the surgery. At 18-month follow-up the patient shows no signs of cranial disease recurrence.

Conclusion

To our best knowledge, we describe the tenth published case of skull metastasis from uterine leiomyosarcoma with dural involvement, treated with complete surgical removal of the tumor followed by radiotherapy, with no signs of recurrence at 18-month follow-up.

Neuroonkologie I/*Neuro-Oncology I*

P049

ZNS-Lymphome- Diagnostik eines Chamäleons mittels MRT-ADC-Mapping
CNS-lymphoma – diagnosing a chameleon by MRI-ADC mapping

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Objective

Primary Central Nervous System Lymphoma (PCNSL) is a rare neoplasm with a high variability on MRI. While FDG-PET CT [1]as the most sensitive imaging tool is rarely available, MR-spectroscopy (MRS), suscebility weighted imaging (SWI) and quantitative ADC-analysis here have been analyzed for their potential use enhancing the diagnostic accuracy.

Methods

22 patients (age 71,5 SD+/-9,5, gender 9♀/13♂) from 2015 till 2022 with unknown primary tumors, homogenous contrast enhancement and heterogenous T2-signals on MRI suspicious of PCNSL were selected for further MRS and ADC-mapping. An age and gender matched pair group of glioblastoma (GBM) patients (n=24) served as a control group. Protocol based Choline/Creatinine (CCR) and Lactat/Creatinine ratios (LCR), SWI as well as quantitative ADC-analysis were evaluated for PCNSL and GBM patients. Imaging was correlated to the histopathological findings following surgical resection or biopsy.

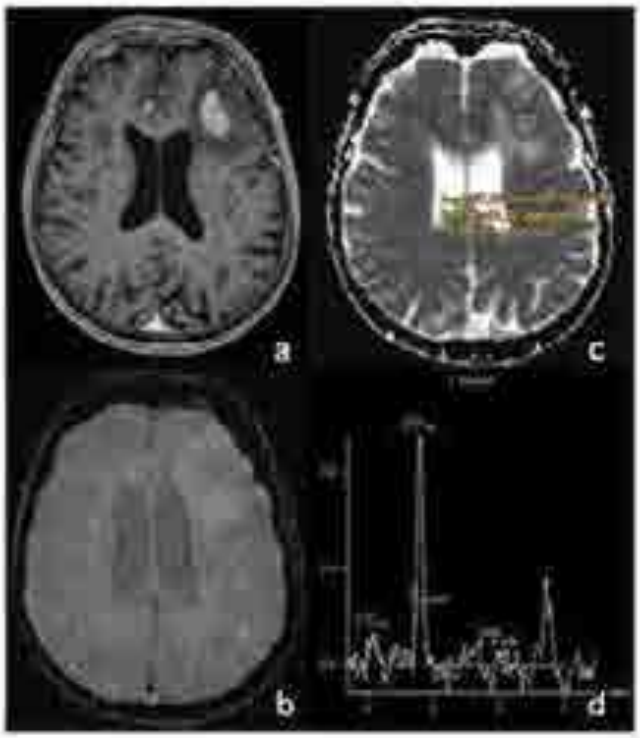
Results

PCNSL and GBM showed no significant features in CCR while LCR was higher in PCNSL compared to GBM (not significant). PCNSL may show just sporadically spot or linear SWI abnormalities while quantitative ADC-analysis (b=1000 s/mm^2) showed significantly lower ADC times in PCNSL (0.70 x 10−3 mm^2/s; SD +/- 0.19) compared to GBM (1.04 x 10−3 mm^2/s SD +/- 0.50), thus leading to a 90% sensitivity rate in the diagnosis of PCNSL.

Conclusion

In addition to conventional MRI-protocols noninvasive quantification of ADC mapping may delineate PCNSL from other brain pathologies with a sensitivity of 90%. While it increases the accuracy of diagnosis in PCNSL, neurosurgical resection or biopsy is still necessary for targeted therapeutics. But ADC mapping here has turned out as a competitive tool already diagnosing PCNSL preoperatively.

Abb. 1



(a) Bilateral frontobasal PCNSL characterized by multifocal, homogeneous enhancing lesion on axial contrast-enhanced T1-weighted MR imaging. (b) Absence of intratumoral susceptibility signals (ITSS) on susceptibility weighted images (SWI) (c) Apparent diffusion coefficient (ADC) map showed little (circles) in the most strongly enhanced tumor area (b=1000sec/mm²). (d) Increased choline peak on MR spectroscopy.

P050

Behandlung, Chirurgische Resektion und Ergebnisse von NF1-assoziierten MPNSTs: Einfluss durch Genetik und Lokalisation.

Management, (Surgical) Treatment and Outcome of NF1-associated MPNSTs: influence of genetics and localization.

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Objective

To evaluate the management and outcome after resection of Malignant Peripheral Nerve Sheath Tumors (MPNST) in patients with Neurofibromatosis Type 1 (NF1).

Methods

We retrospectively reviewed the clinical and functional outcome (motor, sensory, pain) of 16 operated malignant peripheral nerve sheath tumors in 14 NF1 patients.

Results

The mean age at the time of surgery was 27±15 (range 8-54) years. 6 patients exhibited a positive family history of NF1. Among 7 patients with available genetic analysis, 2 patients each carried a missense, splicing, or no mutation. One patient showed a deletion in the *NF1 gene*. Radiological suspicion of potential malignancy (rapid tumor progression, inhomogeneity, enhanced metabolic activity) was the most common indication of surgery (n=9, ≙56%), followed by non-suspicious tumor progression (n=4, ≙25%) and severe pain (n=3, ≙19%). 10 tumors (≙63%), were histologically graduated as high grade, and the remaining 6 (≙38%) as low-grade MPNSTs. Total resection extents were possible in 81% (n=13) whereas only 3 tumors (≙19%) could be partially resected due to either a definite palliative situation or increased perioperative morbidity and mortality. The majority of tumors were localized at the trunk (n=8, ≙50%), followed by head/face/neck/brachial plexus (n=4, ≙25%), and with 13% each by the upper and lower extremities (n=2). High-grade MPNSTs were predominantly localized on the trunk (6/7, ≙86%). In about two third of cases, preoperative motor function improved or maintained (n=11, ≙69%) and worsened in 6 cases (≙31%). Preoperative sensibility level could be maintained or improved in the vast majority of 81% (n=13) and only 3 tumors (≙19%) worsened after surgery. In cases with preoperative pain (n=14), an improvement occurred in all these cases.

Conclusion

Early detection of potential malign or atypic neurofibromas and consecutive complete resection is crucial for further prognosis and survival. In addition, surgery maintains or improves preoperative neurological deficits and reduces pain intensity.

Neuroonkologie I/*Neuro-Oncology I*

P051

Vergrößerte tumefactive perivaskuläre Räume und Hydrozephalus – eine Assoziation oder Koinzidenz?
Enlarged Tumefactive Perivascular Spaces and Hydrocephalus – Association or Coincidence?

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Objective

Perivascular spaces (PVS) appear as small, linear, interstitial fluid-filled structures parallel to the known direction of perforating vessels and surround the small cerebral vessels as they pass the brain parenchyma. An extensive enlargement of PVS is referred to as giant tumefactive PVS (GTPVS). These lesions are mostly asymptomatic and are initially mistaken for cystic tumour formations in many cases. For neurosurgeons, the differential diagnosis must be considered to prevent unnecessary surgical treatment. Nevertheless, several cases of GTPVS are described to cause neurological symptoms due to their size, mass effect and location resulting in obstructive hydrocephalus and therefore the need for neurosurgical treatment.

Methods

We report a case of a 62-year-old male patient with a 4-month history of gait disturbance, followed by memory impairment, urinary incontinence, headache, and vertigo.

Results

Magnetic resonance imaging (MRI) of the neurocranium revealed a multicystic lesion localized in the right basal ganglia with extension into the crus cerebri, which was classified as GTPVS based on the characteristic appearance in MRI (Fig. 1). The repeatedly performed ventriculography indicated the presence of an occlusive hydrocephalus with extensive contrast of the external cerebrospinal fluid spaces, minimal contrast accumulation in the 4th ventricle, and absence of contrast in the 3rd ventricle or lateral ventricles (Fig. 2). The patient underwent endoscopic ventriculostomy of the third ventricle and incision of the lesion. After 4 months, a progression of symptoms occurred and an increase in ventricular width was detected. Therefore, a ventriculoperitoneal shunt was placed.

Conclusion

GTPVS are primarily asymptomatic lesions, rarely leading to neurological deficits, at which point they might require surgical treatment. In cases where patients have typical symptoms indicating the presence of other neurological diseases a coincidence of two phenomena should be considered to define optimal treatment strategies.

Abb. 1

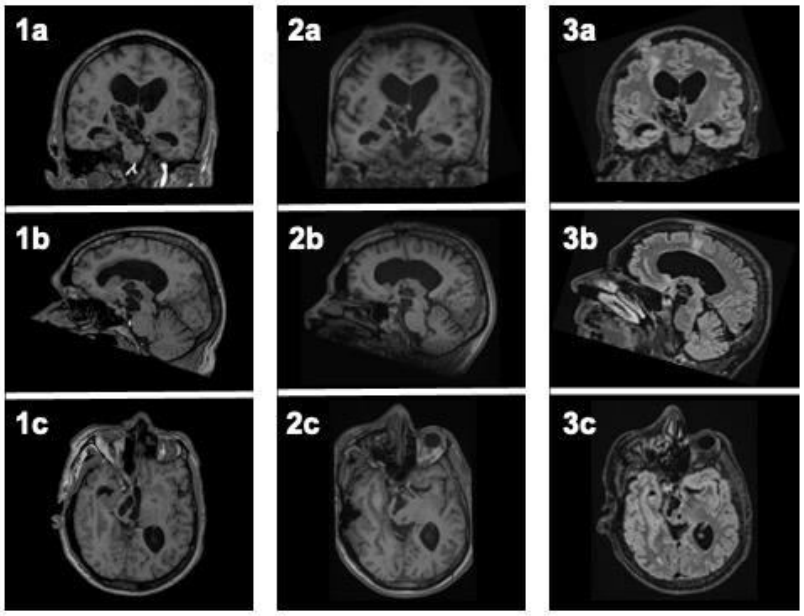

Fig. 1 MRI of the GTPVS during the patients' treatment

1a-c: Preoperative slides
2a-c: Immediately postoperative slides presenting no significant changes in the ventricular dilatation or appearance of the cystic lesions
3a-c: Six weeks follow-up slides showing a re-increase of the ventricular width

Abb. 2

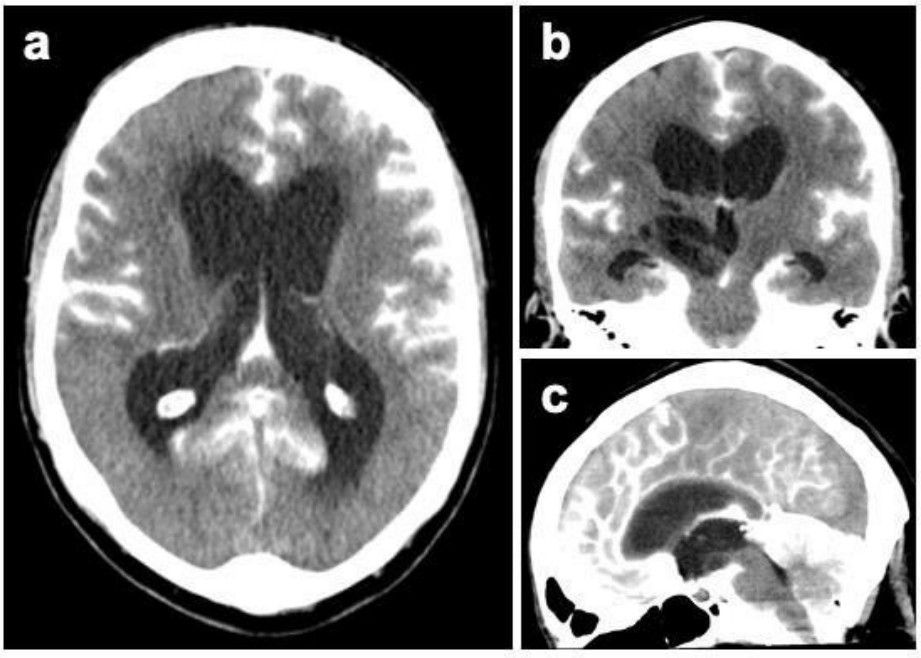

Fig. 2
Preoperative ventriculography showing the obstructive component of the hydrocephalus

Neuroonkologie I/*Neuro-Oncology I*

P052

Ausbleichen der Protoporphyrin IX Fluoreszenz – ein Vergleich der Kinetiken zwischen verschiedenen Geräten für die Fluoreszenz-gestützte Resektion von malignen Gliomen

Bleaching of Protoporphyrin IX fluorescence – comparison of kinetics between different devices designed for fluorescence-guided resection of malignant glioma

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Objective

Fluorescing Protoporphyrin IX (PpIX) is the endogenous dye in 5-aminolevulinic acid (ALA) mediated fluorescence-guided resection (FGR) of glioma. Little is known about the mechanism and kinetics of photodegradation, but it affects FGR of glioma. For intraoperative guidance, PpIX is visualized by a light source for excitation in combination with a dedicated filter system. During PpIX excitation, bleaching of fluorescence occurs. There are different commercially available systems for PpIX visualization. Purpose of this study was to compare real-time kinetics of PpIX photobleaching during excitation with various commercially available devices.

Methods

PpIX solution was exposed to blue and white light excitation, respectively. Photoreaction was stopped according to a predefined time scheme, maximum duration of excitation was 30 min. PpIX was quantified in the samples via liquid chromatography. Five devices were tested: a fluorescence microscope, a surgical loupe device, an endoscope and two exoscopes, all equipped with different light sources for PpIX excitation. Working distances were adapted to the surgical setting.

Results

Kinetics of PpIX degradation varied between the analyzed devices. After endoscopic blue light excitation, PpIX was nearly stable during the evaluation period. Moderate bleaching was detected with the surgical microscope. Exoscope-1 and the loupe device showed 2-fold higher bleaching rates than the microscope. The strongest bleaching was observed with exoscope-2 (3-fold compared to the microscope). Except during illumination with endoscopic blue light, the concentration of PpIX declined exponentially on all devices (Figure 1). Six minutes after blue light excitation, on average 64 ± 11% (mean ± standard deviation) PpIX was still intact. 24 min later, only 23 ± 14% was left. With broadband white light excitation, PpIX was more stable.

Conclusion

Bleaching of PpIX fluorescence appears to occur predominantly during FGR of malignant glioma. White light illumination seems to provoke only minor PpIX degradation. This could affect how we divide resection time between white and blue light during FGR. Although physical principles for PpIX visualization are the same, there are fundamental differences in the stability of the fluorescence signal between devices. If the differences in photobleaching have any effect on the practical use of various devices needs to be tested in future studies.

Abb. 1

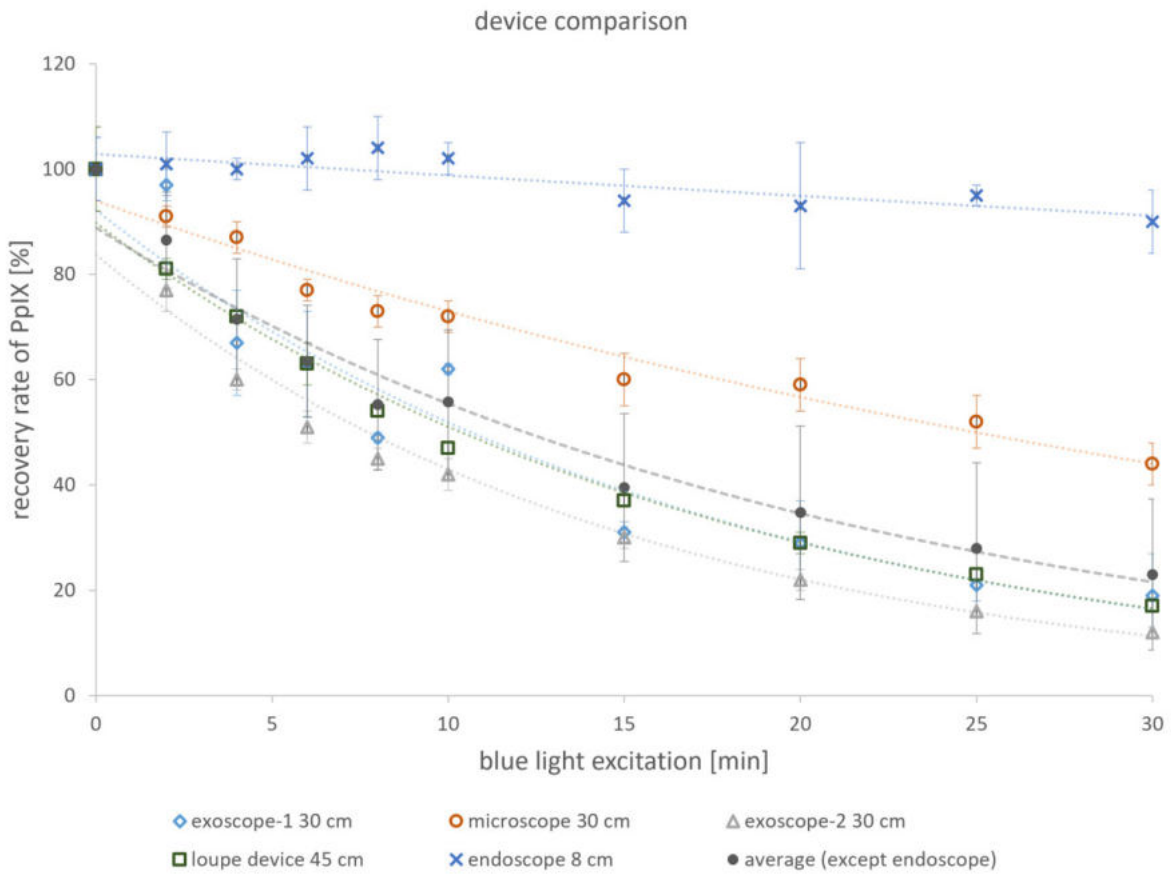

Figure 1: Time-kinetics of PpIX photodegradation with the different devices. Symbols mark average of three replicate measurements, error bars indicate standard deviation.

Neuroonkologie I/*Neuro-Oncology I*

P053

Entwicklung eines Prädiktionsmodels zur präoperativen Vorhersage des WHO Grades und der Tumoraggressivität bei intrakraniellen Meningeomen

Development of a prediction model for preoperative determination of WHO grade and tumor aggressiveness of intracranial meningiomas

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Objective

Determining the aggressiveness of intracranial meningiomas based on diagnostic imaging would provide an attractive opportunity to tailor the treatment strategy. In addition, the integration of radiological, radiomic and histologic factors could help to identify patients who are most likely to develop early tumor recurrence. The aim of this study was to develop a prediction model for preoperative determination of WHO grade and early tumor recurrence of intracranial meningioma

Methods

We performed a retrospective analysis of patients operated on for intracranial meningiomas in our hospital in 2007-2018. Only patients with available preoperative MRI (T1 CE sequences of sufficient quality) were included. MRIs were evaluated for atypical features and WHO grade was estimated by two neuroradiologists. Histological features and WHO grade were taken from histologic report. Meningioma volume extraction and radiomic analysis were performed using 3DSlicer and PyRadiomics software. 4 selection algorithms were used to select 25 most informative radiomic features. For model building using Orange software, 8 machine learning approaches were applied to determine WHO grade and early tumor recurrence. A 10-fold cross-validation was used. Early recurrence was defined as a tumor recurrence within 5 years.

Results

A total of 262 patients (77% women, mean age 57.8 (13.7) years) were included in the study. There were 37 (14%) tumor recurrences, of which … were early and the mean PFS was 124 (5.3) months. There were 78% WHO grade 1, 21% WHO grade 2 tumors, and 26% tumors with atypical histological features. The AUC for estimation of WHO grade by the two neuroradiologists was 0.65 and 0.66 and for determination of aggressive meningioma behaviour 0.53 and 0.54. The best machine learning model for determination of WHO grade was gradient boosting (AUC 0.75). Support vector machines demonstrated the best performance for identifying the tumors with early recurrence (AUC 0.82). The combination of human classifiers and radiomic analysis did not markedly improve model performance.

Conclusion

This study shows that the identification of tumor aggressiveness and early tumor recurrence by radiomic analysis appears to be superior to semantic analysis. Further development of radiomics will achieve a promising tool for preoperative identification of certain tumor characteristics and may become a useful tool in the future.

Neuroonkologie I/*Neuro-Oncology I*

P054

Steuerbarkeit struktureller und funktioneller Konnektomnetzwerke bei Gliompatienten
Controllability of Structural and Functional Connectomic Networks in Glioma Patients

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Objective

Gliomas impact on large-scale neural circuits and systemic microarchitecture of the brain beyond the macroscopically apparent tumor site, but the dynamic interaction between the tumor and the structural and functional connectome is not sufficiently understood. We applied complex dynamic graph network and control theory algorithms on structural and functional MRI connectivity data, in order to investigate controllability of the default-mode network (DMN) in glioma patients compared to healthy controls.

Methods

27 glioma patients (IDHmut=15, IDHwt=12) and 29 matched healthy controls underwent resting-state-fMRI and diffusion-MRI. Based on a whole-brain parcellation, structural (SC) and functional connectivity (FC) matrices were determined for each subject, and connectivity of the DMN was further analysed: Three different pre-processing methods were implemented in order to generate graphs besides the original zero threshold method. Network controllability measures comprising driver nodes (DN: which move the system into specific states of action) and critical nodes (CN: removal would increase the number of drivers needed to maintain controllability), as well as robustness measures were determined for SC and FC of the DMN, and compared between groups

Results

The number of DN within the DMN was decreased in patients, both for SC and FC, with higher losses in the prognostically less favourable IDHwt group. The number of CN was decreased in patients with regard to FC, but not SC, for which IDHmut patients even showed an increase in CN compared to controls. Mainly in the IDHmut patient group, not only losses, but as well topological shifts of DN and CN were found for SC and FC within the DMN. Only few common DN (as well as CN) were found for SC and FC of the DMN within each group. Network robustness was decreased in patients, especially with regard to SC in the prognostically less favourable IDHwt group.

Conclusion

While losses of driver and critical nodes may reflect lesion-induced network degradation, increases in number and topological shifts might relate to network plasticity accompanying the chronic disease course, which is more likely to occur in slower growing tumor lesions. Applying cognitive control theories on structural and functional connectomic patient data opens new avenues for investigating neural network dynamics, which could aid in prognostication of disease evolution and of functional outcome after therapeutic intervention.

P055

Dexamethason in Patienten mit Glioblastom: Systematisches Review und Meta-Analyse
Dexamethasone in Patients with Glioblastoma: A Systematic Review and Meta-Analysis

P. Scheffler[1], A. El Rahal[1], L. Häni[1], D. Kössinger[1], N. Neidert[1], C. Fung[1], J. Beck[1], O. Schnell[1]

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Objective

Glioblastoma is the most common and the most challenging to treat adult primary central nervous system tumor. Although modern management strategies modestly improved the overall survival, the prognosis remains dismal, and treatment side effects often dot the clinical course. Glioblastomas cause neurological dysfunction by destroying CNS tissue and through oedema formation in neighbouring regions of the CNS. The administration of steroids such as dexamethasone is thought to alleviate symptoms by reducing perifocal oedema and restoring neurological function. However, despite its widespread use, the evidence for administration of dexamethasone remains elusive. Therefore, we aimed to review the current evidence concerning the use and outcome of dexamethasone in patients with glioblastoma.

Methods

We performed a systematic review and meta-analysis of the literature according to PRISMA-P guidelines. We performed a restricted search using the keywords "Dexamethasone" and "Glioblastoma"; "Dexamethasone" and "High grade glioma". Records were identified from PubMed, Web of Science, the Cochrane Library and Academic Search Premier. Hazard ratios (HR) for overall survival (OS) and progression-free survival (PFS) were either collected from publications as given, calculated based on the available numeric results, or extracted from Kaplan-Meier plots. Meta-analysis was performed using a random effects model. Results are reported as hazard ratios with 95% confidence intervals (CI).

Results

Data from 21 publications was included in the final analysis. Patients receiving higher doses of dexamethasone had significantly worse overall survival (HR: 1.61, CI: 1.38 – 1.89) and progression-free survival (HR: 1.56, CI: 1.27 – 1.92) than patients receiving lower doses of dexamethasone. In addition, the negative association of dexamethasone on OS and PFS persisted in multiple studies even after adjusting for confounders such as tumor size and Karnofsky Performance Score.

Conclusion

Despite the widespread use of dexamethasone in glioblastoma patients, its use may not be warranted in most patients, as it might be associated with worse long-term outcome. Prospective studies are needed, but we currently conclude that dexamethasone administration should be restricted to selected symptomatic glioblastoma patients.

Neuroonkologie I/*Neuro-Oncology I*

P056

Plasmaproteinspiegel als Biomarker im Glioblastom?
Impact of routine plasma protein level in Glioblastoma

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Objective

Previous investigations have shown that protein kinase pathways can influence the occurrence of Glioblastoma (GBM). However, conventional marker in blood plasma could not be identified in GBM so far. This study aimed to analyze the impact of routine plasma protein level in GBM patients on overall survival (OS) and progression free survival (PFS). It should determine, if plasma protein can be used as a common biomarker regarding the outcome of GBM patients.

Methods

Medical records of adults with GBM treated in our institution between 2005 and 2020 were analyzed regarding demographic-, clinical-, molecular characteristics, as well as laboratory chemistry data at admission before surgery and outcome. Univariate and multivariate analyses were performed to determine significant coherences.

Results

From 1016 patients with a mean age of 61.91 (± 13.38 standard deviation) a recurrent GBM could be identified in 31% (n= 314). The median PFS was 6.77 months. 72.8 % (n= 740) patients showed normal plasma level of protein in the range from 6.4 – 8.3 g/dl, while 25.6% (n= 260) patients showed degraded levels and 1.6 % (n= 17) patients showed increased plasma levels of protein. Age, gender, tumor localization and MGMT status were not associated with the level of plasma protein significantly. A higher BMI influenced plasma protein level ($p = 0.023$). Different protein plasma level did not affect MGMT status ($p = 0.50$). A degraded plasma protein level at admission was significantly associated with a shorter OS ($p < 0.001$) in univariate analysis. Temporal localization of the tumor could be identified as a significant parameter regarding PFS ($p = 0.045$). In multivariate analysis, a longer OS was independently associated with a methylated MGMT status, gross total resection as extent of tumor resection ($p < 0.001$), as well as a younger age ($p = 0.002$). Here, a degraded plasma level of protein showed a trend toward significance ($p = 0.06$).

Conclusion

Routine plasma protein could provide information about OS in GBM. However, further studies are needed to establish a valid, standard plasma biomarker in the management of GBM patients.

Neuroonkologie I/*Neuro-Oncology I*

P057

Palliativversorgung in deutschen neuroonkologischen Zentren
Palliative care in German neurooncological centres

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[2]Universitätsklinikum Frankfurt, Klinik für Neurochirurgie, Frankfurt am Main, Deutschland
[3]Universitätsklinikum Hamburg Eppendorf, Klinik für Neurochirurgie, Hamburg, Deutschland
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[5]Klinikum Fulda, Klinik für Neurochirurgie, Fulda, Deutschland

Objective

Palliative care has been gaining growing attention in the context of neurooncology over recent years. There has been a shift from end-of-life care to early integration and a focus on quality of life in those with incurable diseases. Concepts such as "total pain" acknowledge patients" need for not only medical, but also psychological and spiritual care. The aim of this study was to assess the standard of care for neurooncological patients in certified centres and university hospitals in Germany.

Methods

We sent out a link to a 29-item online questionnaire to all 51 German neurooncological centres certified by OnkoZert, as well as the neurooncological centres of the 6 remaining German university hospitals. The survey is still open and further responses are expected.

Results

To date, specialists from 33/57 centres completed the questionnaire (58% response rate). 26/33 responses were from university hospitals and 12/16 federal states were represented. In all 24 centres there are psychooncology specialists and spiritual counsellors available. However, spiritual care concepts are established in 5/33 centres and only one utilises a standardised screening of spiritual needs. 25/33 centres have separate palliative departments. Palliative issues are regularly discussed in tumour board at 24/33 centres and palliative care specialists attend tumour board in only 11/33 centres. Palliative screening instruments are routinely used in 21/33 centres. However, the time-points for involving palliative care specialist vary widely.

Conclusion

Palliative care approaches and infrastructure vary widely across German neurooncological centres. Specialised psychologists and spiritual counsellors appear to be frequently available. However, there remains scope for standardisation of screening instruments, as well as the time-points and delivery of palliative care in neurooncology.

P058

Neue therapeutische Ansätze zur Behandlung von Glioblastomen
Novel therapeutic targeting rationales for the treatment of glioblastoma

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[2]Philipps Universität Marburg, Neurochirurgie, Marburg, Deutschland
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Objective

Current standard adjuvant therapy of glioblastoma multiforme (GBM) using temozolomide (TMZ) frequently fails due to therapy resistance. Thus, novel therapeutic approaches are highly demanded. Since apoptosis induction in GBM cells is inefficient due to high abundance of apoptosis inhibitors, we tested a strategy of combining apoptosis inducers with anti-apoptosis inhibitors. Thus, we evaluated the efficacy of TMZ, XPO1-Inhibitor, MTX, and Cytarabine (induction of apoptosis) in combination with XPO1-/Bcl-2/Mcl-1 inhibition (rescue of apoptosis) in GBM cell lines.

Methods

Dose-response curves were generated in GBM cell lines and in GBM stem-like cells (GSCs) by using cell titer glow, caspase 3 activity assays, and FACS analyses. Western Blot analyses were performed to determine activation status of p53, CDKN1A, and other p53-related proteins. All combinatorial data were analyzed for cooperativity using isobolograph analyses.

Results

The therapeutic efficacy of the second-generation XPO1 inhibitor Eltanexor was tested for cell viability and apoptosis assays in GBM cell lines and GSCs. For most GBM- derived cells, IC_{50} concentrations for Eltanexor were below 100 nM with the only exception for U251 cells with the highest IC50 value of 260 nM. In correlation with reduced cell viability, apoptosis rates were significantly increased. GBM stem-like cells presented a combinatorial effect of Eltanexor with TMZ on cell viability. Furthermore, pretreatment of GBM cell lines with Eltanexor significantly enhanced radiosensitivity *in vitro*. To explore the mechanism of apoptosis induction by Eltanexor, TP53-dependent genes were analyzed at the mRNA and protein level. Eltanexor caused induction of TP53-related genes, TP53i3, PUMA, CDKN1A, and PML on both mRNA and protein level. Immunofluorescence of GBM cell lines treated with Eltanexor revealed a strong accumulation of CDKN1A, and, to a lesser extent, of p53 and Tp53i3 in cell nuclei as a plausible mechanism for Eltanexor-induced apoptosis. We also tested combinations of AraC, MTX and TMZ with AT101 and A1210477 (selective MCl-1 inhibitors) and noticed a remarkable efficacy in GSCs.

Conclusion

From our data we conclude that monotherapy with Eltanexor and a combination of AraC with Mcl-1 inhibitors is highly efficient in GSCs and can be combined with current adjuvant therapies to provide a more effective therapy of GBM.

Neuroonkologie II/*Neuro-Oncology II*

P059

Spielt die Operation eine Rolle bei der Behandlung von Pinealiszysten ohne Hydrocephalus - Ergebnisse einer Langzeitstudie

Does surgery has a role in the treatment of pineal cysts without hydrocephalus – results of a long-term study

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Objective

Pineal cyst fenestration with either the endoscope or microscope is an established procedure in the management of patients with proven hydrocephalus. Decision making is more difficult if the patients has additional symptoms not attributable to disturbed CSF flow and/or if no hydrocephalus can be seen on CT/MR imaging. The aim of our observational study was to evaluate the effect of surgery in those patients.

Methods

The medical records and MRIs of all patients who underwent surgery for a pineal cyst during the last 15 years were reviewed. Additionally, a telephone interview was done after a mean follow-up time of 98 months. Demographic data, symptoms, pain killer intake before and after surgery and at follow-up were recorded. At follow-up, the patients were asked if they would decide again for surgery or not or would either recommend it for other patients.

Results

The study population consist of 58 patients (37 female, 21 male, mean age at surgery 23 years); 47 patients agreed being interviewed. The remaining 11 patients were unattainable. A total of 18 patients (31 %) had either an own or a family history of migraine. Each patient had more than one discomfort before surgery: Headache (mean VAS 7.3 points) was the major complain (95%), followed by vertigo and subjective double vision (47% each) and sleep disturbances (21%). No hydrocephalus was seen on MRI in 54 patients (93%) and 64% of the cysts were smaller than 1.5cm. 57% of the patients were symptom-free, while 38% reported long-lasting symptom improvement after surgery. The pain killer intake dropped from 79% before to 43% after surgery and to 38% at late follow-up. Accordingly, 97% would recommend surgery to other patients and 91% would undergo surgery again, if needed.

Conclusion

In this large series, we showed that pineal cysts can become symptomatic, irrespective of the presence or absence of a hydrocephalus. As the symptoms are not pathognomonic, the neurosurgeon is left with the challenge to identify the surgical candidates, because the effect of surgery is very good and persists over years.

Neuroonkologie II/*Neuro-Oncology II*

P060

Schnittkulturen des menschlihen Gehirns: ein Paradigma für die neuroonkologische Forschung
Human Brain Slice Cultures: A Paradigm for Human to Human (H2H) Neuroncological Research

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Objective

Glioblastoma (GBM) is among the most common of malignant brain tumours.Over the past several decades, therapies that appeared promising in mice models have failed during clinical trials due to the differences encountered during translation of research from model organisms to humans. To partially mitigate these difficulties in translation, we present a human cortical organotypic culture based GBM model, which allows us to manipulate individual components of the tumour environment in order to investigate the influence of different cell types in the immunosuppressive tumour microenvironment.

Methods

Non neoplastic human neocortical tissue (2 cm away from the tumour core) or entry cortex from epilepsy surgery guided by intraoperative neuro navigation, was cultured for up to 14 days post resection using an optimized medium. The cultured tissue was further injected with patient derived human GBM cells to create an *ex vivo* human model of glioblastoma model. The role of astrocytes in tumour microenvironment was studied using a microglia loss of function model. Tumour growth was monitored using fluorescence microscopy and microglia crosstalk was studied using Flow cytometry and RNA-sequencing analysis.

Results

Our data corroborate differences between astrocytes in human and murine models in different reactive states, showing that the glioblastoma microenvironment is difficult to be accurately modelled using murine models. Results from microglia depletion showed ample evidence of crosstalk between GBM cells, astrocytes and microglia showing the increased intensity of anti-inflammatory cytokine IL10 and TGFb when microglial depletion was carried out.

Conclusion

Due to accessibility and possibility to explore the microenvironment, our established human combined access-tumor tissue model may serve as human to human translational paradigm (H2H) for neuroscience, neuro-oncology, and pharmacotherapy.

Neuroonkologie II/*Neuro-Oncology II*

P061

Die Rolle des Alterns beim Glioblastom
The Role of Aging in Glioblasotma

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Objective

Aging of the human brain is a multifactorial process that is not understood in its complexity. Recent studies demonstrated that elderly brains are enriched for activated glial cells towards inflammatory transformation. Due to the fact that glioblastoma mostly arise in older patients, we aimed to explore similarities between the GBM microenvironment and healthy aging-related transcriptional alterations.

Methods

We performed spatial transcriptomics using Visium 10X Genomics technology, on tumor and healthy access cortex from 22 donors and identified shared transcriptional signatures of tumor and non-malignant samples, correlating with the age of patients. Experimental validation was applied by our human neocortical model using different age groups anf injection of a "young" (45y) or an old" (86y) patient-derived tumor cell line. We performed single-cell RNA sequencing of the tissue model derived cell lines to explore the diversity of a cell line within differently "aged" environments.

Results

Similarity of cell type specific transcriptional differentiation of glial cells in malignant and healthy specimens confirmed an age-related shift towards inflammatory transformation in both, healthy and tumor samples. This inflammatory shift included astrocytes with increased activation of the complement cascade as well as microglia cells / macrophages. To explore the role of the environment in shaping the tumor or vice versa, we characterized both age matched and mismatched human neocortical GBM model, showing that the ageing-environment dynamically shape the intra-tumoral heterogeneity causing differences in tumor growth and cell morphology. ScRNA-seq confirmed the switch from non- to enriched reactive differentiation of tumor cells in the elderly environment.

Conclusion

Our analyses suggest that age-related abnormalities in the human brain are also reflected in glioblastoma. The aging environment is responsible for reactive transcriptional subtypes of glioblastoma and support tumor growth. Our findings support the essential demand for personalized therapies in the elderly population.

Neuroonkologie II/*Neuro-Oncology II*

P062

Anomalieerkennung mittels Diffusions-MRT bei Gliompatienten
Diffusion-MRI for Anomaly Detection in Glioma Patients

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Objective

Defining treatment targets in brain tumor therapy is mainly dependent on structural MRI, which however underestimates tumor extension in malignant glioma due to the diffusely infiltrative nature of the disease. Early detection of tumor infiltration not yet visible on conventional MRI could improve treatment and the therapy-associated prognosis. We developed deep-learning algorithms for diffusion-based anomaly-detection in glioma patients and compared these to conventional MRI.

Methods

32 glioma patients and 28 healthy controls underwent structural and diffusion-weighted MRI preoperatively. Two different anomaly detection methods (an autoencoder <AE> and a reconstruction discrimination network <RDN>) were trained on diffusion-data of healthy controls and then applied in patients. Diffusion-anomalous regions were compared to a ground truth segmentation obtained from T1 and FLAIR images using an ROC curve. The segmentation threshold was determined based on the maximum of a 16x16x16 voxel averaging kernel and evaluated with the Dice score. The segmentation results were further compared by visual inspection to structural follow-up MRI at 18 months postoperatively.

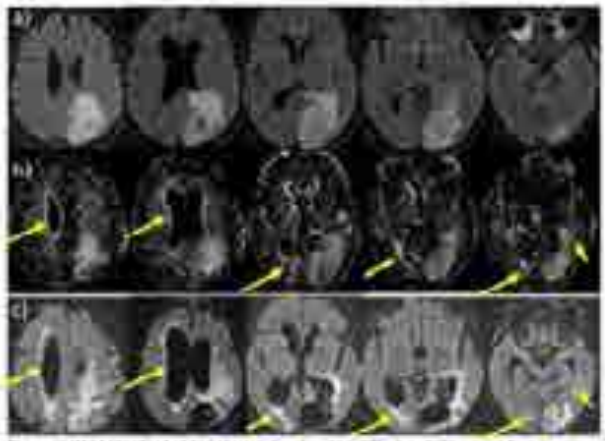
Results

Evaluating different architecture and training hyperparameters comparing the network output against the ground truth, the AE obtained an AUROC of 0.82 and a final Dice score of 0.48. The best RDN obtained an AUROC of 0.772 ($p < .0301$) and a final Dice score of 0.62 ($p < .0016$). The score-difference is due to slightly anomalous areas located by the RDN. The anomaly score of these regions is below the binary segmentation threshold, thus lowering the AUROC score without harming the overall better discriminative performance of this network. These areas characterize regions with potentially altered diffusive properties not yet visible on structural scans, which colocalized in malignant glioma patients to lesions delineated only later on in conventional MRI follow-up data (Fig.1).

Conclusion

Diffusion-based anomaly-detection in glioma patients showed consistency with segmentations obtained from structural scans but indicated in some patients additionally altered areas not yet visible on conventional MRI. Longitudinal studies should investigate whether anomaly-scoring based on diffusion properties can aid in detection of occult tumor infiltration and early identification of itineraries of tumor progression, which could improve prognostication of disease evolution and tumor treatment strategies.

Abb. 1



Neuroonkologie II/*Neuro-Oncology II*

P063

Intraoperative Bestrahlung in der Chirurgie von Gehirnmetastasen ermöglicht die frühere onkologische Systemtherapie.

Intraoperative Radiotherapy in Brain Metastasis Surgery allows faster Transition to Systemic Therapy.

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Objective

In patients with metastatic disease, delay of systemic therapy (CTX) after oncologic surgery due to wound healing issues and postoperative radiotherapy might influence the oncologic outcome. Intraoperative radiotherapy (ioRT) is an emerging option in neurooncology, possibly shortening the time for comprehensive treatment compared to conventional percutaneous radiotherapy (RT). Aim of this study was to compare the transition time to CTX in patients undergoing ioRT or RT.

Methods

We performed a retrospective chart review analysis of patients undergoing surgery for brain metastaes (BM) at our institution with either ioRT or adjuvant RT. Either therapy was applied according to an internal standard operation procedure favoring ioRT if feasible. The time (days) from surgery until the beginning of CTX was compared. Adverse events (AE) after surgery were recorded until the beginning of CTX.

Results

99 patients were analyzed from which 59 underwent adjuvant RT and 40 ioRT. Patients undergoing resection of BMs with ioRT had significantly shorter intervals to CTX (RT vs. ioRT; 65.4 ± 54.3 vs. 32.3 ± 28.0 (mean±SD); $p < .001$). Comparing the interval to CTX between last RT fraction and ioRT showed no significant difference RT vs. ioRT (26.2 ± 55.8 vs. 32.3 ± 28.0 (mean±SD); $p = .52$). AE rates after surgery were comparable in both groups.

Conclusion

ioRT for BM surgery allows faster transition to systemic oncologic therapy than conventional adjuvant RT.

Neuroonkologie II/*Neuro-Oncology II*

P064

Analyse von funktionellen neuronalen Veränderungen bei Patienten mit Hirnmetastasen im sensomotorischen Kortex

Analysis of functional neuronal changes and connectivity in patients with brain metastases in the sensomotor cortex

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Objective

While the influence of a primary brain tumor on the BOLD signal is focus of numerous studies showing that the fMRI signal and activation patterns in the sensomotor cortex are attenuated in the presence of tumors such as glioblastoma, empirical investigation of this influence in patients with metastases is less often examined. Therefore, the aim of this study was to investigate how lateralization of cortical activations and functional connectivity (FC) are affected by the presence of brain metastases exemplary for the sensomotor system.

Methods

In this study, motor fMRI data of 30 patients (16 female and 14 male, mean age 60.27 years) with a brain metastasis (8 left hemisphere, 10 right hemisphere, 12 both hemispheres) and 30 healthy control subjects from the Human Connectome Project were analyzed and compared using Statistical Parametric Mapping (SPM12) with the CONN and LI toolboxes. The extent of lateralization of cortical activation was calculated using the laterality index (LI) in the frontal and parietal lobe, as well as FC between 22 ROIs of the Default Mode, Salience, Dorsal Attention, Fronto Parietal, and Sensorimotor network across both hemispheres.

Results

Analysis of the LI showed no statistically significant differences between patients and controls. When comparing FC of cortical networks, we found attenuated intra-network connectivity in the patients group compared to healthy controls across all networks in the affected and unaffected hemisphere. Similar results were evident in the inter-network connectivity results, especially those involving connections between the Default Mode and Fronto Parietal networks to the ROIs of the other networks. In addition, inter-network connectivity between the Sensorimotor network and the Salience and Dorsal Attention networks was more pronounced in patients.

Conclusion

While the influence of brain metastases in the sensomotor cortex could not be shown to affect the lateralization of cortical activation, the results indicate that FC is altered, similarly to what is already known for FC in primary brain tumors. The attenuated connectivity of networks in both the affected and unaffected hemisphere suggest an influence of the tumor beyond local damage while an increase in inter-network connectivity of the Sensorimotor network may be an indicator for compensatory neuroplastical processes due to the tumor.

P065

Gliom mit fokal Pseudorosetten und fokal pseudopapillären Strukturen- Case Report einer seltenen neuen Tumorentität bei einem Patienten mit initial nachgewiesenem pleomorphen Xanthoastrozytom

High-grade glioma with pleomorphic and pseudopapillary features (HPAP)- a case report of a rare new tumor entity in a patient with initially diagnosed pleomorphic xanthoastrocytoma

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Objective

The identification of high-grade glioma with pleomorphic and pseudopapillary features (HPAP) is a recently described rare entity with new epigenetically defined features of high-grade circumscribed gliomas. We present a case initially diagnosed as pleomorphic xanthoastrocytoma in 2012 and progressed into a rare new tumor entity.

Methods

A 61-year-old male patient underwent surgery and recurrent surgery of histopathology-proven pleomorphic xanthoastrocytoma (PXA, WHO 2) right frontal in 2012, 2014, and 2015. Due to tumor recurrence in 2019, he underwent Cyberknife therapy (18 Gy). Two years later he developed multiple nodular intra- and extra-axial lesions with contact to the dura. He underwent recurrent surgery and, in both lesions, -the extra-and intra-axial- histopathologically again PXA (now WHO 3) could be documented. From April until October 2022, he was treated with 6 cycles of temozolomide due to progression. Because of the rapid and multifocal progression, the atypical growth patterns and the search for possible experimental therapy targets DNA methylation profiling and next-generation sequencing (NGS) were performed. The integrated diagnosis was a glioma, not elsewhere classified. In October 2022 he underwent surgery again for 3 large lesions infiltrating the right frontobasal, temporal and frontoparietal hemisphere since under chemotherapy further progression has been confirmed, and increasing mass effect led to progressive neurological deterioration having resulted in seizures and left-sided hemiparesis. The process from 2012 until now is well documented using MR-Imaging. Patient achieved excellent recovery.

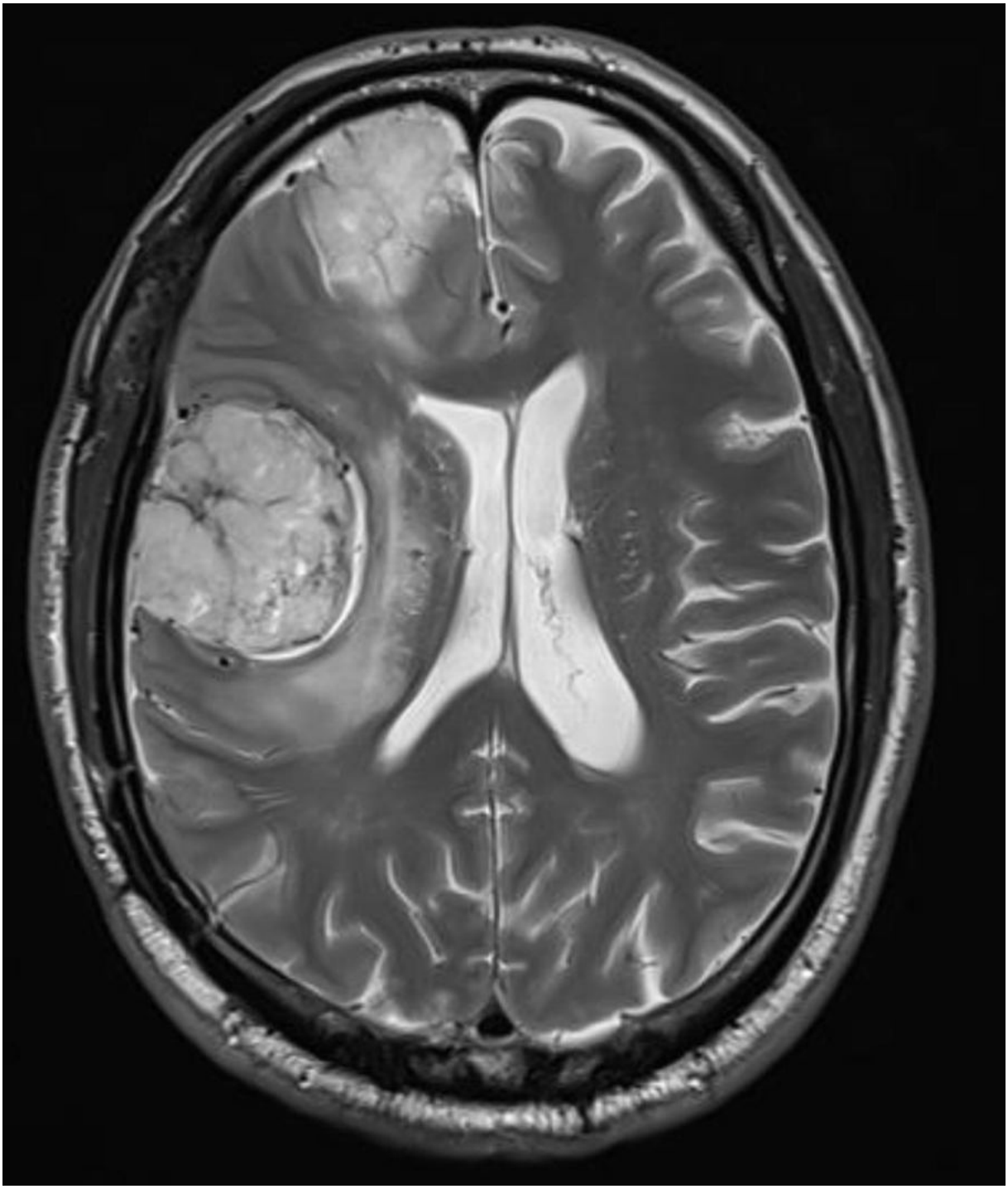
Results

The histological finding was a glioma with pleomorphic and pseudopapillary features. Genetic analysis revealed that there is no allocation to an established reference class. The tumor was IDH1 R132H negative, the nuclear ATRX-expression was obtained, BRAF V600E was negative, H3 G34R was negative and the MGMT-Promoter unmethylated. The integrated diagnosis was a glioma, not elsewhere classified (NEC).

Conclusion

DNA- methylation profiling and NGS are helpful to discover new tumor entities in gliomas which can lead to new therapeutic approaches. In this case, radical surgical therapy including resection of the infiltrated dura is the first line therapy, because radio- and chemotherapy led to progression and despite the extended resection patient had an excellent outcome.

Abb. 1



Neuroonkologie II/*Neuro-Oncology II*

P066

Änderungen der Mikrostruktur des Corpus Callosum nach der Resektion bei Patienten mit höhergradigen Gliomen

Change of white matter integrity of the Corpus Callosum after surgery in patients with high grade gliomas

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Objective

High grade gliomas are very common in adults. To ensure a treatment that does not only lengthen survival, but also improves preservation of neurocognitive functions, reliable methods to measure changes in neurocognitive abilities are necessary. Neurocognitive decline is often based on white matter (WM) lesions. We take the corpus callosum (CC) as a reliable structure to identify decline of WM integrity. We hypothesize a deterioration of WM integrity of the CC after resection due to injury of fiber bundles.

Methods

18 patients with a high grade glioma were included and underwent MRI with Diffusion tensor imaging (DTI) within one week before and within 48 hours after resection. We used the software fsl, Oxford for image processing and determined fractional anisotropy (FA) in three defined volumes of the CC: rostrum, truncus and splenium. Changes in FA after surgery were analyzed using a t-test. The positional relationship of the tumor to the CC was correlated with changes in FA values as well.

Results

Most of the tumors were located in the frontal lobe (69.2%). The CC was infiltrated by the tumor in 7 patients (26.9%), compression or edema of the CC were present in 15 cases (57.7%). There was slight improvement of WM integrity in the rostrum in 10 patients (55.6%), in the truncus in 7 patients (38.9%) and in the splenium in 10 patients (55.6%). None of these changes were statistically significant. For patients with edema or compression of the CC, but no tumor infiltration of the CC (n=6), FA declined significantly in the rostrum (p=.005). In four of these patients (66.7%), edema was evident in the rostrum, explaining the significant correlation in this area. We could not find any further significant correlation between tumor localization and change of WM integrity in the CC.

Conclusion

Contrary to our hypothesis, WM integrity did not change significantly within a maximum period of 48 hours after surgery. This however substantiates that the CC is a robust correlate for WM integrity. We expect further deterioration of WM integrity at a greater time distance from surgery due to demise of fiber bundles.

Whether early significant postoperative deterioration of WM integrity in those patients with compression or edema of the CC is caused by further swelling and manipulation during surgery must be analyzed in a larger patient group.

Neuroonkologie II/*Neuro-Oncology II*

P067

Longitudinale- MRT und [^{18}F]FET-PET Charakterisierung von RCAS-tva-induzierten, PDGFB-getriebenen experimentellen Gliomen

Longitudinal MRI and [^{18}F]FET-PET Profiling of RCAS-tva-Induced PDGFB-Driven Experimental Glioma

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Objective

Glioblastoma are aggressive primary brain tumors with a devastating prognosis despite of multimodal therapy regimes. Longitudinal profiling by MRI and [^{18}F]FET-PET measurements enable the dynamic visualization of metabolic features during tumor development. Options for close-meshed longitudinal imaging time points for characterizing temporal and spatial metabolic alterations during tumor evolution in patients are very limited because patients usually present with already established tumors. The replication-competent avian sarcoma-leukosis virus (RCAS)/tumor virus receptor-A (tva) system offers a high grade of spatial and temporal control of somatic gene delivery *in vivo*. Consequently, the system is a powerful preclinical tool to evaluate novel treatment strategies. In this study, we aimed at using longitudinal MRI and [^{18}F]FET-PET measurements to identify neuroimaging characteristics of the platelet-derived growth factor B (PDGFB)-driven glioma model using the RCAS-tva system.

Methods

We implanted PDGFB transfected DF-1 cells into adult 129S.Tg(NES-TVA)-Cdkn2a$^{-/-}$ mice and performed MRI twice weekly and [^{18}F]FET-PET once per week. We measured growth dynamics and [^{18}F]FET-PET uptake as well as symptom-free survival and post-mortem immunohistochemistry by a selected set of antibodies for characterizing the tumor-associated microenvironment.

Results

We observed reproducible tumor formation with comparable symptom-free survival times in treatment-naïve PDGFB-driven gliomas. Interestingly, the MRI and [^{18}F]FET-PET features were highly comparable to the human glioblastoma, emphasizing the high translational potential of this preclinical glioma model. MRI imaging revealed exponential growth dynamics starting around day 25 after implantation. Furthermore, we observed, a rodent-specific, highly immunogenic tumor microenvironment by immunohistochemistry.

Conclusion

Our study provides further insights into this preclinical model, highlights its translational potential and advocates for an imaging-stratified design of preclinical therapeutic interventions in this preclinical glioma model.

Neuroonkologie II/*Neuro-Oncology II*

P068

Temporale Heterogeneität von DNA Methylierungsklassen zwischen Erstdiagnose und Rezidiv beim *IDH*-Wildtyp Glioblastom

Temporal Heterogeneity of DNA Methylation Subclasses Between Matched Newly Diagnosed and Recurrent IDH-Wildtype Glioblastoma

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[7]Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg i. Breisgrau, Deutschland
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Objective

Spatiotemporal heterogeneity is a major factor contributing to the devastating prognosis of *isocitrate-dehydrogenase (IDH)*-wildtype glioblastoma. Genome-wide DNA methylation profiling allows the stratification into several DNA methylation subgroups of *IDH*-wildtype glioblastoma, which were shown to have a spatial heterogeneity in newly diagnosed tumors. However, the temporal heterogeneity and its clinical relevance of DNA methylation subgroups remains inconclusive.

Methods

Tumor tissue obtained from first and recurrence surgery of 31 patients diagnosed with *IDH*-wildtype glioblastoma was subjected to DNA methylation profiling. DNA methylation profiles were analyzed for temporal heterogeneity and correlated with clinical data, survival outcome and copy number variations. In addition, deconvolution of immune cells and unsupervised hierarchical clustering using pairwise Pearson correlation coefficients of the 10.000 most variable CpG features was performed.

Results

Of all patients with matched tumor tissue, 4 (12.9%) patients had a mismatched brain tumor classifier outcome at recurrence. In the remaining 27 patients, dominant DNA methylation subclass transition was observed in 8 (29.6%) glioblastomas, with mesenchymal subclass transition being the most common (62.5%). Subclass transition was more likely after incomplete removal of contrast-enhanced tumor parts at first surgery ($p = 0.04$). Tumor location, adjuvant treatment, and time between initial and recurrent surgery did not affect transition. The proportion of immune cells from deconvolution data, tumor purity, or specific CpG sites did not correlate with subclass change. Survival analyses showed a comparable outcome for patients with and without subclass transition.

Conclusion

Our findings demonstrate the temporal heterogeneity of DNA methylation subclasses in 29.6% of *IDH*-wildtype glioblastoma. We identified clinical factors and showed that a subclass transition did not impact the survival outcome. However, a possible DNA methylation subclass transition must be taken into consideration for future targeted therapies at recurrence.

Schädelbasis I/*Skull base I*

J-SBNC009

Planung der Schwannom-Operation am Vestibulum anhand von 3-dimensionalen Modellen
Planning of Vestibular Schwannoma Surgery using 3-Dimensional Models

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Objective

Vestibular schwannoma surgery is complex and may present with several pitfalls. Preoperative planning and the understanding of the anatomical variations in each case is a fundamental step for good results and avoidance of complications. Drilling of the internal auditory canal is, in most cases, indispensable to achieve complete tumor resection.

Methods

Six patients with vestibular schwannomas and anatomical variations that could represent difficulties during surgery were selected for this study. After acquiring fine-cut computed tomography scans, 3-dimensional models of the temporal bone of each case using rapid prototyping technique were created. Anatomical aspects as the position of the jugular bulb and semicircular canals in relation to the internal auditory canal and the safe bone removal were evaluated.

Results

Six 3-dimensional temporal bone models helped to better understand the anatomy around the internal auditory canal previously to surgery. This technique enabled an improved comprehension of the relations between the jugular bulb, semicircular canals and to plan the opening of the internal auditory canal. These models could be produced at an average price of US$ 8 each and took about one day to be fabricated.

Conclusion

Production of 3-dimensional temporal bone models previous to vestibular schwannoma surgeries using rapid prototyping technology was possible and permitted a better understanding of anatomical variations. Use of this models helped surgeons to plan the optimal drilling of the internal auditory canal tailored for each case. This technique may, in this way, potentially reduce injuries to the jugular bulb and semicircular canals. Additional clinical studies will be necessary to evaluate this possible advantage.

Abb. 1

Schädelbasis I/*Skull base I*

P071

Medikamentöse Testung bei Vestibularisschwannomen am ex vivo Tumor-Slice-Model
Pharmaceutical Screening in vestibular schwannoma ex vivo tumor slice model

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Objective

Vestibular schwannoma (VS) are benign tumors, which grow bilaterally in most cases of neurofibromatosis type 2 (NF2). In NF2 patients because of different other tumor entities and the high recurrence rate, invasiveness and functional deficits in patients, a systemic approach is urgently needed. However, long lasting systemic treatment strategies are missing until now. We were able to develop an *ex vivo* tumor slice model for pharmaceutical screening in NF2 patients.

Methods

In order to generate our *ex vivo* tumor slice model, freshly obtained tumor tissue was fixed in agorose and cut in 350µm slices. These slices could be cultured for at least six weeks without changes in the tumor microenvironment and without changes in apoptosis or morphology. Nilotinib (20mM), Lapatinib (10µM) and Crizotinib (20µM) treatment over three weeks was evaluated regarding their apoptotic (CC3+/S100+) and antiproliferative (Ki67+/S100+) effect on tumor slices (n=3) via immunofluorescence staining. In comparison, the same experiment was passed in primary cell culture and in untreated slices as control.

Results

The *ex vivo* tumor slice model showed no morphological changes during the pharmaceutical testing and the DAPI stained cell numbers are stable over three weeks. The proliferation rate was 1.25% at the beginning and increased up to 4.5% in week two and three in the untreated model. The proliferation rate could be half after Lapatinib treatment and a quarter after Nilotinib treatment and nearly no proliferation under Crizotinib treatment depending on patient"s individual tumor characteristics. The apoptosis rate was about 1.5% at the beginning and reduced to less than 0.5% after two and three weeks in the untreated slice model. The apoptosis rate was not statistically significant different under the pharmaceutical treatment.In comparison to the treatment in cell culture there was an extensive reduction of the cell count especially after Crizotinib (zero cells vs. 41 cells in the control) and Nilotinib treatment (12 cells vs. 41) and an increase in the apoptosis rate (Nilotinib treatment after 3 weeks: 4 cells vs. 50 cells). Although in this model the development after treatment differed regarding patient"s individual tumor characteristics.

Conclusion

With this tumor slice model pharmaceutical screening on patients individual tumor tissue is possible and perhaps more realistic than testing in primary cell culture. Standard parameters for a medical testing panel has to be developed.

Schädelbasis I/*Skull base I*

P072

Digitale Patient-Reported Outcome Measures zur Erfassung der gesundheitsbezogenen Lebensqualität bei operativer oder konservativer Behandlung von Tumoren des Kleinhirnbrückenwinkels

Digital Patient-Reported Outcome Measures assessing Health-Related Quality of Life in Operative or Conservative Management of Cerebellopontine Angle Tumors

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Objective

Health-related quality of life (HRQoL) assessment is becoming increasingly important in neurosurgery with the trend toward personalized medicine. In benign skull base tumors, patient-centered care requires the knowledge of HRQoL for individual decision making and long-term management. The current study evaluates the systematic assessment of HRQoL in patients with cerebellopontine angle (CPA) tumors using digital patient-reported outcome measures (PROMs) including both generic and specific questionnaires.

Methods

The results of digitally acquired PROMs in patients affected by CPA tumors were retrospectively analyzed, with focus on timing (PROM assessment at baseline and at follow-up after 3 and 12 months) and strategy (operative or conservative management after initial assessment).

Results

Digital PROMs were implemented in 42 patients, with 57.1% vestibular schwannoma, 26.2% meningioma, and 16.7% others. 42.9% underwent surgery after baseline assessment (operative group), and 57.1% followed a wait-and-scan strategy (conservative group). In the operative group, gross total resection was reached in 88.9% and subtotal resection in 11.1%, without recurrence during the follow-up period. No major complications or new major neurological deficits occurred. At baseline assessment, the generic questionnaires 15D and EQ-5D-5L showed similar mean values with operative and conservative management. Mean EQ-VAS was slightly reduced in the operative vs. conservative group (71.3 vs. 74.0). During follow-up, generic questionnaires demonstrated a significantly reduced HRQoL in the operative group after 3 months (which improved after 12 months), and stable values with conservative management. At baseline assessment, the specific PANQOL scale showed lower mean scores in the operative vs. conservative group (68.22/100 vs. 75.33/100). During follow-up after 3 and 12 months, mean values were reduced both with operative (67.85/100 and 60.89/100) and conservative management (71.53/100 and 68.50/100).

Conclusion

The digital assessment of HRQoL appears promising for supporting personalized long-term management of benign skull base tumors. Our data with differing scores of generic and specific questionnaires demonstrate that their combination is essential to cover all aspects. Information on symptom burden and subjective functional status assessed by a combined protocol is needed for treatment decisions and aftercare in order to provide individualized concepts.

Schädelbasis I/*Skull base I*

P073

Hör-Rehabilitation mittels Hirnstammimplantats (ABI) - zwei hilfreiche Methoden zur Klassifizierung elektrophysiologischer und klinischer Ergebnisse

Auditory rehabilitation by brainstem implants (ABI) - Two helpful tools for classifying electrophysiological characteristics and clinical outcome

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Objective

While ABI outcomes are very variable, there are still no uniformly accepted systems for intra- and post-surgical evaluation. Here we apply and present two methods of classification, 1. for fast neurophysiological evaluation to optimize implant placement and 2. for reliable clinical evaluation of patients" benefit from ABI auditory perception.

Methods

In 24 NF2 patients (11 male), the electrically evoked auditory brainstem responses EABR were analyzed for the presence, number and shape of vertex positive peaks: Category A with 3 peaks, Category B with 2 peaks, Category C with 2 peaks and deformation, Category D with one deformed peak and Category E with sole artefact formation. A new Clinical ABI Outcome Classification was developed and applied at 6 to 12 months containing 4 categories: Category 1, Star Performer, with >80% speech understanding in auditory only mono- to polysyllabic test (aMTP) and ability for continuous spoken conversation without any lip reading; Category 2, Good Performer, with >40 to 80% in aMTP and speech understanding combined with lip reading; Category 3, Useful Performance, communication possible with additional measures (lip-reading and written notes); Category 4 Non-useful Performance, no or scarce sound reception.

Results

Stimulation at several sites of the electrode carrier enabled 166 EABR recordings. A a two-peek-formation was identified as the most frequent type in 133 cases (80.1%). EABR showed considerable waveform variation, with P1 developing out of the stimulus artefact, P2 and P3 showing melting and some latency differences. Auditory outcome was useful (Categories 1, 2 or 3) in 88.5% of cases, with Star or Good Performance in about 75% of patients. EABR presence (Classes A to D) predicted auditory rehabilitation outcome correctly in 91%.

Conclusion

The presented E-ABR system is easy to apply, online and offline, and highly predictive of adequate activation of the auditory pathway. The ABI hearing classification combines the internationally well-established MTP test with the patient"s clinical performance in a real-world setting.

Schädelbasis I/*Skull base I*

P074

Chirurgische Techniken und intraoperative Messungen bei einer neuartigen elektrischen Hörprothese zur direkten Stimulation im Hörnerv: das Auditory Nerve Implant (ANI)

Surgical techniques and intraoperative measurements for the implant of a new intracranial hearing prosthesis that stimulates directly the nerve: the Auditory Nerve Implant (ANI)

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Objective

We are currently developing, in collaboration with five institutions and two medical device companies, an intracranial hearing prosthesis that stimulates directly the nerve: the Auditory Nerve Implant (ANI). The ANI is designed to enable hearing rehabilitation for deaf patients for whom the cochlear implant (CI) is not applicable, even with preserved hearing nerve, or leads to poor hearing results. With a penetrating electrode array, the distance between the electrode and the nerve is minimized and the electric field propagation is reduced. The design of the ANI is basically the same as that of a CI with an external speech processor, implant body, and an electrode array, which is inserted into the auditory nerve. The goal is to find surgical techniques and an approach for safe handling, insertion and anchoring of the array. In addition, electrically evoked auditory brainstem responses to superficial stimulation of the auditory nerve will be detected.

Methods

In an iterative process between human preparations and intraoperative experiences, different approaches have been tested and verified. Thereby the handling and anchoring of the array as well as its insertion with a pneumatic system is tested. In the acute experiments this was then verified (without insertion) in a total of 8 patients. The patients underwent an acoustic neuroma removal in which the auditory nerve is exposed. For the measurement of brainstem responses there was a surface electrode was placed on the auditory nerve and electrically stimulated. The responses have been recorded with three needle electrodes on the skull.

Results

The translabyrinthine approach was shown to be the best in terms of handling, placement and anchoring of the array. The auditory nerve could be separated from the vestibular nerve and is located relatively far from the facial nerve. There is also enough bone for insertion and stable anchorage. Brainstem responses could be measured in 2 of 7 patients. To be noted, that due to the tumors and their removal the auditory nerves were already severely affected.

Conclusion

Various surgical techniques for ANI have been tested in human specimens and intraoperative experiences for ANI. The translabyrinthine approach showed the best results. In 2 patients, evidence with the generation of electrically evoked auditory brainstem responses during Surface stimulation of the human auditory nerve was demonstrated.

Schädelbasis I/*Skull base I*

P075

Reklassifizierung von Hypophysenadenomen nach der neuen WHO-Klassifikation – exemplarisch an einer großen retrospektiven Kohorte

Reclassification of pituitary adenomas according to the new WHO classification – exemplified on a large retrospective cohort

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Objective

The classification of pituitary adenomas has been based on immunostaining for hormone expression and ultrastructural features of the adenoma cells. The WHO classification 2017 of pituitary adenomas introduced the expression of the pituitary transcription factors Pit-1, T-Pit and SF-1 in the histopathological diagnosis. Transcription factors determine the differentiation into the hormone-producing cell lines. The aim of this study is to demonstrate the influence of this innovation on the classification of pituitary adenomas in a large retrospective cohort.

Methods

All pituitary adenomas diagnosed at our pituitary center between October 2004 and April 2018 with sufficient tissue available from surgery were retrospectively reassessed according to the new WHO classification by applying the pituitary transcription factors. In total, tissue samples from 921 adenomas could be included in the analyses.

Results

Nonfunctioning adenomas (n=221) and null cell adenomas (n=176) represented the largest subgroup (397 of 921) according to the old classification. Of these, 377 were classified as gonadotrophic adenomas, 14 were assigned to a hormone-producing cell line. Only 6 null cell adenoma remained. Of the 35 plurihormonal adenomas, 27 could be assigned to a specific cell line and only 8 of them remained plurihormonal. These plurihormonal adenomas were PIT 1 positive adenomas (n=6) or with unusual immunohistochemical combinations (n=2). The remaining 489 adenomas were initially classified with expression of 1 or 2 hormones. Of these, the histopathological diagnosis was confirmed in 459 cases (93.9%) and in 12 cases the positive immunostaining of 2 hormones could be assigned to a cell line with 1 main hormone expression. Only one case showed combined staining for prolactin and ACTH and was thus confirmed as a double adenoma. In 18 cases (of 489 adenomas) a different diagnosis resulted due to a changed cell line.

Conclusion

By adding specific pituitary transcription factors, the pituitary adenomas could be subclassified more precisely. Our study shows that most nonfunctioning adenomas according to the old classification are re-classified as gonadotrophic adenomas. Null cell adenomas are by far less frequent than formerly considered. In individual cases, the change of histopathological diagnosis with the reclassification must be into account for the further follow up of the patients.

Schädelbasis I/*Skull base I*

P076

Metastasen der Sella: eine seltene intraoperative Beobachtung nach Vortäuschung eines Hypophysenadenoms im präoperativen MRT

Sellar metastasis: a rare intraoperative finding after preoperative MR imaging of mimicing of a pituitary adenoma

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Objective

The sellar region is an unusual site for metastatic spread, but as patients with metastatic malignancy are living longer, it may become more prevalent. Compression of important anatomy adjacent to the sella may produce disabling symptoms and endocrine derangement, leading to significant morbidity. Furthermore, the preoperative imaging is probably often mimicing an adenoma in these cases.

Methods

To analyse the incidence of sellar metastasis, the authors reviewed their cases with sellar pathologies treated via an endonasal approach between January 2011 and Dezember 2021. Further investigation was performed to evaluate patient demographic, radiological and histological findings and outcome.

Results

Eight of 334 patients (2.3%) treated during this time period revealed in the final histopathology a metastasis. Thereby, malignant tumor history was known in one patient (14%). The preoperative MR and CT imaging suspected a malignant pathology or metastasis in two cases (28%). in 72% oif all cases the MR and CT imaging revealed a piuitary adenoma most likely preoperatively. The average age of the cases was 63.4 years, with histopathological diagnosis of two metastasis of lung cancer, one mestastasis of gastric cancer, one metastasis of kidney, one case of prostatic cancer, one lymphoma and one plasmocytoma. Adenohypophyseal dysfunction (3/7; 42%), abducens palsy (2/7; 28%) and visual field defects (2/7; 28%) were the most common findings at presentation. The mean follow up was 2.4 years. 5 of 7 patients (71%) died during this time period.

Conclusion

The sellar region should not be overlooked as a site of metastasis. Any biochemical or clinical sign of pituitary pathology in a patient with known cancer should raise suspicion for sellar metastasis even if the preoperative imaging argues for a pituitary adenoma most likely. Moreover, the fast development of hormonal dysfunction or ophthalmoplegia is suggestive of metastatic disease even in patients with no known primary.

Schädelbasis I/*Skull base I*

P077

Erfolgschancen wiederholter transsphenoidaler Operationen bei Patienten mit persistierendem und rezidivierendem Morbus Cushing

Outcome of repeat transsphenoidal surgery in patients with persistent and recurrent Cushings disease

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Objective

Transsphenoidal surgery (TSS) is the treatment of choice for Cushing"s disease (CD). Surgery is challenging due to the often very small adenomas. In experienced pituitary centers a high remission rate is reported. Nevertheless, endocrinologists and neurosurgeons face cases with persistent or recurrent CD . In addition to medical treatment, radiation therapy and bilateral adrenalectomy, repeat TSS must also be considered. The aim of this study is to analyse the outcome of repeat surgery and to compare persistent and recurrent CD.

Methods

We retrospectively analysed 59 patients with confirmed CD, who underwent repeat TSS in our department. Both persistence of CD after failed first surgery (n=28) and recurrence of CD (n=31) were the indications for repeat TSS. Thirty-four patients underwent their first surgery externally, 25 patients had both TSS in our pituitary center. All surgeries were performed through a microscopic transsphenoidal approach.

Results

The time interval between the first and the repeat TSS was 0 – 93 months (median 15.5 months) in the case of persistent CD, and 7 – 219 months (median 66 months) in the cases of recurrent CD (p <.0001). A high-quality MRI was performed preoperatively in all cases. A clear adenoma was described intraoperatively in 79.7 % of cases (82.1 % persistent CD, 77.4 % recurrent CD). A histologically confirmation of an adenoma was achieved in 65.5 % of cases (71.4% in persistent CD, 60% in recurrent CD). An early postoperative remission rate of 71.2% was achieved (74.2% in persistent CD, 67.9% in recurrent CD). Long term follow up (n=53) demonstrated a remission rate of 69.8% (75.9% in persistent CD, 62.5% in recurrent CD). Complications only occurred in isolated cases and included one CSF fistula, one epistaxis, one thrombosis and one postoperative cardiac arrhythmia. No mortality occurs.

Conclusion

Persistent and recurrent CD pose a greater challenge for further treatment. If repeat surgery is an option, it should be offered to the patient in an experienced pituitary center. A higher remission rate is achieved in recurrent CD compared to persistent CD. A satisfactory probability of remission with a low complication rate can be achieved in repeat TSS for CD.

Schädelbasis I/*Skull base I*

P078

Minimal-invasive Schädelbasisrekonstruktion mit Gelatinschwamm und Kollagenmatrix
Minimally invasive skull base reconstruction methods using gelatin sponge and collagen matrix

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Objective

Endoscopic transsphenoidal surgery (ETSS) requires consistent reconstruction of skull base defects to avoid the associated postoperative leakage of cerebrospinal fluid (CSF). Various techniques and materials have been used for skull base reconstruction to prevent CSF leakage. Among them, pedicle nasoseptal flap reconstruction is widely accepted as one of the most reliable methods. However, pedicle nasoseptal flap reconstruction carries the risk of complications such as septal perforation, prolonged crusting, and loss of smell. We used a fibrin glue-soaked gelatin sponge (FGGS) for sellar reconstruction without pedicle nasoseptal flap and water-tight dural suturing. The supply of gelatin sponge has been discontinued since 2021, and collagen matrix has recently been substituted. In the current report, we describe our minimally invasive skull base reconstruction methods with FGGS and collagen matrix and analyze their outcomes in patients treated with ETSS for pituitary tumors.

Methods

From 2012 to 2022, 451 ETSS procedures were performed for pituitary tumors at our institution. We excluded 21 patients in whom FGGS or collagen matrix was not used during surgery; thus, 430 patients were included in this study. We conducted a retrospective review of these patients and examined the rate of CSF leakage by Esposito grade.

Results

The patients consisted of 199 males and 231 females, with a median age of 59.0 (range, 8-87) years. The intraoperative CSF leak grade was 0 in 130 cases, Ⅰ in 143, Ⅱ in 88, and Ⅲ in 69. We used pedicle nasoseptal flap in only five cases (grade Ⅱ: 3 cases; grade Ⅲ, 2 cases) (1.2%). The frequency of postoperative CSF leakage requiring repair for each intraoperative CSF leak grade was 0/130 (0%) for grade 0, 3/143 (2.1%) for grade Ⅰ, 4/88 (4.5%) for grade Ⅱ, and 1/69 (1.4 %) for grade Ⅲ. Total CSF leakage was 8/430 (1.9%). Three cases were performed by an inexperienced surgeon who performed fewer than 20 ETSS procedures. Two patients underwent unfamiliar skull base reconstruction. CSF leakage occurred after chemotherapy in patients with lymphoma.

Conclusion

The rate of postoperative CSF leakage in our minimally invasive skull base reconstruction method was only 1.9%. Although many methods of skull base reconstruction have been proposed to prevent postoperative CSF leakage, we believe that uniformity in the method of skull base reconstruction will improve the proficiency of surgeons and lead to even better results.

Schädelbasis I/*Skull base I*

J-SBNC010

Riesiges GH-sezernierendes Adenom der Hypophyse mit Ausbreitung in die hintere Schädelgrube - Fallbericht
Giant Pituitary GH-secreting Adenoma Spreading to the Posterior Cranial Fossa - Case Report

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Objective

This report's aim is to present the clinical progress of a patient with this clinical condition, contributing to the scarce literature on the subject.

Methods

Case report of a patient with giant pituitary adenoma with malignant behavior, with special emphasis on the infiltrative aspect of the middle and posterior fossa and compare it with findings in present literature.

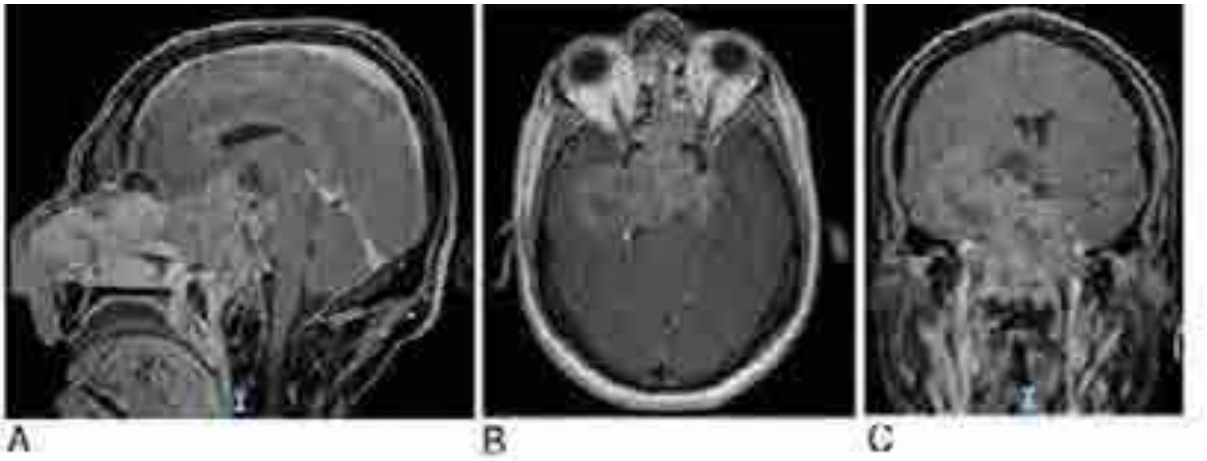
Results

This report presents the clinical progress of a 40 year-old male patient diagnosed with a rare giant growth hormone and adrenocorticotropic hormone secreting adenoma, invading the posterior fossa of the brain. The adenoma was discovered after a car collision - there was no prior knowledge of the lesion. After a CTS performed in the admission, a 9,0 x 7,5 x 7,0cm cystic lesion centered in the clivus was found (Figure 1), invading the cavernous sinus, interpeduncular cistern, left ambiens and prepontine region and compressing the adjacent cerebral parenchyma, anterior left cerebellar peduncle, and pontine region, including mesial temporal region and the right nucleo-capsular region. At neurologic evaluation, displays right third cranial nerve paralysis and sixth bilateral cranial nerve paralysis, right facial paresis, dysarthria, dysphonia and dysphagia with no strength loss and an active movement of four members.

Conclusion

GH secreting adenomas are usually benign but, in this case, a not yet described in literature pattern was found. Therefore, the aim of this study is to expose clinical, pathological, and surgical findings in diagnosis of pituitary adenomas with posterior extension.

Abb. 1



Trauma I/*Trauma 1*

J-SBNC011

Epidemiologische Analyse von traumatischen Hirnverletzungen in Brasilien
Epidemiological analysis of traumatic brain injury in Brazil

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Objective

To understand the etiological profile of traumatic brain injury (TBI) in Brazil in the years 2021 to 2022.

Methods

A literature review was conducted using SciELO, LILACS, VHL and PUBMED databases. The terms used in the search were: Traumatic Brain Injury, and/or Etiology, and/or Epidemiology. Articles from the years 2021 to 2022 were included in order to address the most recent update. English, Portuguese and original articles were included. Five studies were used.

Results

Four of the five studies reviewed reported that the etiology of most outpatient TBI hospitalizations is motorcycle accidents. However, the findings of one of these studies contradict such data, showing not only traffic accidents, but also several other external causes related to deaths, regardless of age, which can lead to TBI, such as falls, being run over by a car, physical aggression, car accidents, and firearm-related trauma. It observed that motorcycle accidents lead the ranking of the main etiological causes of TBI with (57.6%); followed by falls (13.7%); pedestrian accidents (13.4%); physical aggression (8.4%); car accidents (4.1%); firearm trauma (1.2%), and others (1.6%).

Conclusion

Studies show that most traumatic brain injuries are related to traffic accidents, but this is not the only etiology. In addition, TBI entails an aggravating public health problem for the population. The present article had a small number of recent samples, because robust epidemiological studies on TBI in Brazil are still scarce.

Trauma I/*Trauma 1*

P079

Hirndruck bei älteren Patienten mit Schädel-Hirn-Trauma: Schwellen neu definieren
Intracranial pressure in elderly patients with traumatic brain injury: redefining thresholds

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Objective

In the setting of traumatic brain injury (TBI), current guidelines advocate for the establishment of intracranial pressure monitoring (ICP) to guide therapeutic decision-making. The RESCUEicp trial established a threshold of 25 mmHg to indicate decompressive craniectomy as a life-saving measure. Nevertheless, controversy surrounds ICP monitoring in elderly TBI patients, as it does not appear to yield better outcomes. We hypothesize that this is due to different ICP thresholds for malignant intracranial hypertension in the elderly.

Methods

We conducted a retrospective study of elderly patients, aged 65 years or older, treated at our center for TBI from October 2008 until October 2018. Only those patients who underwent ICP monitoring during the first 72 hours after trauma were included in the analysis. Hourly ICP values were registered for every patient. GCS at admission was documented, as well as patient comorbidities, as objectivized by the Charlson Comorbidity Index. The primary outcome was mortality at 6 months.

Results

35 patients were included in the analysis. Mean age was 78 years (range: 65-90). Most patients were male (n=24/35 [69%]). Mean GCS at admission was 9 (range: 3-15). Mean CCI was 2 (range: 0-7). Mortality at 6 months was n=12/35, 34%. Mean ICP in survivors over the first 72 hours after TBI was 7.11 mmHg (SD=1.00), whereas it was 10.8 mmHg (SD=1.72) in those patients who perished. This difference was statistically significant ($p<.001$). In a ROC curve analysis of ICP vs mortality, the AUC was .982, $p<.001$. ICP≥8 mmHg had a sensitivity of 97.2% and a specificity of 83.3% to identify patients at risk for mortality at 6 months.

Conclusion

Our data questions the assumed futility of ICP monitoring in the elderly and suggests that the threshold for indicating further therapy in this patient population might be lower than the one commonly assumed in TBI. Further studies are needed to validate these findings.

P080

Das ICP Monitoring zeigt kurzfristige Veränderungen an, retrospektive Analysen zwischen Druckspitzen und Zeitdauer sind nicht zum live Monitoring geeignet. Die Icon basierte Darstellung ist ein vielversprechendes Konzept um potentiell bedrohliche Trends darzustellen.

ICP monitoring visualizes short term ICP fluctuation. Approaches recognizing dependencies between the ICP magnitude and duration are not intended for live patient monitoring. Icon-based visualization of ICP is a promising alternative new concept with benefits in immediate trend assessment.

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Objective

Conventional intracranial pressure (ICP) monitoring devices visualize short term ICP fluctuation, but do not intuitively illustrate subtle, potentially hazardous ICP trends over a longer time-period. Visual analytic approaches that recognize dependencies between the ICP magnitude and duration through two-dimensional color plots for instance, do exist. Due to their retrospective nature however, such approaches are not intended for live patient monitoring. The objective of the current study is to develop an intuitive ICP visualization tool, that facilitates a quick assessment of ICP trends during a user-defined time interval, by means of visual navigation of continuous ICP values of a patient on an intensive care unit.

Methods

We applied a participatory design approach involving an interdisciplinary team of neurosurgeons, sociologists and computer scientists. The concept has been iteratively refined, whereby each cycle comprised a discussion of the current visualization concept with medical experts and a subsequent technical implementation of their feedback. Our concept aimed at an intuitive representation of the ICP by exploiting visual metaphors at two levels. First, we selected an icon based visual object to represent the key domain i.e., ICP. Then we mapped the parameters to specific features of the icon and encoded the changes of data as icon variations based on predefined cut-off values. We further implemented a navigation tool as a "play back" function of single consecutive icons of a variable time-period.

Results

The base icon schematically portrays the outlined profile of a human head engulfing a simplified depiction of a brain. The scalar ICP values are mapped to the brain"s volume, using the "inflation under pressure" metaphor, i.e., the higher the value, the larger the volume and the shallower the grooves (sulci). Using color as an explicit visual feature with a high po-up effect, the ICP is further categorized as normal (grey), elevated (light red) or pathological (dark red). Finally, situations that require immediate attention, namely if ICP is pathologically high or elevated for more than 15 minutes, are visually emphasized by arrows which appear around the head symbolizing an urgent need to "release pressure".

Conclusion

Icon-based visualization of ICP is a promising alternative concept to conventional graphical representation, yielding benefits particularly in immediate trend assessment.

Abb. 1

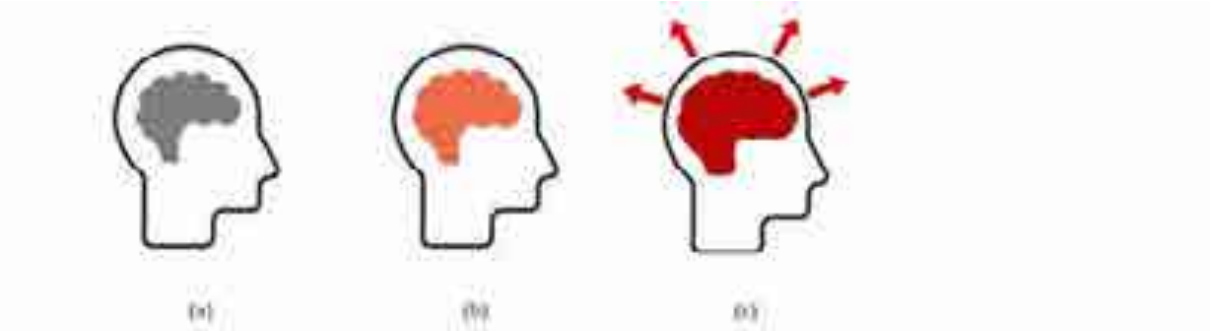

Figure 1: Icon-based ICP visualization. 1a: the original icon, used for normal ICP values; 1b: the orange brain color indicates, an elevated ICP, the brain volume is increasing, the folding becomes less distinct; 1c: the dark red brain color indicates a pathological ICP. the brain has been further "inflated", the arrows around the head signalize a need of action.

Trauma I/*Trauma 1*

P081

Beeinflussung der ICP-Messung via Luftkammer-Systeme durch intracerebrale Hämatome
Intracerebral hematomas are capable of altering air-pouch intracranial pressure monitoring

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Objective

Air-pouch balloon-assisted probes have proven to be simple and reliable tools for intracranial pressure (ICP) monitoring. However, we experienced reproducible falsely high ICP-values by measuring ICP in the intraparenchymal hematoma. Thus, the aim was to analyze the influence of ICP-probe placement with regard to measured ICP-values.

Methods

Two Spiegelberg 3PN-sensors were simultaneously inserted into a closed drain system and were connected to two separate ICP-monitors thereby allowing for simultaneous ICP-measurements under gradual increase of pressure in a controlled fashion. Once the pressure was verified using two identical ICP-probes, one probe was coated with blood in an effort to replicate placement within an intraparenchymal hematoma. Pressures were recorded and compared using the coated and control probe. As translational purpose, two ICP-probes (1:brain parenchyma,2:hematoma) were inserted in a patient with large intracerebral hemorrhage and ICP-values were compared.

Results

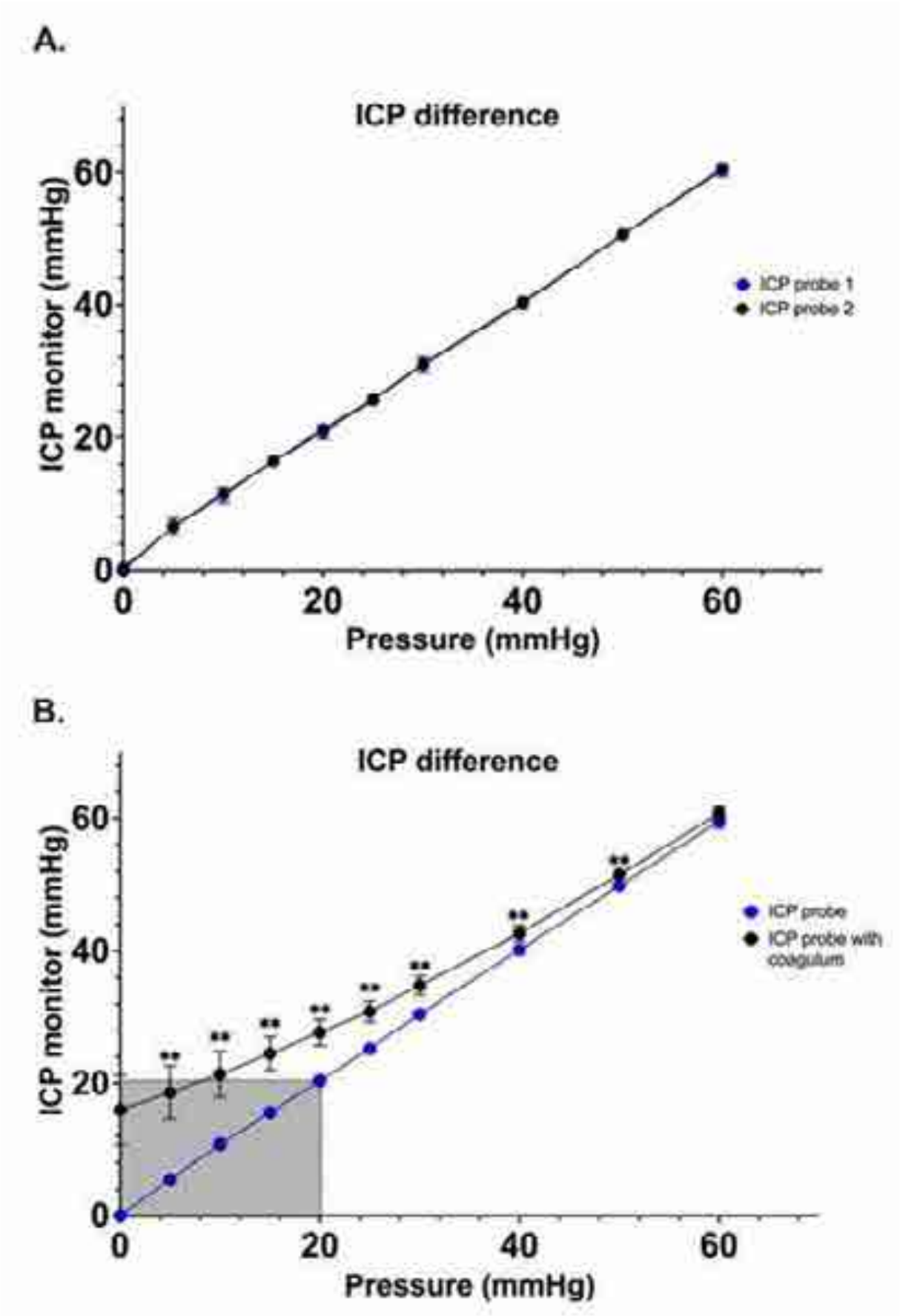
The experimental set-up demonstrated a reliable correlation between both control ICP-probes. Interestingly, the ICP-probe covered with clot displayed a significantly higher average ICP-value when compared to the control probe between 0mmHg and 50mmHg ($p<0.001$); at 60mmHg there was no significant difference noted. Critically, this trend in discordance was even more pronounced in the clinical setting with the ICP-probe placed within the hematoma cavity having reported significantly higher ICP-values as compared to the probe within brain parenchyma.

Conclusion

Our experimental and clinical pilot highlight a potential pitfall in ICPmeasurement that may result secondary to probe placement within hematoma. Such aberrant results may lead to inappropriate interventions in an effort to address falsely elevated ICPs.

Abb. 1

Abb. 2


A.
ICP difference
ICP monitor (mmHg)
0
20
40
60
Pressure (mmHg)
ICP probe 1
ICP probe 2
B.
ICP difference
ICP monitor (mmHg)
0
20
40
60
Pressure (mmHg)
ICP probe
ICP probe with coagulum

Trauma I/*Trauma 1*

P082

Zeigt der Intensivmonitor den richtigen Cerebralen Perfusionsdruck? Vergleich von Monitorausgabewerten mit Rohdaten aus Hochfrequenzaufzeichnungen

Does the intensive care monitor show the correct cerebral perfusion pressure? Comparison of monitor output values with raw data from high-frequency recordings

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Objective

CPP is calculated from the difference between MAP and ICP. The processing of the underlying raw data is not standardized. Post-processing of the data in monitor systems by averaging and/or filtering may lead to significant deviations. The purpose of this study is to compare monitor output values and raw data and to examine the suitability of conventional values to serve as a basis for clinical decisions.

Methods

39 patients from our ICU with ICH who had a complete 60-minute recording from 2 a.m. on the first day after probe implantation were included. ICP, BP, ECG, pulse oximetry, and various ventilation parameters were collected as raw data. Data were recorded at 100 Hz and automatically stored on a scientific server system.

Similarly, the CPP output from the Draeger Infinity Delta XL system was recorded. The starting point of each ICP and MAP signal for all 39 data sets was identified and synchronized in time according to a method proposed by Schönenberg-Tu et al [1]. MAP and ICP were determined for each heartbeat. The area integrals of the MAP and ICP pressure curves were calculated for this purpose and each was divided by the time of the cardiac cycle (MAParea and ICParea). The CPParea is then obtained from MAParea- ICParea. The data collected was then compared with the monitor output data.

Results

The Shapiro-Wilk test showed that the data of CPParea and CPPdraeger do not follow a Gaussian normal distribution. The significance level was calculated using the Wilcoxon sign rank test and medians. There is a significant difference for each data set. CPPdraeger was higher in 24 and lower in 15 patients compared to CPParea. The difference in medians ranges from -43mmHg to +54mmHg. Figure 1 shows timelines for 3 different patients. CPPdraeger is significantly lower in amplitude than CPParea. This may result from the use of filters and/or averaging. Figure 2 shows examples of the variable distribution of measured perfusion pressures in different patients.

Conclusion

The CPParea values calculated from raw data deviate from the output monitor data to varying degrees. The question arises to what extent the values available at the patient's bedside are suitable as a basis for therapeutic decisions. No standard has been defined for the collection of the underlying values. The question of comparability arises as to whether the relevant treatment guidelines are based on non-standardized data collection and, if so, whether they should be reviewed based on standardized data.

Abb. 1

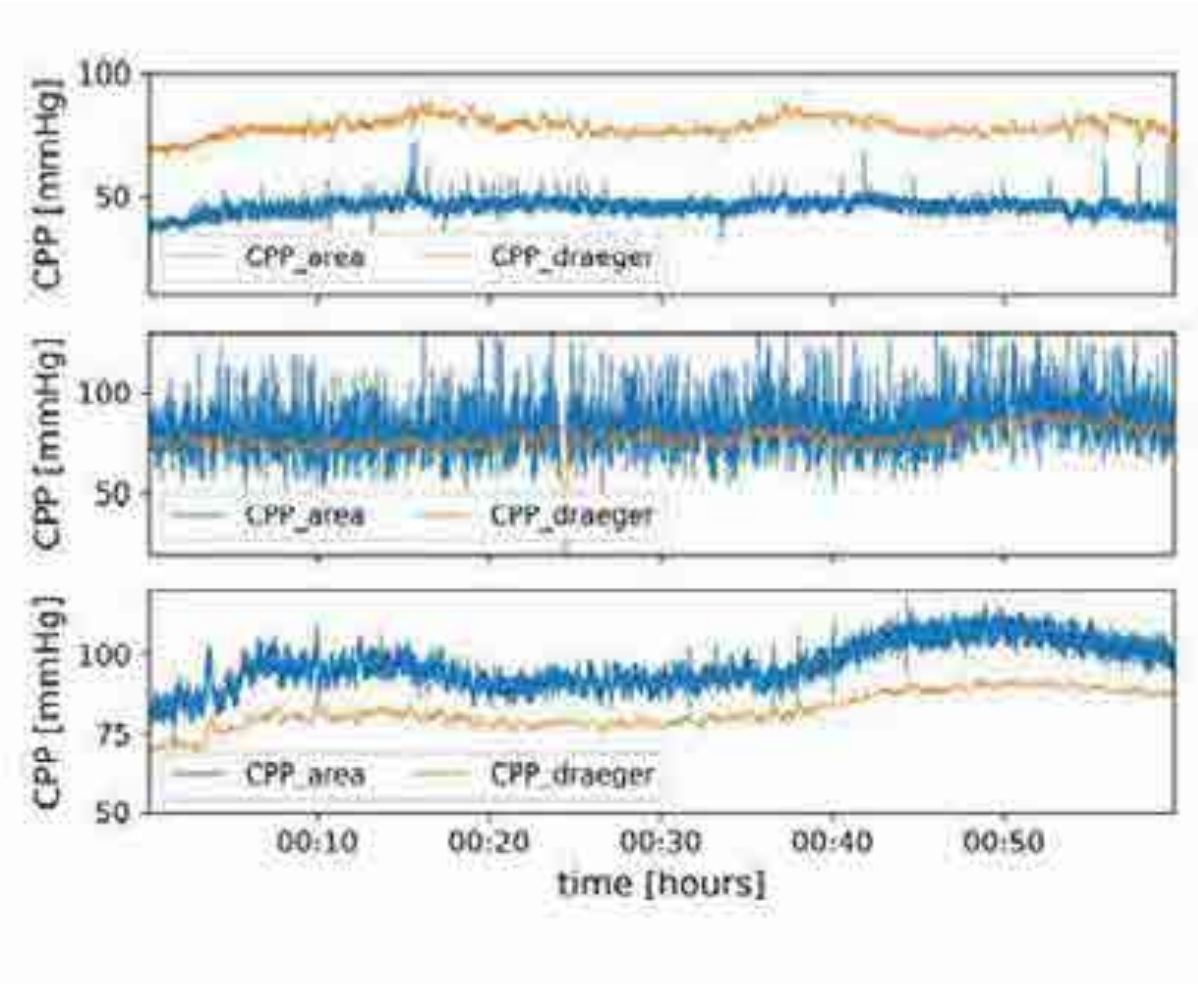
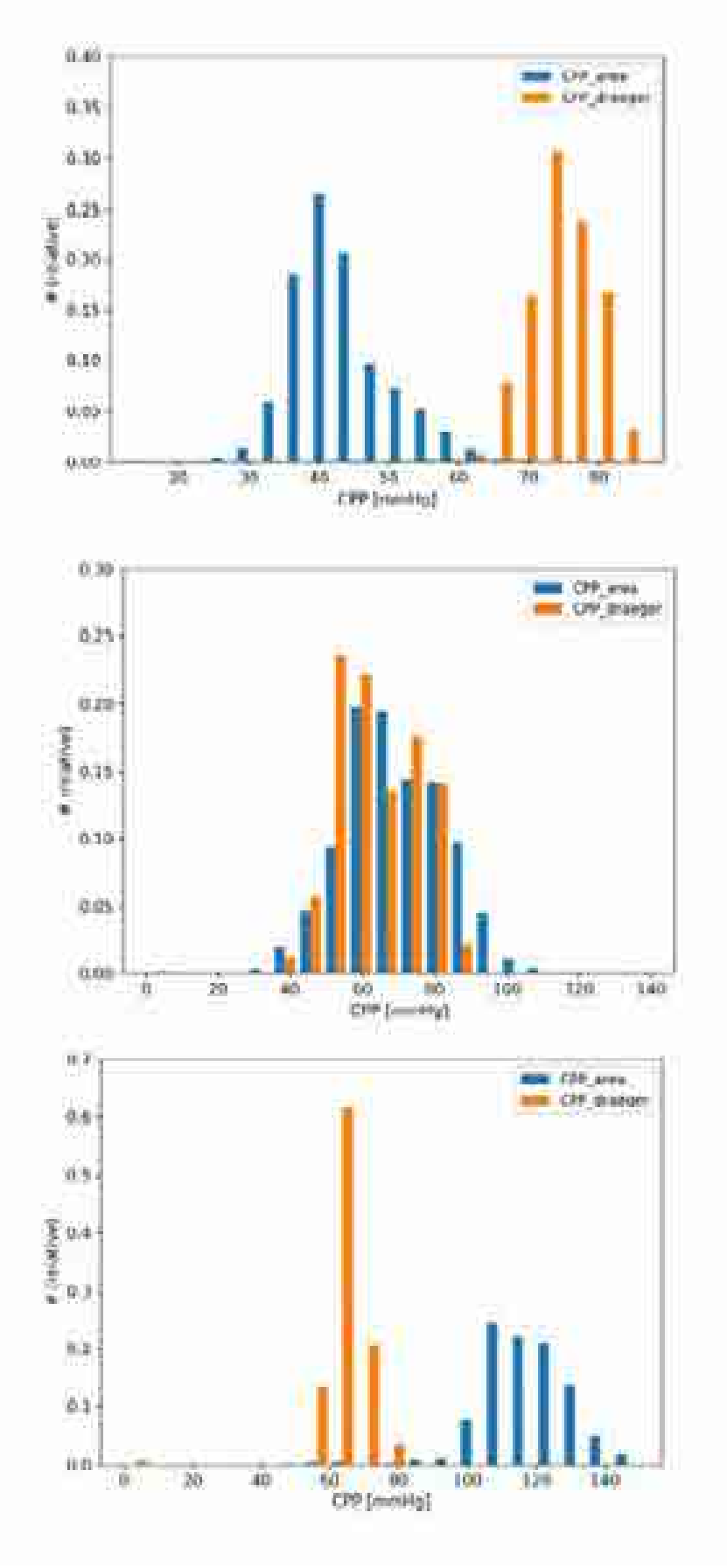

CPP [mmHg]
100
50
CPP_area
CPP_draeger
CPP [mmHg]
100
50
CPP_area
CPP_draeger
CPP [mmHg]
100
75
50
CPP_area
CPP_draeger
00:10
00:20
00:30
00:40
00:50
time [hours]

Abb. 2



P083

Der Stellenwert der Pupillometrie bei Patienten mit leichtem Schädel-Hirn Trauma: eine laufende prospektive Studie

The merit of quantitative pupillometry in patients with mild traumatic brain injury: A prospective pilot study

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Objective

Traumatic brain injury (TBI) is a highly prevalent cause of morbidity and mortality worldwide. Quantitative pupillometry (QP) has been established as an effective, affordable, easy-to-use, and reliable tool in the neurocritical care setting that may be used to assess and predict neurological effects or the occurrence of traumatic intracranial hemorrhage (ICH) after TBI.Our pilot study therefore aims to investigate the role of QPin patients with mild TBI, as potential adjunct to head computed tomography (CT), to predict and identify neurological deficits and the presence of ICH.

Methods

This is an on-going prospective study collecting pupillometry data from patients who sustained TBI (ranging from mild to severe) as well as with tumors compressing structures of the optic system. Pupillometry using the automated NPi 200® pupillometer was performed in 17 patients after mild TBI. The neurological pupillometry index (NPi) ranges between 0-4.9 and quantifies the pupil reactivity with values >4.0 considered physiological. The NPi was analyzed as computed parameter and correlated with the occurrence of ICH on CT.

Results

A total of 17 patients with a mean age of 57.8 years (SD 25.9) with mild TBI were enrolled into the study. All patients presented with persistent headaches, dizziness, vomiting and experienced loss of consciousness for several seconds. Overall mean GCS was 14.2 points (SD 0.5). In 11 patients an ICH was detected on CT, while in 6 patients no pathology was seen. Interestingly, patients presented with ICH as detected on CT imaging, had significantly lower NPi index bilaterally compared to patients without (ICH: NPi right eye: 3.7 SD 0.1, NPi left eye: 3.6 (SD 0.2) vs. no ICH: NPi right eye: 4.4 SD 0.3, NPi left eye: 4.5 (SD 0.4); $p<0.001$).

Conclusion

Our preliminary findings suggest that reduced NPi (<4) was associated with the presence of ICH as detected on CT; thus, indicating that the point of care assessment of NPi might predict the occurrence of ICH in patients sustaining TBI. Thereupon, widespread deployment of NPi assessment might be a considerable parameter when examining the necessity of CT. This could potentially lead to a substantial decrease of patient radiation exposure and its associated risks.

Trauma I/*Trauma 1*

P084

Interkorrelation zwischen intrakranieller Druck Steigerung und der Selected Correlation Analysis auf der neurochirurgischen Intensivstation

Intercorrelation between intracranial pressure increase and selected correlation analysis in patients at the neurosurgical intensive care unit

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Objective

Selected correlation analysis (SCA) is a method to detect impaired autoregulation combined with severe brain swelling by calculating a correlation-based index sc using fixed-length windows of arterial blood pressure (ABP) and intracranial pressure (ICP) signals. If sc is higher than a predefined significance level and the correlation is positive, the windows are labeled scp, indicating the above-mentioned pathophysiology. As scp is a dichotomous index, we examined whether the quantitative extent of sc under scp conditions has any relevance. We analyzed the intercorrelations between the sc value and the mICP of the appropriate windows.

Methods

We included 19 patients (9 female and 10 male) with a median age of 44 years, treated for subarachnoid hemorrhage (SAH; n = 14) or traumatic brain injury (TBI; n = 5). The median initial GCS was 7, no decompressive craniectomy was performed. SCA was used to extract all windows labeled scp (sc > 0.0556) and the according mICP values were calculated. First, we dissected the mICP in steps of 10 mmHg and the sc values in steps of 0.056. Subsequently, we calculated the number of scp-labeled windows that match an element of this grid. From this preprocessed information, we determined two groups of probability distributions. We calculated the probability of a specific sc value under the condition of scp and a certain mean ICP (mICP); conversely, we calculated the probability of a specific mICP values under the condition of scp and a specific sc value.

Results

The probability distributions clearly show that an elevated mICP is related to an increased sc value. The sc values for a mICP between 30 and 40 mmHg was found between 0.500 and 0.566, whereas the sc values for a mICP value between 10 and 20 mmHg ranged between 0.083 and 0.139. The situation changes drastically when we look at the probability distributions concerning the sc value. Even for sc values between 0.500 and 0.566 the most likely mICP was found between 10 and 20 mmHg.

Conclusion

Our data show that, besides the dichotomous classification between scp or no scp, the extent of the sc value contains additional information. It relates to ICP crises which are among the most dangerous events during neurosurgical ICU treatment. Additionally we see that high sc values also occur with inconspicuous mICP. This leads to the hypothesis, that high sc values with moderate mICP could serve as a predictive factor for immanent ICP crises.

Trauma I/*Trauma 1*

P085

Bedeutung der Dicke des Schläfenmuskels bei chronischem subduralem Hämatom
Significance of temporal muscle thickness in chronic subdural hematoma

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[2]Universitätsmedizin Rostock, Institut für Diagnostische und Interventionelle Radiologie, Kinder- und Neuroradiologie, Rostock, Deutschland
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[4]Unfallkrankenhaus Berlin, Neurochirurgie, Berlin, Deutschland

Objective

Reduced temporal muscle thickness (TMT) was verified as an independent negative prognostic parameter for outcome in brain tumor patients. Independent thereof, chronic subdural hematoma (CSDH) is a neurosurgical condition with high recurrence rates and unreliable risk models for poor outcome. Since sarcopenia was associated with poor outcome, we investigated the possible role of TMT and the clinical course of CSDH patients

Methods

This investigation is a single center retrospective study on patients with CSDH. We analysed radiological and clinical data sets of 171 patients with surgically treated CSDH at a University Hospital from 2017-2020

Results

Our analysis showed a significant association between low-volume TMT and increased hematoma volume ($p<0.001$), poor outcome at discharge ($p<0.001$) and reduced performance status at 3 months ($p<0.002$)

Conclusion

TMT may represent an objective prognostic parameter and assist the identification of vulnerable CSDH patients.

Trauma I/*Trauma 1*

P086

Embolisation der Arteria meningea media als erfolgreiche Alternativ- oder Zusatzbehandlung des chronischen Subduralhämatoms- Erste Ergebnisse der Registerstudie für chronische Subduralhämatome

Middle meningeal artery embolization as a successful alternative or add-on treatment for chronic subdural hematomas- first results from the register study for chronic subdural hematomas

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Objective

Chronic subdural hematomas (cSDH) and recurrence is a common condition in multimorbid high aged individuals with a high cardiovascular risk profile and various risk factors. The establishment of the cSDH registry in 2022 allows for systematic analysis of this heterogeneous patient cohort. Primary objective is the determination of the best possible treatment concept for each individual. In this study we analyzed the effect of middle meningeal artery embolization (eMMA) in our study cohort.

Methods

The first results of this prospective register study evaluated data of 38 patients treated in our department from 1/22 to 9/22. eMMA was performed in 10 patients for prophylactic indication and in 4 patients with an asymptomatic recurrence with no need for surgery. Angiography was performed in general anesthesia using selective microcatheterization of the MMA. Embolization was performed using differently sized microspheres (Embozene, 45-400m) and coils. The frontoparietal branch was the most embolized branch in 64%. Cerebral imaging (cCT/cMRT) was performed to evaluate the imaging outcome 3 months after treatment using coronar scans to measure the thickness of hematomas and midline shift.

Results

Medical history of only 3 patients in this cohort was negative for cardiovascular diseases, 92% of the patients were positive for multiple cardiovascular risk factors. 63% were in need for oral anticoagulation (OAC) or antiplatelet therapy on a regular basis. In 89% the initial therapy of the cSDH was surgery, in 84% via burr hole trepanation, in 5% with initial mini craniotomy. Complications were found in 5% with secondary hemorrhage and in 3% with wound healing deficit, which were treated surgically. All in all, eMMA was performed in 37% with no complications like secondary bleedings, wound healing disorders or neurological deteriorations in our cohort recorded. Following eMMA, no patient needed further treatment, neither surgical nor interventional. The initial neurological deficits were improved in all patients compared to initial presentation. No patient developed new neurological deficits. The mean mRS improved from 2,3 (range 0-5) at initial presentation to a mean of 1,3 (range 0-3) at follow up examination.

Conclusion

eMMA, as a minimally invasive procedure with low-risk adverse event profile, can be considered as an alternative or add-on treatment in asymptomatic patients with cSDH or recurrence and in multimorbid patients who cannot pause OAC due to their high-risk cardiac profile.

P087

Anti-Inflammatorische Therapie bei chronischem Subduralhämatom: Ein systematischer Review und eine Meta-Analyse von prospektiven, randomisierten, doppel-blinden und placebokontrollierten klinischen Studien

Anti-Inflammatory Drug Therapy in Chronic Subdural Hematoma: A Systematic Review and Meta-Analysis of Prospective Randomized, Double-Blind and Placebo-Controlled Trials

M. Vychopen[1], E. Güresir[1], J. Wach[1]

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Objective

Although anti-inflammatory drug therapy has been identified as potentially beneficial for patients suffering from chronic subdural hematoma (cSDH), contemporary literature presents contradictory results. In this meta-analysis, we aimed to investigate the impact of anti-inflammatory drug therapy on mortality and outcome.

Methods

We searched for eligible randomized, placebo-controlled prospective trials (RTCs) on PubMed, Embase and Medline until July 2022. From 97 initially identified articles, five RTCs met the criteria and were included in our meta-analysis.

Results

Our results illustrate significantly lower rates of recurrent cSDH (OR: 0.35; 95% CI: 0.21-0.58, p = 0.0001) in patients undergoing anti-inflammatory therapy. In the subgroup of patients undergoing primary conservative treatment, anti-inflammatory therapy was associated with lower rates of "switch to surgery" cases (OR: 0.30; 95% CI: 0.14-0.63, p = 0.002). Despite these findings, anti-inflammatory drugs seemed to be associated with higher mortality rates in patients undergoing surgery (OR: 1.76; 95% CI: 1.03-3.01, p = 0.04), although in the case of primary conservative treatment, no effect on mortality has been observed (OR: 2.45; 95% CI: 0.35-17.15, p = 0.37).

Conclusion

Further multicentric prospective randomized trials are needed to evaluate anti-inflammatory drugs as potentially suitable therapy for asymptomatic patients with cSDH to avoid the necessity of surgical hematoma evacuation on what are predominantly elderly, vulnerable, patients.

Trauma I/*Trauma 1*

P088

Strahlenbelastung von CT Kontrolle bei Patienten mit chronischem subduralem Haematom, die zuerst mit einem Mini-Bohrloch behandelt wurden.

Radiation exposure in patients undergoing twist-drill craniostomy for chronic subdural hematoma

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Objective

Chronic subdural hematoma (CSDH) is known to recur in up to 40% of patients who undergo neurosurgical evacuation, and amongst those who undergo twist drill craniostomy (TDC) a full evacuation of the CSDH is seldomly achieved. Thus, patients with TDC often undergo follow-up CT scans. Nevertheless, studies have shown that routine follow-up CT after CSDH evacuation does not correlate with any clinical benefit. In this study, we attempted to establish the radiation exposure (RE) of patients undergoing TDC for CSDH, and whether this RE is clinically warranted.

Methods

We conducted a retrospective analysis of patients undergoing TDC for CSDH at our department over a five-year period. Patients routinely underwent postoperative CT scan on the first day after surgery, and subsequent scans in two-week intervals if CSDH remnants were seen and/or clinical deterioration ensued. RE was calculated in mSv. CT scans were correlated to clinical deterioration and therapeutic consequences, as number-needed-to-treat (NNT).

Results

A total of 184 patients were included in the analysis, of which 125/184, 68% were males. Mean age was 77 years (SD=10.9). Mean GCS at admission was 14 (SD=2.4). Patients received on average 7 CTs postoperatively (range: 1-17), totalling 957 CT scans. Over the follow-up period, only 57 (6%) CT scans correlated to clinical deterioration (NNT=17). 98 (10%) of all the CT scans had a therapeutic consequence (NNT=10). Mean cumulative radiation dose was 15 mSv (range: 2.1 – 33.7 mSv), the equivalent of 150 transatlantic flights.

Conclusion

Routine CT scans of patients undergoing TDC for CSDH do not seem to detect patients at clinical risk, thus posing the question as to whether or not RE is warranted during patient follow-up

Abb. 1

Radiation exposure in patients undergoing twist-drill craniostomy for chronic subdural hematoma

Marcel Krucker, Daniel Behme, Veit Rohde, Silvia Hernandez-Duran

Background: Chronic subdural hematoma (CSDH) is known to recur in up to 40% of patients who undergo neurosurgical evacuation, and amongst those who undergo twist drill craniostomy (TDC) a full evacuation of the CSDH is seldomly achieved. Thus, patients with TDC often undergo follow-up CT scans. Nevertheless, studies have shown that routine follow-up CT after CSDH evacuation does not correlate with any clinical benefit. In this study, we attempted to establish the radiation exposure (RE) of patients undergoing TDC for CSDH, and whether this RE is clinically warranted.

Materials and methods: We conducted a retrospective analysis of patients undergoing TDC for CSDH at our department over a five-year period. Patients routinely underwent postoperative CT scan on the first day after surgery, and subsequent scans in two-week intervals if CSDH remnants were seen and/or clinical deterioration ensued. RE was calculated in mSv. CT scans were correlated to clinical deterioration and therapeutic consequences, as number-needed-to-treat (NNT).

Results: A total of 184 patients were included in the analysis, of which 125/184, 68% were males. Mean age was 77 years (SD±10.9). Mean GCS at admission was 14 (SD±2.4). Patients received on average 7 CTs postoperatively (range: 1-17), totalling 957 CT scans. Over the follow-up period, only 57 (6%) CT scans correlated to clinical deterioration (NNT=17). 98 (10%) of all the CT scans had a therapeutic consequence (NNT=10). Mean cumulative radiation dose was 15 mSv (range: 2.1 – 33.7 mSv), the equivalent of 150 transatlantic flights.

Conclusion: Routine CT scans of patients undergoing TDC for CSDH do not seem to detect patients at clinical risk, thus posing the question as to whether or not RE is warranted during patient follow-up.

Trauma I/*Trauma 1*

P089

Das chronische Subduralhämatom bei 80- und 90 Jährigen: Klinische Charakteristika und Verläufe
Chronic subdural hematomas in octa- and nonagenerians: Clinical characteristics and outcome

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Objective

Chronic subdural hematomas are one of the most common neurosurgical pathologies with the elderly being the most affected age group. However, especially in octa- and nonagenarians, cSDHs might not be as "benign" as formerly suspected. We, therefore, aimed to describe possible underlying factors that resulted in the complications, neurological deterioration and recurrences of surgically treated cSDH patients aged ≥ 80 years.

Methods

All patients with a surgically treated chronic subdural hematoma presenting to a neurosurgical maximal care provider between 2006 and 2017 were retrospectively assessed and only adult patients aged ≥ 80 years were included for further analysis. Demographic and clinical variables were collected and outcomes at discharge as well as the rate of recurrence within 90 days were analyzed.

Results

Over a period of 11 years, 288 elderly cSDH patients (mean age 84,8±3,89 years, 63% (n=182) male) could be identified. Their most common comorbidity was arterial hypertension (52%, n=149) and most of them (61%, n=176) were taking antithromotic medication. The most frequent symptoms were palsy (21%, n=60) and coordination deficits (20%, n=57). A midline shift of 8,09mm ± 4,5mm was present 181 patients (63%). Evacuation of the cSDH was performed via burr hole trephination in 87,5% (n=252) of cases with subdural drains placed in almost all patients (96%, n=276). Complications (e.g. cardiovascular, pulmologic, infectiologic, surgical) were common (39%, n=111) but the rate of revision surgery (8%, n=22) and in-hospital mortality (1,4%, n=4) were low. At the time of discharge 2,5±1,34 days after surgery, the mean Karnofsky Performance Index had only slightly improved from 62±16 to 67±32 but 83 % of patients (n=240) reported improvement of their main symptom. Unsurprisingly, patients with 0-1 comorbidities had a significantly reduced risk of complications (OR=0,4; CI 95% 0,27;0,72; P<0,05), and a higher chance of ameliorated symptoms upon discharge (OR 3,1; CI 95% 1,7;5,8; P<0,05). The rate of cSDH recurrence requiring de novo surgery within 90 days was 10% (n=30).

Conclusion

Chronic subdural hematomas are a common neurosurgical pathology in octa- and nonagenerians. Rates of revision surgery or mortality are surprisingly low and postoperative improvement of symptoms is reported by a substantial number of patients. However, missing amelioration of symptoms is associated with the cumulation of comorbidities, implying that frail patients are prone to worse outcomes.

Wirbelsäule I/*Spine I*

P090

Kinematische Bewegungs- und Gleichgewichtsparameteranalyse bei neurologischen Gangstörungen
Kinematic Movement and Balance Parameter Analysis in Neurological Gait Disorders

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[4] , contributed, equally, Deutschland

Objective

Characterizing gait disorders in neurological diseases is at present mainly dependent on clinical observation and difficult to objecti- or quantify. Compared to spatiotemporal movement parameter analyses, kinematic movement parameters have less commonly been described in neurological gait disorders. We used an inertial movement analysis system combined with pedobarography, in order to analyze kinematic movement parameters in different neurological gait disorders compared to healthy controls.

Methods

31 patients with neurological gait disorders (9 normal pressure hydrocephalus <NPH>, 6 lumbar spinal stenosis <LST> , 16 cervical myelopathy <CM> patients) were compared to a ´common reference´ group of 14 healthy controls. Using an inertial measurement system, movement parameters were acquired during 3 different walking conditions, and postural sway was measured by pedobarography with the eyes opened and closed. 7 different kinematic parameters (comprising the range of motion <RoM> in different joint angles <shoulder/hip/knee/ankle> and stride time), and 4 different pedobarography parameters (force distribution, anterior-posterior <ap> and lateral movement, passed centre of pressure <COP> distance) were compared between groups (between-subject factor) and conditions (within-subject factor), using a mixed model ANOVA.

Results

Group effects were found for all movement and balance parameters, except for stride time and force distribution. All parameters significantly differed between conditions except for ankle plantarflexion. NPH patients differed compared to controls in all movement parameters except for stride time, while balance parameters differed only with regard to AP movement. LST patients differed compared to controls in the RoM of the shoulders, hip, and ankle, with differences in balance parameters regarding AP movement and passed COP distance. CM patients differed compared to controls only in the RoM of the hip and ankle, but in nearly all balance parameters except for force distribution.

Conclusion

Inertial measurement systems and pedobarography may allow to identify specific kinematic movement and balance parameter patterns of different neurological gait disorders, which may aid in increasing diagnostic accuracy and in objectifying clinical outcome after therapeutic intervention.

P092

Die 3D-Navigation ist nützlich für die dorsale zervikale Foraminotomie, insbesondere an der unteren Halswirbelsäule

3D Navigation is useful for posterior cervical foraminotomy, especially of the lower cervical spine

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Objective

Unilateral monosegmental radiculopathy, caused by foraminal soft disc nerve root compression, can be safely and effectively treated with posterior cervical foraminotomy (PCF). Intraoperative fluoroscopy is the most widely used method for level localization. However, the error rate increases, especially in obese patients and the lower cervical spine.

Methods

In this retrospective observational study, we analyzed a total of 45 patients (mean age 54 ± 9 years, mean BMI 29 ± 7, 22 females and 23 males) who underwent PCF using intraoperative 3D navigation (O-armTM System, Medtronic) between 08/2017 and 04/2022. Two-tailed t-tests were used for simple difference comparison of preoperative, postoperative and follow-up (FU, 48 ± 28 days) values for neck pain (visual analogue scale, VAS), radicular pain (VAS) and paresis (muscle strength according to Janda). The same was done for level-dependent group comparisons by dividing the group according to the location of disc herniation (C2-C6 and C6-T1).

Results

A significant neck and radicular pain reduction was achieved postoperatively (both $p<.0001$) and during FU (both $p<.0001$). Similarly, significant improvement of the paresis was reached postoperatively ($p<.0001$) and during FU ($p<.001$). 81,3 % of the patients had an intraoperative blood loss of less than 100 ml. Mean time of surgery was 92 minutes (± 28) with 6 days (± 3) as the mean length of stay. There were no significant group differences between upper (C3-C6) and lower (C6-T1) cervical spine concerning symptom relief (all $p>.05$). All surgery levels were identified correctly. Anterior revision surgery was performed in 3 patients because disc herniation could not be completely removed from dorsal.

Conclusion

Intraoperative 3D navigation was successfully used for PCF in our patient cohort, resulting in significant symptom relief. Especially during procedures on the lower cervical spine and cervicothoracic junction, 3D navigation simplified orientation and thus ensures an equivalent outcome as on the upper cervical spine.

P094

Angualtionsabweichungen in iCT navigierter dorsaler Instrumentierung der Wirbelsäule. Eine interims-Anayse von intraoperativ geplanten Trajektorien vs. definitver Schraubenlage.

Angulation-Errors in iCT navigated dorsal instrumentation of the spine. An interim analysis of intraoperatively planned trajectories vs. definitive screw placement.

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Objective

Navigated screw placement is of increasing importance in spinal instrumentation surgery. Especially cervical pedicle screw placement is considered safe only with the use of a navigated approach. However, even intraoperative CT (iCT) navigated pedicle screw placement is prone to error. Recently we have been confronted with the question of whether intraoperatively planned screw trajectories can be considered true with respect to actual screw placement and how angulation errors correlate with screw-misplacement.

Methods

Between March and December 2021 we prospectively recorded intraoperatively planned trajectories of 279 screws in 54 patients placed throughout the spine (104 cervical; 93 thoracic; 76 lumbar; 6 sacral) using BrainLab Curve Planning Station. 3D coordinate systems of planning and control CT scans were merged an vectors of individual screws compared to planed trajectories.

Results

Initially 81% of all screws were placed accurately (<2mm), 14% showed minor (<4mm) and 5% major perforations of the pedicle wall. The mean axial angulation error was 3.4° ± 2.9 and sagittal 3.6° ± 3.7. Rotational (axial) angulation error was higher in the cervical (median 3.4 95%CI 3.6-4.8) then in the thoracic (2.3 95%CI 2.3-3.4) spine (p=0.016).
Overall axial and sagittal angulation error correlates positively with increase in Gertzbein&Robbins grade (Spearmans r: 0.19 and 0.23).
Major pedicle wall breaches (>4mm) were found in cases of median sagittal angulation error of 8.3° (95%CI 4.1°-16°) while accurately placed screws featured a median sagittal error of 2.4° (95%CI 2.7°-3.4°). Median axial angulation errors in major misplacements were 4.4° vs. 2.5° regarding acceptably placed screws in our cohort.

Conclusion

iCT remains a solid tool to facilitate accurate dorsal instrumentation throughout the spine. Rotational error of actually achieved compared to intraoperatively planned trajectories is confined to a minimum. However, angulation error correlates with pedicle violation and cannot be eliminated completely. The specific regional mobility of the spine must be kept in mind when applying pressure on the navigated drill-guide during pediculation to minimize angulation error.

Wirbelsäule I/*Spine I*

P096

Rigide vs. semi-elastische Bildfusionsgenauigkeit in der thorakolumbalen navigierten Wirbelsäulenchirurgie
Rigid vs. Semi-elastic Image Fusion Accuracy in Thoracolumbar Navigated Spine Surgery

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Objective

Preoperative planning of pedicle screws is routinely used in complex spine surgery for (roboter-assisted) navigated pedicle screw placement, analyzing challenging anatomy and accelerating the intraoperative workflow. However, due to differing patient position pre- and intraoperatively and spinal flexibility, co-registration and thereby accurate transfer of preoperatively planned screws to intraoperative 3-dimensional imaging data remains challenging. Most commonly, rigid image fusion is utilized applying partly multiple monosegmental fusion procedures to reduce registration inaccuracies. Alternatively, a semi-elastic fusion can be used to map intraoperative and preoperative image data by deforming the preoperative images. This study aimed to investigate the accuracy of semi-elastic and monosegmental rigid image fusion.

Methods

A retrospective single-center study of 16 patients who underwent spinal surgery was performed. All patients received preoperative as well as intraoperative CT imaging prior to screw placement. In all cases for each visualized vertebra intravertebral landmarks were defined. Subsequent monosegmental rigid fusions as well as a semi-elastic fusion was performed (Elements Image Fusion & Elements Curvature Correction Spine, Brainlab, Munich, Germany). For all fusions the Euclidean distance between transferred and reference landmarks was calculated and averaged across each vertebra.

Results

In total a mean of 4.00 ± 1.65 rigid as well as one semi-elastic fusions were performed per case. The mean Euclidean distance across all vertebrae was 0.50 ± 0.27 mm (thoracic: 0.43 ± 0.25 mm, lumbar: 0.59 ± 0.27 mm) for rigid and 0.32 ± 0.15 mm (thoracic: 0.34 ± 0.16 mm, lumbar: 0.29 ± 0.14 mm). In all cases and all vertebrae, semi-elastic fusion was at least as precise as standard rigid fusion, especially in the lumbar area, semi-elastic fusion showed even significantly ($p < 0.001$) improved results.

Conclusion

Statistically significant differences were found between both models regarding the landmark accuracy, with even higher accuracies in case of the semi-elastic image fusion. Rigid image fusion has to be repeated several times, especially in the case of bi- or multisegmental screw placement, which is time-consuming, error-prone and therefore not applicable for most surgeries. Therefore, as only one fusion step is performed in semi-elastic fusion, this approach represents a considerable step towards efficiency in thoracolumbar navigated spine surgery.

Wirbelsäule I/*Spine I*

P097

Der One-Stop-Shop Approach: Navigierte 360 Grad-Instrumentierung der lumbalen Wirbelsäule in einer einzigen Patientenlagerung

The one-stop-shop approach: Navigating lumbar 360-degree instrumentation in a single positioning

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Objective

Treatment strategies of patients suffering from pyogenic spondylodiscitis are a controverse topic. Percutaneous dorsal instrumentation followed by surgical debridement and fusion of the infectious vertebral disc spaces is a common approach for surgical treatment. Technical advances enable spinal navigation for dorsal and lateral instrumentation. This report investigates combined navigated dorsal and lateral instrumentation in a single surgery and positioning for lumbar spondylodiscitis in a pilot series.

Methods

Patients diagnosed with 1- or 2-level discitis were prospectively enrolled. To enable posterior navigated pedicle screw placement and lateral interbody fusion (LLIF) patients were positioned semi-prone in 45-degree fashion. For spinal referencing, a registration array was attached to the pelvic or spinal process. 3D scans were acquired intraoperatively for registration and implant control.

Results

27 patients suffering from 1- or 2-level spondylodiscitis with a median ASA of 3 (1-4) and a mean BMI of 27.9±4.9 kg/m2 were included. Mean duration of surgery was 146±49 min. Mean blood loss was 367±307 ml. A median of 4 (4-8) pedicle screws were placed for dorsal percutaneous instrumentation with an intraoperative revision rate of 4.0%. LLIF was performed on 31 levels with an intraoperative cage revision rate of 9.7%.

Conclusion

Navigated lumbar dorsal and lateral instrumentation in a single operation and positioning is feasible and safe. It enables rapid 360° instrumentation in these critically ill patients and potentially reduces overall intraoperative radiation exposure for patient and staff. Compared to purely dorsal approaches it allows for optimal discectomy and fusion while overall incisions and wound size are minimized. Compared to prone LLIF procedures, semi-prone in 45-degree positioning allows for a steep learning curve due to minor changes of familiar anatomy.

Wirbelsäule I/*Spine I*

P098

Der vordere Zugang zum zervikothorakalen Übergang über eine partielle Sternotomie: Ein Bericht einer klinischen Serie über technische Machbarkeit, postoperative Morbidität und frühe chirurgische Ergebnisse

Anterior access to the cervicothoracic junction via partial sternotomy: A clinical series reporting on technical feasibility, postoperative morbidity, and early surgical outcome

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Objective

Surgical access to the cervicothoracic junction (CTJ) is challenging. The aim of this study was to assess technical feasibility, early morbidity and outcome in patients undergoing anterior access to the CTJ via partial sternotomy.

Methods

Consecutive cases with CTJ pathology treated via anterior access and partial sternotomy at a single academic center from 2017-2022 were retrospectively reviewed. Clinical data, perioperative imaging and outcome were assessed with regards to the aims of the study.

Results

A total of 8 cases, four (50%) bone metastasis, one (12.5%) traumatic instable chance fracture (B3-AO-Fracture), one (12.5%) thoracic disc herniation with spinal cord compression, and two (25%) infectious pathologic fractures (12.5%) from tuberculosis and spondylodiscitis, (Median age was 49.88 years, interquartile range (IQR) 21, range 22 – 74 years of age, 75% male) were analyzed. 75% cases had an *American Society of Anesthesiologists (ASA)* grade 2. The median *Spinal Instability Neoplastic Score* (SINS) was 14.5 (IQR: 5, range 9 – 16) indicating high degree of instability in treated cases. Four cases (50%) underwent additional posterior instrumentation. All surgical procedures were performed uneventfully with no intraoperative complications. Median length of hospital stay was 11.5 days (IQR: 9, range 6-20) including median 1 day on intensive care unit (ICU). Two cases (25%) developed slight to moderate postoperative dysphagia with unrestricted oral diet. No in-hospital mortality was observed. Radiological outcome was unremarkable in all cases with no case of implant failure. One case died due to the underlying disease during follow-up. The median follow-up was 2.6 months (IQR: 23.8, range: 1–45.7 months).

Conclusion

Our series indicates that the anterior approach to the cervicothoracic junction and upper thoracic spine via partial sternotomy is a safe and effective option to treat anterior spinal pathologies. Careful case selection is essential to adequately balance clinical benefits and surgical invasiveness for these procedures.

Wirbelsäule I/*Spine I*

P099

Risikofaktoren für neurologische Defizite nach OLIF
Risk factors for motor weakness following oblique lumbar interbody fusion

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Objective

Oblique lumbar interbody fusion (OLIF) is known as a minimally invasive technique for disc space fusion which protects the intrapsoas nerves. Nevertheless motor weakness after OLIF has been known to occur in some cases. This study aimed to report the incidence and potential risk factors for motor weakness following OLIF.

Methods

We enrolled 38 patients and 59 segments who underwent OLIF. Computed tomography was performed before and after OLIF. Radiologic data including psoas muscle (cross-sectional area, Hounsfield unit (HU), fat portion grade), bone mineral density and clinical data, including age, sex, presenting symptoms, visual analog scale score, operating segments, and postoperative complications, were collected. We divided the patients into groups with and without neurologic deficit. Transient deficits were considered as such up to 1 month after surgery. Neurologic status was evaluated preoperatively and postoperatively at 2 days, 1 week, 1 month, and 3 months. Number of levels, disc height, foramen height and osteophyte length were measured and compared between the 2 groups.

Results

The neurologic deficit group included 4 patients with transient (10%) und 2 (5%) patients with permanent weakness, whereas non-neurologic deficit group included 35 patients (85%). The neurologic deficit group included 10 segments (8%), whereas the non-neurologic deficit group included 114 segments (92%). The disc and foramen heights did not differ significantly between the groups with and without neurologic deficit; however, the psoas retraction time, osteophyte lengths and multilevel surgery more than 3 levels were higher in the neurologic deficit group.

Conclusion

In our study, psoas retraction time, osteophyte lengths and multilevel surgery were found to be potential risk factors for motor weakness after OLIF. For patients with severe multilevel degeneration with long osteophytes may have neurologic complications and show delayed recovery from postoperative weakness.

Wirbelsäule I/*Spine I*

P100

Schraubenentfernung bei Schraubenfehllage 30 Jahre nach Implantation: Chancen und Risiken
Delayed screw removal 30 years after lumbar screw malpositioning: chances and risks

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Objective

Screw malpositioning (SMP) is a known complication of lumbar fusion surgery, which potentially makes screw revision necessary. Screw revision after decades in case of SMP with nerve compression or even injury is a difficult decision as it poses the risk of causing further injury with functional impairment and unpredictable chances of improvement.

Methods

A 79-year-old woman presented to our outpatient clinic with a 30-year history of radiating pain in both legs (most probably in the left leg L5 and S1 dermatomes and the right leg S1 dermatome). She also had claudication that did not improve under conservative treatment. The patient history revealed that 30 years ago, she had undergone lumbar fusion surgery at the levels from L4 to S1 due to spondylolisthesis in an external hospital (the screw system was not mentioned in the surgical report). A computed tomography scan revealed an SMP of the screw at the level of L5 on the left side (grade III) and both screws at the level of S1 (right: grade III, left: grade II). Furthermore, two screws were broken.

Two different treatment options were discussed in our spine board: 1. screw removal and 2. symptomatic therapy with spinal cord stimulation.

Being aware of the potential complications, the patient decided to undergo screw revision.

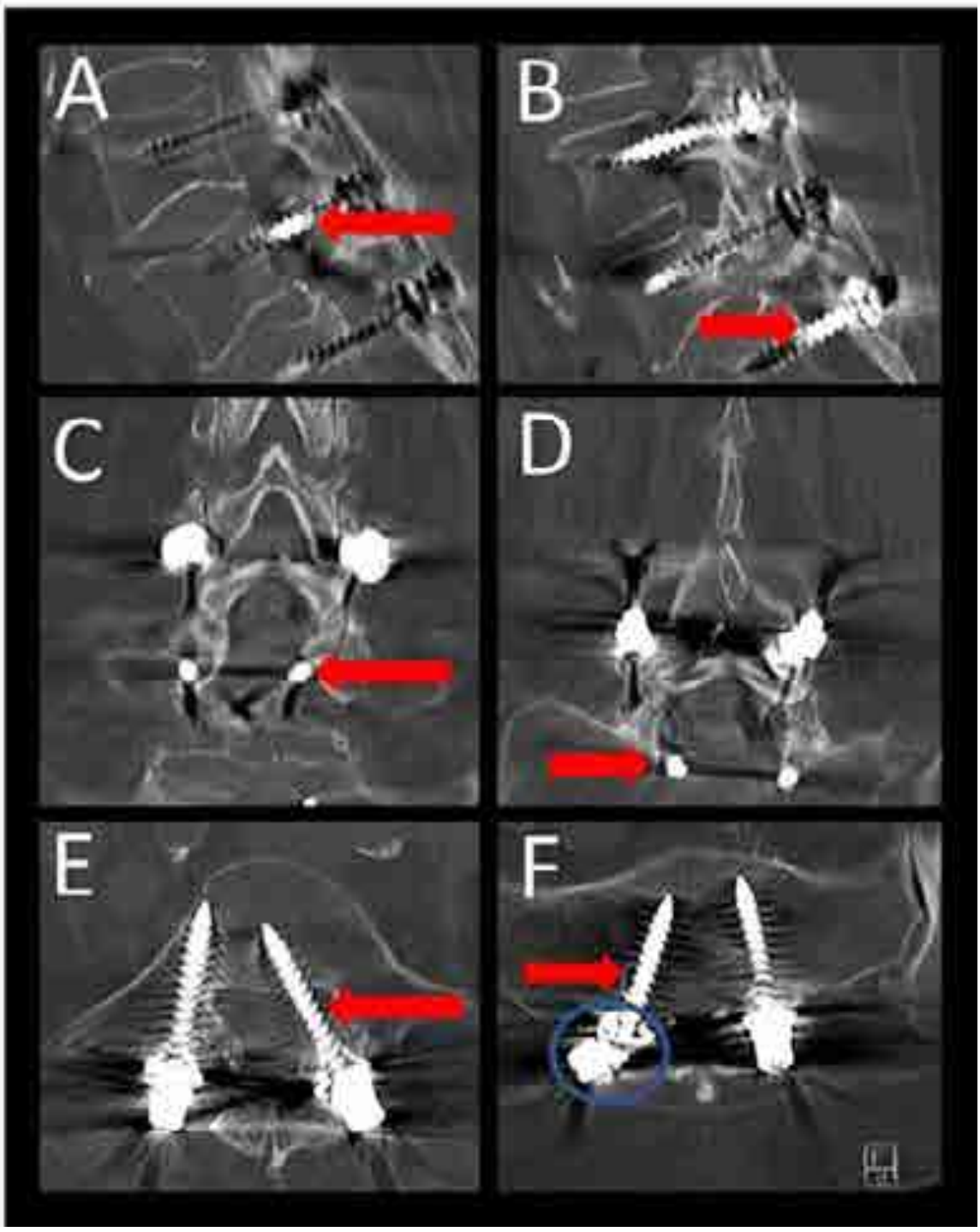
Results

Screw removal was performed under intraoperative monitoring (IOM). Since the screw rescue system did not fit, the rods were cut by drilling in ´key points´. The rods and intact screws were removed. Under the microscope, drilling for decompression and inspection of the left L5 and right S1 nerve roots was performed and the anterior broken screw parts were removed. IOM remained stable during surgery. The patient recovered from the surgery without developing any new deficit. The pain was completely resolved after three days.

Conclusion

There are no guidelines about SMP management after decades with nerve compression or injury. Revision surgery in a spine center under IOM (including nerve control under microscopic visualization) should be considered as an option to alleviate pain.

Abb. 1



Wirbelsäule I/*Spine I*

P101

Häufigkeit von medizinischen und chirurgischen Komplikationen nach elektiven Operationen an der Lendenwirbelsäule

Incidence of medical and surgical complications after elective lumbar spine surgery

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Objective

The demographic change results in an ever increasing number of older patients with pre-existing medical conditions who require spinal surgery, and recovery is often severely impaired by procedure-related complications. The purpose of this retrospective study was to determine patients at risk of medical and surgical complications.

Methods

Using our database, we reviewed 1,244 patients with lumbar degenerative disk disease, spinal stenosis, and instability, who had undergone surgery at our department between 2009 and 2014. We screened for medical complications (thromboembolic and cardiac events) and surgical complications (hemorrhage, wound infection, and CSF fistula). Furthermore, a matched 1:1 control group consisted of 103 patients without any surgical and medical complications in the randomly selected period of May 2009 to October 2014.

Results

93 patients (46 women, 47 men), mean age 70 years (range 33–86 years, median 67.4 years), with complications were identified (overall morbidity 7.6%): 22.6% (n=26) had medical complications and 77.4% (n=89) surgical complications. In 93 patients (46 females, 47 males), mean age 70 years (range 33-86 years, median 67.4 years), a total of 115 complications were noted (overall morbidity of the 93 patients 7.6%): 22.6% (n = 26) medical complications and 77.4% (n = 89) surgical complications. Age and pre-existing conditions were independently associated with medical complications ($p<0.001$). Infections (pneumonia and sepsis) were correlated with multi-segmental interventions ($p=0.009$), duration of surgery ($p=0.009$), and pre-existing conditions ($p=0.014$). Surgical complications were significantly correlated with age ($p=0.016$) and duration of surgery ($p=0.014$) and occurred significantly more often in patients with instability ($p<0.001$). Wound healing disorders were associated with coagulopathy ($p=0.013$) and transfusion ($p<0.001$).

Conclusion

We identified predictors that help identify patients at risk of medical ~~or~~ and surgical complications. These correlations should be taken into account when advising older patients with pre-existing conditions on lumbar spine surgery.

Abb. 1

Complication	Risk factor	Odds ratio	95%-confidence interval		P-value
Blood transfusion					
	Age >60 years	17.009	1.77	254.766	0.038*
	Instability	74.794	5.986	934.615	0.001***
	Multi-segmental surgery	26.706	2.300	310.062	0.009*
CSF fistula					
	Duration of surgery	1.008	1.001	1.016	0.036*
Wound healing disorder/Infection					
	Instability	9,.49	1.860	44.033	0.006**

Table 1: Multivariate analysis of risk factors for surgical complications

Abb. 2

Complication	Risk factor	Odds ratio	95%-confidence interval		P-value
Wound healing disorder/Infection					
	Previous nephrological disease	21.545	1.062	436.883	0.046*
	Multi-segmental surgery	6.908	1.257	37.957	0.026*

Table 2: Multivariate analysis of risk factors for medical complications

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P102

Epidurale Rückenmarkstimulation bei ausgeprägtem Freezing of gait
Spinal cord stimulation for severe primary progressive freezing of gait

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Objective

Primary progressive freezing of gait (PPFG) is a rare disorder associated with atypical parkinsonism which often is refractory to medical treatment. Since deep brain stimulation of targets such as the subthalamic nucleus or the pedunculopontine region have not shown stable longterm improvement, there is a need to explore new treatment paradigms. Here we report on a pilot study of spinal cord stimulation evaluating its safety, tolerability and efficacy in PPFG.

Methods

Both patients had a diagnosis of PPFG with a history of freezing for 5 and 6 years, respectively. Patient 1 was a 77-year-old woman, patient 2 was a 68-year-old man. Freezing was refractory to dopaminergic medication in both instances. There were frequent falls and patients were severely disabled by freezing. Epidural electrodes for spinal cord stimulation were implanted at mid-thoracic levels, in patient 1 via a small laminotomy (plate electrode), and in patient 2 via a transcutaneous approach. Upon test stimulation both patients had marked improvement of freezing which was objectified by standardized videotaping and assessment. For chronic stimulation a frequency of 40 Hz was used at a pulse width of 320 and 450 microsec, respectively, with an amplitude producing paraesthesias (up to 6 V).

Results

Patient 1 benefitted from short-lived improvement for four weeks, and patient 2 for a period up to six months. Thereafter the initial benefit could not be sustained despite multiple attempts of modifying the stimulation settings.

Conclusion

Spinal cord stimulation for severe freezing of gait shows transient benefit, however, with limited longterm perspectives. Future studies are needed to explore alternative stimulation algorithms such as artificial intelligence and adaptive routines.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P103

Klinische Effektivität von adaptierten Stimulationsparadigmen bei Patienten mit persistierendem spinalen Schmerzsyndrom (Typ I und II)

Clinical efficacy of new patient-adapted stimulation patterns for SCS therapy in patients with persistent spinal pain syndrome (type I and II)

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Objective

In patients with chronic axial back pain, results of spinal cord stimulation are still heterogeneous regrading comparable therapeutic response between systems and stimulation paradigms used. New patient-adapted stimulation seem to lead to a clinically significant pain reduction in this commonly low-responder patient population. We therefore examined the efficacy of two types of patient adapted stimulation on pain intensity in patients with persistent spinal pain (PSP).

Methods

We used two types of patient-adapted SCS systems, in which settings can be customized to address the patients´ individual needs. One system offered stimulation with respect to the glial cell activation (group I), the second one permanent neurophysiological adaptation (group II).

A total of 12 patients were included (PSP, type I and II). Group I: this system was primarily used in PSP type I (surgery naïve) patients. (n=6, m=4, f=2; mean age: 63.3 years). Group II included predominantly patients with PSP type II (with previous surgery (n=6, m=3m f=3, mean age: 64,5 years).

Stimulation was adapted according to the paraesthesia coverage under tonic stimulation (group II) and via glial activation measurement in group I.

For both groups, pain intensity was recorded with the VAS score was recorded at baseline and at follow up (Group I: 12-24 weeks, II: 6 -12 weeks postsurgery).

Results

The overall pain intensity in group I was mean 6.3/10 points (range 5-8) at baseline and 2.8/10 (range 1-5) postoperatively. In 3 out of the 6 patients, stimulation achieved an average pain relief of >75%. In 5 of 6 patients, the average VAS was reduced by at least 3 points. One patient did not benefit from the therapy (Pain Relief <30%) and was explanted after 6 months.

The pain intensity in group II was given as an average of 7.8/10 VAS (range 6-9) preoperatively and 3.2/10 VAS (range 2-5) postoperatively. Mean pain relief was >50% in 5 of 6 patients and >70% in 2 patients.

Conclusion

Our preliminary results suggests that patient adapted stimulation improves treatment response, especially in PSP type I patients. Further prospective investigations are necessary to assess future therapeutic approaches in spinal cord stimulation.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P104

Effekt der Niedrigfrequenzstimulation des Spinalganglions auf die Behandlung neuropathischer und nozizeptiver Schnerzen

Effect of Low-Frequency Dorsal Root Ganglion Stimulation in the Treatment of Neuropathic and Nociceptive Pain

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Objective

The role of stimulation parameters in dorsal root ganglion stimulation (DRG-S), especially of stimulation frequency, is not well understood. Previous studies documented higher effectiveness for frequencies as low as 20 Hz, but there is evidence that even lower values could lead to better outcomes. In this study, we investigate the influence of low-frequency DRG-S.

Methods

We report on the results of a randomized double-blind clinical trial with crossover design. Patients with an already implanted DRG-S system were included and randomly tested with 4 Hz, 20 Hz, 60 Hz and sham stimulation. Amplitude was adjusted to subthreshold values for each frequency. Each frequency was tested for 5 days, followed by a 2-day wash-out period. Patients were assessed using VAS, McGill Pain Questionnaire, EQ-5D-5L and Beck Depression Inventory.

Results

17 patients were included. Time between inclusion in this study and primary implant was 32.8 months. Baseline stimulation frequency was 20 Hz in all patients. Mean baseline pain intensity was VAS 3.2 (SD 2.2). With 4 Hz stimulation, VAS was 3.8 (SD 1.9), with 20 Hz VAS 4.2 (SD 2.0) and with 60 Hz VAS 4.6 (SD 2.7). Worst pain control was seen with sham stimulation with a VAS of 5.3 (SD 3.0). Stimulation with 4 Hz achieved lower VAS scores, but this was only statistically significant when compared to sham ($p = 0.001$). A similar trend favoring 4 Hz stimulation was seen using the Beck Depression Inventory, but in this case no statistical significance was found. Outcomes of McGill Pain Questionnaire and EQ-5D-5L favored 20 Hz stimulation, but again without statistical significance.

Conclusion

Low-frequency stimulation might be most effective in dorsal root ganglion stimulation for chronic neuropathic pain. Longer wash-out and observational periods might be necessary to show clear differences in frequency response.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P105

Die laterale Implantation von Elektroden zur direkten Nervenwurzelstimulation erzielt eine suffiziente Schmerzreduktion bei Patienten mit neuropathischen Schmerzen durch einen pseudo-DRG Effekt

Implantation of direct nerve root stimulating leads in patients with radicular and pseudoradicular pain syndromes can produce an therapeutic "pseudo-DRG" effect

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Objective

Dorsal root ganglion stimulation (DRGS) is an established option for the treatment of radicular and pseudoradicular neuropathic pain. However, placement of DRG-stimulating leads can be challenging to the surgeon. We present a series of patients with neuropathic pain in whom we were able to achieve sufficient pain relief by nerve root stimulation via lateral location of spinal cord stimulation (SCS) electrodes, thus creating a "pseudo-DRG" effect.

Methods

Between March 2021 and December 2022, we treated 5 patients (3 male, 2 female ; median age 55 years) with chronic unilateral or bilateral neuropathic pain. All patients presented a positive response to diagnostic infiltration. In each case, the procedure was performed under local anesthesia for intraoperative testing of the stimulation. Eight contact ring electrodes were placed laterally under intraoperative radiographic control, aiming to place at least one lead directly at the nerve root thus exerting stimulation in a "pseudo-DRGS" fashion. Pain diaries including numeric rating scores as well as plain radiographs and intra- and postoperative impedance values were measured in all patients at 1 week and 3 months postoperatively.

Results

All patients presented with mean NRS values of >5 at baseline (mean NRS 8.3±0.73). All procedures were performed without complications. The trial phase was performed for seven days after implantation. All patients achieved a reduction of greater than 50% in their pain intensity as self-reported by numeric rating scale (p=0.04, mean NRS 4±0.56). All patients underwent implantable pulse generator (IPG) implantation for continuous stimulation. At three months after implantation, pain intensity was still significantly reduced when compared to preoperative values (p=0.03, mean NRS 3.5±0.86). Over time, one patient experienced mild caudal dislocation of the electrode without any clinical relevance. No patient had to undergo revision of either electrodes or IPGs.

Conclusion

Implantation of lateral SCS electrodes appears to sufficiently reduce symptoms of both radicular and pseudoradicular neuropathic pain syndromes of various origins. The procedure is easy to perform for neurosurgeons who are familiar with SCS implantation. Postoperative radiographic examination and clinical evaluation of subjective and objective measures of pain intensity demonstrates a sufficient long-term reduction of pain in these patients.

Abb. 1

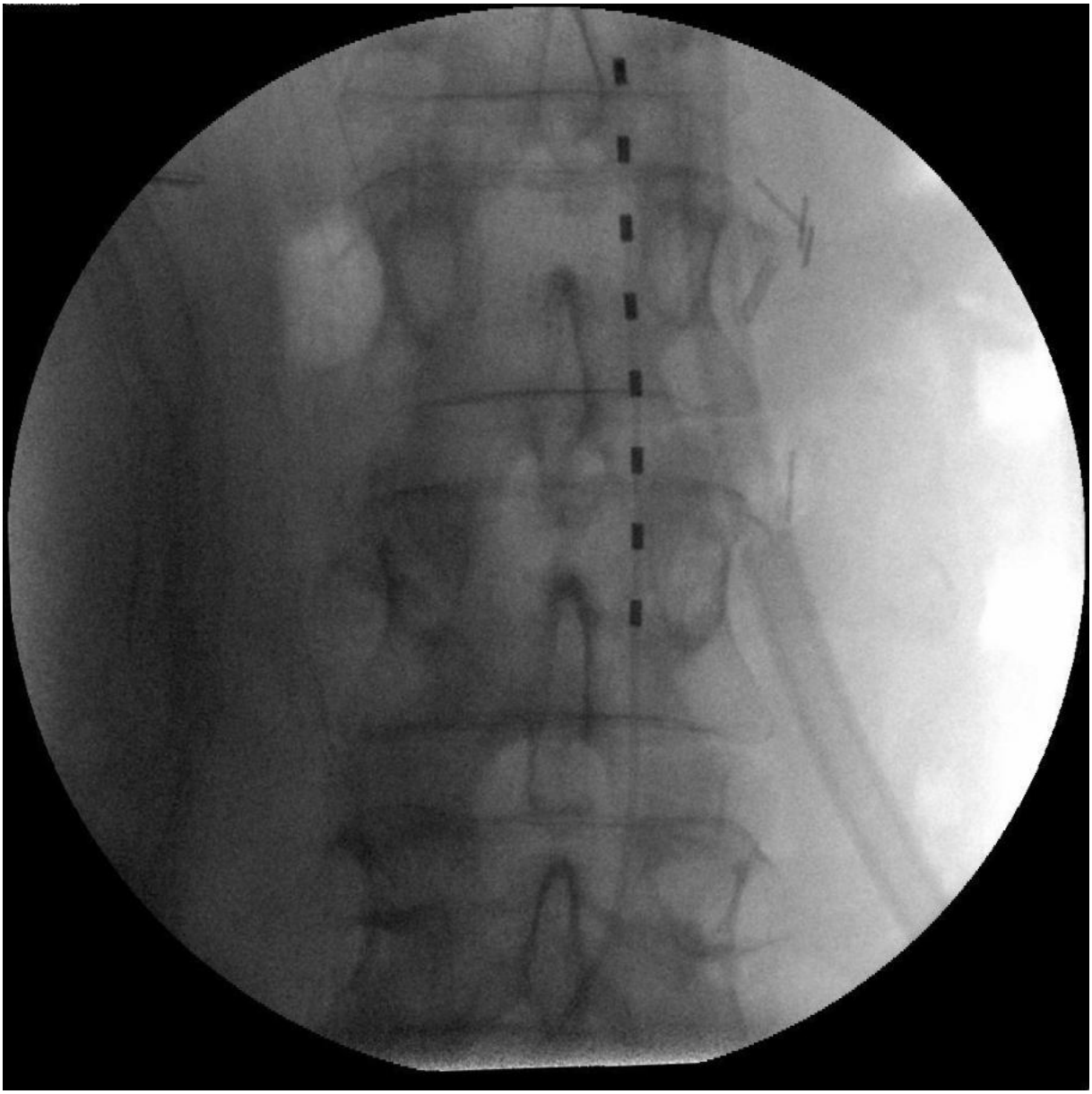
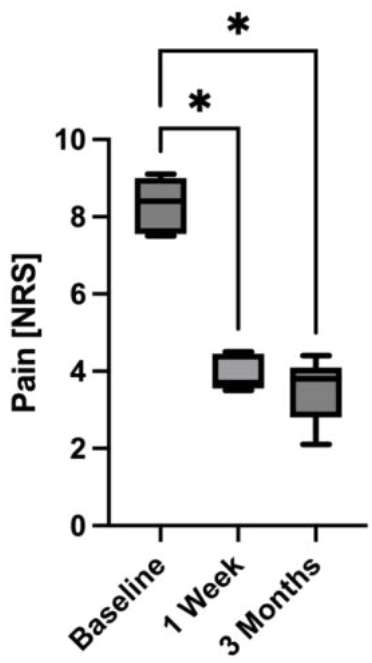


Abb. 2



Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P106

Schmerzreduktion durch periphere Nervensimulation bei patientin mit chronischen Knieschmerzen – Eine Therapiealternative?

Peripheral Nerve Stimulation reduces pain in patients with chronic knee pain – a treatment alternative?

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Objective

The increasing average age of our population results in a high incidence of chronic degenerative knee pathologies. Several surgical procedures can help patients to improve. However, the amount of patients with chronic postsurgical knee pain is estimated with 16-20%. Neuromodulation techniques like SCS and Dorsal Root Ganglion Stimulation have already been used to treat chronic knee pain. The evidence of selective treatment due to peripheral nerve stimulation (PNS) is very low so far because of the absence of suitable neuromodulation systems for the distal part of the lower limbs. The aim of this study was to show the effectiveness and safety of a wireless PNS system to treat chronic intractable knee pain via saphenous nerve stimulation.

Methods

27 patients with chronic intractable postsurgical knee pain have been tested via landmark- guided peripheral nerve stimulation of the branches of the saphenous nerve. All implantations were performed with a wireless PNS system and external battery to avoid lead migration due to cross-joint lead positions. Data was collected prospectively. Outcome scores and pain medication were followed in outpatient visits scheduled 3, 6, 12 and 24 months after permanent implantation.

Results

All patients benefited significantly from PNS and were implanted with a permanent device. The mean NRS (NRSpreop. =8.1 +/- 0.7) was reduced after trial period and after three months follow-up (NRSpostop.= 2.7 +/- 1.5, NRS3 months= 2.5 +/- 1,6). Additionally, patients were able to reduce pain their opioid medication from 85 Morphine Milligram Equivalents (MME) preoperatively to 15 MME three months after surgery.

Conclusion

Wireless PNS of the branches of the saphenous nerve is a simple, selective, safe and elegant technique for patients with chronic knee pain. The land-mark guided implantation is less invasive than classical neuromodulation techniques like Spinal Cord or DRG-stimulation. Complication rates are low and durations of surgeries are short. Short-term results are promising and show considerable pain and opioid reduction. However, long-term results are pending.

P107

Die autonome Testung von chronischen Schmerzpatienten unter Burst Motorkortexstimulation: Prädiktion oder Mythos?

Burst motor cortex stimulation promotes pain relief and changes of autonomic parameters in chronic post-stroke pain: preliminary findings

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Objective

To evaluate the impact of Burst motor cortex stimulation on pain and autonmic function in chronic poststroke pain patients

Methods

In three patients with chronic post-stroke pain, we assessed pain-perception (VAS) and parameters of autonomic cardiovascular modulation at supine rest, during parasympathetic challenge with six cycles per minute metronomic deep breathing, and during sympathetic challenge, i.e. active standing. *Directly after implantation* (MCS OFF) and *after four months of Burst MCS*, we compared *resting* parameters of total autonomic modulation (total powers of R-R interval modulation [RRI-total-powers], RRI standard deviation [RRI-SD], RRI coefficient of variation [RRI-CV]), parasympathetic modulation (normalized RRI-high-frequency-powers [RRI-HFnu-powers], square root of the mean squared differences of successive RRIs [RMSSD]), sympathetic modulation (normalized RRI-low-frequency-powers [RRI-LFnu-powers]), the index of sympatho-vagal balance (RRI-LF/HF-ratios), and baroreflex sensitivity (BRS). Furthermore, we compared expiratory–inspiratory-ratios (E/I-ratio) during parasympathetic activation by *metronomic deep breathing*, and RRI-30/15-ratios reflecting the degree of heart rate changes upon sympathetic stimulation, i.e. *active-standing*.

Results

Although VAS-values already improved after four months of stimulation (VAS 8 vs VAS 4.5), RRI- and BP-values were similar before and after treatment. Yet, at rest, parameters of parasympathetic (RRI-HFnu-powers 0.24 vs 0.38, RRI-RMSSD 7.7 vs 14.7 ms), total autonomic modulation (RRI-total-powers 129.3 vs 406.2 ms2, RRI-SD 11.6 vs 18.5 ms, RRI-CV 1.9 vs 3.7), and BRS (1.9 vs 2.3) increased and parameters of sympathetic tone (RRI-LFnu-powers 0.76 vs 0.62), and sympatho-vagal balance (RRI-LF/HF-ratio 3.4 vs 1.9) decreased between measurement 1 and 2 in our three patients. During parasympathetic stimulation, E/I-ratio slightly increased, while upon sympathetic stimulation 30/15-ratios remained unchanged between the two assessments.

Conclusion

Four months of 40 Hz stimulation was associated with an increase of parameters reflecting total, as well as parasympathetic autonomic modulation and baroreflex sensitivity. In contrast, sympathetic tone declined in our three patients, suggesting stimulation-associated improvement not only in subjectively perceived VAS pain-scores, but also in objectifiable parameters of autonomic cardiovascular modulation.

Abb. 1

	1. Measurement	2. Measurement
Assessment at rest		
RR-Interval (ms)	641,0	676,7
Systolic blood pressure (mmHg)	138,8	140,8
Parameter of sympathetic modulation		
RRI-LFnu-power	0.76	0.62
Parameter of parasympathetic modulation		
RRI-HFnu-power	0.24	0.38
RRI-RMSSD (ms)	7.7	14.7
Parameter of total autonomic modulation		
RRI total powers (ms^2/Hz)	179.3	406.2
RRI-SD (ms)	11.6	18.9
RRI-CV (%)	1.9	3.7
Parameter of sympatho-vagal balance		
RRI-LF/HF-ratio	3.4	1.9
Baroreflex Sensitivity (ms/mmHg)	1.9	2.9
Assessment during metronomic breathing		
E/I-ratio	1.01	1.16
Assessment during active standing		
30/15-ratio	1.05	1.05

Table 1 - Mean values of RR-intervals, systolic blood pressure and autonomic cardiovascular parameters at rest and during autonomic challenge maneuvers directly after implantation and after 4 months of 40 Hz stimulation

RRI: RR-interval; LFnu: low frequency normalized unit; HFnu: high frequency normalized unit; RMSSD: square root of the mean squared differences of successive RRIs; SD: standard deviation; CV: coefficient of variance; E/I-ratio: expiratory–inspiratory ratio; 30/15-ratio: ratio between the shortest RRI around the 15th heart beat and the longest RRI around the 30th heart beat after standing up

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

J-SBNC013

Systematische Übersicht: Neuromodulation zur Behandlung chronischer Schmerzen
Systematic Reviwe: Neuromodulation for the management of chronic pain

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Objective

Systematically review the effectiveness of several neuromodulation techniques for the management of chronic neuropathic pain, including Deep Brain Stimulation (DBS), Motor Cortex Stimulation (MCS), Spinal Cord Stimulation (SCS) and Posterior Insula Stimulation (PIS).

Methods

PubMed, EMBASE and Cochrane Library databases were searched from 1990 to 2022. The strategy of search concentrated on the following key-words: "neuropathic pain", "chronic pain", "deep brain stimulation", "motor cortex stimulation", "spinal cord stimulation", "insula stimulation" and "neuromodulation". Studies that provided data regarding the immediate and long-term effectiveness of the neuromodulation technique, anatomical stimulation target and NP etiology were included.

Results

The most frequent etiologies of NP were phantom limb pain and central post-stroke pain (CPSP) in the MCS group; CPSP, phantom limb pain and spinal cord injury (SCI) in DBS patients; and complex regional pain syndrome (CRPS) and failed back surgery syndrome (FBSS) in the SCI group. Pain improvement varied between 35 to 80% in the MCS group and 50-60% in the DBS group. In the SCS group, successful rates varied between 38 to 89%.

Conclusion

MCS, DBS and SCS were considered well stablished techniques for the management of neuropathic pain. However, we believe there is not enough evidence yet to support the routine use of PIS. At last, we concluded that the literature was not able to provide a definitive answer regarding which technique should be used for each disease. The results were extremelly diverse depending on the service and neurosurgeons preference.

Abb. 1

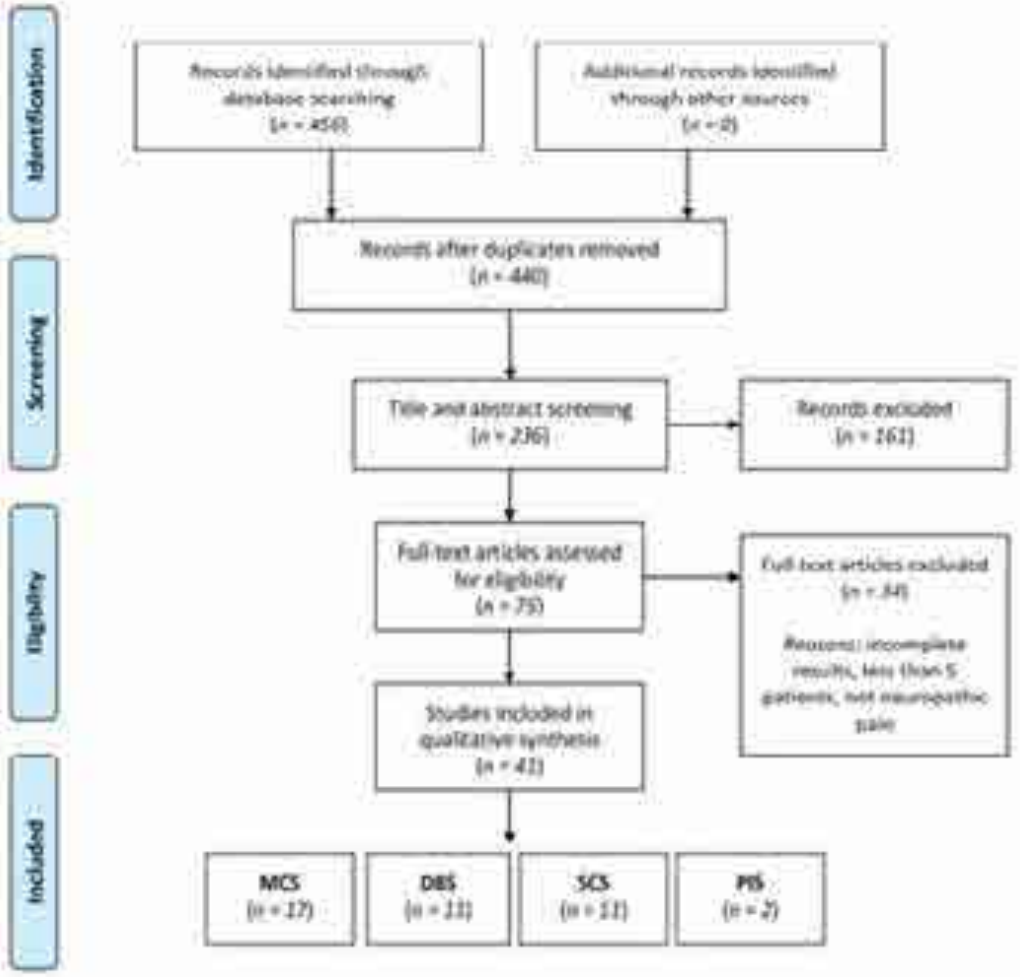

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flowchart showing the selection process

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

J-SBNC014

Intrathekale opioidpumpe zur behandlung von schmerzen bei krebspatienten
Intrathecal opioid pump in the treatment of pain in oncologic patients

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Objective

Intractable pain in cancer patients reduces the quality of life and increases the use of oral opioids without effectiveness in treatment. Therefore, the intrathecal opioid pump becomes an option, allowing a reduction in drug dose and mortality while increasing treatment efficacy.

Methods

Systematic review of literature in PubMed searching for "intrathecal opioid" and "cancer pain". The main points for the follow-up of an oncologic patient, who underwent an intrathecal opioid pump implantation were included.

Results

Patient 1: Male, 63 years old, prostate cancer with bone metastasis with refractory bone pain preoperatively 7/10 and postoperatively 3/10 (NRS). Patient 2: Female, 21 years old, rhabdomyosarcoma in the left mandible, refractory pain 7/10 in mandibular nerve territory and 3/10 (NRS) post-procedure. Patient 3: Male, 31 years old, anal cancer, intense anorectal and lower limb pain refractory to odd ganglion block, with no improvement after the procedure.

Conclusion

Refractoriness to other drug therapies and the trial of intrathecal therapies should be considered before the procedure. The case series presented shows the potential of the treatment, which was able to reduce pain intensity by more than 50%, in two patients. However, the technique has limitations, and one of the patients reported did not achieve symptomatic improvement even with the use of intrathecal morphine. The implantation of an intrathecal opioid pump is undoubtedly an option with great therapeutic potential in refractory pain.

P108

Intraoperative Laser Speckle Bildgebung zur Beurteilung der Elektrodenplatzierung während Radiofrequenzablation des Ganglion gasseri

Intraoperative laser speckle imaging to assess electrode placement during radiofrequency ablation of the trigeminal ganglion

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Objective

For optimal clinical results of radiofrequency ablation (RFA) of the trigeminal ganglion, correct probe positioning is crucial. Preclinical findings have shown that intraoperative laser speckle imaging (iLSI) may help to optimize probe positioning by measuring skin perfusion during electrode placement. Against this background, the present pilot study reports the first experience of using iLSI during RFA electrode placement at the trigeminal ganglion in humans.

Methods

This pilot study was performed in 5 patients that underwent unilateral RFA of the trigeminal ganglion for treatment of refractory trigeminal neuralgia. After induction of general anesthesia, an iLSI device was positioned 30cm above and perpendicular to the surface of the face. Skin perfusion was continuously recorded at 25Hz / 8.3ms in the arbitrary perfusion unit "Flux". After a 30-second baseline measurement, the RFA probe was inserted under fluoroscopic guidance until the desired target area at foramen ovale was reached. During this process, the facial perfusion response was visualized and quantitatively analyzed within 16 corresponding regions of interest (ROIs) covering the ipsi- and contralateral V2+V3 skin surface area (8 ROIs per side) for matched comparison of the perfusion change above the treatment and contralateral (control) side calculated as mean±95% confidence interval.

Results

In all cases, iLSI was successfully performed. In 4/5 patients, a sudden ipsilateral perfusion increase was visualized in the color-coded iLSI perfusion map above the V2+V3 skin surface area at the time-point of fluoroscopically confirmed electrode positioning at the target area. For all 5 patients, this translated into a significant ipsilateral perfusion increase of 23.3±19% compared to baseline (*p=0.021 vs. baseline), which remained significantly greater than the contralateral perfusion change of 4.5±10% (p=0.31 vs. baseline; *p=0.0248 for ipsilateral vs. contralateral). In all patients, no complications or adverse events in regard to the RFA procedure or iLSI were observed.

Conclusion

Non-invasive iLSI during RFA for trigeminal neuralgia is technically feasible, safe and may serve as a tool for real-time confirmation of correct electrode positioning. The benefit of iLSI for optimization of electrode placement and the predictive value of perfusion changes regarding clinical efficacy will be investigated in a prospective trial.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P109

Multimodales Behandlungskonzept bei medikamentenrefraktärer MS assoziierter Trigeminusneuralgie

Multimodal surgical management program of multiple sclerosis-related medically refractory trigeminal neuralgia: A single center experience

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Objective

Trigeminal neuralgia (TN) is the most common craniofacial pain disorder that frequently affects patients with multiple sclerosis (MS). Common surgical treatments for MS associated TN include radiofrequency ablation (RFA) and subcutaneous trigeminal nerve field stimulation (sTNFS). Studies regarding therapies for MS-associated TN are limited; furthermore, these therapies are rarely offered in a center with multimodal surgical treatment.

Methods

In this retrospective study over two years, all patients who have been treated with surgical therapy were analyzed for pre- and postoperative pain intensity, frequency of attacks, complications, and side effects of therapy.

Results

The N=12 MS associated TN patients were with a mean age of 59 years significantly younger than patients with classic TN (p=0.037). MS association resulted in higher initial pain intensity in TN according to VAS scale compared to other types of TN (p=0.032). The mean VAS was reduced from 9 to 4 postoperatively. RFA was the most common therapy in N=10 patients. For MS-associated medically refractory TGN, RFA was the first line therapy compared to other types of TN (p=0.001). Patients with MS related TN received repeated surgical therapy significantly more often than other types of TN (p=0.026). N=1 (8.3%) patient had a surgical complication.

Conclusion

RFA remains the first-line intervention for MS-associated medically refractory TN, providing good pain reduction, but will most likely need to be repeated several times over the course of the patient's life.

Funktionelle Neurochirurgie I/*Functional neurosurgery I*

P110

Vorhersage von Komplikationen bei Mikrovaskulärer Dekompression von Spasmus Hemifazialis: welche Faktoren spielen eine Rolle?

Predictors of complications in Microvascular decompression for hemifacial spasm!

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Objective

Microvascular decompression (MVD) is the operative procedure adopted and accepted as curative for hemifacial spasm (HFS). Several potential risks or complications might accompany the procedure. We present the different complications that might accompany the operation, their etiology, and recommended strategies to tackle them.

Methods

Our prospectively maintained database for MVD was retrospectively reviewed. Relevant demographics, patient related data, operative technique, outcome, and different complications were extracted. Descriptive analysis as well as both uni- and multivariable analyses for the factors that might influence the seventh, eighth and lower cranial nerves were performed.

Results

Favorable outcome 12 months after surgery exceeded 90%. Mean follow-up period (SD) is 4.3 (3.2) years. Immediate complications reached 18.8%. Complications persisted only in 7.14% and included persistent hearing affection (5.95%) and residual facial palsy (HB 2-3) (<1%).

Transient complications included CSF fistulae (3.10%), lower cranial nerves affection (3.81%), meningitis (0.71%), and brainstem ischemia (0.24%). One patient died due to herpes encephalitis. Inferential statistics declared that immediate disappearance of the spams and male gender are correlated with postoperative facial palsy. Compressions involving VA and AICA can predict postoperative hearing deterioration and VA compressions could lead to postoperative lower cranial nerves affection.

Conclusion

Despite safety and effectiveness of MVD for treating HFS, proper discussion of the complications with the patient should take place. Optimal intraoperative positioning, sharp arachnoid dissection, and endoscopic visualization under facial and auditory neurophysiological monitoring are the corner stones for a safe MVD.

Funktionelle Neurochirurgie II/*Functional neurosurgery II*

P111

Diagnostischer Wert der rahmenbasierten stereotaktischen Biopsie im Zeitalter molekularer Neuropathologie: Eine Querschnittsstudie

The diagnostic value of frame-based stereotactic biopsies in the age of precision oncology: A cross-sectional study

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Objective

Stereotactic frame-based biopsies only deliver a limited amount of tissue for neuropathology studies. With the increasing role of molecular genetics in the diagnostics of intracranial lesions, sufficient tissue for sequencing studies is of paramount importance. This study explored the rate of successful diagnosis after stereotactic frame-based biopsies of intracranial lesions in a high-throughput neurooncology center.

Methods

145 consecutive patients undergoing frame-based stereotactic biopsies in 2020 and 2021 at our neurosurgical department were included in this retrospective analysis. Aspects of histological and molecular (methylomics, panel-sequencing) neuropathology analysis in addition to clinical and radiological variables were analyzed. Cases were classified as conclusive, likely-conclusive (sufficient diagnosis with non-satisfying sequencing information), and inconclusive neuropathological diagnosis.

Results

Of 145 cases analyzed, astrocytic tumors were suspected in n= 94 (67%) of patients. In n= 136 cases (94%), a conclusive diagnosis was possible. For 3 cases (2%), diagnosis was established with missing molecular data due to insufficient DNA. In 6 cases (4%), a non-conclusive (tumor) diagnosis was met, with 5 cases showing an insufficient amount of DNA. Diagnoses comprised mainly WHO 4 glioblastomas (56%), WHO 3 gliomas (2%) in addition to WHO 1 and 2 gliomas (n=7, 5%), CNS lymphomas (n=23, 16%), inflammatory diseases (n=10, 7%) and normal or reactive tissue (n=3, 3%). Methylomics were pivotal in providing an integrated diagnosis in 52% of tumor cases (panel sequencing in n=28, 30% of tumors). In a univariate analysis, insufficient DNA was associated with an insufficient diagnosis or a diagnosis with missing molecular data ($p<0.001$). Analyses of planned and implemented trajectories of cases with insufficient DNA and/or non-conclusive diagnosis or diagnosis without molecular data revealed that areas of interest within the lesion were reached in 15 out of 16 cases

Conclusion

Albeit its delivery of a limited amount of tissue, stereotactic frame-based biopsies bear an excellent histopathological and molecular genetic diagnostic yield, with rare cases of missing molecular data or rarely insufficient diagnosis. Given the proven surgical precision of biopsy trajectories, optimizing the cellular and DNA content of specimens might enhance their diagnostic utility even further.

Funktionelle Neurochirurgie II/*Functional neurosurgery II*

P112

Kegelstrahl-CT-Registrierung von rahmenbasierten stereotaktischen Biopsien
Cone-beam CT registration of frame-based stereotactic biopsies

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Objective

Computed tomography (CT) is the standard of care for registration in frame-based stereotactic procedures. Meanwhile cone beam CT capable devices find their way in multidisciplinary hybrid operating rooms. We hereby report our experience with cone-beam CT in registration for stereotactic biopsies.

Methods

16 candidates for stereotactic biopsy underwent registration using cone beam CTs by the Siemens Pheno Artis and a Fischer Revison-U open ceramic stereotactic ring. The registration and trajectory planning was done by the Brainlab iPlan Software. As a historic group 11 patients with conventional CT based registration were analysed.

Results

In all 16 patients, the registration could be completed using the cone-beam CT. Here, the latter 10 patients received a 360 degree large volume protocol to enlarge the field of view (FOV). The median procedural time in the cone beam registration group compared to the conventional CT registration was 1.85h vs. 2.28h, respectively (p=0.0092). Three patients also received a cone beam CT scan to rule out biopsy-associated complications.

Conclusion

Cone-beam CT by pheno artis is capable for frame based stereotactic registration. Procedure time can be saved through on-site registration in a hybrid operating room.

Funktionelle Neurochirurgie II/*Functional neurosurgery II*

P113

Aktiv krümmbare Kanülen für die stereotaktische Neurochirurgie – erste Schritte in einem interdisziplinären Ansatz

Active curved cannula in stereotactic neurosurgery – First steps in an interdisciplinary approach

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Objective

Neurosurgical stereotactic procedures are planned and performed with straight trajectories. For the insular or pineal region, or in patients with a certain degree of brain atrophy, alternative approaches using curved trajectories to the target would be useful. In a collaborative DFG-project, engineers, neurosurgeons, and mathematicians investigate the potential application of an actuation system for curved cannulas in stereotactic neurosurgery with concentric tube continuum robots (CTCRs). The authors present the development of a CTCR platform for use in combined engineering and medical research.

Methods

A system for mechanical actuation of the CTCR allowing an easy exchange of tubes, precise actuation at the tubes" base and precise measurements of the robot"s backbone w.r.t. time were used. Validation was performed with a photogrammetric measurement system. Target precision and follow-the-leader-deviations by movements of the cannulas was assessed. For a set of automatically planned configurations by numerical optimization, the real robot behaviour was compared to state-of-the-art models of the elastostatic behaviour. To investigate the precision of target accuracy in a neurosurgical setting, metal artifacts of the actuation system and the nickel-titanium curved cannulas within predefined targets were assessed in a CT-device using a stereotactic head model. Further, a porcine brain cadaver model was used.

Results

The actuation system"s artifacts did not disturb the image quality of the region of interest. CT-scans identifying the conduct of the curved cannula within the brain parenchyma did not show signs of marked tearing of the porcine brain, but a higher degree of interfering artifacts of the cannula was found increasing with the amount of porcine cadaver tissue surrounding the cannula tip. However, despite optimal target point accuracy in the planned configurations by numerical optimization, first practical applications of curved cannulas had a target point deviation of up to 4 mm.

Conclusion

While there is significant progress from a theoretical point of view particularly in mechanical engineering and mathematic modeling, a medical application of CTCRs is still in its infancy. Detailed studies addressing the actuation system"s precision at the target point in a physical model as well as the effect and potential damage on brain parenchyma by the deviation of the cannula within the parenchyma are needed.

Funktionelle Neurochirurgie II/*Functional neurosurgery II*

P114

Ein höherer BMI korreliert mit einem ungünstigerem postoperativen Outcome nach Hypoglossus Nerven Stimulation bei Obstruktiver Schlaf Apnoe.

Increased BMI correlates with less favorable postoperative outcomes after hypoglossal nerve stimulation for obstructive sleep apnea

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Objective

Obstructive sleep apnea (OSA) is associated with high morbidity. Hypoglossal nerve stimulation has become a new treatment strategy for OSA, demonstrating good success rates. Beyond predefined inclusion and exclusion criteria, no precise data are available enabling individual preoperative risk assessment. Here, individual patient factors presumably affecting the outcome of hypoglossal nerve stimulation were analyzed to improve preoperative risk stratification.

Methods

Fourteen patients treated with unilateral hypoglossal nerve stimulatior implantation (Inspire Medical Systems, Inc, Maple Grove, Minnesota) were analyzed retrospectively. Assessed risk factors included: hypertension, diabetes mellitus, depression, smoking, alcohol consumption, body mass index (BMI), and disease duration. Treatment success was defined as a reduction in the postoperative apnea-hypopnea index (AHIpost) to ≤ 20 events/h, with a relative reduction of at least 50% compared to baseline. Statistical analysis was performed using unpaired t-test, pearson correlation, and exact fisher test.

Results

A significant reduction in preoperative AHI to AHIpost was observed in all patients (*46.33 ± 10.62 vs. 16.00 ± 5.87; p<0.0001*). BMI correlated significantly with AHIpost scores *(95% CI 0.1519 to 0.8974; p=0.018*). Based on predefined criteria, significant treatment success was observed in 50% of patients. Compared with the "*responder group*", "*excellent responders*" demonstrated a significantly higher BMI (*95% CI 0.4393 to 6.504; p<0.05*). Diabetes (*p=0.66*), hypertension (*p=0.61*), disease duration (*p=0.51*), smoking (*p=0.41*), depression, and alcohol consumption (*p=0.32*) were not significantly associated with AHI differences.

Conclusion

Individual risk stratification of patients may contribute to a better outcome and associated patient satisfaction. Our results show that BMI may represent an independent risk factor regarding the response to hypoglossal nerve stimulation. Patients who benefited less from therapy demonstrated a significantly higher BMI than "excellent responders". Among the other risk factors assessed, there appears to be a differential impact concerning AHI reduction, although not statistically significant. Predefined eligibility criteria seem therefore to allow favorable outcome-based selection, as otherwise, postoperative AHI values may remain increased despite a significant reduction.

Funktionelle Neurochirurgie II/*Functional neurosurgery II*

P115

Weniger ist mehr - Die 2-Schnitt Methode der Implantation eines Systems zur Hypoglossus Stimulation - eine retrospektive Auswertung und Vergleich mit der 3-Schnitt Methode hinsichtlich der Atemsensorkurve

Less is more - Retrospective analysis of the two-incision implantation technique for hypoglossal nerve stimulation and comparison of respiratory sensing lead curves against the three-incision technique

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Objective

Breathing-synchronised hypoglossal nerve stimulation is a treatment option for suitable patients with severe obstructive sleep apnea. The classical implantation technique requires three incisions: anterior submandibular to place the stimulating electrode on the hypoglossal nerve, subclavicular to place the impulse generator and on the lateral chest wall to place the sensor lead. More recently, a two incision technique has been propagated whereby the sensor lead is placed deeper to the IPG pocket. Our department switched to the 2-incision technique in May 2021 and we set out to compare the two methods in respect to the generated breath curves at implantation and clinical follow-up parameters.

Methods

Cases operated between October 2020 and September 2022 were included. Parameters considered included age, gender, BMI, OR time, positioning of the sensor lead, preoperative Apnea-Hypopnea Index (AHI) and Epsworth Sleepiness Scale (ESS). The generated breath curves were categorised by an independent expert blinded to the surgical technique into "good" and "satisfactory" curves regarding conduciveness to optimal stimulation.

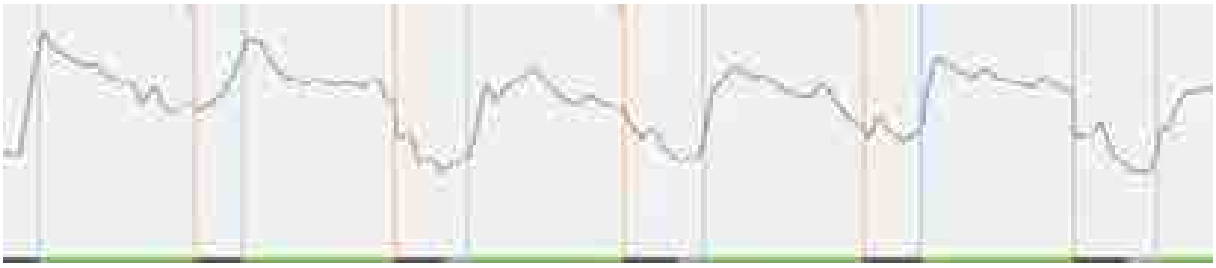
Results

24 patients were included. 5 of these were operated with the 3-incision technique. There were no significant differences in the recorded parameters among the two groups. The expert opinion on the breath curves did not vary between groups. Mean OR time was marginally shorter in the 2-incision group by 4% (138.2 minutes for the 2-incision vs. 144 minutes for the 3-incision group). This might however be attributed to increasing surgeon expertise over time.

Conclusion

The 2-incision technique generates breath curves at par with those generated with 3-incision implants. The limited patient data collected in this analysis suggests the OR-time can be reduced using the 2-incision technique. There were no cases of postoperative infection in our patient group but it can be postulated that a 2-incision implant might have a lower risk of infection due to the reduced wound surface.

Abb. 1



P116

Die Stimulation des Nervus hypoglossus zur Behandlung der obstruktiven Schlafapnoe korreliert mit einer Reduktion von Depressionssymptomen

Hypoglossal nerve stimulation for treatment of obstructive sleep apnea correlates with reduction of depression symptoms

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Objective

Obstructive sleep apnea (OSA) remains a highly prevalent disease with substantial morbidity and mortality. Hypoglossal nerve stimulation has shown to be a promising therapeutic approach for patients that respond insufficiently to standard treatment with continuous positive airway pressure (CPAP). Former studies have proven good effects of nerve stimulation on objective outcome parameters like Apnea-Hypopnea Index, whereas more information is needed regarding the impact on mood and global quality of life.

Methods

A single-center prospective analysis of 10 patients undergoing surgery for unilateral hypoglossal nerve stimulator implantation (Inspire Medical Systems, Inc, Maple Grove, Minnesota) between 2020 and 2022 was performed. All participants included underwent examination with two questionnaires at baseline prior to surgery and at follow up six months after activation of the stimulator: the Becks Depression inventary (BDI 2) for mood assessment, where lower scores indicate less depression symptoms, and the Quality of Life Scale questionnaire, where higher scores indicate more favorable outcomes.

Results

There was a reduction of the mean score in the Becks Depression inventary from 16.5 (165/10) prior to hypoglossal nerve stimulation to 10.6 (106/10) at follow up visits, indicating a relative reduction of 36%. A small effect was observed in the analysis of the Quality of Life Scale questionnaire: The average score of 79.2 showed an increase to 80.9 points.

Conclusion

Treatment of OSA with hypoglossal nerve stimulation does not only improve objective outcome parameters but is also associated with improvement of mood in a six month period after implantation.

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Lokal induzierter Hörverlust durch intracochleäre Neomycin-Injektion bei juvenilen Ratten führt zu Hyperaktivität und ausgeprägten Spielverhalten, verbunden mit gestörtem strategischen Lernen.

Hearing loss after intracochlear neomycine-injektion in juvenile rats leads to hyperactivity and pronounced play-fighting, together with disturbed strategic learning

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Objective

In children, hearing loss has been associated with hyperactivity, disturbed social interaction, and cognitive deficits. Whether hearing loss is causal for these disturbances, or whether the dynamic interplay with deficient acquisition of spoken language and speech understanding plays a role, is unknown. To investigate the effect of hearing loss on behavioral deficits in a confined setting, especially in the absence of language which may act as confounding factor, we here tested the impact of hearing loss in juvenile rats on motor, social, and cognitive behavior.

Methods

In juvenile (postnatal day 14) male Sprague Dawley rats hearing loss was induced under general anaesthesia with intracochlear injection of neomycin (n=13). Sham-operated (n=8) and naive rats (n=8) served as controls. One week after surgery auditory brainstem response (ABR) -measurements verified hearing loss after intracochlear neomycin-injection, respectively intact hearing in sham-operated and naive controls. Thereafter, all rats were tested for locomotor activity (open field) and coordination (Rotarod), as well as for social interaction during development in weeks 1, 2, 4, and 8 after surgery, followed by training and testing for spatial learning and memory (4-arms baited 8-arms radial maze test).

Results

In the open field deaf rats moved faster and covered a greater distance than sham-operated and naïve controls (both $p<0.05$). The motor coordination on the Rotarod was not disturbed in deaf rats ($p>0.05$). During social interaction, deaf rats showed significantly more play fighting during development ($p<0.05$), whereas other aspects of social interaction, such as following, were not affected. Learning the radial maze test was not disturbed in deaf rats ($p>0.05$), but retesting after eight weeks indicated a long-term memory deficit.

Conclusion

Hearing loss in juvenile rats leads to hyperactive behavior and pronounced play-fighting during development, together with deficits in long-term memory, suggesting a direct link between hearing loss and behavioral deficits. This model offers the opportunity for deeper investigation of developmental deficits resulting from hearing loss without language as potentially confounding factor.

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Die kabelgebundene Aufzeichnung neuronaler Aktivität hat keinen Einfluss auf die Leistung von Ratten in einem hoch anspruchsvollen Aufmerksamkeitsparadigma

Cable-bound recording of neuronal activity does not affect rat`s performance in a highly demanding attentional paradigm

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Objective

In neuroscience, rodent models are used to study fundamental questions of neuronal information processing. For this purpose, electrodes are intracranially implanted and secured by headstages to allow cable-bound recordings in behavioral paradigms, which may cause motor restraint and stress with possible impact on animal`s test performance. We were interested whether intracranial implantation of electrodes and first cable connection for recording of neuronal activity would affect rat`s performance in a highly demanding cognitive task, the three-tone auditory oddball paradigm. Furthermore, event related potentials (ERPs) were analyzed to detect potential motion-related artefacts attributed to cable-bound recordings in free moving rats.

Methods

Rats (n=9) were trained in a three-tone auditory oddball paradigm, where rats have to respond by nose poke to a rare target tone (5 kHz, rewarded by a casein pellet), while ignoring a rare distractor (1.5 kHz) and frequent standard tone (3 kHz). After reaching a predefined success criterion of correct responses to the target tone and correct rejection of the standard and distractor tones (80%, each), electrodes were stereotactically implanted in the medial prefrontal cortex (mPFC) under general anesthesia and perioperative pain control. After one week recovery from surgery, rats were retrained for criterion in the oddball paradigm for evaluation of the effect of first cable connection on rat`s performance and recording of neuronal activity.

Results

One week after surgery, the response to the target tone was significantly reduced for two days ($p<0.05$), while reaction time was not affected. Furthermore, false pokes to the distractor tone was enhanced on days two and three after surgery ($p<0.05$), while rejection of the standard tone was not affected. First cable connection for neuronal recording did not affect the hit rate, the reaction time and the number of false pokes. Analysis of the ERPs did not reveal substantial motion-related disturbances of neuronal recordings.

Conclusion

Together, intracranial surgery and cable-bound recording of neuronal activity does not substantially affect rat`s performance in behavioral paradigm with high cognitive load and allows analysis of ERPs with high quality

Funktionelle Neurochirurgie II/*Functional neurosurgery II*

J-SBNC016

Masseterisch-Gesichtsanastomose: Ein Bericht über drei Fälle
Masseteric-Facial Anastomosis: A Report of Three Cases

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Objective

The pathways of the facial nerve are variable, and knowledge of that is essential. The worst impact caused by facial paralysis is related to quality of life, especially regarding the self-esteem and social acceptance on the part of the patients, leading to social isolation and disruption on their mental health. The objective of this report is to present a literature review and three cases of Masseteric-Facial Anastomosis.

Methods

We performed a literature review of papers related to surgeries for masseteric-facial nerve anastomosis and compiled the results in table; then, we compared these data with those obtained from our cases.

Results

A 33-year-old female patient, with a stage-T3 acoustic neurinoma, presented with a moderate dysfunction (grades II to III) according to the House-Brackmann (HB) Facial Nerve Grading System, after 9 months, she underwent another elective surgery for masseteric-facial nerve anastomosis, which resulted in full recovery of function four months postoperatively. A 43-year-old male patient, with a stage- T4B trigeminal schwannoma, underwent a resective surgery and presented grade-VI dysfunction according to the HB scale, after six months of the resective surgery, the patient underwent a hypoglossal-facial anastomosis surgery to improve facial function, which was not possible due to the technical conditions. And a female patient with a stage-T4A acoustic neurinoma presented grade-IV dysfunction according to the HB scale, two months postoperatively, presented grade-III paralysis on the HB scale, being able to close the eyes more and smile somewhat more widely, expressing excellent surgical results.

Conclusion

The masseteric nerve is the one that shows the best prognosis among all the cranial nerves that could be used, but it is also necessary to perform well the surgical technique to access the facial branch and consequently achieve a better masseteric-facial nerve anastomosis.

Abb. 1

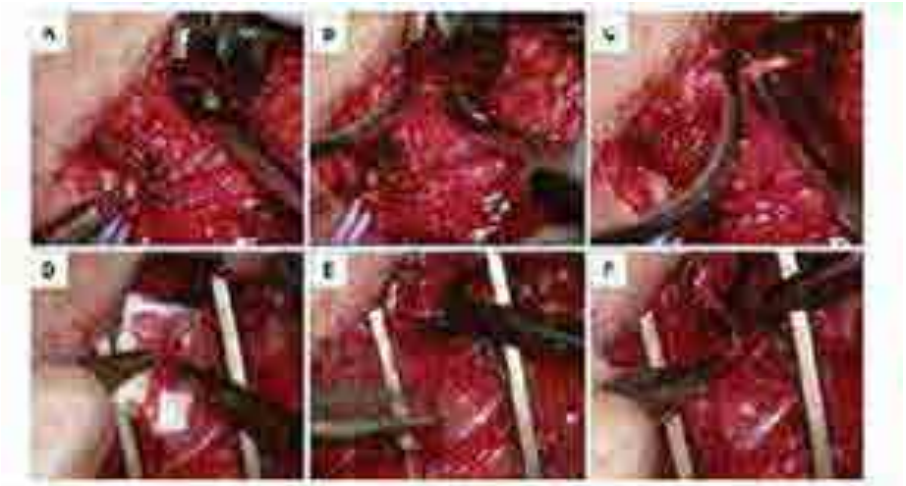

Abb. 2

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P119

Sicherheit von transkranieller Magnetstimulation in neurochirurgischen Patient*innen
Safety of navigated transcranial magnetic stimulation in neurosurgical patients

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Objective

Navigated transcranial magnetic stimulation (nTMS) can be used for preoperative planning as well as postoperative therapy in neurosurgical patients. While the method is generally considered safe, recent studies in healthy subject suggest a potential impact on the activity of the sympathetic nervous system (SNS). The aim of the present study was to assess the safety of different, commonly used nTMS protocols by investigating the impact on the SNS, as well as patient reported anxiety and discomfort.

Methods

15 healthy controls and 15 neurosurgical patients underwent a single session of nTMS-based mapping. To address the safety of TMS, we recorded an electrocardiogram, electrodermal activity, state anxiety as measured with the STA-I/ STOA and perceived discomfort during the measurement. Changes in these outcomes were compared between baseline and a follow-up immediately after stimulation. In case of a significant effect of nTMS, we also assessed the duration of the effect by comparing the baseline with a second follow-up 15 minutes later.

Results

Results of a linear mixed model analysis showed a main effect of nTMS with a decrease in heart rate and correspondingly an increase in inter-beat intervals immediately after the stimulation. This effect did not last until the second follow-up. Independent of the nTMS, patients presented with a higher heart rate and lower inter-beat interval compared to healthy subjects. Patients also showed a reduced electrodermal activity, visible in a smaller skin conductance response amplitude and skin conductance level. No significant changes in state-anxiety values were observed during nTMS. All subjects tolerated the stimulation well, reporting no significant discomfort or pain.

Conclusion

NTMS is safe to use in neurosurgical patients as it does not introduce lasting changes in sympathetic nervous system activity or anxiety. Still, minor short-term changes of heart rate parameters were observed.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P120

Machbarkeitsanalyse hinsichtlich des intraoperativen neurophysiologischen Monitorings bei der Resektion extramedullärer Rückenmarkstumore im höheren Lebensalter

Feasibility of Multimodal Intraoperative Neurophysiological Monitoring for Extramedullary Spinal Cord Tumor Surgery in Elderly Patients

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Objective

Extramedullary spinal cord tumors (EMSCTs) are mostly benign tumors which are increasingly diagnosed and operativeley treated in the higher age of life in the context of an aging western population. While there are hints that monitoring of both MEPs and SSEPs could be influenced by age and age-related comorbidities, no study has ever systematically evaluated the feasibility and value of multimodal IONM for EMSCT surgery in elderly patients.

Methods

We retrospectively evaluated all patients with microsurgical EMSCT resection under continuous multimodal IONM with SSEPs, MEP and EMG between 2016-2020. Epidemiological, clinical, imaging and operative/IONM records as well as detailed individual outcomes were analyzed and compared for the cohort</>65yrs.

Results

Mean age was 45yrs in cohort<65yrs (n=109) and 76yrs in cohort>65yrs (n=64), while baseline and operative characteristics (sex, BMI, comorbidities, symptoms, tumor features and operative duration/blood loss) did not sign. differ between both cohorts. Mean baseline SSEPs' latencies (left-right average as surrogate marker) were sign. higher in the cohort>65yrs for both median nerve (20.9ms vs. 22.1ms; p<0.01) and tibial nerve (42.9ms vs. 46.1ms; p<0.01) with no sign. differences for SSEPs' amplitudes. Furthermore, stimulation intensity to elicit intraop. MEPs was sign. higher in the cohort>65yrs (left-right-averaged quotient of ID1-muscle to abductor-hallucis-muscle as surrogat marker; 1.6 vs. 2.1, p<0.001). Intraoperatively, SSEPs and MEPs monitoring were feasible in 99%/100% and 99%/98% for the cohort</>65yrs with no sign. differences in rates for significant IONM-changes during surgery (SSEPs: 0.9%/1.6%; MEPs: 2.8%/4.7%). Postoperatively, 3.7% of the patients had a transient new motor deficit (permanent in 2.8%) and 3.7% a new sensory deficit (permanent in 0.9%) for the cohort<65yrs, while 4.7% had a transient new motor deficit and 4.7% a new sensory deficit (permanent in 1.6%) in the cohort>65yrs (no sign. differences between both cohorts). Sensitivity of IONM was 29%/50%, specifity 99%/98%, PPV 67%/75% and NPV 95%/95% for the cohort</>65yrs. Overall, age was no negative risk factor for IONM-feasibility or rate of significant IONM-changes in regression analysis.

Conclusion

Multimodal IONM is both feasible and reliable for EMSCT surgery in elderly patients. An age-related prolongation of SSEPs" latencies and demand for higher stimulation intensities for MEPs' elicitation has to be considered.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P121

Selektive und unselektive Stimulation in transkraniell motorisch evozierten Potenzialen zur Überwachung der Integrität des kortikospinalen Traktes während der operativen Behandlung von supratentorillen Tumoren

Selective and unselective stimulation in transcranial motor evoked potentials for monitoring of the integrity of corticospinal tract during surgery for supratentorial tumors

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Objective

Evaluation of transcranial motor evoked potentials (MEP) is one of the established methods to monitor the integrity of the corticospinal tract during surgery for supratentorial tumors. One of the pitfalls of this methods, however, is the risk of bypassing the lesion through high or unselective stimulation, which might cause the stimulation to occur at the level of brain stem. The aim of this study is to differentiate between current intensity (threshold level) needed for a selective stimulation of corresponding corticospinal tract and the one that lead to a stimulation at the level of the brain stem

Methods

We prospectively included patients who were operated on for resection of a brain tumor without preoperative motor deficit between 2018 and 2022. After induction of anesthesia and prior to skin incision, corkscrew electrodes were installed on the scalp and MEP were elicited using each of the following combination: C1-C2, C3-C4 and C4/C3-Cz (according to International 10–20 system) and recorded bilaterally from musculus abductor pollicis brevis (APB) and threshold level was determined separately for each muscle for each of the electrode combination. The stimulation was deemed to occur at the level of brain stem when MEP could be elicited from the ipsilateral APB.

Results

56 patients with mean age of 60 years were included. MEP could be recorded in all patients. Mean threshold level for contralateral APB was 43 mA for C3-C4, 55mA for C4/C3-Cz and 65mA for C1-C2, $p<0.001$. Mean threshold level for ipsilateral APB was 132 mA for C4/C3-Cz, 128 mA for C1-C2 and 92 mA for C3-C4, $p<0.001$. Mean ratio of threshold level of ipsilateral APB to that of contralateral APB was 200% (max. 280%, min. 120 %) for C1-C2, 217% (max. 288%, min. 133%) for C3-C4 and 248% (max. 364%, min. 140% for C4/C3-Cz), $p<0.001$.

Conclusion

C4/C3-Cz was the most selective electrode combination for eliciting contralateral MEP. The risk of electrical stimulation to take place at the level of the brain stem seems to start from a 120% increase in current intensity comparing to the threshold level of contralateral muscle.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P122

Überwachtes maschinelles Lernen zur Identifizierung von Muskeln anhand von MEP-Spuren - ein Proof-of-Concept-Design

Supervised machine learning methods to identify muscles from MEP traces - a proof of concept design

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Objective

Even for an experienced neurophysiologist, it is challenging to look at a single, unlabeled, raw motor evoked potential (MEP) and to identify the corresponding muscle. The clinical utility might be limited, however, this is an excellent model to evaluate machine learning paradigms to intraoperative neurophysiologic monitoring (IOM) data. Here we demonstrate that supervised learning is feasible on MEPs without preselection, preprocessing or normalization of the data.

Methods

MEP data of 6 patients undergoing supratentorial surgeries was used for classification. We selected two muscles from upper extremities ((Extensor brachioradialis (EXT) and abductor pollicis brevis (APB)) and two from lower extremities (Tibialis anterior (TA) and abductor halluces (AH)). A supervised clustering method, the k-nearest neighbor (k-NN) classification, was used to categorize MEPs according to the four recorded muscles. We split training and testing data for every trial into 75%-25% and computed the accuracy across 10 classifications. To improve the k-NN, we included a neighborhood component analysis (a metric learning method) and demonstrated increased accuracy. We performed classifications for each patient and across patients within each extremity.

Results

Classifying MEPs within the upper extremities (EXT and APB) or lower extremities (TA and AH) of individual patients, the accuracy reached between 85-94%. When pooling the MEPs from all six patients together, the accuracy was 86%. Classifying MEPs of all four muscles simultaneously, the accuracy dropped between 67-85% on individual patients and 78% on the combined data.

Conclusion

In a proof of concept, we show that MEPs may be reliably classified by a supervised algorithm with surprisingly high accuracy without any preprocessing or normalization of the data. This is a first step to evaluate the quality of machine learning algorithms to predict MEP alterations. Preprocessing steps may further improve the accuracy of the classification.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P123

Niedrig-frequente repetitive transkranielle Magnetstimulation in Patient*innen mit motorischen Defiziten nach Resektion eines Gehirntumors: Eine randomisierte, doppelt-verblindete, sham-kontrollierte Studie

Low-frequency repetitive transcranial magnetic stimulation in patients with motor deficits after brain tumor resection: a randomised, double-blind, sham-controlled trial

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Objective

Surgical resection of motor eloquent tumors poses the risk of causing postoperative motor deficits which leads to significantly reduced quality of life in these patients. Currently, rehabilitative procedures are limited with physical therapy being the main treatment option. The present study investigated the efficacy of repetitive navigated transcranial magnetic stimulation (rTMS) for treatment of motor deficits after supratentorial tumor resection.

Methods

30 patients with a worsening of upper extremity motor function after tumor resection were recruited in this randomised, double-blind, sham-controlled trial. They were randomly assigned to receive rTMS treatment (1Hz, 110% RMT, 15 minutes, 7 days) or sham stimulation to the motor cortex contralateral to the lesion followed by physical therapy. Motor and neurological function as well as quality of life were assessed directly after the intervention, one month and three months postoperatively.

Results

There was no significant difference between both groups in the primary outcome, the Fugl Meyer score three months postoperatively (Group difference [95%-CI]: 5.05 [-16.0; 26.1]; p=0.631). Patients in the rTMS group presented with better hand motor function (BMRC scores) one month postoperatively. Further, a subgroup of patients with motor eloquent ischemia showed better NIHSS scores in the rTMS compared to the sham condition at all timepoints.

Conclusion

Low-frequency rTMS facilitated the recovery process in selected subgroups of patients, but not in the full cohort. Long-term motor deficits were not impacted by rTMS. Due to the reduced life expectancy in this patient group a shortened recovery duration of functional deficits can still be of high clinical significance.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P125

Tractometrie zur Bestimmung der hemisphären Dominanz bei Hirntumorpatienten
Tractometry to determine language hemispheric dominance in brain tumour patients

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Objective

Identifying language hemispheric dominance prior to surgery is of great interest for neurooncological and epilepsy surgery. Due to the invasive nature of the Wada test, efforts have been made do establish reliable non-invasive alternatives, primarily using functional MRI. Recently, it was shown that the white matter tracts also reflect hemispheric dominance, in particular the arcuate fascicle. In this study, we assess to which extent tractometry, i.e. the study of microstructural characteristics along the tracts, of the language network can inform on hemispheric dominance in brain tumour patients.

Methods

From a consecutive monocentric cohort of 74 patients with previously untreated supratentorial glioblastoma scheduled for surgery, 13 patients were included in this analysis who showed no tumour-related interruption of any major language network tracts by tumour. All patients received diffusion weighted images (DWI). For hemispheric dominance assessment, the Edinburgh Handedness Inventory (EHI) was used as a proxy. DWI were acquired and processed using standard protocols and procedures, culminating in the diffusion tensor estimation and microstructural metrics calculation, like fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). Tractography reconstruction and tractometry were performed using TractSeg. Bilateral tracts of interest included: arcuate fascicle (AF), third segment of the superior longitudinal fascicle (SLFIII), and uncinate fascicle (UF), of both hemispheres. Correlation analyses was conducted between the diffusion metrics and EHI scores along each tract segment.

Results

According to the EHI (median = 82, range [-100,100]), one patient was classified as purely left-handed, one ambidextrous and the others as majorly right-handed. No significant correlations between the EHI and any diffusion metric were found along the tract segments. However, when comparing the tract profile along the segments, the FA of the left AF showed a significantly different profile compared to that of the right AF, especially in the posterior segments. This is potentially due to the right-handed-biased cohort.

Conclusion

While significant correlations between diffusion metrics and handedness were not found, differences in the tract profiles across hemispheres were, which might be useful to assess hemispheric dominance. A multicentric confirmative analysis including left-handed patients is planned.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P126

Vergleich verschiedener Stimulationsmuster zur Identifizierung des primär sensorischen Kortex mittels Intraoperativer Optischer Bildgebung

Comparison of different stimulation paradigms for identification of primary sensory cortex with Intraoperative Optical Imaging

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Objective

Intraoperative Optical Imaging (IOI) is a marker free and non-invasive imaging technique that is able to visualize functional areas of the human cerebral cortex. In the past we evolved the method as a clinical tool for identification of the primary sensory cortex (PSC) during surgical interventions. The method is based on the detection of subtle changes in cortical optical properties with a camera systems. Those changes are induced due to stimulation of the specific function that should get visualized. Here, we are comparing two different stimulation patterns and their influence on the imaging results.

Methods

Measurements were performed on five patients that underwent surgical resection of lesions near the PSC (2 male, 3 female, median age 66 years). IOI was performed directly after craniotomy and exposition of the cortical surface. In each patient, two different electrical stimulation paradigms were applied on the median nerve. The first one consisted of alternating 30-second rest and 30-second stimulation trials over 9 minutes. In the second paradigm the trial times were shortened to 15 seconds for each trial whereas the overall recording time of 9 minutes was kept constant. To assess the quality of the calculated IOI activity maps, the mean level of activation (A_{act}) as well as a spatial signal-to-noise ratio (SNR) were calculated for each patient and compared between both paradigms.

Results

The results reveal that in 4 out 5 patients the activity maps created from 15-second stimulation pattern had a higher overall level of activation on sensory cortex ($A_{act15} = 0.38$ vs. $A_{act30} = 0.27$). On the other hand, the 15-second stimulation pattern also revealed in 4 out 5 patients a lower spatial SNR compared to 30-second paradigm ($SNR_{15} = 4.58$ vs. $SNR_{30} = 6.54$). This indicates, that the 15-second paradigm leads to a higher level of activation but a less localized and more widespread activity across different cortical regions. Therefore, the 30-second stimulation pattern is more suited for the purpose of the imaging method.

Conclusion

The results are leading to the conclusion, that the stimulation paradigm, consisting of 30 second trials, is better suited for identification of the PSC during the surgical intervention.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P127

Hirnimpedanzspektroskopie - Ein neues System zur intraoperativen Gewebedifferenzierung
Brain impedance spectroscopy - A technique for intraoperative tissue differentiation

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Objective

The electrical properties of biological tissue are characterized by its electrical conductivity and its relative permittivity. These tissue properties are highly relevant in, both, clinical and basic research contexts. Impedance measurements are expected to enable intraoperative differentiation between healthy and tumorous brain tissue in real time and without altering the characterized tissue. The application of these techniques to living human brain tissue has the potential to enhance intraoperative diagnostics.

Methods

We developed an experimental setup for intraoperative impedance measurements, consisting of an ISX-3 mini impedance analyzer (Sciospec Scientific Instruments GmbH, Bennewitz, Germany) and a custom made 4-point electrode with a tip size of 0.4x0.4 mm. We conducted brain impedance measurements on porcine brain in vitro as a proof-of-principle. Furthermore, we conducted experiments to investigate the pressure dependency of the measured impedance.

Results

In in vitro measurements, we were able to differentiate grey and white matter within our probe through significantly different spectral impedances. Contact pressure as a source of variation could be ruled out within physiological borders, i.e. realistic intraoperative contact pressures, by showing that the coefficient of variation in the measured impedance is under 3%. Further, we fit the measured impedances to an equivalent circuit model and compared the resistances of grey and white matter brain tissue based on the model parameters.

Conclusion

We could show that the influence of contact pressure on impedance measurements is very small compared to the difference between grey and white matter brain tissues and can be neglected in the investigated use case. Therefore, we could prove the practicability and usability of impedance measurements for intraoperative tissue differentiation.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

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Gliale Hirntumore in der konfokalen Laserendomikroskopie
Confocal laser endomicroscopy in glial tumors

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Objective

Surgical resection is the primary treatment option for malignant gliomas and needs to be efficient and safe. Confocal laser endomicroscopy is a tool to examine tissue directly without the need for fixation or staining.

We aim to analyze how different histomorphological features are visualized by confocal laser endomicroscopy solely based on autofluorescence and identify reliable diagnostic criteria to analyze glial matter and glial tumors with respect to cell of origin and malignancy that are independent of the examiner and their experience with confocal laser endomicroscopy.

Methods

We examined 125 glioma biopsies. Each specimen was first analyzed using a 670 nm confocal laser endomicroscope, then processed into hematoxylin and eosin stained frozen sections. All confocal images and frozen sections were evaluated for the following criteria: presence of white matter, grey matter or tumor; cellularity, nuclear pleomorphism, changes of the extracellular glial matrix, microvascular proliferation, necrosis and mitotic activity. Accuracy, sensitivity, specificity and positive and negative predictive values were assessed for each histomorphological feature. We compared differences in visualization of these features in tumor versus peritumoral tissue, astroglial versus oligodendroglial tumors and low-grade versus high-grade tumors.

Results

Diagnostic criteria to analyze cellularity, nuclear pleomorphism, changes of the glial matrix, vascularization and necrosis in glial tumors were identified.

These criteria proved useful in differentiation tumor from peritumoral tissue: Tumor was diagnosed with an accuracy of 91.2 %. Sensitivity was 94.17 %, specificity 77.27 %. The positive and negative predictive values were 95.1 % and 73.91 %, respectively. All criteria mentioned above differed significantly ($p=0.013$ or less each) in visualization in tumor and peritumoral matter. Oligodendroglial tumors showed significantly less nuclear pleomorphism in confocal laser endomicroscopy than astroglial tumors ($p<0.001$). Visualization of necrosis aids in the differentiation of low-grade and high-grade gliomas ($p<0.001$).

Conclusion

Autofluorescence-based confocal laser endomicroscopy proved not only useful in differentiation between tumor and brain tissue, but revealed useful clues to further characterize tissue without processing in a lab. Possible applications include improvement of extent of resection and safe harvest of representative tissue for histopathological and molecular genetic diagnostics.

Neurophysiologie, IOM, Bildgebung und Spektroskopie/*Neurophysiology, IOM, imaging and spectroscopy*

P129

Schnelle intraoperative Tumorerkennung von spinalen Tumoren mit stimulierter Raman-Histologie
Rapid intraoperative tumor detection in spinal tumors using stimulated Raman histolog

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Objective

Fresh frozen tissue samples and hematoxylin & eosin (H&E) staining are currently the gold standard for rapid intraoperative tumor analysis. Recent works have introduced machine learning based deep convolutional neural network (CNN) analysis of label-free stimulated Raman histology (SRH) samples as a simple, fast alternative for fresh frozen samples in cranial lesions, enabling the surgeon to acquire a result within minutes. Recently we developed a new CNN to distinguish tumor and non-tumor SRH-samples in intracranial lesions. This work aims to investigate whether this algorithm validated for intracranial tumors can be applied in spinal tumors as well.

Methods

Small human spinal tumor tissue samples (1-3mm3) for SRH were acquired parallel to the regular pathological assessment and squeezed onto a histological slide resulting in a flat tissue layer of max. 10 mm2. Random areas of 2x2 mm within the sample were chosen for SRH analysis and the CNN was run afterwards. The pathological diagnosis was made in a typical routine workflow. CNN-based predictions were compared to final pathological diagnosis.

Results

57 patients who underwent surgery for a spinal tumor were included. The samples included 18 different tumor entities. Of these, 136 SRH samples were generated, 7 were excluded for bad quality. The CNN correctly classified 17/18 entities as tumor/non-tumor, with an epidermoid cyst being the only non-tumor entity to be wrongly labeled as tumor. No sample was incorrectly labeled as "no tumor".

Conclusion

SRH based rapid intraoperative histological tissue sample assessment has great potential as a tool to generate fast histological feedback and to support intraoperative decision making. Together with the developed CNN this workflow can reliably detect the presence of tumor independent of tumor entity and conventional H&E frozen samples. Next to aiding the surgeon to achieve gross total resection, future developments could enable machine learning based tumor classification analogous to the classification CNN developed for intracranial lesions.

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Asservierung von biologischen Proben als Qualitätsindikator eines zertifizierten pädiatrisch-onkologischen Zentrums – die neurochirurgische Perspektive

Tumor sample collection as a quality indicator in a certified pediatric oncology center – the neurosurgical perspective

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Objective

Pediatric central nervous system (CNS) tumors require histological and molecular diagnostics to reach an integrated diagnosis. Molecular data is used for risk stratification of current therapies. Tumor samples are further needed for patient-specific experimental approaches. Thus extensive collection of samples is important, but requires substantial infrastructure and staffing. Here we review the experience at a pediatric oncology center certified by the Deutsche Krebsgesellschaft.

Methods

We report the results of an internal audit of neurosurgical performance with regard to intraoperative biological material collection from 2015 to 2019. Data was collected from electronic records in a retrospective anonymized fashion. Types of biological material collected intraoperatively were: a) tumor tissue obtained with grasping forceps, b) surgical aspirate obtained with filters from suction or ultrasound aspiration and c) 5ml EDTA blood samples. For technical reasons, cerebrospinal fluid and normal CNS tissue were rarely obtained during surgery and are thus not included in the audit. However, CSF specimens are routinely obtained by lumbar puncture approximately 14 days after surgery.

Results

In the audit period, 184 pediatric CNS lesions underwent resection or biopsy (17% pilocytic astrocytoma, 16% medulloblastoma, 15% high-grade glioma, 12% ependymoma, 40% other). Tissue for routine diagnostics was obtained in all cases, mostly along with ETDA blood samples, corresponding to SIOPE priority 1 (= highest). Tissue and/or surgical aspirate for internal and external research was obtained in 164 cases (89%), corresponding to SIOPE priority 2 (= highly important). In 107 cases (58%) tumor cell cultures were established, potentially enabling patient-specific treatment approaches

Conclusion

Biomaterial collection according to SIOPE categories 1 and 2 was achieved in 100% and 90% of neurosurgical operations within the framework of a certified pediatric oncology center. This should be regarded an essential prerequisite for precision medicine and access to new therapies. We consider biomaterial collection a neurosurgical quality indicator, which should be subject to active auditing and benchmarking.

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Molekulare Einteilung der H3F3A-Wildtyp, EGFR-mutierten WHO Grad 4 diffusen Mittelliniengliomen

Distinct molecular subclasses of H3F3A-wildtype, EGFR-altered pediatric-type diffuse midline gliomas WHO CNS grade 4

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Objective

Histone gene H3K27-altered diffuse midline glioma (DMG) are malignant tumors that occur in all age groups. In this study, we report comprehensive genomic profiling from *H3F3A*-wildtype, *EGFR*-altered DMG, as a distinct and newly recognized subset of pediatric-type DMG.

Methods

Tumors were profiled in the comprehensive genomic profiling (CGP) program at Foundation Medicine between 2013 - 2020. Information from pathology reports, histopathology review, and patient clinical data was assessed.

Results

We collected demographic and genomic data from 39 pediatric patients with *H3F3A*-wildtype, *EGFR*-altered HGG (17 females, 22 males; median age: 8.5 years, range 1-18 years). Female patients were younger at first diagnosis compared to male (median age 7 years vs. 10 years). All cases were microsatellite stable (MSS). The *EGFR*alterations consisted of 30 mutations and 9 amplifications. The mutations were distributed across the entire gene with no clear hotspot location. Our genomic data converged to identify three distinct molecular patterns. The first and most common group contained *TP53* mutations (n = 17, 43.5%), showed no association with patient sex (8 females, 9 males), contained *ATRX* mutations (n = 3) and *CDKN2A* deletions (n = 5); these tumors did not harbor pathogenic mutations in *TERT*p, *PIK3CA/PIK3R1, BCOR/BCORL1*, *STAG2*, or *SETD2*. The second group featured *TERT*p-mutant tumors (n = 10), were more common in males (70%), and often demonstrated additional mutations in *PIK3CA/PIK3R1* (n = 4), *BCOR/BCORL1* (n = 4), *CDKN2A*/B (n = 4), and *SETD2* (n = 2). The third group (n = 12) lacked *TERT*p and *TP53* mutations and had a heterogeneous spectrum of non-recurrent mutations, including one *CDKN2A/B* deletion.

Conclusion

We have identified three distinct molecular subclasses that defined specific genomic tumor subgroups in pediatric-type *EGFR* altered DMG. Overall, these data increase our understanding of the pathobiology of this DMG subset and can guide the design of clinical trials.

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Inflammatorisches Microenvironment in Medulloblastomen - eine Pilotstudie
Inflammatory microenvironment in medulloblastoma - a pilot study

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Objective

Medulloblastomas (MB) are the most common malignant primary brain tumors in children. The prognosis of patients diagnosed with these tumors varies greatly and is mainly dependent on molecular subgroups. The exact reasons for clinically distinct behavior of those groups are not yet know. Inflammatory microenvironment may contribute to local infiltration and metastasis as well as resistance to therapy. In this study, the impact of several immunohistochemical markers and the association with molecular subgroups was assessed in a cohort of children with brain tumors.

Methods

In this study, 27 tumor samples underwent tissue microarray (TMA) processing and subsequent immunohistochemical staining. The expression of GD2, CD276, EphA2, L1CAM and Her2 was assessed. Results of (epi)genetic testing and molecular subgroup classification were compared with immunostaining.

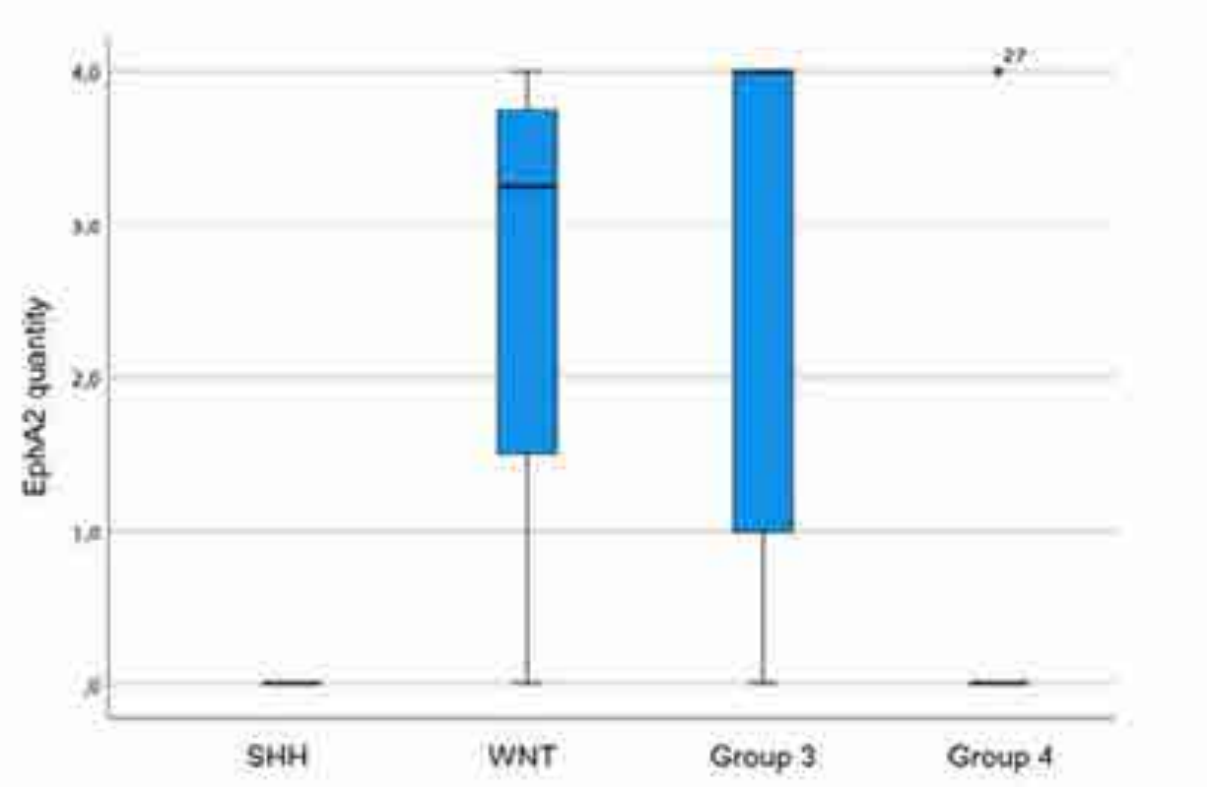
Results

TMA-based immunostaining yielded stable and repeatable results with a high throughput. WNT-MB as well as Group 3-MB showed significant expression of EphA2. CD276 is expressed in MB in all molecular subgroups. Thus this might serve as a good target for further evaluation.

Conclusion

TMA is an optimal tool for assessment of multiple antigens in large patients populations and samples. It is a cheap method with a high throughput and yields results consistent with literature on classic immunostaining. Expression of EphA2 might be associated with migratory properties in MB. Association to outcome has to be assessed in larger cohorts. CD276 is expressed universally in all molecular subgroups and might serve as a promising target for individualized therapy.

Abb. 1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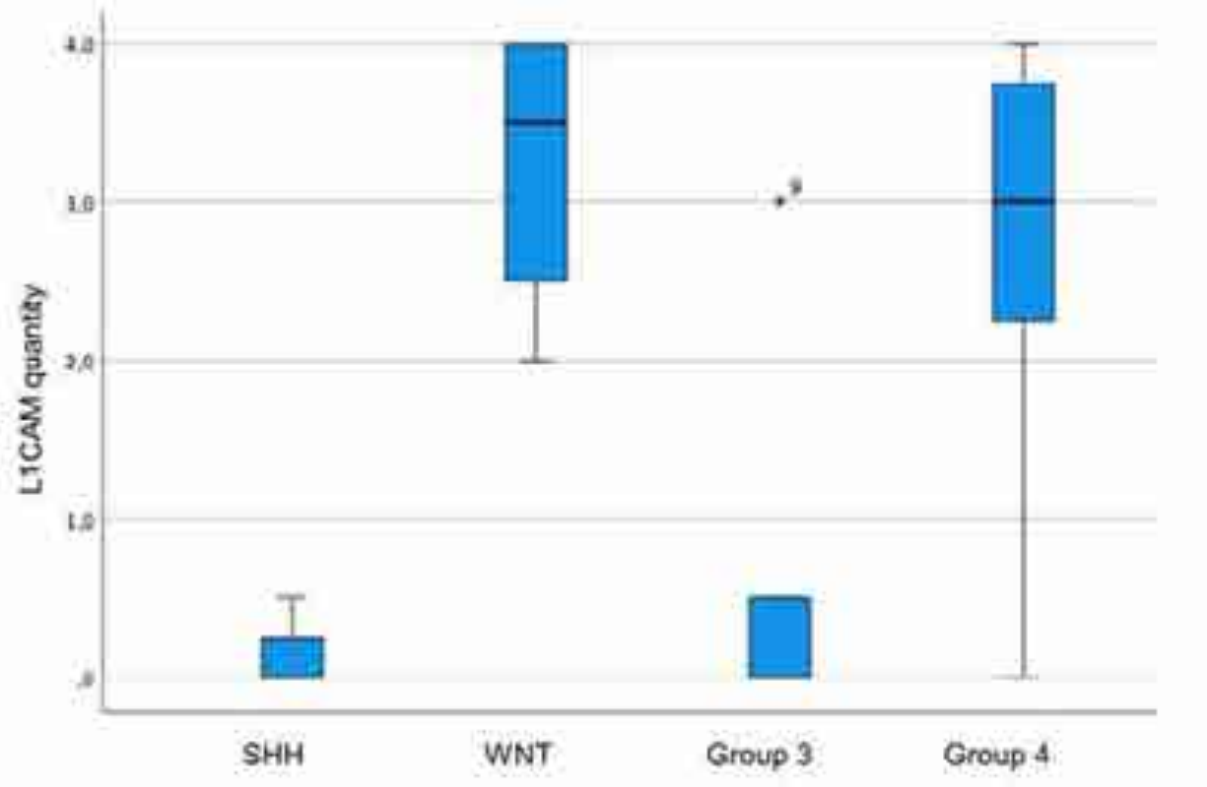
3,0
2,0
1,0
,0
27
SHH
WNT
Group 3
Group 4

Abb. 2


L1CAM quantity
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3,0
2,0
1,0
,0
9
SHH
WNT
Group 3
Group 4

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Fall-Kontroll-Studie zum Auftreten des postoperativen Fossa-posterior-Syndroms bei Kindern - abhängig von intraoperativen Faktoren?

Case-control study on the occurrence of postoperative posterior fossa syndrome in children - dependent on intraoperative factors?

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Objective

Posterior fossa syndrome (PFS) is a complex syndrome of great neurological impairment occuring most commonly after neurosurgical resection of infratentorial lesions in children. Literature reveals the histology of the lesion, midline location, infiltration of the brainstem or superior cerebellar peduncle associated with the development of an PFS. However, there is shortage of knowledge on the surgeon"s role and intraoperative factors in this context. Thus, we aimed to examine the association between intraoperative features and PFS.

Methods

The study population included pediatric patients at the University Medical Center Hamburg-Eppendorf, Germany, between 2013-2022 who had a space-occupying lesion in the cerebellum and required surgical therapy. Patients were included if they developed PFS after surgery. Controls were matched to cases for age months at diagnosis using coarsened exact matching. We fitted logistic regression models using weights assigned to the observations" stratum for each intraoperative variable using PFS (yes/no) as the outcome variable and case-control indicator variable as the independent variable adjusting for age months at diagnosis. As intraoperative features we examined the administration of dexamethasone, coagulative factors, mannitol, usage of preoperative CSF drain, either by ventricular drainage or by ventriculocisternostomy, the operative approach and the extend of resection.

Results

Of 168 eligible pediatric patients (mean age (SD) months 91.9 (62.4), female 38.8%), PFS occurred in 26 patients. We found a significant association between PFS and intraoperative use of dexamethasone (OR=3.73, 95% CI=[1.01, 13.82]), coagulation factors (OR=4.50, 95% CI=[1.02, 19.92]), and CSF drainage (OR=3.91, 95% CI=[1.19, 12.83]). Other features did not show any significant differences between the groups.

Conclusion

Despite the small sample size, the results suggest a relationship between the intraoperative procedure and the occurrence of PFS. Further studies are needed to investigate relevant homeostatic variables and possible influences of the intraoperative methods to name reversible and influenceable causes of PFS.

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Analyse der bihemisphärischen Sprachbeteiligung bei Kindern mit sprachassoziierten Läsionen mittels rTMS
Analysis of bihemispheric language involvement in children with language-associated lesions using rTMS

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Objective

Language dominance in the developing brain is the subject of current research and may vary widely across individuals. Previously, repetitive transcranial magnetic stimulation (rTMS) was used to examine language-involved cortical regions and to assess language lateralization in adults. However, only little is known about the use of rTMS to study plasticity of language function in children with language-associated lesions.

Methods

A consecutive prospectively collected cohort of 18 children with language-associated lesion underwent bihemispheric rTMS mapping prior to surgery (with 100 stimulation sites on each hemisphere). The evaluation of the speech mapping was performed by 2 experienced investigators with many years of rTMS experience in a consensus-based manner. Feasibility and side effects were documented as well as the error rate and error category of each hemisphere.

Results

Repetitive TMS mapping was feasible in all 18 patients (median age: 13; range: 4-17; left sided lesion: 16 cases) without any relevant side effects. Eight patients (44%) had a tumor, 7 patients (39%) suffered from cortical dysplasia and 3 patients (17%) had a perinatal stroke / hemorrhage. Fifteen patients underwent surgery, of whom language function worsened in 2 patients, improved in 4 patients, and remained the same in 9 patients postoperatively. We observed rTMS-induced errors in both hemispheres in all children, with more errors in the left hemisphere (LH) (mean 8.7 vs. 6.0) ($p = .008$). Five children (28%) had more or equal errors in the right hemisphere (RH), which never resulted in postoperative deterioration of language function in these children. This language lateralization to the RH was detected only in children with focal lesions (tumors, dysplasia) and not in patients with perinatal stroke / hemorrhage. Additionally, these were non-significantly older than the children with more erros in the LH (median age: 17y vs. 13y) ($p = .150$). Children with impaired (preoperative) language development never showed language lateralization to the RH ($n = 7$; $p = .036$).

Conclusion

Bihemispheric rTMS speech mapping is feasible in children. Significantly more errors were observed in the LH, however, errors could also induced in the RH in all cases. Age-appropriate language development was associated with right hemispheric language involvement, which was observed only in focal lesions and never resulted in deterioration of language function.

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Evaluation der Sicherheit einer perioperativen Behandlung mit Dexamethason pädiatrischer Patienten mit Low-grade Gliom

Evaluating the safety of perioperative dexamethasone treatment: A retrospective analysis of a single center pediatric low-grade glioma cohort

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Objective

In addition to surgical management, corticosteroids have proven to be beneficial in the management of acute symptoms related to CNS tumors, and have been widely used for many decades, with dexamethasone (DM) representing the most commonly used agent. However, lately published in vitro data possibly indicates a DM-induced suppression of oncogene-induced senescence (OIS) in a preclinical pediatric low-grade glioma (pLGG) model, which, alongside data associating perioperative DM treatment with reduced event-free survival in adult glioma, raises questions concerning the safety of DM treatment in pLGG.

Methods

A total of 172 patients with pLGG were retrospectively analyzed concerning the impact of perioperative DM application on postoperative short- and long-term tumor growth velocity and progression-free survival (PFS). Three-dimensional volumetric analyses of sequential MRI follow-up examinations were used for assessment of tumor growth behavior.

Results

Mean follow-up period accounted for 60.1 months. Sixty-five patients (45%) were perioperatively treated with DM in commonly used doses. Five-year PFS accounted for 93% following gross-total resection (GTR) and 57% post incomplete resection (IR). Comparison of short- and long-term postoperative tumor growth rates in patients with vs without perioperative DM application showed no significant difference (short-term: 0.022 vs 0.023cm^3/month, respectively; long-term: 0.019 vs 0.023cm^3/month, respectively). Comparison of PFS post IR (5-year-PFS: 65% vs 55%, respectively; 10-year-PFS: 52% vs 53%, respectively) and GTR (5- and 10-years-PFS: 91% vs 92%, respectively) likewise showed similarity.

Conclusion

This data emphasizes the safety of perioperative DM application in pLGG, adding further evidence for decision making and requested future guidelines.

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Niedriggradige pädiatrische Hirnstammtumoren – Charakteristica, Chirurgisches Management und Langzeit-Outcome

Characteristics, surgical management and outcome of pediatric low-grade brainstem-gliomas - a single center cohort study

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Objective

In children with pediatric low-grade gliomas (pLGG) maximal safe surgical resection is the treatment of choice and yields good long-term stability. Posterior fossa pLGG with involvement of brainstem (BS-pLGG) are due to the eloquent structures a subgroup with high risks at surgery. Nevertheless, surgery has an important role, since chemotherapy rarely decreases tumour volumes and radiation should be avoided in children before completion of puberty. We analyzed children with BS-pLGG for pre-operative characteristics, neurological outcome and recurrence/progression patterns.

Methods

41 children operated in our institution on BS-pLGG from 2005 to 2021 were included. Patients (pts) fulfilling radiological or molecular characteristics of DIPG were excluded.

Results

Mean age at diagnosis was 7.61 years (range 8 mo-17y). Pts were anatomically stratified in 3 groups: I) cerebello-peduncular & brainstem n=17; II) 4 th ventricle & brainstem (n= 11) ; and III) purely brainstem (medulla, pons or both) n=13. Interval from symptom onset to diagnosis was overall 10.6 mo (range 2wks - 6y), in Group I 3.3 mo, in Group II 12.5 mo and in Group III 16.8 mo. 5 pts had neoadjuvant therapy at outside institutions prior to surgery. 34 tumors were pilocytic astrocytomas (85%), 5 gangliogliomа, 1 RGNT and 1 diffuse astrocytoma. Postoperative mean follow-up (FU) was 90 mo (12mo-13y). 5 pts (12%) underwent GTR. 17 pts (42%) showed no progression of tumour residuals. 10 patients (24%) underwent re-operation due to tumour progression after a mean interval of 33 mo. 9 pts (22%) received chemo/radiation due to postoperative tumor progression. There was no perioperative mortality nor during FU. Postoperatively, 75 % of pts developed mostly transient moderate to severe deficits (dysphagia 12%, sleep apnea 10%, mutism 10 %, ataxia 54%, cranial nerve dysfunction other than dysphagia 31%). Long-term neurological outcome was favorable, 38 pts (93%) recovered within 1y to mild disabilities, not relevant for daily life (69%) or had no residual deficits at all (24%). 3 (7 %) had permanent disabilities interfering with everyday life activities, but allowing schooling.

Conclusion

The study suggest, that surgery in BS-pLGG can be associated with excellent survival rates plus favorable long-term neurological outcome. A multimodal approach with maximal safe resection, re-resection, chemo- and radiotherapy as designed in interdisciplinary tumour boards is mandatory.

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Die halbsitzende Lagerung in der pädiatrischen Neurochirurgie - Gefahren und Fallstricke aus 10 Jahren Erfahrung

The Semi-Sitting Position in Pediatric Neurosurgery – Pearls and Pitfalls of a 10-Years" Experience

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Objective

To investigate pearls and pitfalls of the semi-sitting positioning in pediatric neurosurgery with special focus on related morbidity and surgical practicability.

Methods

All pediatric cases of the author"s department were evaluated retrospectively. Those, who underwent procedures in semi-sitting position between 12/2010 and 12/2020 were included into final analysis. Results were compared to all children operated in prone position for posterior fossa lesions within the same time frame.

Results

A total of 42 posterior fossa surgeries were performed in 38 children between 01/2010 and 10/2020. Data of 24 surgeries in prone position in 22 children was analyzed in comparison. Mean age at surgery was 8.9 years (13 months – 18 years). Three children (7.9%) were diagnosed with persistent foramen ovale preoperatively. Surgery could be completed in all cases. Incidence of VAE was 11.9%. There was no VAE related hemodynamic instability, infarction or death. Endoscopic techniques were applied safely in 14 cases (33.3%). Postoperative pneumocephalus occurred significantly more frequently in semi-sitting procedures ($p<0.05$) but without need for intervention. One child (2.4%) showed postoperative skull fracture and epidural bleeding due to skull clamp application. Clinical status immediately after surgery was improved or stable in 33 of the cases (78.6%).

Conclusion

Attentive performance and an experienced surgical team provided; the semi-sitting position remains a safe option for posterior fossa surgery in the pediatric population. Precautious skull clamp application and appropriate monitoring is highly recommended. With a comparable complication profile, the semi-sitting position offers excellent anatomical exposure, particularly for the application with endoscopic visualization.

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Inkrementelle Bedeutung von FOHR und Tumorgröße bei der Prädiktion des Hydrozephalus nach Resektion pädiatrischer Kleinhirntumore

Incremental prognostic value of the FOHR and tumor diameter for persistent hydrocephalus in pediatric patients with posterior fossa tumors

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Objective

The Fronto-occipital horn ratio (FOHR) has been suggested to be added to the modified Canadian Preoperative Prediction Rule for Hydrocephalus (mCPPRH) to increase its performance. We aimed to examine the incremental (added) prognostic value of the FOHR in addition to tumor diameter.

Methods

We identified a cohort of pediatric patients with posterior fossa tumors who subsequently underwent resection. The variables of the mCPPRH were collected including age, transependymal edema, moderate to severe hydrocephalus, metastasis, and preoperative tumor diagnosis in addition to FOHR and tumor diameter. As defined by the mCPPRH model, the outcome was persistent hydrocephalus within 6 months of tumor diagnosis, as defined by the occurrence of either ventricular shunting or endoscopic third ventriculostomy. The incremental prognostic value of the preoperative FOHR and tumor diameter was determined separately and in combination. Incremental prognostic value, using logistic regression analysis, was assessed by delta *c*-statistic between models with and without these variables. The c-statistic quantifies the ability of a prediction model to discriminate between patients with and without the event of interest. The c-statistic ranges from 0.5 to 1, where 1 refers to perfect discrimination.

Results

The preoperative FOHR and tumor diameter were available for 101 and 98 of the 114 patients respectively. The mean FOHR was 0.40 (SD 0.079). The mean tumor diameter was 36.8 mm (SD 14.8). The odds ratio of FOHR was 1.2 (95% CI 0.3 - 4.5, p = 0.76). The odds ratio for tumor diameter was 1.1 (95% CI 0.6 – 2.0, p = 0.88). The c-statistic equaled 0.83 for all models. Consequently, the delta *c*-statistic was redundant.

Conclusion

In this preliminary analysis, the FOHR and tumor diameter show to have no significant incremental prognostic value for persistent hydrocephalus after PFT resection in our pediatric patient cohort. The results should be taken with caution, as the sample size is relatively small. Larger sample sizes are needed to confirm these results and assess the incremental value of other variables of interest such a tumor location.

Pädiatrische Neuro-Onkologie Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Neuro-Oncology Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

J-SBNPed003

Klarzelliges Meningeom bei einem Kind: Fallbericht und systematische Literaturrecherche
Clear cell meningioma in a child: Case report and systematic literature review

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Objective

Clear Cell Meningioma (CCM) consists in a rare variant of meningiomas that generally occur in children. This uncommon tumor behaves aggressively, and recurrence rates are high. Clinical manifestations are atypical, and the treatment generally involves surgery. The objective of this report is to present literature review and a case of a CCM in the temporal base with posterior extension in dumbbell shape in a child.

Methods

We performed a systematic review to define the most common characteristics of this rare tumor. PubMed and Lilacs were the databases used for the literature search. We included 17 studies that met our criteria. To further our research, we included the case report of a 3-year-old female child with CCM operated in our service.

Results

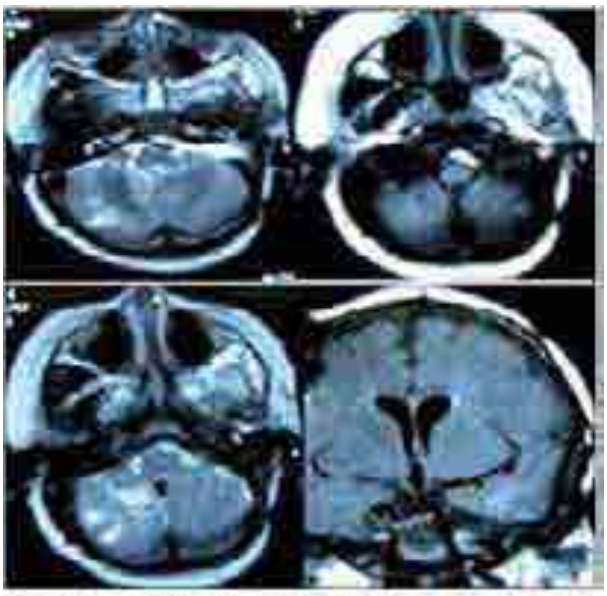
CCMs were more frequent in the pediatric population than in adults, especially in females. Gross tumor resection and MIB-1 index ≤ 3 were the parameters related to a smaller recurrence rate. Subtotal tumor resection was followed by radiotherapy in most adult cases. SMARCE-1 mutation could be found in several patients.

Conclusion

CCMs are rare meningiomas that occur especially in children. The aggressiveness and high recurrence rates difficult the management of this disease. There is still a lot to be discussed about these rare tumors, demanding further research.

Abb. 1

Abb. 2



Pädiatrische Neuro-Onkologie Joint Session mit der Brasilianischen Gesellschaft für Pädiatrische Neurochirurgie (SBNPed)/*Pediatric Neuro-Oncology Joint Session with the Brazilian Society of Pediatric Neurosurgery (SBNPed)*

P139

Enterogene Zysten des ZNS: Embryologische, histologische und neurochirurgische Aspekte 3 Fallberichte und Literaturübersicht

Enterogenous cysts of the central nervous system: embryological, histological and neurosurgical aspects. Report of three cases and review of the literature

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Objective

Enterogenous cysts of the central nervous system are rare lesions with an epithelial lining which is similar to the gastro-intestinal mucosa. Various embryological causes and mechanisms for their development are discussed in the literature but still many questions are not answered yet. In reviewing the literature we found a maximum of 140 cases reported. We present 3 patients and discuss details of diagnosis including questions of imaging and histological as well as neurosurgical aspects.

Methods

We analysed our own patient group with surgically treated cystic lesions of brain and spinal cord. In 3 meanwhile adult patients (1 female, 2 male) an enterogenous cyst was diagnosed. All patients are still in our follow-up. Clinical data as well as the results of MRI imaging controls before and after surgery and histological findings were reviewed and found complete.

Results

Our patient group included 3 patients: one female patient was treated at the age of 15 years in another department and referred for treatment of spinal cyst recurrence to us. 2 male patients were operated for cranial enterogenous cysts at the age of 20 and 38 years respectively. The cysts were localised at the level of the conus medullaris in one case and found supratentorially on the left side with our 2 other patients. Recurrences were seen in the female patient requiring meanwhile 3 reoperations. In one case of supratentorial localisation the lesion was thought to be an arachnoid cyst first for many years and finally turned out to be an enterogenous cyst when surgery was done for increasing cyst volume. In another case a left fronto-parietal cyst was diagnosed and treated in the context of a traumatic brain injury requiring surgery.

Conclusion

Enterogenous cysts of the CNS are rare diseases . The operative procedure itself is challenging due to often unclear dissection planes as there is only a very fine membrane between the cyst and the intact nervous tissue. So there is an increased risk of recurrences as preserving neurological function is the main goal. Except surgical treatment there are no real other treatment options . A close clinical and radiological follow-up is important to detect tumor recurrences on time and treat them surgically if necessary.

Vaskuläre Neurochirurgie II/*Vascular neurosurgery II*

P140

Volumetrische Analyse einseitiger chronischer subduraler Hämatome und ihrer neurologischen Auswirkungen nach Bohrlochtrepanation und subduraler Drainage

Volumetric analysis of unilateral chronic subdural hematoma and its impact on neurological outcome after burr hole trephination and subdural drainage

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Objective

To investigate the minimum volume reduction of chronic subdural hematoma (CSDH) required to achieve immediate and significant neurological improvement. A retrospective study was conducted on patients in whom burr hole trephination, irrigation and drainage of unilateral CSDH was performed.

Methods

100 consecutive, symptomatic patients were included in this retrospective study (71 males, 29 females, mean age 71,3 years, range from 23 to 91 years). Receiver operating characteristic (ROC) curve analysis was obtained to identify the optimal cut-off volume (in percentage) of CSDH reduction by clinical testing and improvement of the dedicated neurological deficit within the initial hospital stay.

Pre-and postoperative CSDH volumes were obtained from computed tomography (CT) and the relative reduction of the preoperative hematoma volume in percentage was statistically balanced against the improvement of the neurological categories: motor deficit, aphasia, psychomotor abnormalities, headache and seizures.

Results

The most common preoperative symptoms were psychomotor abnormalities (n=58), motor deficits (n=52), headache (n=38), aphasia (n=34), and seizures (n=11). Overall, 78% (n=78) experienced clinical improvement within the hospital stay.

The mean preoperative hematoma volume was 102.95 ml (range from 21.9 ml to 201.4 ml) and the average postoperative hematoma was 54.9 ml (range from 1.61 ml to 253 ml). The mean volume reduction was 46.95 ml (49,94%).

This relative volume reduction significantly influenced improvement of motor deficits (p=0.016), psychomotor abnormalities (p= 0.002), headache (p=0.026). Accordingly, general improvement was related to a relative reduction of 43% (AUC= 0.708, p=0.001). We could not calculate a significant cut-off of volume reduction for aphasia (p =0.377) and seizures (p= 0.169).

Conclusion

We could define cut-off values for volume reduction in CSDH patients with regard to improvement of dedicated neurological deficits. Generally, symptom relief was achieved due to reduction of 43% of the initial hematoma volume.

Abb. 1

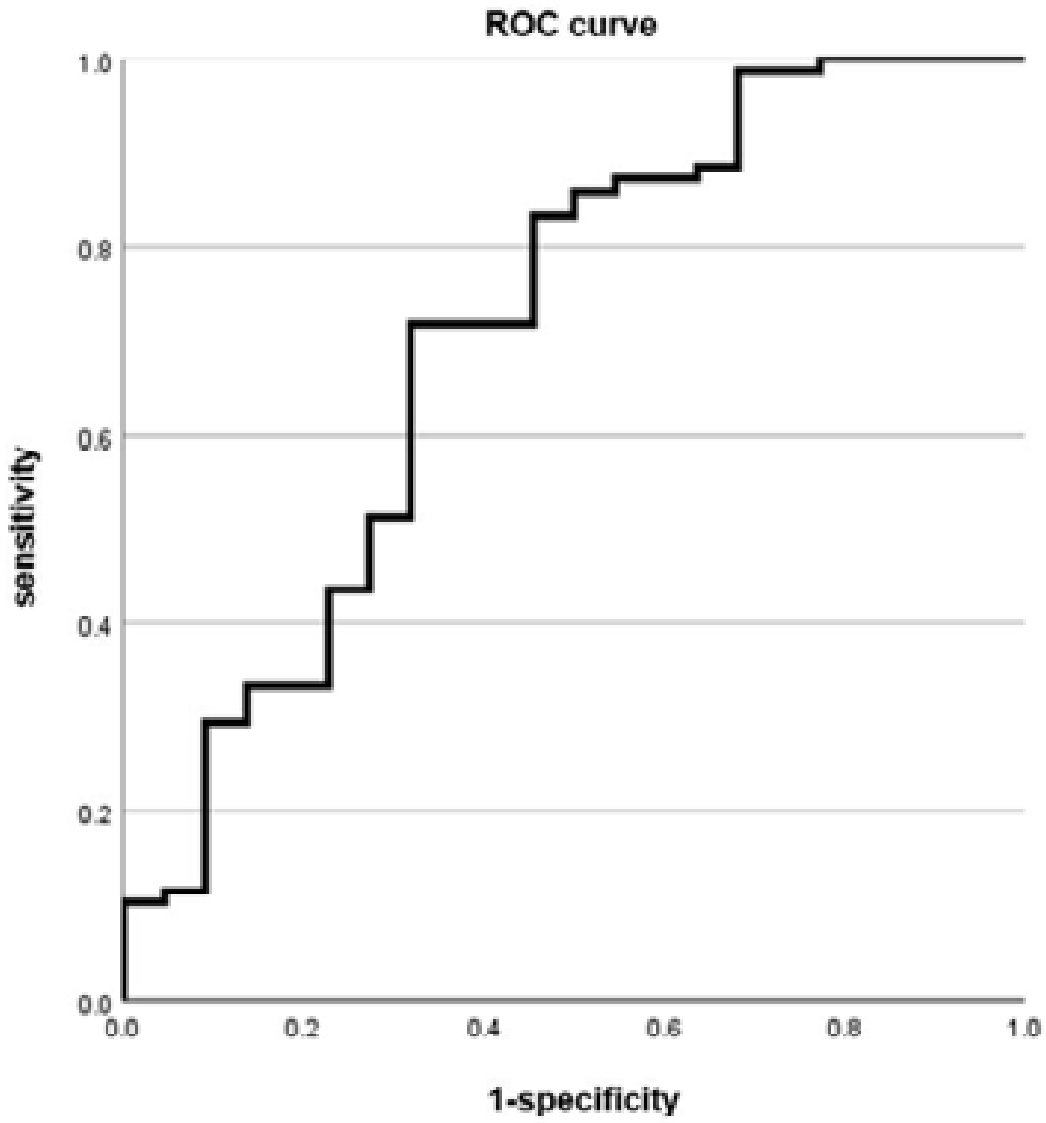
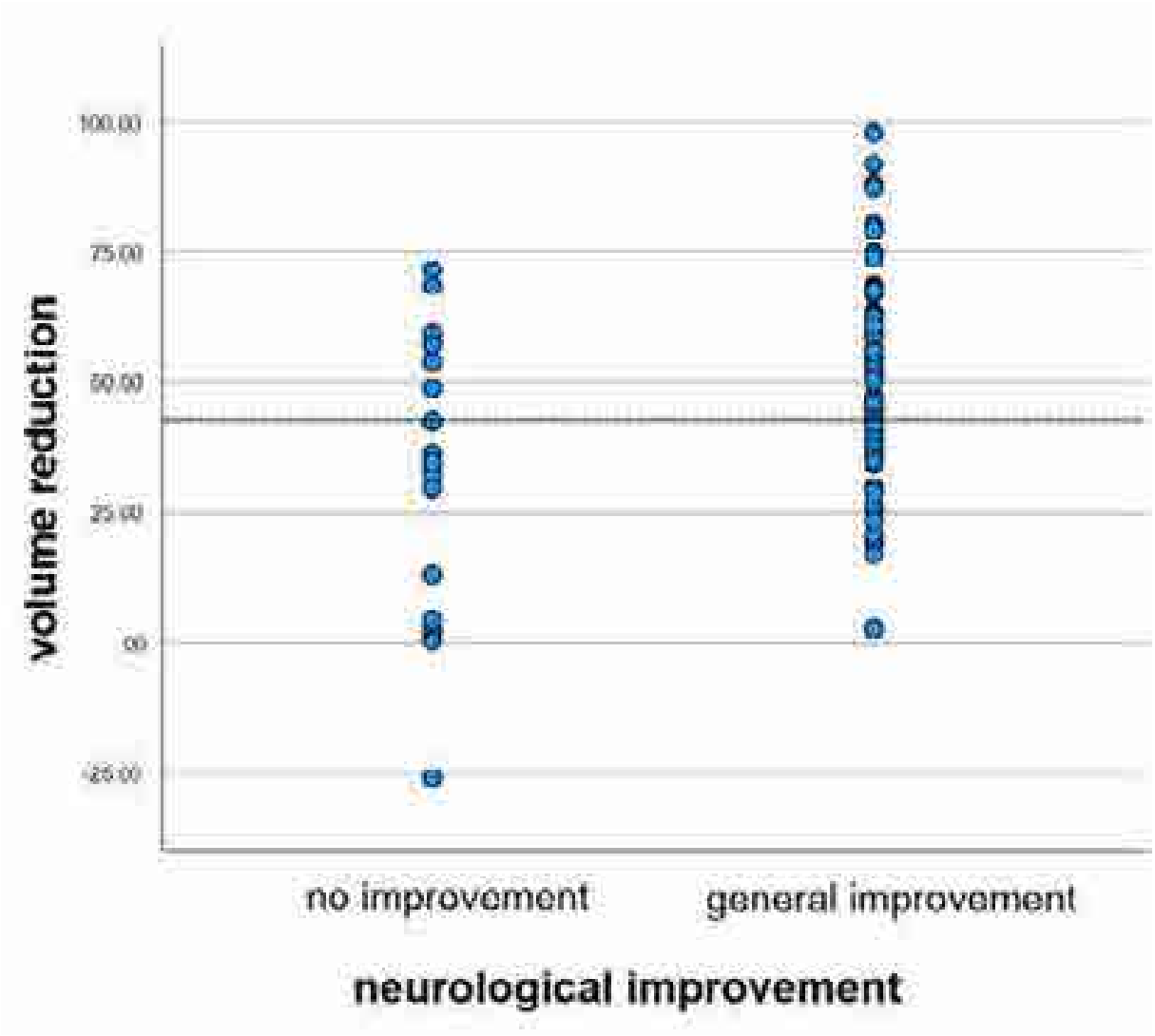


Abb. 2


100.00
75.00
50.00
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00
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volume reduction
no improvement
general improvement
neurological improvement

P141

De novo intrakranielle Aneurysmenbildung nach Verschluß der Arteria carotis interna: Eine systematische Überprüfung von Ätiologie, Diagnose und Behandlung

De Novo Intracranial Aneurysm Formation after Internal Carotid Artery Occlusion: A Systematic Review of Etiology, Diagnosis, and Treatment

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Objective

Acute ACI occlusion may lead to hemodynamic perfusion deficits leading to compensatory spontaneous hypertension that is a known risk factor to develop ICAs. Here, we review different etiologies of ACI occlusion, follow up, time to develop de novo ICA aneurysm and treatment options.

Methods

We searched the PubMed database using the terms "internal carotid artery occlusion" and "de novo aneurysm". A review of literature on etiology, diagnosis, and treatment of internal carotid artery occlusion and de novo aneurysm was conducted. The studies involving the management of internal carotid artery occlusion and de novo aneurysm were selected. In this review article, we mainly summarized the etiology, diagnosis, and treatment strategy of de novo aneurysm after internal carotid artery occlusion.

Results

A total of 23 articles were included. 183 patients [52 (28.4%) males, 75 (41.0%) females, and 56 (30.6%) unclear] suffered ICA occlusion at the mean age of 44.8±18.4 (range between 6 to 81) years. 120 (65.6%) patients caused by balloon occlusion of ICA for the treatment of aneurysms was the most common etiology of ICA occlusion. Mean time to develop de novo aneurysm in patients with ACI occlusion was 7.08 years. Follow up imaging was carried out with DSA, CTA or MRI. The most common site of occurrence of de novo aneurysms occurred 10 (30.3%) ACOM followed by 4 (12.1%) left MCA, 4 (12.1%) BA, 3 (9.1%) left P1/P2 PCA, 3 (9.1%) right P1/P2 PCA, 3 (9.1%) left cavernous and supracavernous segment of ICA, 2 (6.1%) VA, and 2 (6.1%) A1 segment and A1-A2 junction, respectively. The mean diameter of de novo aneurysms was 8.1±5.8 (2.5 to 25) mm. Surgical clipping was performed in 13 (39.4%) cases followed by 8 (21.2%) coil embolization and/or stent assisted, 4 (12.1%) EC-IC high-flow bypass, 2 (6.1%) STA-MCA bypass and occlusion of the BA and anastomotic aneurysm resected, 1 (3.0%) ECA-MCA bypass and occlusion of the basilar trunk. 2 (6.1%) cases had no treatment and 3 (9.1%) cases were unclear.

Conclusion

De novo aneurysms formation after ICA occlusion is much more frequent than in general population. Hence, the patients with ACI occlusion need strict follow up. The patients with haemodynamic perfusion deficits may benefit from cerebral revascularization to control spontaneous hypertension and formation of de novo ICAs.

Abb. 1

Table 2. The summary of characteristics in patients with ICA occlusion.

ICA occlusion patients	**No. of patients** (n, %)
Total	183 (100)
Age (years, mean±SD)	44.8±18.4 (6 to 81)
Gender	
Male	52 (28.4)
Female	75 (41.0)
Unclear	56 (30.6)
Etiology of ICA occlusion	
Balloon occlusion of ICA for the treatment of aneurysms	120 (65.6)
ICA ligation for the treatment of aneurysms	6 (3.3)
Coils occlusion of ICA for the treatment of aneurysms	5 (2.7)
Selverstone clamping ICA for the treatment of aneurysms	4 (2.2)
ICA aneurysms only mentioned endovascular occlusion	4 (2.2)
ICA clipping for the treatment of aneurysm	1 (0.5)
Bilateral ICA stenoses	1 (0.5)
Arteriosclerotic stenosis of supra-clinoid ICA	1 (0.5)
Left ICA occlusion due to a small left hemispheric cortical infarct	1 (0.5)
Unclear	40 (21.9)

Abb. 2

Table 4. The summary of characteristics of de novo aneurysm in patients with de novo aneurysm formation followed by ICA occlusion.

De novo aneurysm	**No. of patients** (n, %)
Total	33 (18.0) †
Age (years, mean±SD)	42.3±18.2 (6 to 70)
Sex	
Male	14 (47.4)
Female	16 (48.5)
Unknown	3 (9.1)
Symptoms	
Headache	16 (48.5)
Visual disturbance	6 (18.2)
Ptosis	2 (6.5)
Loss of consciousness	5 (15.2)
Neck stiffness	6 (18.2)
Nausea and vomiting	4 (12.1)
Neck pain	1 (3.0)
Retroorbital pain	1 (3.0)
Increased deep tendon reflexes in the four extremities	1 (3.0)
Progressive dyspnea	1 (3.0)
No described the symptoms only SAH displayed with images	5 (15.2)
No mentioned	5 (15.2)
De novo aneurysm diameter (mm, mean±SD)	8.1±5.8 (2.5 to 25)
De novo aneurysm Location	
ACOM	10 (30.3)
A1 segment and A1-A2 junction	2 (6.1)
Right PCOM, left and right IC-PCOM	3 (9.1)
Left MCA	4 (12.1)
Right MCA branch	1 (3.0)
Vertebrobasilar	2 (6.1)
Basilar artery	4 (12.1)
Right vertebral	1 (3.0)
Left P1/P2 PCA	3 (9.1)
Right P1/P2 PCA	3 (9.1)
P1 segment	1 (3.0)
Left SCA	1 (3.0)
Left cavernous and supracavernous segment of ICA	3 (9.1)
Right cavernous portion	1 (3.0)
Left ophthalmic artery	1 (3.0)
Right pericallosal artery	1 (3.0)
Cavernous pseudoaneurysm	1 (3.0)
De novo aneurysms treatment	
Clipping	13 (39.4)
Coil embolization and/or stent assisted	8 (21.2)
EC-IC high-flow bypass	4 (12.1)
STA-MCA bypass + Occlusion of the BA and Anastomotic aneurysm resected	2 (6.1)
ECA-MCA bypass + Occlusion of the basilar trunk	1 (3.0)
No treatment	2 (6.1)
Unclear	3 (9.1)

Legend: †=the total number of de novo aneurysm patients divided by the total number of ICA occlusion patients.

Vaskuläre Neurochirurgie II/*Vascular neurosurgery II*

P142

Topographische Verteilung von Entzündungsfaktoren in einem Ratten Seitenwand-Aneurysma-Modell behandelt mit Coiling

Topographic distribution of Inflammation factors in a rat sidewall aneurysm model treated with coiling

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Objective

Aneurysm healing after endovascular treatment relies on biological processes such as neointima formation and organization of the early intraluminal hematoma into mature scar tissue. Thereby, activation and deactivation of the inflammation cascade plays an important regulatory role. We hypothesize, that in addition to the timely evolution, also the topographic distribution of inflammation factors is of paramount importance for successful aneurysm healing.

Methods

Decellularized saccular sidewall aneurysms were microsurgically created in Lewis rats. They were treated by coiling and compared to the natural course of untreated aneurysms after 3 days (n=16), 7 days (n=19) and 21 days (n=8). Upon follow-up, aneurysms were harvested, macroscopically inspected and light microscopically assessed for healing and inflammation status. Furthermore, immunohistochemistry was performed to visualize inflammation cells (CD45, CD3, CD20, CD31, CD163, HLA-DR, tryptase clone AA) and an in-situ hybridization was performed for soluble inflammation markers (Il6, MMP2, MMP9, TNF-α, FGF23, VEGF). These factors were assessed in four regions of interest (ROIs): aneurysm wall (proximal and distal), neointima, intraluminal (in the thrombus) and in the adjacent vessel wall.

Results

Coiled aneurysms showed an enhanced pattern of thrombus organization and neointima formation, whereas those without coils demonstrated a heterogeneous pattern of thrombosis, thrombus recanalization, and aneurysm growth (p=0.02). Whereas pro-inflammatory cytokines were ubiquitously detected in all four ROIs, inflammation cells tended to accumulate inside the thrombus, and to a lesser extend in the neointima (p=0.001). Inside the evolving thrombus, there was a concentration of B-lymphocytes, M1-macrophages and mast cells (p= p<0.0001), whereas endothelial cells accumulated directly in the neointima (p<0.0001). Their presence is associated with complete aneurysm healing.

Conclusion

The presence of proinflammatory cells plays a crucial role in aneurysm remodelling after coiling: Whereas thrombus organization is hallmarked by a pronounced intra-thrombotic inflammation reaction, neointima formation is characterised by direct invasion of endothelial cells, which promote complete aneurysm healing. The presented topographic distribution of regenerative inflammatory processes may pave the way for future treatment modalities that enhance aneurysm healing after endovascular therapy.

Vaskuläre Neurochirurgie II/*Vascular neurosurgery II*

P143

Implementierung eines semiautomatisierten und Deep Learning-basierenden Analyseprozesses für Ganzhirnvolumetrien bei erwachsenen Patienten mit Moyamoya Angiopathie

Implementation of a semi-automated and deep learning-based analysis process for whole brain volumetrics in adult patients with Moyamoya angiopathy

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Objective

Deep learning (DL)-based algorithms have become a mainstream approach to analyse brain imaging data. To applicate whole-brain volumetry (WBV) tools for MRI of Moyamoya angiopathy (MMA) patients, we built a semi-automated pipeline with state-of-the-art DL-based volumetry software for one-stop access to WBV data of up to 135 different regions of interest (ROI).

Methods

In total, 292 high-resolution T1w (3D MPRAGE) MRI datasets from routine pre- and/or postoperative imaging of 104 adult MMA patients and 129 healthy persons (control group (CG)) were included. The semi-automated pipeline included the preprocessing of MRI data for conversion, anonymization and defacing, followed by analysis using two deep learning-based segmentation software programs: FastSurfer (FS) and AssemblyNet (AN), as well as the multi-atlas label fusion technology-based method vol2Brain (VB). Manual quality control (QC) of potential segmentation errors was performed by visual inspection. Descriptive and comparative analysis were conducted between the patients with MMA and the healthy control group, which were matched for age and sex.

Results

Average processing time was less than 60min. QC revealed no or minor segmentation errors in 74.2% (FS) and 77.3% (AN) of all MMA datasets, while in CG 100.0% (FS, AN, VB) was achieved. Intrarater analysis between softwares (QC FS & AN) showed a very strong correlation with Kappa κ, = 0.79, p <.0001. In the Chi²- tests, there were no significant differences in the achieved QC considering ischemia except for FS and right-sided ischemia (p<.05, Stuart's τc = 0.12). The WBV of cortical grey matter (-7.9% [CI95%3.1-12.7] p<0.01; FS) and white matter (-6.3% [CI95%1.1-11.5], p=0.019; FS) were significantly lower in patients with MMA compared to the age- and gender matched healthy controls. MMA patients with infarcts had significant (p<0.0001) brain volume loss compared to controls, but this was not observed in patients without infarcts regardless of Suzuki grade.

Conclusion

We implemented a user-friendly, semi-automated pipeline for DL-based WBV in Moyamoya patients. While the distinctive brain changes seen in patients with MMA pose a challenge for software algorithms, our QC has demonstrated high workflow reliability and favoured AN in MMA patients with ischemia. Incorporating DL brain volumetry as a new data source will allow for future multimodal disease analysis and may have the potential to aid in decision making of indicating bypass-surgery and non-invasive disease monitoring.

Abb. 1

1. Visualizing segmentations with (a.) MRIcoGL and (b.) 3DSlicer

P146

Vorläufige Analyse der Wirkung der lokalen Anwendung von menschlichem basischem Fibroblasten-Wachstumsfaktor zur Verstärkung der Neointima-Bildung in einem Ratten-Seitenwand-Aneurysma-Modell

Preliminary analysis of the effect of local application of human basic fibroblast growth factor to enhance neointima formation in a rat sidewall aneurysm model

G. Boillat[1,2], J. Rey[1,2], S. Wanderer[1,2], L. Andereggen[1,2], M. Von Gunten[1,3], L. Remonda[4], S. Marbacher[1,2], B. Grüter[1,2,4]

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[2]Kantonsspital Aarau, Division of Neurosurgery, Aarau, Schweiz
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Objective

Long-term aneurysm occlusion after endovascular treatment relies on cell-mediated processes including thrombus organisation and neointima formation. Thereby, basic fibroblast growth factor (bFGF) is a potent stimulator for this remodelling process by enhancing fibroblast migration. Therefore, local intra-aneurysmal application of human bFGF is hypothesised to promote aneurysm healing in an experimental rat sidewall aneurysm model.

Methods

Vital and decellularized saccular sidewall aneurysms were microsurgically created in 24 Lewis rats and treated with bioembolization material (bioabsorbable thread) soaked with 5ug (n=6),10ug (n=6) and 20ug (n=6) of bFGF. A control group (n=6) received the biomaterial alone without bFGF. Histological specimens were harvested at 21 days follow-up. Healing status, local inflammation and degree of neointima formation was microscopically evaluated.

Results

All specimen of the control group showed a neointima formation with a complete occlusion of the aneurysm"s orifice. All groups with bFGF application showed a poorer aneurysm occlusion rate, with a an enhanced neointima formation upon the biomaterial instead at the orifice of the aneurysm. This was observe with a dose-response effect: In the 5ug bFGF-group, the neointima upon the biomaterial tended to be thin and incomplete, and an incomplete neointima still appeared at the orifice of the aneurysm. In the 10ug bFGF-group, intraluminal perfusion in a dog-ear pattern was observed. In the 20ug bFGF-group, the neointima mostly covered the bioimplant isolating it from the aneurysm wall and allowing a persisting perfusion in between. The effect observed was more pronounced in decellularized aneurysms compared with vital ones.

Conclusion

Local application of bFGF by means of a bioimplant seems to enhance cellular migration and neointima formation on the surface of the embolization material with a dose-effect response. However, it results in a poor occlusion of the aneurysm orifice. A larger series is needed to confirm these results and to provide quantitative analyses.

Vaskuläre Neurochirurgie II/*Vascular neurosurgery II*

J-SBNC022

DNA des Torque-Teno-Virus wird in der Wand des intrakraniellen Aneurysmas gefunden - spielt es eine ursächliche Rolle?

Torque Teno Virus DNA is found in the Intracranial Aneurysm Wall – Is there a causative role?

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[2]University of Ribeirão Preto, Department of medicine, Ribeirão Preto, Brasilien
[3]Barão de Mauá University Center, Medicine, Ribeirão Preto, Brasilien
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Objective

Torque Teno Virus (TTV) is a recently discovered virus with high prevalence worldwide, that has been associated with vascular diseases. The aim of this study is to investigate the prevalence of TTV molecular DNA in the intracranial aneurysm (IA) artery walls

Methods

Samples of IA walls were collected after microsurgical clipping from 35 patients with IA (22 ruptured /13 unruptured cases). The samples were submitted to molecular DNA extraction using the EasyMag automatized extractor and performed with Qiagen DNA extraction Minikit 250. The samples underwent PCR examination with primers for β-globin as internal control using the Nanodrop 2000 spectrophotometer. A quantitative (real-time) PCR with TTV-specific primers was performed. Clinical and radiological data of patients included was collected.

Results

TTV was detected in 15 (42.85%) cases, being 10 (45.4%) ruptured and 5 (38.4%) unruptured (p=0.732) lesions. Multiple IAs accounted for 14 (40%) cases. Five cases (17.2%) had TTV+ and multiple aneurysms (p=0.73). Association between presence of virus and aneurysm rupture was not statistically significant (p=0.96).

Conclusion

This study demonstrated a relatively high prevalence of viral DNA in the walls of IAs. This is the first study to identify the presence of TTV DNA in IA"s samples, which was found more often in ruptured lesions. This is an exploratory study, therefore, larger studies are required to clarify the relationships between inflammation, viral infection, IA formation and rupture.

P147

Sequenzielle Multiplex-Untersuchung von Zytokinen im Serum und Liquor von Patienten mit aneurysmatischer Subarachnoidalblutung: eine Pilotstudie

Sequential multiplex cytokine profiling of serum and CSF in patients with aneurysmal subarachnoidal hemorrhage: a pilot study

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Objective

Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating event. A substantial part of the morbidity and mortality observed in patients with aSAH is attributed to delayed cortical ischemia (DCI) which can occur in the first few days and weeks after aSAH. The pathophysiology of DCI is not fully understood but immunological processes are thought to play a substantial role. We therefore set out to investigate the immunological sequelae in serum and CSF of aSAH patients.

Methods

Patients with aSAH were prospectively enrolled and serum and CSF were sequentially sampled for as long as the patient remained in the ICU. Levels of 40 human cytokines were determined using Luminex multiplex technology. Clinical data was also recorded.

Results

20 patients were enrolled (17 female, mean age 56 years). Aneurysms were treated with clipping (n=11) or coiling (n=8) within 24 hours of hospital admission. 1 spinal aneurysm at Th1 occluded spontaneously without intervention. 5 patients had DCI while in the ICU, 9 patients suffered from procedure-related ischemia. 6 patients did not have any cerebral ischemia. Individual cytokine expression profiles were created for each patient. In the DCI group, we observed an increase of inflammatory cytokines in serum and CSF within 3 days before the first radiological detection of DCI, especially of Interleukin (IL)-6, IL-8, IL-15 and interferon gamma-induced protein (IP)-10. Group comparisons were not statistically meaningful due to the small sample size.

Conclusion

Multiplex cytokine profiling of serum and CSF in patients with aSAH revealed highly individual expression patterns, specific for serum and CSF. Further prospective studies are needed to determine whether specific cytokine expression profiles can be tied to adverse clinical events.

Vaskuläre Neurochirurgie II/*Vascular neurosurgery II*

J-SBNC023

Dekompressive Kraniektomie bei malignem ischämischem Schlaganfall - retrospektiver Überblick: Erfahrungen in einem brasilianischen medizinischen Zentrum

Decompressive Craniectomy for Malignant Ischemic Stroke retrospective review: Experience in Brazilian Medical Center

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Objective

This study aimed to identify prognosis factors associated with clinical outcome, including timing of the procedure, and postoperative mortality.

Methods

We analyzed surgical characteristics associated with prognosis in 145 patients who underwent decompressive craniectomy (DC) secondary to malignant ischemic stroke (MIS) between 2013 and 2018, assessing clinical outcome at discharge and 6 and 12 months after discharge. Our inclusion criteria were DC secondary to MIS in adult patients with raised intracranial pressure signs. All patients underwent DC within <48 Hours of onset.

Results

Our analysis showed that although patients from cities >100 km from the neurosurgical center had a worse prognosis, only the surgical head side (left vs. right, = 0,001), hospitalization length (P < 0.001), and e timing of procedure (P « 0.001) were statistically relevant in having worse outcomes. Patients operated on the left side had a worse prognosis and those submitted to surgery between 12 and 36 hours had the best prognosis.

Conclusion

The timing of procedure, surgical side, and hospitalization length were independent predictors in determining the prognosis of patients who underwent DC after an MIS. Our results showed a better outcome for patients who underwent CD on the non-dominant side, with statistical relevance.

P148

Segmentierung von aneurysmatischen subarachnoidalen Blutungen basierend auf einem konvolutionalem neuronalen Netzwerk: Eine Durchführbarkeitsstudie an einem internen Datensatz

Convolutional neuronal network based aneurysmal subarachnoid hemorrhage segmentation: A feasibility study on an inhouse dataset

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Objective

The volume of aneurysmal subarachnoid hemorrhage (aSAH) is a consistent predictor of mortality and long-term functional outcome. However, in clinical routine, the three-dimensional manual calculation is time consuming and may be prone to manual error. This study was designed to assess the performance of a neuronal network based segmentation of aSAH on admission computed tomography (CT).

Methods

Ethics approval was granted by local authorities (EA1/291/14). The ground truth (segmentation mask) was manually generated by an experienced neurosurgeon. Binary segment analysis of cortical and basal aSAH was performed using BRAVE-NET, a multiscale 3-D convolutional neural network (CNN) model. Model performance on lesion segmentation and volumetric measurement of cortical and basal aSAH were evaluated by comparing the model results with the segmentations performed by the neurosurgeon. Training-validation-test split was randomly performed 49-10-10 out of 69 patients with aSAH.

Results

Sixty nine patients with a median age of 54 [46; 63] were included. 65 % of patients were female. Presence of intraventricular hemorrhage (IVH) was noted in 42 patients, presence of intracerebral hemorrhage (ICH) in 26 patients. A substantial amount of subarachnoid blood was noted in cortical regions in 41 patients. Visual inspection of the test set revealed more accurate overlays of aSAH in cortical regions than in regions closer to the skull base with a higher number of false negative results in the basal cisterns. Pathologies other than aSAH, like ICH and IVH, produced false positive results. The median dice coefficient of the validation and test sets were 0.51 and 0.46, respectively.

Conclusion

This first assessment of our in-house aSAH CT dataset revealed a moderate performance of the CNN model for delineation of cortical and basal aSAH. Whether the performance of the CNN model based segmentation can be improved by exclusion of previously treated patients with artifacts, data augmentation, and inclusion of other pathologies in the segmentation has to be shown in future studies.

P149

Mozart in the Brain - Einfluss klassischer Musik nach aneurysmatischer Subarachnoidalblutung
Mozart in the Brain - Impact of Classic Music in Aneurysmal Subarachnoid Hemorrhage

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Objective

Aneurysmal subarachnoid hemorrhage (aSAH) is accompanied by cerebral vasospasm and delayed cerebral ischemia (DCI). It is well known that certain classical music improves the outcome of neurological patients. Among other things, it could be shown that classical music can lead to dilatation of the cerebral blood vessels in healthy controls. The aim of this study was to investigate the impact of classical music in patients with aSAH.

Methods

In this prospective pilot study, 20 aSAH patients were recruited. Up to 3 examinations were carried out from day 6, in which the patients listened to W. A. Mozart's Symphony No. 40 in G minor (KV 550; duration approx. 28 min) via headphones and parallel to this, the flow velocities in the right middle cerebral artery (MCA) were continuously measured using transcranial Doppler (TCD), which was fixed to the head using a DiaMon® mount. For each minute of the study, an average was taken from all available TCD values. In addition, heart rate, blood pressure and other physiological and laboratory parameters were evaluated. The level of statistical significance was set to <0.05.

Results

A total of 50 measurement sessions were carried out in 20 patients. The median Hunt&Hess grade was 2, the median modified Fisher Scale was 2.5. A total of 7 patients (35%) developed a DCI during their clinical course. The TCD values showed, starting from a mean baseline value of 77.0 cm/s, a decrease to 71.8 cm/s at minute 14. Corresponding effects were observed for respiratory rate (19.0 to 17.6 /min at minute 3) and to a lesser extent for heart rate (70.3 to 68.0 /min at minute 23) and systolic blood pressure (172.8 to 139.4 mmHg at minute 8). The serum cortisol value decreased from 189.3 to 179.0 nmol/L during the examination. Nevertheless, none of these observations reached the level of statistical significance in the context of high variability between sessions.

Conclusion

No significant physiological effect was detected after exposure to classical music in the investigated aSAH cohort. Physiological data of aSAH patients was overall noisy, suggesting potential variation in the susceptibility to auditory stimulation. Nevertheless, we observed an overall trend towards a more relaxed physiological state over exposure time. This may warrant future investigations aiming to identify factors determining susceptibility or resistance to auditory stimulation in neurocritical care subpopulations and to evaluate potential clinical implications.

P150

Multiple Korrespondenzanalyse und Clusteranalyse von kranialen duralen arteriovenösen Fisteln basierend auf deren gefäßarchitektonischen und anatomischen Eigenschaften

Multiple correspondence analysis and automatic clustering of cranial dural arteriovenous fistulas based on angio-architectural and anatomical features

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Objective

Although rare, cranial arteriovenous fistulas are complex vascular malformations that have a rupture risk with potential devastating consequences. Despite this fact, the exact angio-architectural features associated with increased risk of bleeding complications are at best insufficiently defined. Here we propose a simple machine learning algorithm based on multiple correspondence analysis and k-means clustering as a means of defining those features that best identify the at risk fistulas.

Methods

15 patients (median age=60, range=36-82, female=6, male=9) with symptomatic cranial arteriovenous fistulas were so far characterized retrospectively in terms of the anatomical and angio-architectural features as evaluated on conventional subtraction angiography: Location of the fistula, nidus architecture, venous drainage anatomy, presence of pial feeders, outflow stenosis, sinus thrombosis and presence of flow associated aneurysms. Using custom-written routines in R and Python, we performed a multiple correspondence analysis (MCA)-based dimensionality reduction of the pooled data followed by k-means clustering along the dimensions with greatest inertia.

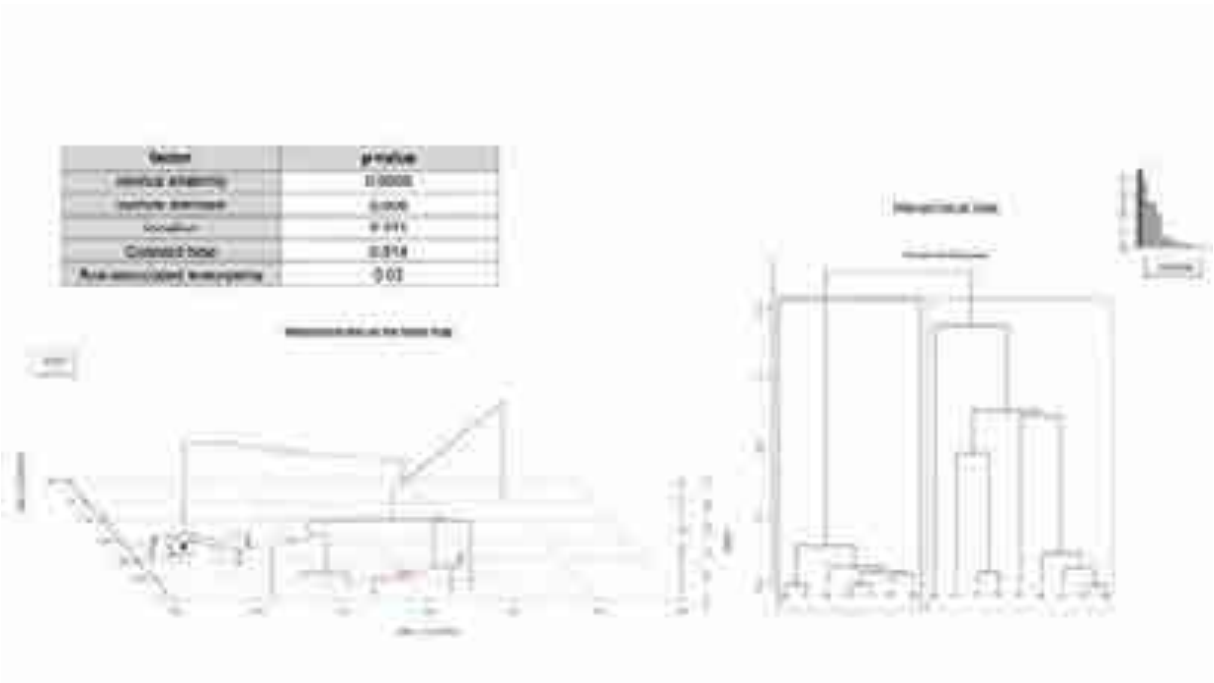
Results

The most common anatomical location of the fistulas was transverse sinus/sigmoid sinus junction (6/15, 40%) followed by tentorial (4/15, 26%), occipital (4/15, 26%) and ethmoidal (1/15, 6%). The nidus architecture was mostly of the multi-feeder/multiple fistula points type (10/15, 66%). Venous anatomy characterized by ectasia was present in 46% of fistulas whereas outflow stenosis of the draining veins was encountered in 66% of cases. The drainage pattern was over cortical veins in 86% of the fistulas. We found that the factors with the largest inertia explaining the variance of the data were the venous anatomy (p=0.0005) and presence of outflow stenosis (p=0.006). Intriguingly, clustering along these dimensions assigned 85% of the ruptured fistulas to the same group (cluster 1 in Figure 1, numbers correspond to individual patients), without prior knowledge of the bleeding status. Comparatively, the Cognard classification achieves the same clustering with a p=0.01.

Conclusion

Dimensionality reduction using MCA coupled with a clustering algorithm (k-means) can correctly identify ruptured dural arteriovenous fistulas based on simple features of the conventional subtraction angiography.

Abb. 1



Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P151

Die körperliche Fitness scheint kein prognostischer Faktor für das neurologische Outcome bei Patienten mit aneurysmatischer Subarachnoidalblutung zu sein

Physical fitness does not appear to be a prognostic factor for neurological outcome in patients with aneurysmal subarachnoid hemorrhage

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Objective

Recently, the temporalis muscle area (TMA) was identified as a useful surrogate parameter for the estimation of skeletal muscle mass, a correlate of physical fitness itself (Ranganathan et al., 2014; Leitner et al., 2018). A retrospective pilot study with 127 patients identified the temporal muscle thickness (TMT) and the TMA to be possible prognostic factors for the neurological outcome in patients with aneurysmal subarachnoid hemorrhage (aSAH) (Katsuki et al., 2021). In the present study, we wanted to test this observation in a larger patient cohort.

Methods

All patients with aSAH treated at our neurovascular centre from 05/2012 to 09/2022 were retrospectively included if usable initial CT imaging (before surgical/endovascular treatment) was available. All CTs were aligned identically to the skull base and the TMA was measured 5mm above the orbital roof. The TMT was measured in four different locations: 1.) At the level of the Sylvian fissure, 2.) at the thickest point, 3.) at the mid-level of the muscle, 4.) at the inferior level of the Sylvian fissure. Since the thickness measurements at different locations were highly correlated, a weighted average (projection on the first principal component) was calculated. Logistic regression analyses with the dichotomized mRS score 6 months after aSAH as the outcome parameter were performed (0-2 = good outcome, 3-6 = poor outcome). Besides age, sex, WFNS grade and Fisher score, either TMT at the Sylvian fissure, the weighted average of TMT, or TMA were used as predictors.

Results

We included 625 of 707 patients with aSAH in this study. Of these, 66% were female, the median age was 56 and 16% of patients had an mRS of 3-5 after 6 months. The mean TMT at the level of the Sylvian fissure was 5.9 mm in males and 4.7 mm in females. The mean TMA was 225 mm^2 in females and 381 mm^2 in males. WFNS grade ($p < 0.0001$) and age ($p < .05$) correlate significantly with the dichotomized mRS after 6 months. No correlation was found between the dichotomized mRS after 6 months and the TMT at the Sylvian fissure ($p = 0.37$), the weighted average of TMT ($p = 0.63$), or the TMA ($p = 0.63$).

Conclusion

In contrast to the published literature, no correlation was found between TMT / TMA and neurologic outcome after aSAH in our patient cohort of 625 patients. Further studies in other patient populations are needed to resolve the uncertainty of the prognostic utility of TMA and TMT in patients with aSAH.

Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P152

Auswirkungen einer Schilddrüsenhormonersatztherapie auf den Verlauf und das funktionelle Ergebnis einer aneurysmatischen Subarachnoidalblutung.

Impact of thyroid hormone replacement therapy on the course and functional outcome of aneurysmal subarachnoid hemorrhage.

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Objective

In patients with cerebral ischemic stroke, presence of hypothyroidism was reported to be associated with favorable outcome. We aimed to analyze the value of thyroid hormone replacement therapy (THRT) due to pre-existing hypothyroidism on the clinical course and outcome of aneurysmal subarachnoid hemorrhage (SAH).

Methods

SAH individuals treated between January 2003 and June 2016 were included. Data on baseline characteristics of patients and SAH, adverse events and functional outcome of SAH were recorded. Study endpoints were cerebral infarction, in-hospital mortality and unfavorable outcome at 6 months. Associations were adjusted for outcome-relevant confounders.

Results

109 (11%) of 995 individuals had THRT before SAH. Patients with THRT showed lower incidence of intracranial pressure increase >20mmHg (40.6% vs 45.2%), decompressive craniectomy (22.9% vs 26.2%), delayed ischemic neurologic deficit (26.1% vs 31.2%) and fever (71.7% vs 79.8%) during SAH. Risk of intracranial pressure- or vasospasm-related cerebrovascular events was inversely associated with presence of THRT (p=0.047). In multivariate analysis, THRT was independently associated with lower risk of cerebral infarction (adjusted odds ratio [aOR]=0.64, p=0.045) and unfavorable outcome (aOR=0.50, p=0.018), but not with in-hospital mortality (aOR=0.69, p=0.227).

Conclusion

THRT due to pre-existing hypothyroidism seems to be protective in SAH, decreasing burden of ischemia-relevant cerebrovascular events and resulting in lower rate of cerebral infarction and unfavorable outcome. Further experimental and clinical studies are required to confirm our results and elaborate the mechanistic background of the effect of hypothyroid dysfunction and THRT on course and outcome of SAH.

Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P153

Rapid Ventricular Pacing in einem kommunalen Zentrum für zerebrovaskuläre Neurochirurgie - Erste interdisziplinäre Erfahrungen

Rapid Ventricular Pacing in a Community Center for Cerebrovascular Neurosurgery - First Interdisciplinary Experience

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Objective

The aim of this study was to establish intraoperative rapid ventricular pacing (RVP) and to test its methodological applicability in a community center for cerebrovascular surgery. Intraoperative rapid ventricular pacing (RVP) leads to a time -controlled blood pressure regulation in the sense of hypotension while maintaining perfusion of the vascular system.

Methods

Intraoperative rapid ventricular pacing was performed in 4 of 33 patients with aneurysms of the anterior and middle arterial supply and in 4 of 10 patients with arteriovenous malformations or dural AV fistulas in the period from May 1, 2022 to January 1, 2023 during elective surgical treatment. Only patients without any cardiac pathology, as examined in the preoperative workup, were included. The pacing catheter was tested after placement and positioning of the patients. Intraoperative stimulation was performed for 2-3 times and for a maximum of up to 90 sec. Follow up examinations included neuropsychological evaluations and neuroimaging studies.

Results

In all patients, an immediate decrease of blood pressure with preserved residual perfusion could be achieved. At the end of pacing, the normotensive baseline was reached after a few cardiac actions without an exaggerated reaction. Both aneurysms and vascular malformations showed significantly reduced turgor, which facilitated dissection/elimination. Perioperative cardiac complications did not occur.

Conclusion

The establishment of rapid ventricular pacing is also possible in a community setting with careful consideration of safety controls. The workflow could be improved and shortened after a few trial runs. Thus, without the disadvantages of interruption the blood flow (cardiac arrest/temporary clipping) or unpredictable blood pressure manipulation and in close cooperation of the neurovascular team, patient care in more complex cerebrovascular clinical pictures is possible.

Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P155

Die Behandlung von rupturierten blister-like Aneurysmen mittels Flow-divertern
Treatment of ruptured blister-like intracranial aneurysms with flow diverters

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Objective

Clipping or coiling are established treatments for dome protection and aneurysm occlusion in patients presenting with aneurysmal subarachnoid hemorrhage. Blister-like aneurysms, however, are considered difficult to clip as well as to coil. Primary flow diversion (FD) might be an alternative, but it has been used rarely because of the necessity for dual antiplatelet therapy (AT) and the delayed remodeling and occlusion of the aneurysm.

Methods

We retrospectively evaluated the outcome of FD for treatment of ruptured blister like aneurysms. We only included aneurysms, which were judged not to be amenable for clipping or coiling by an experienced vascular neurosurgical and neuroradiological team. Aneurysms in which FD was performed as an adjunct to primary coiling and fusiform-dissecting aneurysms were excluded.

Results

Four consecutive patients with a ruptured blister-like aneurysm were treated with FD. The mean age was 55 years. Three aneurysms were located at the internal carotid artery and one at the middle cerebral artery. The mean aneurysm size was 2,5x2,3 mm. The mean interval from SAH to FD was 9,7 days (range 1-19). All patients had a Hunt and Hess score of 2. Prior to FD an external ventricular drain (2/4) or a lumbar drain was inserted (2/4). AT consisted in all patients of an i.v. loading dose of aspirin and an i.v. bolus of eptifibatid followed by continuous administration over the next 12 hours. 3/4 patients received a loading dose of clopidogrel. Postprocedural mono- or dual AT was maintained with aspirin and/or clopidogrel. There were no intra-procedural complications. Complete neck coverage was achieved in all cases. Placement of a single flow diverter resulted in immediate aneurysm occlusion in 2 aneurysms. One incompletely occluded aneurysm re-ruptured 7 days after initial FD and was treated with placement of 3 additional flow diverters. One patient had an in-stent thrombosis which occurred 5 days after a second FD was placed (7 days after primary FD) and was successfully treated with mechanical thrombectomy and stent angioplasty. Neurological outcome at 3 months ranged between 0 and 2 on a modified Rankin scale.

Conclusion

FD is a valuable treatment option for ruptured blister-like aneurysms deemed difficult to treat by conventional microsurgical or endovascular techniques. While immediate aneurysm occlusion is possible, there is a risk of early re-rupture or in-stent thrombosis. Patients need to be monitored carefully in the early post-interventional period.

Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P156

Sedierungsregime in anaeurysmatischer Subarachnoidalblutung und Vasospasmus.
Sedation regimes in aneurysmal subarachnoid hemorrhage and vasospasm.

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Objective

In this study, we aim to elucidate whether different sedation regimes have an influence on the incidence of vasospasm in SAH.

Methods

We analyzed patients who underwent sedation during their SAH treatment at our institution over a five-year period. We stratified patients according to the sedation regime into two groups: (A) those who primarily received propofol and sufentanil; (B) those who primarily received ketamine and midazolam. The incidence of vasospasm, diagnosed by transcranial Doppler sonography, was compared between the two groups by means of a Chi square test. Secondary endpoints included the incidence of cerebral infarctions and outcome at discharge, objectivized by the Glasgow Outcome Scale (GOS). Significance was assumed at a value of $p<.05$.

Results

A total of 82 patients were included in the analysis. Of these, 25 (30%) underwent sedation with (A), while the remaining 57 (60%) underwent sedation with (B). In the (B) group, 36 (63%) of patients suffered vasospasm, whereas only 8 (32%) of those in group (A) did. This difference was statistically significant ($p=.009$). Nevertheless, there was no statistically significant difference in the incidence of cerebral infarctions between both groups: 18 (32%) vs 11 (44%) ($p=.279$). Similarly, no difference in outcome, as stratified by GOS, could be observed ($p=.060$).

Conclusion

In our study, sedation with propofol and sufentanil appears to have a protective effect against vasospasm. Nevertheless, this effect did not translate into less cerebral infarction or better functional outcome. More studies are needed to elucidate the effect of sedatives in SAH.

Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P157

Terson-Syndrom bei Patienten mit aneurysmatischer Subarachnoidalblutung - eine 10-Jahres-Analyse
Terson syndrome in patients with aneurysmal subarachnoid hemorrhage – a 10-year analysis

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Objective

Terson syndrome (TS), an intraocular hemorrhage associated with subarachnoid hemorrhage (SAH), occurs in up to 46% of all SAH patients. Despite its high incidence, TS is underrepresented in the literature and SAH patients are sometimes not systematically evaluated for the presence of TS in clinical practice.

The aim of this work is to raise awareness of TS and to describe risk factors associated with its occurrence in a large cohort screened over a 10-year period.

Methods

All patients treated with aneurysmal SAH in our hospital between 10/2010 and 05/2020 were included in this retrospective study. The frequency of ophthalmologic screening by indirect funduscopy, as well as their results were investigated. In addition, collection and statistical analysis of epidemiological and clinical data were performed using chi-square, Kruskal-Wallis, ANOVA test, and multivariate regression and ROC analysis. Level of significance was set at $p<0.05$.

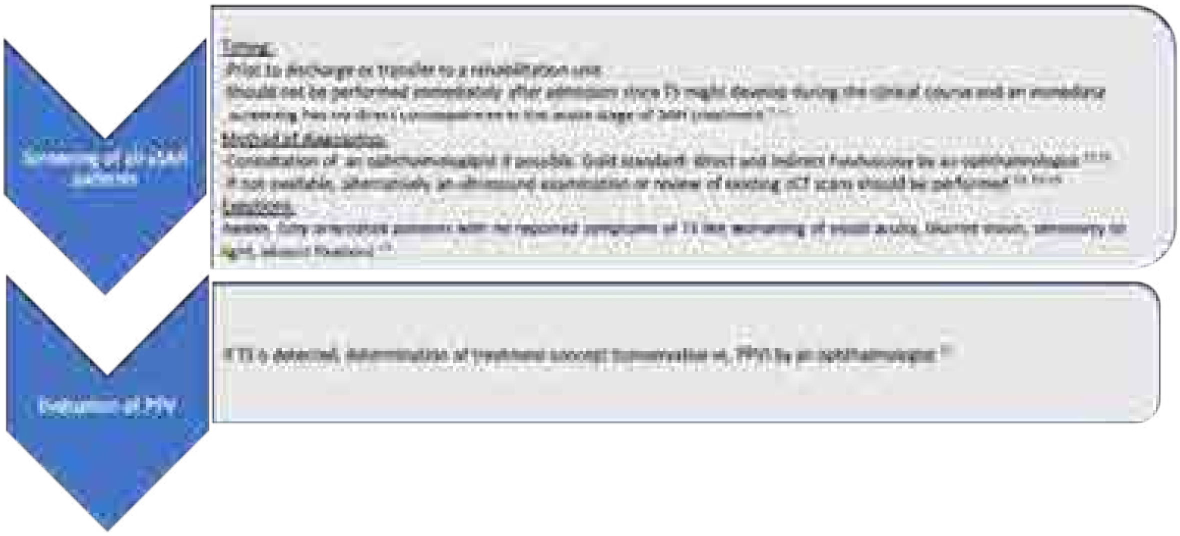
Results

Between 10/2010 and 05/2020, 617 patients were treated for SAH in our clinic. Of these, 367 patients (59.5%) were ophthalmologically examined for the presence of TS. The rate of TS in the examined patients was 21.3% (n=78). Patients with TS had significantly higher Fisher and World Federation of Neurosurgical Societies (WFNS) scores ($p<0.0001$). Regression analyses showed WFNS grade ($p=0.003$) and occurrence of epileptic seizures (ES) ($p=0.002$) as independent predictors of TS occurrence as did ROC analyses with a significant AUC of 0.66 for the combination of WFNS grade and seizures. In 12 (15.4%) patients with a total of 14 eyes, the TS had to be surgically treated by vitrectomy, which resulted in significant improvement of visual function in all patients: Mean preoperative best corrected visual acuity was 0.03 (sd 0.08) versus 0.76 (sd 0.21) postoperatively ($p<0.001$).

Conclusion

Terson syndrome is a common complication in patients with SAH, affecting approximately 1 in 5 patients. A higher WFNS grade and the occurrence of ES are associated with TS, therefore screening for TS should be performed in these patients. Summarizing the existing literature and the 10-year experience of our facility, we recommend the approach shown in Figure 1.

Abb. 1



Vaskuläre Neurochirurgie III/*Vascular neurosurgery III*

P158

Evaluation des SOFA-Scores als ein Tool zur Prädiktion von verzögerten Infarkten nach Subarachnoidalblutung
Evaluation of the SOFA score as a tool to predict delayed cerebral infarctions after subarachnoid hemorrhage

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Objective

Delayed cerebral ischemia (DCI) is a major complication after spontaneous subarachnoid hemorrhage (SAH). Inflammation is an important factor contributing to the development of DCI. The sequential organ failure assessment (SOFA) score is used in intensive care medicine to monitor organ failure and predict mortality of sepsis, and presents a holistic picture of inflammatory processes.The objective of this study was to determine whether the SOFA score obtained in the first 48h post-SAH could be used to predict the occurrence of delayed cerebral infarctions after SAH.

Methods

We retrospectively evaluated all SAH patients admitted to our neurosurgical intensive care unit during a 3-year period. Patients were included if a cranial CT scan obtained 14-28 days post-SAH and clinical data were available to determine the SOFA scores, patient characteristics, Hunt&Hess score (H&H), and World Federation of Neurosurgical Societies score (WFNS). Cranial CT scans were evaluated for the occurrence of delayed cerebral infarctions by a neuroradiologist. The threshold to predict delayed cerebral infarctions was determined for each score to maximize the sum of sensitivity and specificity.

Results

149 patients were screened, 71 fulfilled the inclusion criteria. 70.4% were female, mean age was 57.3±14.46 years. Median SOFA score was 4, median H&H was 3, median WFNS was 3.The SOFA score was significantly associated with occurrence of DCI ($p<0.0001$,) as well as H&H ($p=0.002$, OR=0.32) and WFNS ($p=0.02$).The calculated threshold for the SOFA score was ≥ 6 points with a positive predictive value (PPV) of 0.17 and a negative predictive value (NPV) of 0.87, a sensitivity of 0.4 and a specificity of 0.67. The thresholds were 5 points for the H&H score (PPV 0.12, NPV 0.7, sensitivity 0.59, specificity 0.18), and 5 points for the WFNS score (PPV 0.12, NPV 0.79, sensitivity 0.75, specificity 0.14).

Conclusion

The SOFA score is regularly documented in intensive care medicine and therefore available for most SAH patients treated on the ICU. SOFA score predicted the development of delayed cerebral infarctions with high NPV, similar to the established H&H and WFNS scores, while the predictive values were rather superior to the established scores. The SOFA score could therefore provide additional information to select patients at risk of delayed cerebral infarctions.

P159

Eine kosten- und zeiteffiziente Methode zur Generierung von *ex vivo* Glioblastom-Organoiden

Introducing an innovative and time-effective method to generate ex vivo patient-derived glioblastoma organoid models

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Objective

Glioblastoma multiforme (GBM) is the most prevalent primary brain tumor found in adults with a poor survival rate despite vigorous treatment. A suitable and realistic *ex vivo* model is still missing. Patient-derived, 3D organoid models (PDO) emerged recently illustrating the phenotypic and molecular heterogeneity of GBM and maintain the predominant features of their respective parental tumors. However, generating PDOs by dissecting the tumor tissue manually is time-consuming and costly. Therefore, we describe a new method of manufacturing PDOs directly from patients" freshly dissected tumor tissue using an automatic tissue chopper.

Methods

Glioblastoma multiforme (GBM) is the most prevalent primary brain tumor found in adults with a poor survival rate despite vigorous treatment. A suitable and realistic *ex vivo* model is still missing. Patient-derived, 3D organoid models (PDO) emerged recently illustrating the phenotypic and molecular heterogeneity of GBM and maintain the predominant features of their respective parental tumors. However, generating PDOs by dissecting the tumor tissue manually is time-consuming and costly. Therefore, we describe a new method of manufacturing PDOs directly from patients" freshly dissected tumor tissue using an automatic tissue chopper.

Results

The process of manufacturing PDOs using the chopper took in average two hours in comparison to five hours using the manual method. The automatically manufactured PDOs tended to round faster, leading to almost double the number of PDOs during the second week. After four weeks of culture, 735 PDOs were acquired automatically in comparison to 519 manually. Moreover, we manually developed 171 PDOs from the second patient, but 278 automatically. From the fourth patient we achieved similar results with 168 PDOs manually, but 250 automatically. Proliferation and apoptosis rates were similar among the two methods.

Conclusion

Usage of the automatic tissue chopper was proven to be time and cost effective whilst generating larger numbers of PDOs with same proliferation and apoptosis rates. This method could enable a higher throughput for drug screening in immunotherapy in PDOs of GBM patients.

P160

Mikroglia-vermittelte Effekte von Dexamethason auf das Auswachsen von Glioblastomzellen in einem organotypischen Rattenhirnschnittmodell (OBSC) und die Rolle der CXCL2/CXCR2-Achse

Microglia-mediated dexamethasone effects on glioblastoma (GBM) outgrowth in a rat organotypic brain slice co-culture (OBSC) and the role of the CXCL2/CXCR2-axis

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Objective

High numbers of GAMM (glioblastoma-associated macrophages/microglia) were correlated with poor clinical outcome in glioblastoma (GBM). Nevertheless, the specific role of the peripherally located microglia on tumor outgrowth remains elusive. Moreover, it has been shown that the frequently applied dexamethasone (DEX) significantly impacts on the immunological microenvironment. Here we further investigate the intertwined roles of microglia, the CXCL2/CXCR2-axis and DEX in our rat *ex vivo* model.

Methods

Brains from d6-d12 rats were cut into 350 µm slices and put on special 0.4 µm pore inserts. Three different cell lines (GBM rat cell lines 9L and S635 and a control rat astrocyte cell line) were vitally stained (CellBrite), formed into spheroid like structures on agarose and put on the OBSC. With previous treatment of the OBSC with PLX5622 (CSF1-R-antagonist) we generated microglia-depleted slices.

DEX and CXCR2-inhibitors were added to the medium and tumor outgrowth was quantified after 7 days.

Additionally, a membrane-based semi-quantitative proteome profiler (XL Rat Cytokine, biotechne) was used to screen for differential cytokine signaling in the supernatants.

Results

Both GBM cell lines showed less outgrowth on microglia native slices (fig. 1a).

DEX treatement lead to a pronounced spheroid condensation on plastic, especially for 9L (fig. 1c). This detrimental effect of DEX on the cell line was also seen on the OBSC for 9L (fig. 1d).

For the S635 cell line, DEX treatment of the OBSC lead to a pronounced outgrowth, but only when microglia is present on the slices (fig. 1b & 1e).

In our screening for differential cytokine signaling, we found an enhanced signal for CXCL2 secretion in the microglia native condition, for the control slices without spheroid no CXCL2 signal was detectable and for the DEX conditions we found an intermediate secretion in our pooled samples (fig. 2a). To look further into the CXCL2-signaling, we treated the slices with different CXCR2-inhibitors. We found enhanced outgrowth with the CXCR2-inhibitor Navarixin (fig. 2b) and Danirixin (not shown) when microglia is present. Dexamethasone modulated this effect towards enhanced overall outgrowth (fig. 2b).

Conclusion

The mere presence of microglia mediates a tumor outgrowth reducing effect, whereas microglia seems to mediate a tumor outgrowth promoting effect when DEX is applied. CXCR2-inhibition appears to reduce the microglial anti-tumor outgrowth effect with and without DEX.

Abb. 1

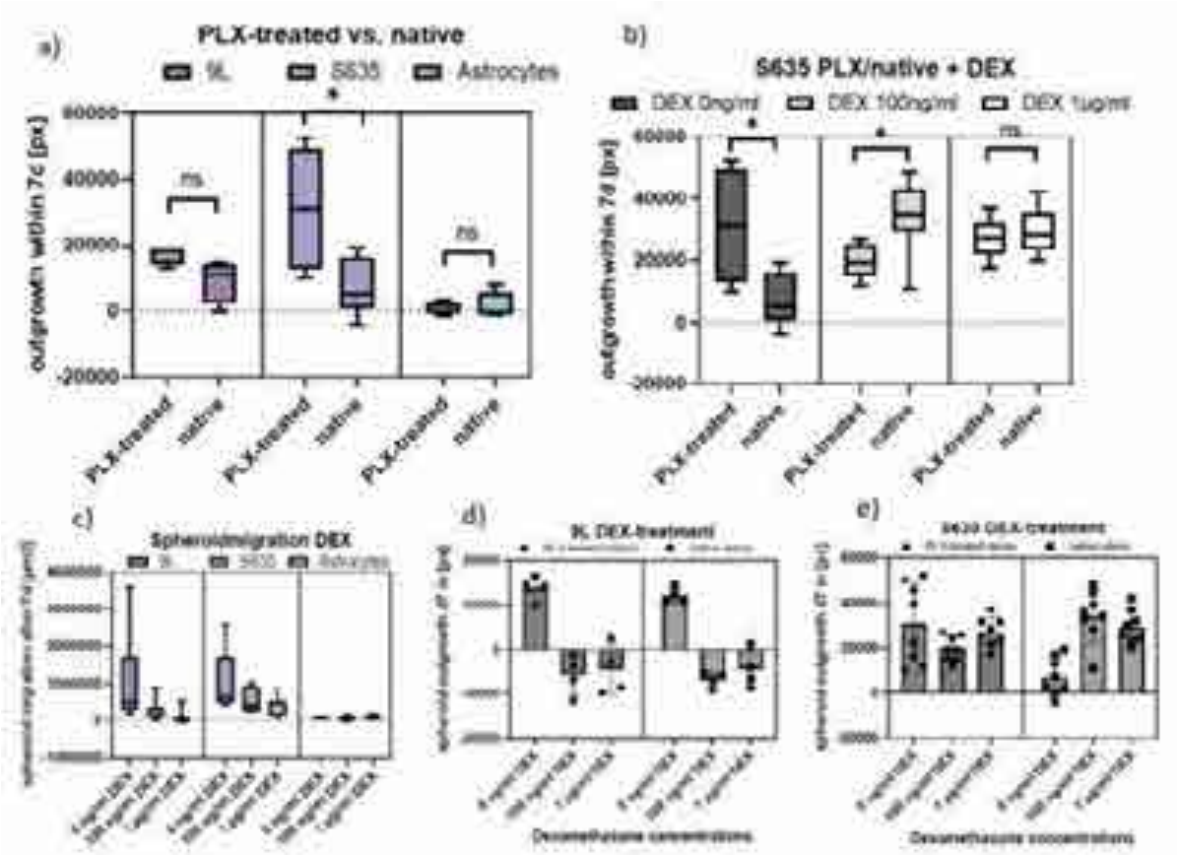
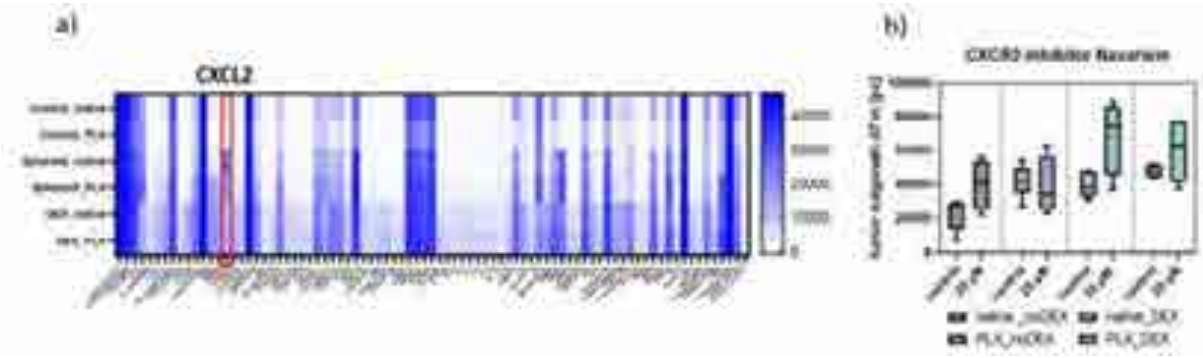


Abb. 2



P161

Glykierung beeinflusst die Expression von Sialyltransferasen von Glioblastom Zelllinien und führt zu Polysialylierung

Glycation interferes with sialyltransferase expression of glioblastoma cell lines and leads to increased polysialylation

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Objective

As known for other tumours, glioblastoma (GBM) cells prefer aerobic glycolysis for energy production (Warburg effect). This results in an increase of the reactive by-product Methylglyoxal (MGO), which leads to irreversible glycation resulting in protein functions" alterations. Previous studies have shown that glycation affects polysialylation, another common characteristic of cancer cells. Polysialylation, which results from upregulation of sialyltransferases modulates cell-cell-adhesion, invasion and immune recognition, is marked as a hallmark of cancer. In this study, we examined the influence of MGO on sialyltransferases in glioma cell lines and human astrocytes (hA).

Methods

The cell lines U251 (WHO grade 4, GBM), LN229 (WHO grade 4, GBM), U343 (WHO grade 3, glioma) and human astrocytes (hA) were treated with MGO and subsequently sialyltransferase expression was analysed on the mRNA level using qPCR. Polysialylation was examined with immunoblotting. In addition, RNAseq analysis of eight patient primary cultures from tumours with different glioma grades were evaluated on the sialyltransferase expression profile.

Results

The glioma cell lines and primary cultures showed a differential gene expression (DIGE) pattern of sialyltransferases. Interestingly, U251 expressed both sialyltransferases responsible for polysialylation (ST8SIA2 and ST8SIA4), LN229 only expressed the ST8SIA4 and U343 none. Glycation led to upregulation of all sialyltransferases in the LN229 cell line and ST8SIA4 in the U251. In contrast, MGO did not affect the sialyltransferase expression or lead to downregulation in the remaining cell lines. Polysialylation was detected in the cell lines expressing the corresponding sialyltransferases and was increased after glycation in the LN229 and U251.

Conclusion

Expression of sialyltransferases showed differential gene expression between the cell lines and patient primary cultures, which could be due to different glioma subtypes and genetic background. Glycation showed cell line specific effects on the expression of sialyltransferases. Polysialylation was increased after glycation, which could result in a more aggressive phenotype, due to the involvement in cancer hallmark processes such as immune evasion, resistance to apoptosis and enhancing invasion.

P162

Inhibition der Protein Tyrosin Phosphatase PTP1B mittels Claramine inhibiert die EGF induzierte Wachstumsstimulation in Glioblastomzellen durch Inhibition des MAPK Signalweges

Inhibition of the protein tyrosine phosphatase PTP1B by the small molecule inhibitor Claramine inhibits the growth stimulation of EGF in glioblastoma cells via inhibition of the MAPK pathway

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Objective

As most EGFR targeted therapies did not show a significant increase of progression free survival and overall survival of glioblastoma patients, novel ways of inhibiting tumor promoting pathways, such as MAPK and AKT signaling, need to be identified. Interestingly, the protein phosphatase PTP1B resembles a regulator of the activation of the EGFR pathway and also interferes with MAPK and Akt signaling. In this study, we used the selective PTP1B inhibitor Claramine to evaluated the role of PTP1B in downstream signaling of EGFR in glioblastoma cells.

Methods

Ten different glioblastoma cell lines were cultured in DMEM supplemented with 10 % FCS, 1 % glutamine, and 1 % penicillin/streptomycin. The CellTiter-Glo Luminescent Cell Viability Assay (CTG, Promega, Mannheim, Germany) was employed to determine viable cells by measuring ATP in cell lysates. Immunoblotting of protein samples of T98G lysates treated with EGF and/or Claramine was used to evaluate the activation of the EGFR, ERK1/2, and Akt.

Results

We identified 4 GBM cell lines responding to EGF by incubating them with 10 ng/ml and 100 ng/ml EGF for two days in FBS-free and FBS-containing DMEM media (Figure 1). The cell lines U343, T98G, MZ18, and MZ54 exhibited a significant increase in cell viability under EGF treatment in medium without FBS. To determine whether Claramine does interfere with the growth of GBM cells stimulated by EGF, cells from the lines T98G and MZ54 were incubated in the absence and presence of EGF (10 ng/ml and 100 ng/ml) and in the absence or presence of Claramine (5 µM). Here, Claramine abolished EGF-induced increased cell viability. Immunoblotting showed an activation of the MAPK pathway under EGF stimulation in T98G cells. Coincubation with Claramine and EGF reduced the activation of the MAPK pathway comparable to the control group (Figure 2).

Conclusion

These results show that Claramine inhibits the MAPK pathway downstream of the EGFR. Thus, selective PTP1B inhibition gives the opportunity to inhibit EGFR-induced MAPK pathway activation in glioblastoma cells and may thereby overcome resistance against EGFR-targeted therapies.

Abb. **1**

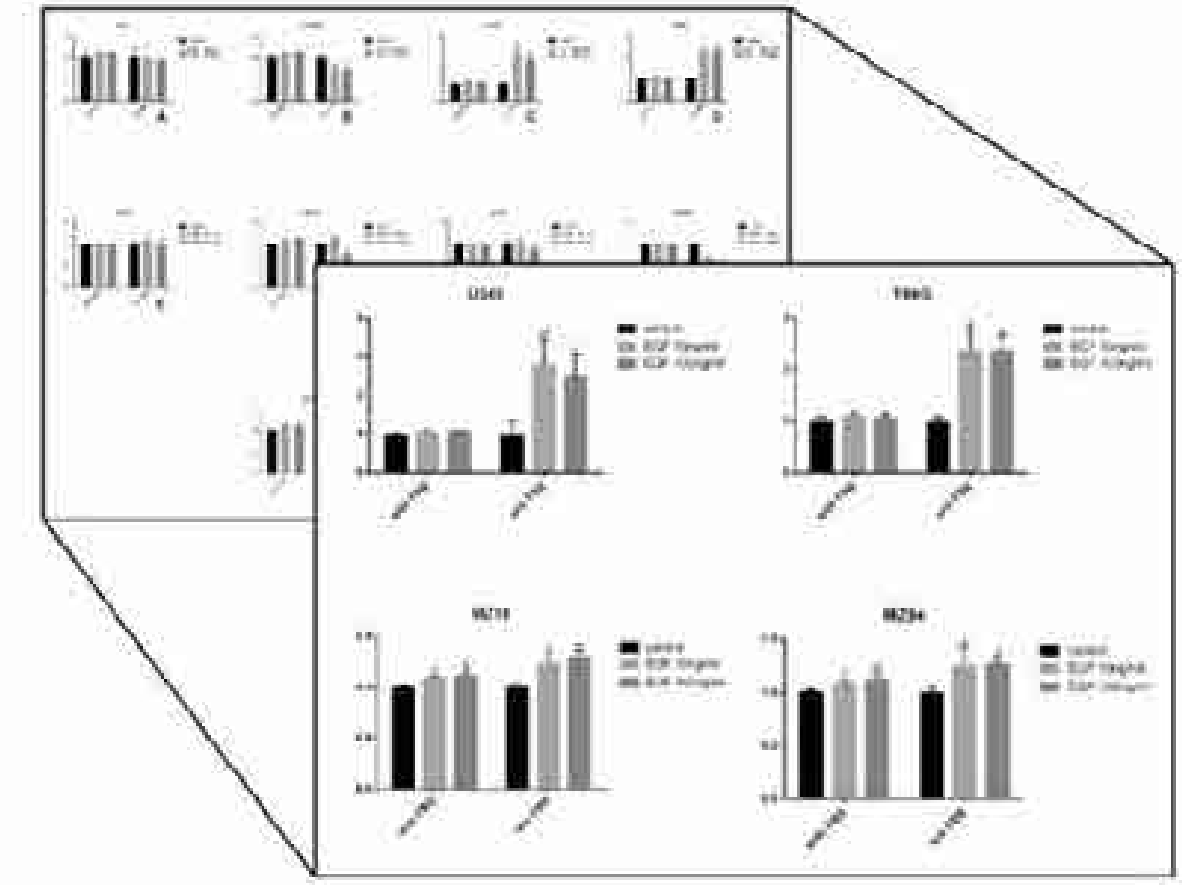

Figure 1. Determination of cell viability of 10 different GBM cell lines in the presence of EGF. The foreground panel represents the responsive cells.

Abb. 2

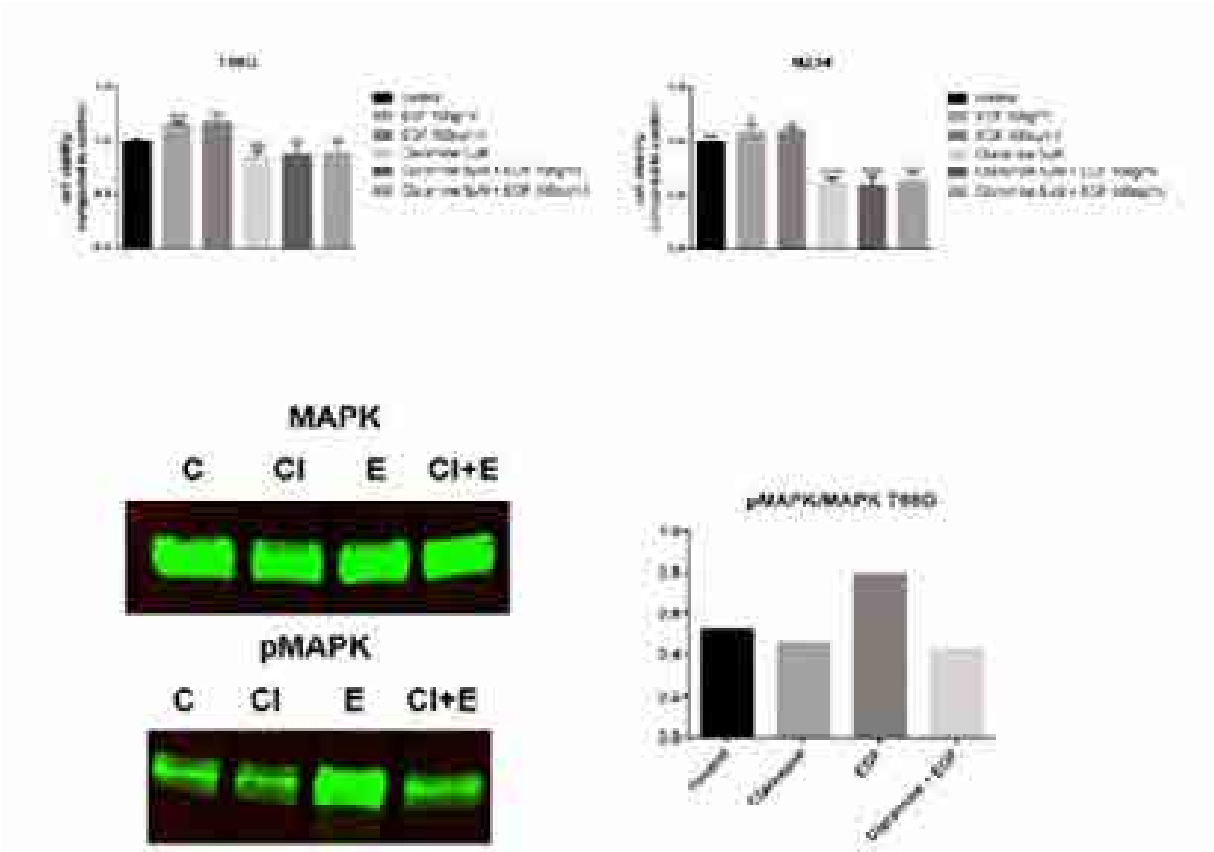

Figure 2. Viability of cells from the GBM lines T98G and MZ54 under the influence of EGF and Claramine (upper panel). Activation of the MAPK pathway under the influence of EGF and Claramine (lower panel).

P163

Ein neuartiger PCR-basierter Assay zur Identifizierung von IDH1 und TERT Promoter Hotspot Mutationen in zellfreier DNA

A novel PCR-based assay for the detection of IDH1 and TERT promoter hotspot mutations in cell-free DNA

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Objective

Molecular markers have become increasingly important for the diagnosis of tumors of the central nervous system. Among the most frequent genetic alterations in gliomas are mutations in the isocitrate dehydrogenase 1/2 and the TERT promoter region, which are routinely analyzed for the classification of gliomas. As the analysis of liquid biopsies (e.g. cell-free DNA from plasma or CSF) has become an important area of research, highly specialized methods for the genetic analysis of minute amounts of DNA are required. We sought to develop a robust and straightforward, PCR-based assay for the detection of these hotspot mutations.

Methods

Sequence-specific PCR primers were designed for wildtype DNA, IDH1 R132H and TERT promoter C228T/C250T mutations. By leveraging modified, wildtype-specific oligonucleotides, the amplification of wildtype DNA is inhibited, while mutated DNA can be freely amplified by PCR (Figure 1). A control primer pair flanking the analyzed region allows for internal control of successful PCR amplification. Amplicon sizes were chosen to be <200 bp for optimal analysis with highly fragmented cell-free DNA. cfDNA was extracted from cell culture medium from U251 (C228T) and T98G (C250T) glioblastoma cell lines or plasma of non-tumor controls using the QIAamp Circulating Nucleic Acid Kit (Qiagen). DNA was then quantified with the Qubit dsDNA HS Assay Kit (Thermo Fisher Scientific).

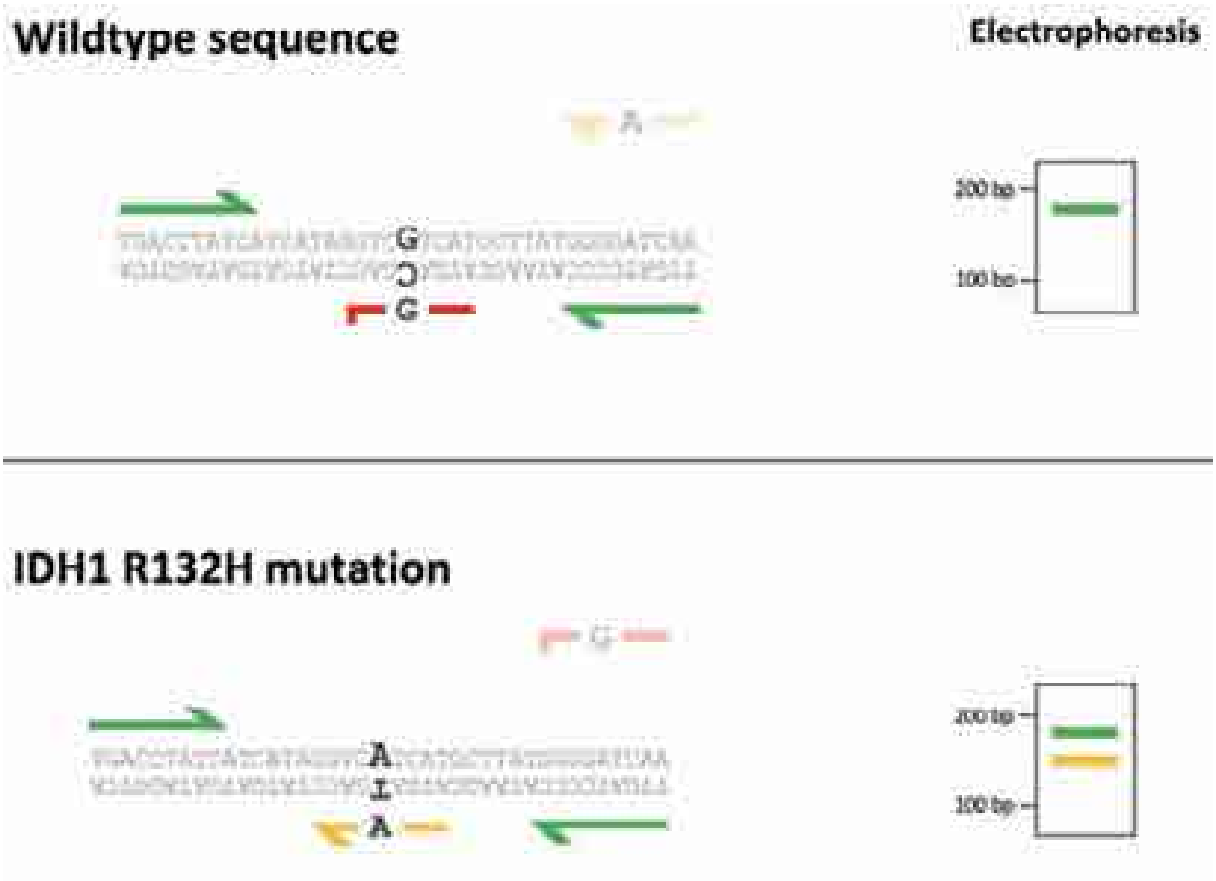
Results

The assay shows 100% correlation with Sanger sequencing results in bulk cell line DNA. For cfDNA, decreasing amounts of DNA were tested. Amounts of < 1 ng per reaction were sufficient for reliable detection of TERT promoter mutations. The limit of detection for tumor-derived cfDNA was analzed by spike-in experiments and showed reliable detection of the mutation for mutant allele fequencies > 5%. Specificity of the PCR assay was 100% as no mutations could be detected in plasma cfDNA samples from non-tumor patients (n=10).

Conclusion

Here we describe a rapid and straight-forward PCR-based detection method for glioma hotspot mutations with high specifictiy and sensitivity that can be broadly applied to bulk DNA, cfDNA and potentially single cells. Due to the flexibility of primer sequences, the presented method can easily be modified to detect further mutations, i.e. H3 K27M.

Abb. 1


Wildtype sequence
Electrophoresis
200 bp
100 bp
IDH1 R132H mutation
200 bp
100 bp

Neuroonkologie experimentell III/*Experimental Neuro-Oncology III*

P164

Die DNA-Methylierungsanalyse ist eine effektive Methode zur Identifizierung von Tumoren in mutmaßlichen, jedoch immunohistochemisch nicht-spezifizierbaren, neuroonkologischen Fällen

DNA-methylation profiling is an effective asset for identification of tumors in suspected, yet immunohistochemically unspecifiable, neuro-oncological cases

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[2]Charité - Universitätsmedizin Berlin, Department of Neuropathology, Berlin, Deutschland
[3]German Cancer Research Center (DKFZ), German Cancer Consortium (DKTK), Partner Site Berlin, Heidelberg, Deutschland
[4]University Medicine Greifswald, Institute of Pathology, Greifswald, Deutschland
[5]Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Berlin, Deutschland
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Objective

Patients with a suspected neurooncological disease on radiographic images and no histopathological evidence of a tumor on the surgically retrieved tissue, pose a great challenge for clinicians and neuropathologists. DNA methylation-based classifications and copy number variation (CNV) analysis allow robust brain tumor classification. As we recently had provided preliminary data of this technique, to be effective in classification of histopathologically unspecifiable or negative cases, we intended to evaluate its diagnostic properties in a case series.

Methods

We screened all neurosurgical cases, which underwent surgery at our institution between 2009 and 2021, with suspected neurooncological, but negative or unspecific histopathological diagnosis. We differentiated two groups: cases with cell-enriched, reactive tissue (+/- single tumor cells), insufficient to fully classify the lesion according to criteria of WHO for CNS tumors (group 1) and cases without histological evidence of tumor cells (group 2). In both groups, DNA methylation profiling was applied. Endpoints were diagnostic results of DNA methylation profiling (classifier Score ≥0.9) and evidence/no evidence of tumorigenic CNV alterations and eventually feasibility to make a diagnosis according to WHO 2021 criteria for brain tumors.

Results

23 cases with unspecifiable histopathological diagnosis were identified, out of whom 5 (21.7%) were confirmed as healthy brain tissue via DNA-methylation profiling, whereas the eventual diagnosis of tumorigenic tissue was provided in 18 (78.3%) cases. 14 of these were assigned to group 1, 4 cases to group 2. In 6 cases of group 1 (42.9%) DNA-methylation profiling resulted in a successful tumor classification (score ≥0.9) compared to 1 case (25%) in group 2. CNV indicated tumorigenic alterations in 9 (64.3%) patients in group 1 and 2 (50%) patients in group 2. Specific tumor alterations in the CNV were found in 8 (57.1%) patients in group 1 and in 1 (25%) patient in group 2. Combining CNV and DNA-methylation profiling, a final tumor diagnosis according to WHO 2021 criteria was feasible in 9 (64.3%) cases in group 1 and 3 (75%) cases in group 2. Median time from surgery to histopathological diagnosis was 6 and 7 days and 32.5 and 31 days for integrated diagnosis (group 1 vs. group 2).

Conclusion

Molecular diagnostics with DNA-methylation profiling and CNV analysis substantially increases the likelihood of a definitive diagnosis according to 2021 WHO criteria for these challenging cases.

Neuroonkologie experimentell III/*Experimental Neuro-Oncology III*

P165

Die Rolle des Onko-Metaboliten (R-2-Hydroxyglutarat) in der Mikroumgebung des IDH-mutierten Glioblastoms
The role of onco-metabolite (R-2-hydroxyglutarate) in the IDH mutant glioblastoma microenvironment

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Objective

Tumor-associated astrocytes in the microenvironment of IDH wild type glioblastoma contribute to anti-tumor immunity and support pro-oncogenic signaling. Due to the unique metabolic niche in IDH mutated glioma, the role of astrocytes remained unexplored. Here, we characterized the spatiotemporal adaptation and cell-cell communication pattern of astrocytes in IDH-mutant glioma.

Methods

We purified and transcriptionally profiled astrocytes from 9 patients with confirmed IDH1-R132H mutation, by means of RNA-sequencing and the data were analyzed using the established pipelines. Spatially resolved transcriptomics was performed in 6 patients. Using SPATA2 and weighted correlation network analysis, we integrated cell specific signatures and spatial transcriptomics profiling. We validated our findings using human organotypic slice model inoculated with IDH-mutant cell line or treated with oncometabolite 2-hydroxy glutarate.

Results

Our results from RNA sequencing showed a inflammatory transformation of astrocytes within the microenvironment of IDH-mutated tumors significantly correlated with signatures of the A1-phenotype of reactive astrocytes. Using our established human neocortical GBM model inoculated with IDH mutant tumor and R-2HG treatment, we showed that we were able to activate inflammatory transcriptional programs in astrocytes, mediated by the presence of microglia. Further, by spatially mapping the transcriptomic profiles of purified microglia, we were able to confirm that microglia also demonstrate inflammatory activation in IDH mutated glioma. This inflammatory astrocyte transformation is associated with a loss of neurotransmitter homeostasis (disrupted levels of glutamate) in the treated sections, as has been previously reported in IDH mutated tumors. Additionally, R-H2G increased neuronal spiking rate in, pointing to potential excitotoxicity.

Conclusion

Our work provides a crucial contribution towards understanding the role of R-2HG in the IDH mutant glioma microenvironment and sheds light on the significant microenvironmental differences to IDH wild-type glioma.

P166

Nimodipin schützt Schwann-Zellen und neuronale Zellen, nicht aber Tumorzellen vor Cisplatin-assoziiertem Zelltod

Nimodipine treatment protects Schwann cells and neuronal cells but not tumor cells from cisplatin-induced cell death

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Objective

Cisplatin-based chemotherapy still represents the standard therapy for many solid tumors. However, treatment often leads to neurotoxicity and the development of peripheral neuropathy including paresthesia and loss of motor functions, limiting patients' quality of life. In previous studies, we demonstrated a protective effect of nimodipine treatment on cell stress of Schwann cells and neuronal cells. Therefore, the aim of this study was to analyze the effect of nimodipine on cisplatin-treated Schwann cells, neuronal cells and tumor cells.

Methods

The Schwann cell line SW10 and the neuronal cell line RN33B were used to investigate the neuroprotective effect of nimodipine, as well as the tumor cell lines A549 (non-small cell lung carcinoma) and SAS (squamous cell carcinoma) to exclude a protective effect on tumor cells. To investigate the influence of pretreatment with nimodipine under cisplatin therapy on cell survival, lactate dehydrogenase activity in the cell supernatant was used as a marker for cell death. In addition, propidium iodide was used to detect dead cells and CellRoxGreen (Thermo Fisher Scientific) to determine oxidative stress via fluorescence microscopy. The level of nimodipine-dependent regulated and apoptosis-related proteins LMO4, Akt, CREB and Stat3 were analyzed using western blot.

Results

The cytotoxic effect of cisplatin was reduced up to 38% in neuronal cells and up to 60% in Schwann cells by pretreatment with nimodipine, while a reduction of dead cells was also evident in immunofluorescence. However, no decrease in the cytotoxic effect was detected for the tumor cell lines by nimodipine pretreatment. In Schwann cells and neuronal cells the downregulation of LMO4 induced by cisplatin was counteracted by nimodipine. Furthermore, an activation of anti-apoptotic signaling pathways was demonstrated. Surprisingly, the opposite effect could be demonstrated in the tumor cell lines.

Conclusion

Nimodipine pretreatment had a neuroprotective effect on Schwann cells and neuronal cells without reducing the cytotoxic effect of the chemotherapeutic agent cisplatin on tumor cells. Thus, the treatment with nimodipine may represent a new approach against neurotoxically side effects in cisplatin chemotherapy.

P167

ALA-RDT in GBM: Protokoll einer Phase I/II Dosiseskalationsstudie zur radiodynamischer Therapie mit 5-Aminolevulinsäure bei Patienten mit erstmaligem Rezidiv eines Glioblastoms

ALA-RDT in GBM: Protocol of the Phase I/II dose escalation trial of radiodynamic therapy with 5-Aminolevulinic acid in patients with first recurrence of glioblastoma

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Objective

Despite improvements in surgical as well as adjuvant therapies over the last decades, the prognosis for patients with glioblastoma remains poor. Five-Aminolevulinic acid (5-ALA) is already used successfully in resective surgery and as a photosensitizer for photodynamic therapy. New findings reveal potential as a radiosensitizer in combination with ionizing radiation. Our study aims to determine the maximum tolerated dose of 5-ALA concurrent to radiotherapy, as well as its tolerability and impact on survival parameters.

Methods

We initiated a phase I/II dose escalation study, treating patients with first recurrence of glioblastoma with oral 5-ALA concurrent to radiotherapy (RT). This prospective single-center study based in the University Hospital Münster aims to recruit 30 patients between 18 and 75 years with histologically verified first recurrence of MGMT-non-methylated glioblastoma in good performance status (KPS ≥ 70), starting November 2022. Following a 3+3 dose-escalation design, patients having undergone re-resection will receive a 36 Gy RT including radiodynamic therapy fractions (RDT). RDT constitutes of oral administration of 5-ALA before the irradiation session. Two cohorts will additionally receive two fractions of neoadjuvant treatment three and two days before surgery. To determine the maximum tolerated dose of repeat 5-ALA-administration, the number of RDT-fractions will increase, starting with one to a maximum of eight, while closely monitoring for safety and toxicity. Follow-up will be performed at two and five months after treatment. Outcome measures are event-free-, progression-free-, and overall-survival. Additionally, 5-ALA metabolites and radiobiological markers will be analysed throughout the course of therapy and tissue effects after neoadjuvant treatment will be determined in resected tissue.

Results

"ALA-RDT in GBM" is the first trial to evaluaterepeated administration of 5-ALA as a radiosensitizer for treatment of recurrent glioblastoma in human patients.

Conclusion

Recruitment for this study is currently ongoing. This trial is registered under www.cliniclatrials.gov (Identifier: NCT05590689)

Neuroonkologie III/*Neuro-Oncology III*

P168

Hirnmetastasen bei urogenitalen Primärtumoren – Demographie, klinischer Verlauf und Follow-up
Brain metastasis from urogenital cancer –demography, clinical course, and follow up

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[4]Klinikum Fulda, Department of Neurosurgery, Fulda, Deutschland

Objective

To asses demographic and clinical parameters, treatment, and course of disease in patients with brain metastasis (BM) from urogenital cancer.

Methods

We retrospectively identified patients who underwent resection of BM from urogenital primary tumors. We analysed and described clinical and treatment related parameters with respect to histology, time to occurrence and systemic/ BM-specific treatment.

Results

We included 57 patients with a mean age of 60.2 (range 28-79) years at diagnosis of primary tumor and 67 (range 31-84) years at BM diagnosis. Two thirds were male. Histology was renal-cell carcinoma in 19 (33.3%), prostate carcinoma in 15 (26.3%), bladder carcinoma in 14 (24.6%), as well as cervical and ovarial cancer in 4 (7.0%) and 3 (5.3%) patients, respectively. Two patients hat a leiomyosarcoma and primary peritoneal cancer (1.8% each).

Treatment for primary tumor included resection (78.9%), neo-adjuvant and post-operative chemotherapy (8.8%/28.1%), neo-adjuvant and post-operative radiation (1.8%/15.8%), and immuno-/targeted therapy (35.1%). Many patients received a combination of the latter.

The mean interval between primary tumor and BM diagnosis was 47 months (range -1 to 241). At the time of BM diagnosis, in 77.1% of patients the primary tumor was controlled and 42.1% had no systemic metastases. Almost all patients (96.5%) suffered from BM-related symptoms, 66.7% had a preoperative KPS ≥70. Most patients had one BM (71.9%), while 22.8% had 2-3 and 5.3% >3 BM. Gross-total resection was achieved in 93.0%. Adjuvant local BM-Treatment comprised focal radiation therapy (63.2%), whole-brain-radiation therapy (15.8%), and stereotactic radiosurgery (5.3%). 20 patients (35.1%) received chemotherapy and 16 (28.1%) (additional) targeted therapy.

13 patients (22.8%) suffered from ≥1 BM relapse. At the time of the analysis, 31 (54.4%) patients had died; cause of death was cerebral (16.1%), systemic (32.3%), or remained unkown (48.4%). The mean overall survival (OS) was 61 months (range 2-244) and 14 (range 0-85) after initial tumor and BM, respectively. Surgical complication rate was 15.8%.

Further survival analysis was omitted due to subgroup sizes.

Conclusion

Even though, renal cell carcinoma is reported among the frequent primary tumor causing BM, in our cohort prostate and bladder carcinoma showed a similar frequency. Patients with BM from urogenital cancer seem to have a rather comprised physical status and suffer from a high surgical complication rate.

P169

Langzeitüberleben nach der Diagnose von Hirnmetastasen – klinischer Verlauf und Follow-up
Long-term survival after the diagnosis of brain metastasis – the clinical course and follow-up

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Objective

To asses demographic and clinical parameters, treatment, and course of disease in patients surviving longer ≥ 5 years after the diagnosis of brain metastasis (BM).

Methods

We retrospectively identified patients who were treated for BM and survived ≥ 5 years after initial BM diagnosis. We analysed and described clinical and treatment related parameters with respect to histology, time to occurrence and systemic/ BM-specific treatment

Results

We included 68 patients with a mean age of 55 years (range 24-81) at diagnosis of primary tumor and 57 (range 85-84) at initial BM diagnosis. Histology was non-small-cell lung cancer in 28 (41.2%), melanoma in 17 (25.0%), breast cancer in 13 (19.1%), renal carcinoma and small-cell lung cancer in 3 (4.4%) each, and four rare tumors in one case each (1.5%). Treatment for primary tumor included resection (73.5%), chemotherapy (51.5%), radiation (35.3%), interferon therapy (17.6%), and immuno-/targeted therapy (54.4%). Most patients received a combination of the latter. The mean interval between primary tumor and BM diagnosis was 33 months (range -2 to 277). At the time of BM diagnosis, 60.3% of patients presented with systemically stable disease, 63.2% showed BM related symptoms, 95.6% showed a KPS ≥70. Most patients had one BM (66.2%), while 22.1% had 2-3 and 11.8% >3. Initial treatment for BM comprised resection (52.9%), stereotactic radiosurgery (33.8%), whole-brain-radiation therapy (4.4%), and interstitial brachytherapy (2.9%). Approximately half of the patients (44.1%) suffered from ≥1 BM relapse at initial treatment site. At the time of the analysis, 13 (23.5%) patients had died; cause of death was cerebral in two, systemic progression in three and unknown in eight patients. The mean overall survival (OS) rates were 123 months (range 64-361) and 90 (range 59-246) after initial tumor diagnosis and BM, respectively. All patients suffering from melanoma who had received interferon therapy (n=8) survived. Neither systemic status at BM diagnosis nor the administration of novel treatment agents or chemotherapy after BM diagnosis influenced OS. Further survival analysis was omitted due to subgroup sizes.

Conclusion

Despite the usually fatal course after BM development, some patients show long-term survival. Whether specific genetic parameters have a particular impact in this subgroup of patients, warrants further investigation.

Neuroonkologie III/*Neuro-Oncology III*

P170

Operative Therapie von Läsionen der Pinealis-Loge: Machbarkeit, Morbidität und funktionelles Outcome- Erfahrungen aus einem klinischen Zentrum

Surgical treatment of lesions of the pineal region: feasibility, morbidity and functional outcome- a single center experience.

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Objective

Pineal region lesions can impose a challenge for surgical access due to the deep location, narrow field of view and intricate vascular anatomy. However, the pineal region often harbors rare malignancies, thus, obtaining a histological diagnosis is mandatory. Furthermore, these lesions are often symptomatic and require a safe maximal resection. We analyzed the outcome following surgery of lesions of the pineal region concerning functional and histological results as well as surgical morbidity.

Methods

All patients who underwent surgical treatment for a pineal region lesion between September 2013 and May 2022 at our institution were included in the study. Retrospective evaluation of tumor size, clinical symptoms at presentation, type of surgical access, duration of surgery, complication rate, necessity for re-operation and histology was performed. Functional status prior to and post surgery was evaluated using the modified Rankin Scale (mRS). Median mRS values pre- and post surgery were compared using student's t-test.

Results

Data of 35 patients (19 male, 16 female) were available for final analysis. Mean age at diagnosis was 39 years. Most patients (30/35, 86%) received a supracerebellar infratentorial approach (SIA). In 3 of the remaining 5 patients ventriculocisternostomy (VST) combined with endoscopic biopsy was conducted, and 2 patients received a staged approach (VST followed by SIA). Median surgical time was 170 minutes for the SIA and 53 minutes for the VST. Median in-hospital stay was 10 days. Histology revealed a pineal cyst in most patients (34%), followed by pineal tumor of intermediate differentiation CNS WHO 2-3 (14%). Further pathologies included a pineocytoma CNS WHO 1 (n=5), germinoma (3), pilocytic astrocytoma (3), metastasis (3), epidermoid (1), meningioma (1), haematoma (1) and pineoblastoma (1). Surgical mortality rate was 0 %, while morbidity was 28% (10/35) including transient trochlear or/and oculomotor palsy (4/10), cerebospinal fluid fistula (CSF) (3/10), thalamic infarction (1/10) and bleeding (2/10). A revision surgery was performed in 5/10 of these patients, either for evacuation of bleeding or correction of CSF-fistula. The median mRS improved from 2 prior to surgery to 1 post surgery ($p = 0.047$).

Conclusion

Surgical access is a safely feasible option for pineal region lesions when performed by an experienced surgeon and provides both histological clarification and functional improvement.

Neuroonkologie III/*Neuro-Oncology III*

J-SBNC026

Intramedullärer B-Zell-Lymphom-Tumor: Fallbericht und systematische Überprüfung
B-cell Lymphoma Intramedullary Tumor: Case Report and systematic review

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Objective

The main objective of the present study is to report a surgical case treated for a large diffuse B-cell lymphoma, in addition to presenting the results of a systematic review of primary intramedullary spinal cord lymphoma.

Methods

The study protocol was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. A systematic search of the MEDLINE electronic database was performed to identify studies reporting clinical features of children and adults who presented with an intramedullary lymphoma. Manuscripts were excluded if the full-text article was not available, original data was not reported (e.g. review articles) or if the main disease was not intramedullary lymphoma. A structured data extraction form was employed to standardize the identification and retrieval of data from manuscripts. To enlighten the discussion, a case is also presented.

Results

21 studies were included, reporting a total of 25 cases (20 male and 5 female patients), ranging from 15-79 years (average 52,72 years). Only 10 cases reported the follow-up as 4 patients lost to follow-up and 11 papers did not report it. The average follow-up was 1,73 years (from 2 weeks to 6 years).

Our treated case is a female, 82 years-old, Fitzpatrick II, diagnosed and treated for non-Hodgkin lymphoma 7 years ago, admitted with mental confusion and memory loss for the past 2 months. One day before admission, she displayed Brown-Séquard syndrome. An expansive lesion from C2 to C4 in the cervical spinal cord was found and a hypersignal spinal cord adjacent was described at the bulb medullary transition to C6-C7 level. A primary spinal cord tumor was considered, as well as a melanoma metastasis, due to the lesion"s flame-pattern. The patient presented a partial recovery of symptoms and a reduction of the spinal cord edema after being empirically treated with corticosteroids, but the lesion maintained its extent. Subsequently, a large diffuse B-cell lymphoma with non-germinal center was found in open body biopsy, infiltrating neural tissue.

Conclusion

Intramedullary lesions can be related to several pathologies, such as tumors and lymphomas, even if etiology is different, clinical presentation is most of the time similar. Occurrence of Brown-Séquard syndrome is commonly concurrent to those lesions and is valuable evidence of a spinal cord hemisection. It"s important to stress the value of surgical procedures to conclude neurological diagnosis.

Neuroonkologie III/*Neuro-Oncology III*

P171

Perioperative Bewertung und Überwachung des intrakraniellen Drucks durch die Bestimmung des Durchmesser der Sehnervenscheide bei NF2-assoziierten intrakraniellen Falxmeningeomen.

Perioperative evaluation and monitoring of intracranial pressure by optic nerve sheath diameter measurements in NF2-associated intracranial meningiomas of the falx.

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Objective

To evaluate long-term intracranial pressure in Neurofibromatosis Type 2 (NF2) patients who have been operated on intracranial meningiomas of the falx with/without infiltration of part of the cerebral venous sinus.

Methods

We retrospectively measured bilateral optic nerve sheath diameter (ONSD) with T2-weighted magnetic resonance imaging (MRI) scans of the orbit in 7 NF2 patients with 14 operated intracranial falx meningiomas during their pre- and postoperative follow-up. The mean ONSD of both eyes was calculated for further evaluation.

Results

All tumors were operated on due to critical growth progression. Headache was the most common symptom before surgery (5/14) in 36%, followed by new focal neurological deficits in 29% (4/14) and one patient with nausea and vomiting (7%). None of the patients were treated with a shunt system before surgery. 128 MRI-based ONSD measurements were performed in a mean follow-up of 68 ± 67(3-179) months before and 27 ± 35 (1-103) months after surgery. ~71% (10/14) of tumors were totally resected (Simpson grade 1) and the majority of tumors (10/14, ≙71%) infiltrated parts of the cerebral venous sinus. Symptoms postoperatively improved in 86% (12/14) and only 2 cases (2/14 ≙ 14%) exhibited new neurological deficts and postoperative seizures. Up to the last MRI directly before surgery, there was a non-significant ($p > 0.05$) and approximately 2% increase in mean preoperative ONSD values (6.32 ± 1.09 mm) compared to the mean baseline ONSD values (6.16 ± 1.16 mm). Nevertheless, a significant decrease ($p = 0.001$) in mean ONSD values after surgery could be observed (5.79 ± 1 mm). At the last follow-up MRI, values were still stably lower (5.69 ± 1.04 mm) with a minimal tendency to further decrease (approximately 2%).

Conclusion

Falx meningiomas with contact or infiltration to parts of the cerebral venous sinus seem to play an important role in increased intracranial pressure in patients with NF2. Timing of surgery is crucial to avoid the long-term effects of increased pressure. Regular ONSD measurements by ultrasound or MRI could help to find the ideal timing and assess postoperative outcomes. Other influencing and correlating factors such as volumetry, collateral formation, and intracranial tumor burden in general are under investigation

P172

Resektion von Meningeomen nahe motorisch eloquenter Areale unter Zuhilfenahme präoperativer navigierter transkranieller Magnetstimulation - eine Vergleichsstudie

Resection of meningiomas in motor eloquent regions aided by preoperative navigated transcranial magnetic stimulation – a comparative analysis

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Objective

Navigated transcranial magnetic stimulation motor mapping is a reliable tool for preoperative risk stratification prior to resection of intra-axial lesions. The utility of presurgical motor mapping for meningiomas located close to the motor cortex has not been investigated in a comparative analysis.

Methods

Patients with meningiomas located in the central region were retrospectively analyzed. Patients undergoing nTMS mapping for motor function (Nexstim NBS 5, Nexstim Oy, Helsinki, Finland) were compared to a cohort of patients of our institution who did not receive presurgical motor mapping. All patients were treated between April 2016 and October 2022. Clinical examinations, imaging studies, nTMS examinations and surgical protocols were analyzed.

Results

61 patients (55.7% female) aged 62.4 ± 15.8 years were included. 29 patients received presurgical nTMS with or without nTMS-based DTI fibertracking (TMS-group) and 32 were operated on without functional imaging (non-TMS-group). Both groups did not differ in gender (p=0.61), age (p=0.93), tumor volume (p=0.77), and location (p=0.64). Preoperatively, 19 patients presented with hemiparesis, 2 with isolated paresis of the upper extremity, 7 with isolated lower limb paresis, 4 with disturbance of fine motor skills. Preoperative motor status did also not differ among the two groups (p=0.84). Surgical time was shorter in the non-TMS-group (p=0.048) but complication rates did not differ (p=0.16).

Concerning the TMS-group, compression of the nTMS-hotspot gyri was associated with presence of a preoperative motor deficit (p=0.01) as well as postoperative deterioration in motor function (p=0.04). In contrast, the resting motor threshold could not predict poor motor outcome after tumor removal (p=0.5).

At discharge from hospital, motor function deteriorated in 8 patients in the TMS-group and in 10 patients in the non-TMS-group, whereas motor status improved in 5 patients in each group (p=1.0). Among those patients, who underwent surgery without a preoperative motor deficit, no patient developed a new permanent deficit (at 3 months postoperatively) in the TMS-group whereas 4 patients suffered from a new permanent motor deficit (p=0.13).

Conclusion

nTMS motor mapping could not preserve patients from developing a new postoperative deficit but nTMS motor mapping data allows excellent risk stratification in the presurgical planning process for intracranial motor-eloquent meningiomas.

Neuroonkologie III/*Neuro-Oncology III*

P173

Spirituelle Belastung neuroonkologischer PatientInnen: Eine Erhebung in Ostdeutschland
Spiritual care in Neuro-oncology: A challenging problem in Eastern Germany?

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Objective

Neuro-oncological diseases are associated with high morbidity and mortality and subsequently with a significant burden for patients and their relatives. According to the Total Pain concept, ailments can be categorized into physical, psychological, social and spiritual burden. While physical and, increasingly, psychological complaints are regularly addressed in everyday clinical practice, social and, above all, spiritual complaints hardly play a role.

The aim of the present work was to evaluate the frequency of spiritual complaints in a tertiary neuro-oncological care centre in Eastern Germany.

Methods

Over a six-month period (02/2021 – 07/2021), all patients treated in our neurooncologic out-patients clinic were routinely asked to answer a palliative care questionnaire. The screening tool used was the palliative care basic assessment (modified MIDOS). This questionnaire addresses spiritual complaints related to God and loss of faith. Psycho-oncological distress and quality-of-life was assessed by the EORTC-qlq-C30, -BN20 questionnaire and the distress-thermometer

Data were collected and analysed using Prism 9 (GraphPad Prism).

Results

The present analysis includes a cohort of 419 neuro-oncological patients treated in 609 consultations. 168 patients suffered from malignant and / or life-threatening neoplasms (40 %). 252 patients were female, 168 male. Median age was 57 years (18 – 87 years).

In 15 / 609 consultations (2.4 %), patients reported spiritual discomfort related to God and in 18 consultations (2.9 %), a loss of faith as a problem. Interestingly, questions about spiritual complaints or a loss of faith were completely rejected by patients in 86 and 85 consultations (14 % each), respectively.

Spiritual complaints had no impact on psycho-oncological distress and overall quality of life ($p > 0.05$).

Conclusion

Less than 3 % of our neuro-oncology patients report spiritual problems or a loss of faith. On the other hand, almost 15 % reject the question about spiritual complaints. Spiritual complaints probably play a minor role in this cohort in Eastern Germany. Further studies are needed to identify spiritual complaints and need for spiritual care in Germany as a whole to be able to treat palliative care patients according to the total pain model.

P174

Postoperative Wundheilungsstörungen bei Glioblastom-Patienten: Fluch oder Segen?
Surgical site infections after glioblastoma surgery: boon or a bane?

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Objective

Surgical site infections (SSI) are among the most common postoperative complications. Glioblastoma multiforme is the most frequent malignant brain tumor and its treatment is associated with poor outcome. The effect of surgical site infections on the course of Glioblastoma patients is unclear since available data are limited and contradictory. The aim of this study is to investigate the effect of surgical site infections on glioblastoma"s course.

Methods

The medical records of all patients undergoing surgery for high-grade glioma between 2010 and 2020 in our institution were scanned and those with surgical site infections after glioblastoma resection were identified and compared to an age-matched control group. Median survival time after primary surgery and length of stay in hospital were compared between both groups.

Results

Out of 759 patients undergoing primary surgery for high-grade glioma, 35 patients with postoperative surgical site infection after glioblastoma resection were identified and 20 (8 men and 12 women aged between 10 and 70) were included in this study. 15 patients were excluded because of lack of complete follow-up data. The control group consisted of 20 age-matched patients without SSI (11 males and 9 females aged between 11 and 86). Median survival time in patients with SSI was 437 days and 353 in the control group (p=0.63). The total length of all hospital stay was 43 ± 6 days in the SSI group and 22 ± 2 days in the patients without SSI (p=0.0012).

Conclusion

Our data suggest that surgical site infections do not influence survival time in glioblastoma patients. However, they lead to more frequent and longer hospitalizations, an additional reduction in quality of life.

Neuroonkologie III/*Neuro-Oncology III*

P175

Prognostische Relevanz von Änderungen der Tumor-Volumina zwischen Resektion und Bestrahlung in IDHwt Glioblastomen

Frequency and prognostic relevance of volumetric MRI changes in contrast- and non-contrast-enhancing tumor compartments between surgery and radiotherapy of IDHwt glioblastoma

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Objective

In glioblastoma, tumor regrowth on MRI between surgery and postoperative radiochemotherapy has been commonly described. However, frequency and prognostic relevance in IDH-wildtype glioblastoma diagnosed per WHO 2021 classification are unclear.

Methods

In this retrospective, single-center study we included 64 consecutive cases, for whom magnetic resonance imaging (MRI) was available for both, volumetric assessment of extent of resection immediately after surgery as well as volumetric target delineation before initiation of adjuvant radiochemotherapy.

Results

Time interval between both MRIs was 15.5 ± 1.9 days. Overall, median new contrast-enhancement volume was seen in 21/64 individuals (33%, 1.5 ± 1.5 cm^3) and new non-contrast lesion volume in 18/64 patients (28%, 5.0 ± 2.3 cm^3). Multidisciplinary in-depth review revealed that new contrast-enhancement was either due to: (I) progression of contrast-enhancing tumor remnants in 6/21 patients; and (II) distant contrast-enhancing foci or breakdown of the blood-brain-barrier in previously non-contrast-enhancing tumor remnants in 5/21 patients, whereas it was unspecific or due to ischemia in 10/21 patients. For non-contrast-enhancing lesions, 3/18 had progression of non-contrast-enhancing tumor remnants and 15/18 had unspecific changes or changes due to ischemia. There was no significant association between findings consistent with tumor regrowth and less favorable outcome (overall survival: 14 vs. 19 months; $p = 0.423$).

Conclusion

These findings support the rationale that analysis of postsurgical remaining tumor-volume for prognostic stratification should be done on immediate post-operative MRI (<72h) as unspecific changes are common. However, tumor regrowth including distant foci may occur in a subset of *IDH*-wildtype glioblastoma patients diagnosed per WHO 2021 classification. Thus, MRI imaging prior to radiotherapy should be obtained to adjust radiotherapy planning accordingly.

Abb. 1

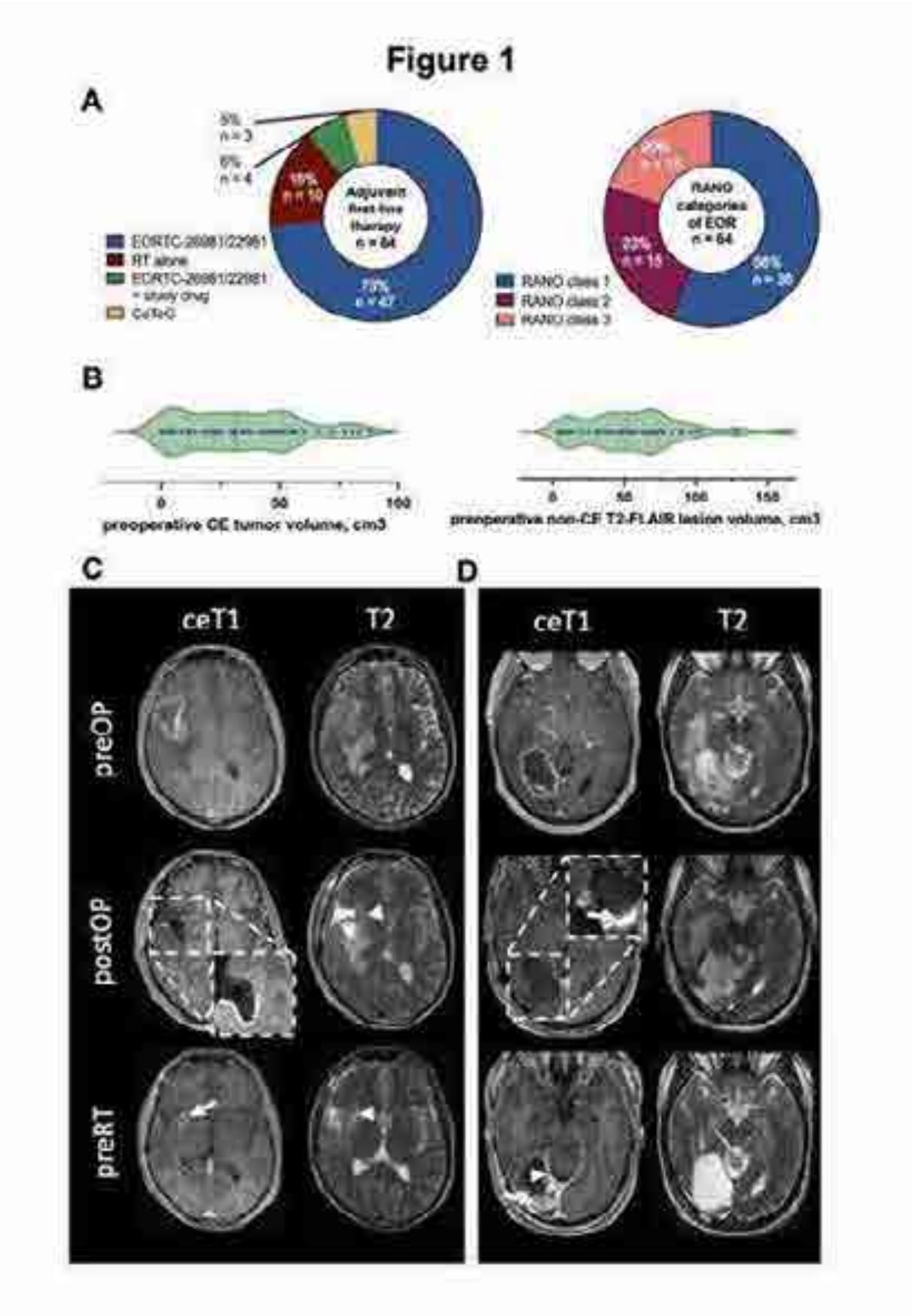
Figure 1
A
5%
n = 3
6%
n = 4
19%
n = 10
Adjuvant
first-line
therapy
n = 64
70%
n = 47
EORTC-26981/22981
RT alone
EORTC-26981/22981
+ study drug
CeTeG
RANO
categories
of EOR
n = 64
22%
n = 14
36%
n = 23
RANO class 1
RANO class 2
RANO class 3
B
0
50
100
preoperative CE tumor volume, cm3
0
50
100
150
preoperative non-CE T2-FLAIR lesion volume, cm3
C
D
ceT1
T2
preOP
postOP
preRT
ceT1
T2

Abb. 2

Table 1: Baseline characteristics for patients with glioblastoma, IDH-wildtype, CNS WHO grade 4

Characteristics are given for all patients with glioblastoma, IDHwt, CNS WHO grade 4 (n=64), patients without (n = 42) and with (n = 22) volumetric changes on MRIs between surgery and radiotherapy. *Abbreviations: CE* – contrast-enhancing; *CCNU* – lomustine; *CeTeG* – TMZ+CCNU/RT → TMZ+CCNU; *EOR* – extent of resection; *EORTC-26981/22981* – TMZ/RT → TMZ; *KPS* – Karnofsky Performance Status; *MGMT* - O6-methylguanine-DNA-methyltransferase; *non-CE* – non-contrast-enhancing; *Post-OP*: post-operative; *Pre-OP* – pre-operative; *Pre-RT* – pre-radio(chemo)therapy; *RT* – radiotherapy; *TERT* – telomerase reverse transcriptase; *TMZ* – temozolomide.

		Patients without volumetric changes	Patients with volumetric changes	Total	*p*-value
Overall, n (%)		42 (66%)	22 (34%)	64 (100%)	
Age, years (%)	Mean	61.6	57.2	60.1	0.123
	18-35	1 (2%)	0 (0%)	1 (2%)	
	36-50	7 (17%)	4 (18%)	11 (17%)	
	51-65	16 (38%)	13 (59%)	29 (45%)	
	>65	18 (43%)	5 (23%)	23 (36%)	
Sex, n (%)	Female	11 (26%)	10 (45%)	21 (33%)	0.163
	Male	31 (74%)	12 (55%)	43 (67%)	
Clinical performance	Pre-OP KPS, median (range)	80 (60-100%)	90 (20-100%)	85 (20-100%)	0.133
	Post-OP KPS, median (range)	80 (50-100%)	90 (50-90%)	80 (50-100%)	0.394
	New postoperative deficit, n (%)	3 (7%)	5 (23%)	8 (13%)	0.111
MGMT promotor, n (%)	Methylated	12 (29%)	10 (45%)	22 (34%)	0.268
	non-methylated	30 (71%)	12 (55%)	42 (66%)	
TERT promotor, n (%)	Wildtype	10 (24%)	0 (0%)	10 (16%)	***0.012**
	Mutated	32 (76%)	22 (100%)	54 (84%)	
Tumor localization, n (%)	(sub)-cortical	38 (90%)	18 (82%)	56 (88%)	0.430
	Multifocal	1 (2%)	4 (18%)	5 (8%)	
	Deep-seated	2 (5%)	0 (0%)	2 (3%)	
	Cerebellar	1 (2%)	0 (0%)	1 (2%)	
	Dominant hemisphere	20 (48%)	10 (45%)	30 (47%)	0.999
Tumor volumes, cm³; mean ± SEM	Pre-OP CE	30.9 ± 3.8	34.1 ± 5.3	32.0 ± 3.1	0.624
	Pre-OP non-CE	47.7 ± 5.4	66.0 ± 6.2	53.9 ± 4.2	***0.009**
	Post-OP CE	0.5 ± 0.2	2.3 ± 1.2	1.1 ± 0.4	0.256
	Post-OP non-CE	2.2 ± 0.9	12.2 ± 4.1	5.7 ± 1.9	***0.007**
	Pre-RT CE	0.5 ± 0.2	6.2 ± 2.5	2.4 ± 0.9	***0.001**
	Pre-RT non-CE	2.2 ± 0.6	19.8 ± 5.4	8.3 ± 2.1	***0.001**
RANO categories of EOR in glioblastoma, n (%)	RANO class 1	28 (67%)	8 (36%)	36 (56%)	***0.033**
	RANO class 2	6 (14%)	9 (41%)	15 (23%)	
	RANO class 3	8 (19%)	5 (23%)	13 (20%)	
Adjuvant therapy	EORTC-26981/22981	28 (67%)	19 (86%)	47 (73%)	0.137
	RT alone	9 (21%)	1 (5%)	10 (16%)	
	EORTC-26981/22981 + study drug	3 (7%)	1 (5%)	4 (6%)	
	CeTeG	2 (5%)	1 (5%)	3 (5%)	

Neuroonkologie III/*Neuro-Oncology III*

Neuroonkologie IV/*Neuro-Oncology IV*

J-SBNC027

Infratentorieller suprazerebellärer versus okzipitaler transtentorieller Zugang bei Tumoren der Zirbeldrüse
Infratentorial Supracerebellar Versus Occipital Transtentorial Approach for Tumors of the Pineal Region

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Objective

Despite the deep localization of tumors of the pineal region, surgical resection has become safer and more effective, and now plays an essential role in their management. Tissue diagnosis allows initiation of chemotherapy or radiotherapy, and resection may be curative or improve the efficacy of adjuvant therapies. Infratentorial supracerebellar (ITSC) and occipital transtentorial (OTT) are the most commonly used approaches to resect pineal tumors. The aim of this study is to describe feasible criteria for better approach indication based on our surgical experience.

Methods

42 patients were divided for tumor resection, using the angle of the tent surface in sagittal MRI view in the selection of the approach: Group 1 (25 ITSC); Group 2 (15 OTT); Group 3 (2 combined approaches).

Results

Group 1 was successful in total removal. One visual impairment, hydrocephalus was observed in one patient with postoperative meningitis, and another with postoperative hematoma. Group 2 had 13 total resections, one visual impairment and transient contralateral hemianesthesia. Group 3 resulted in one air embolism and one ventriculitis after ventriculoperitoneal shunt. There was no surgical mortality recorded.

Conclusion

A 42 pineal tumor cases descriptive analysis showed minimal complications. The ideal approach is well decided based on the angle between tentorial surface and vertical midline on sagittal plane.

Neuroonkologie IV/*Neuro-Oncology IV*

J-SBNC029

Zentrale extraaxialen expansive Läsionen die Meningeomen nachahmen – eine Literaturübersicht
Central extra-axial expansive lesions mimicking meningiomas – a literature review

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Objective

Meningiomas represent 13% to 26% of intracranial tumors and the most common extra-axial lesion. They manifest radiologically as an isointensity to slight hypointensity lesion, relative to grey matter on T1-weighted sequences and isointensity to slight hyperintensity relative to grey matter on the T2 sequences. However, some studies reported that in 7.2% of cases, despite very similar characteristics to meningiomas on imaging exams, the lesions might lead to misdiagnosis. We aim to demonstrate radiological characteristics of meningioma-mimics to reduce misdiagnosis.

Methods

A PubMed database search was conducted by the following combined formula: (Meningioma) AND (mimicking) AND (extra-axial lesions). Additional resources were added after screening the references of the included papers. This literature review summarizes the current accuracy status of MRI for differential diagnosis of meningiomas, focusing on the radiological grading (such as presence of dural tail sign, calcifications and areas of central necrosis). We further analyze the red-flags that should alert radiologists to consider meningioma-mimics.

Results

There are five imaging features that suggests meningioma-mimics: bone erosion, dural displacement sign marked T2 hypointensity, marked T2 hyperintensity, absence of dural tail. Other suspect sign of meningioma mimic is the dural displacement sign. Perfusion-weighted magnetic resonance imaging is crucial for differentiation of meningiomas and other extra-axial tumors. Hemangiopericytimas, lymphomas and schwannomas are the most common mimic lesions. Also, metastatic disease, melanoma, hemangiopericytomas, glioblastomas, lymphomas, tuberculosis and sarcoidosis can mimic meningiomas as well.

Conclusion

There is a range of tumors, neoplastic or non-neoplastic, that can mimic the radiological aspects of meningioma, and since the type of tumor impacts directly on treatment strategy, it is extremely important to perform accurate differential diagnosis preoperatively and also early differentiation to provide adequate treatment.

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Analyse demografischer und versorgungspezifischer Parameter im Rahmen der stationären neurochirurgisch-onkologischen Behandlung bösartiger Neubildungen des Gehirns (ICD10-C71) im Pandemiejahr 2020/21

Analysis of demographic and care-specific parameters in neurosurgical- and oncologic- treatment of malignant neoplasms of the brain (ICD10-C71) during the Covid-19 pandemic period 2020/21

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Objective

The Covid-19 pandemic leads to competing risks of the Covid-19 disease compared to the primary tumor disease in neuro-oncological patients in Germany. This work analyzes demographic and care-specific parameters of the neurosurgical- and oncological treatment of malignant neoplasms of the brain during the Covid-19 pandemic period 2020/21 in order to achieve a patient-centered care optimization in the future.

Methods

Patient data sets from a German health insurance register during Covid-19 pandemic period 2020/21 were evaluated retrospectively for the ICD10 C71 (malignant neoplasm of the brain). Demographic parameters (age, gender), duration of treatment and diagnostics, care and treatment options (biopsy, resection, chemotherapy, radiotherapy) were categorized and analyzed using OPS-codes. Patient data records with same ICD10 and OPS coding from the period 2017-2019 were used for comparison. The total number of registered patients for the periods averaged 9.145 million patients/month.

Results

In general, there was a decrease in the absolute and relative ICD10 C71 cases with a specific decrease in the course of the pandemic by -14% (1st wave in 3-6/2020) and -17% (2nd wave 10/20-2/21). The evaluation of the OPS codes also showed reduced surgical (biopsy/resection) and treatment options (radiation therapy/chemotherapy). Gender and age-specific subgroup analyzes demonstrated a significant case reduction in in the 2nd wave for men (-21%) compared to women (-14%). Age-specifically, the group of men >40 years was also more affected in the 2nd wave (-26%) than the group of women (-14%). The analysis of the inhouse hospitalization (median 7-8 days) revealed a shorter time period for men (7d) during the pandemic phases.

Conclusion

During the Covid-19 pandemic period 2020/21 a decrease in hospital cases and oncologic treatments (OPS codes) in neuro-oncological patients with the ICD10 C71 could be proven . There was no increase in the number of cases or procedures as catch-up effects in the 2020/21 study period. Therefore, capabilities should be created for the future period. Age and gender-specific abnormalities during the Covid-19 pandemic phases must be taken into account in future preclinical and clinical diagnostic settings.

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Entwicklung einer Problemliste für Angehörige neuroonkologischer Patient*innen

Unmet needs and relevant problems in caregivers of adult neuro-oncological patients – development of a problem list

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Objective

The diagnosis of a brain tumor represents high burden for patient but also caregivers. Therefore, psychosocial screening tools for caregivers adapted to neuro-oncological tumor entities are urgently required but do not exist. The aim was to develop a problem list for a holistic need assessment tailored to the unmet needs of brain tumor patients" caregivers for an application in combination to the distress thermometer scale.

Methods

First, items of high relevance for the caregivers were identified on basis of retrospective analyses. Second, qualitative interviews with caregivers were conducted in two study centers. We performed a qualitative content analysis applying inductive/deductive categorizations of the reports.

Results

The qualitative interviews included n=13 main questions and up to 4 sub-questions focusing on changes in relationship, social live, emotional, physical, financial, spiritual problems and information needs. The interview was conducted during the outpatient visit. A total of 50 caregivers were interviewed (n=25 in each center). Main unmet needs were time constrains (n=34, 68%) and less time for themselves (n=36, 72%). The majority of the caregivers wished for psychological support (n=28, 47%) and first contact with psycho-oncologists after first diagnosis n=30 (60%) or in case of the patient"s clinical deterioration (n=26, 52%). A total of 30 (60%) caregivers wished dyad interventions on demand, but not frequently. However, n=32 (64%) caregivers reported at the same time, that they would finish their psycho-oncological sessions when clinical deterioration of the patient occurred (due to lack of time). Reported unmet information needs were communication with health personnel, how to find sources of strength, strategies for problem solving, conflict resolution and disease management.

Conclusion

The interviews reflected the unmet needs of brain tumor patients" caregivers and an adapted problem list might allow for a more targeted assessment of their specific burdens.

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Langzeitergebnisse und neuroonkolog. Management von Patienten mit primären IDH-WT Glioblastom-Ergebnisse einer monozentrischen 10-Jahres-Analyse

long term results and neurooncological management of patients with primary IDH-wild type glioblastoma-results of a single centre 10 year analysis

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Objective

Overall survival (OS) of patients with primary IDH- WT glioblastoma (pGBM) remains poor, although new treatment protocols were introduced. The aim of our study was to analyse the OS of patients with pGBM, who were treated in a non controlled, everyday neurooncological practice and to evaluate factors with significant correlation to OS.

Methods

Single centre, retrospective analysis of patients with IDH-WT pGBM, treated between 2010 and 2020. Data collection was based on the c37.CancerCenter web based tumour documentary system. Kaplan Meier analysis and log rank test were applied to analyse the effect of sex, age, tumour location, molecular status, extent of tumour resection and adjuvant neurooncological treatment on OS.

Results

193 patients with pGBM were included (108 male [56%], 85 female [44%]). Mean OS was 14.7 (± 22) months.16 patients were alive at the primary OS endpoint of analysis. 4 (2.1%) patients had OS >10 y, 9 (4.6 %) > 5 y, 13 (6.7%) >4 y, 18 (9.3%) >3 y, 28 (14.5%) >2 y, 75 (38.8%) > 1 y, 118 (61%) > 6 months and 145 >3 months. 98 patients (60.7%) had MGMT promoter hypermethylation. 95 (49.2%) patients underwent biopsy, 60 (31%) complete resection (CR) and 31 (16%) subtotal resection (SR). 107 (55.4 %) patients were treated with concomitant radio-chemotherapy (R/C) : 89 (46.1%) Stupp, 6 (3.1%) CeTeG, 4 (2%) Perry, 2 (1%) paediatric HIT protocol and 6 (3.1%) other. 48 patients (24.8%) received monotherapy (29 [15%] temozolomid; 18 [9.3%] radiotherapy, 1 [0.5%] PC-regime). 39 patients (20.2%) received best supportive care. TTF was applied to 21 (10.8%) patients. Surgery for tumour recurrence was performed in 21 (10.8%) patients. Age < 65years (mOS 28.4 m), MGMT hypermethylation (mOS 26.5 m), CR (mOS =29.7 m), R/C (mOS Stupp=26.5 m), temozolomide monotherapy (mOS=14.5 m) and surgery for tumor recurrence (mOS 37.6 m) had a significant positive influence on OS (p<0.001). Moreover frontal tumour location (mOS=23.6m, p<0.014) , use of TTF (mOS=19.8 m, p<0.033) and higher number of adjuvant therapy cycles (mOS>3cycles 44.0 m, p<0.001) were also significantly positive correlated to OS.

Conclusion

If treatment protocols from randomized controlled trials (RCT´s) are implemented into the daily neurooncological praxis according to patient"s specific characteristics the OS of nonselected patients treated outside RCT´s may be comparable to patients OS included in previous RCT´s.

Abb. 1

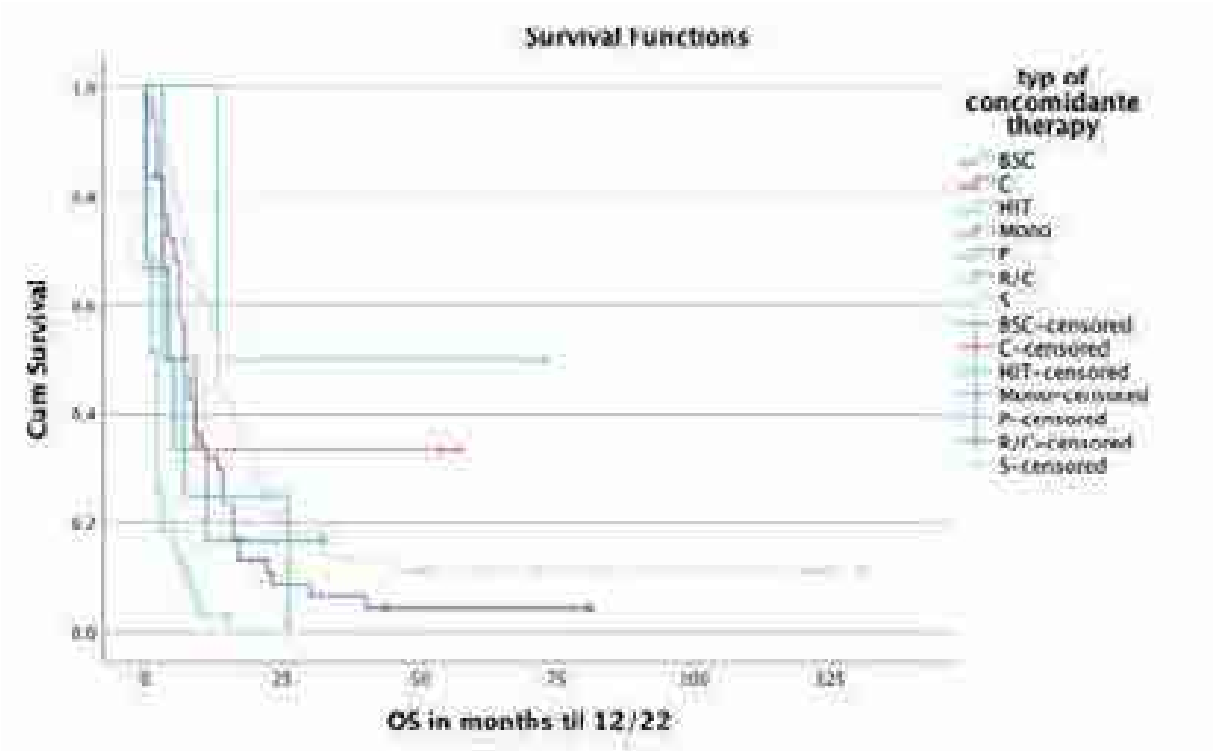
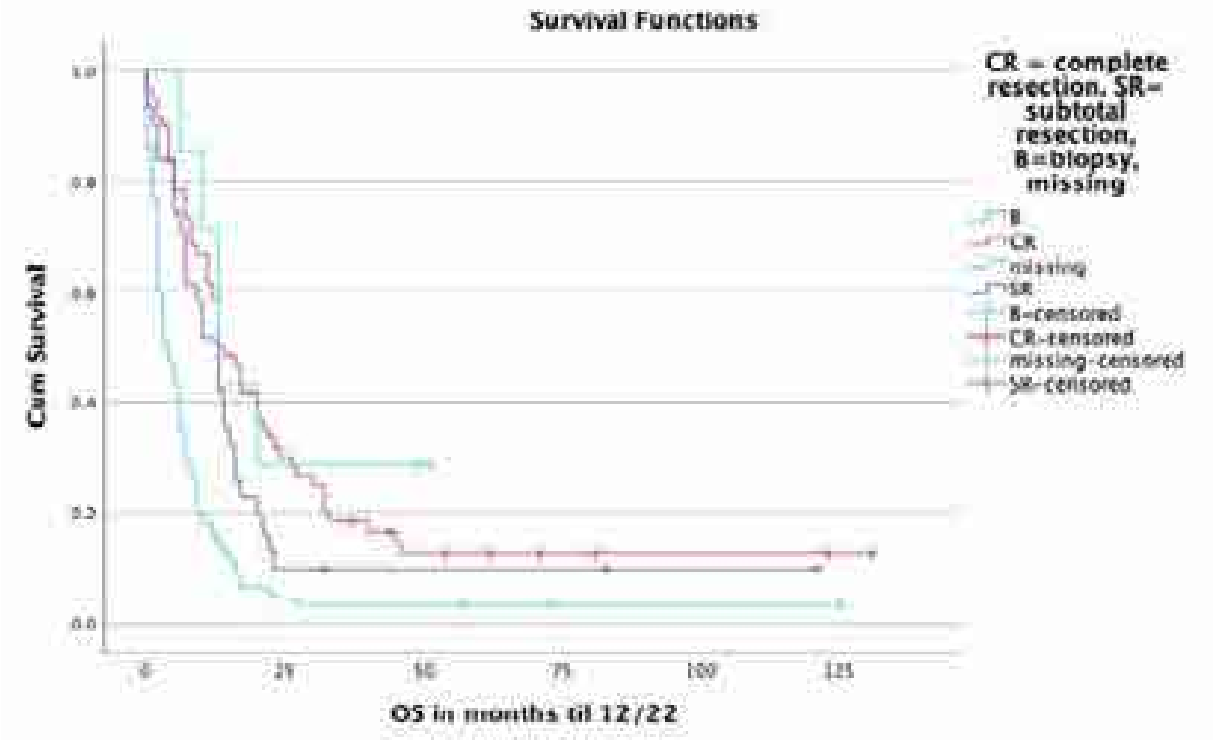

Survival Functions
typ of concomidante therapy
BSC
C
HIT
Mono
P
R/C
S
BSC-censored
C-censored
HIT-censored
Mono-censored
P-censored
R/C-censored
S-censored
Cum Survival
OS in months til 12/22

Abb. 2


Survival Functions
CR = complete resection, SR= subtotal resection, B=biopsy, missing
B
CR
missing
SR
B-censored
CR-censored
missing-censored
SR-censored
Cum Survival
OS in months til 12/22

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Vergleich von epiduralem und kortikalen Motormapping bei Resektion supratentoriell eloquent lokalisierter Hirntumore

Comparison of epidural and cortical motor mapping in supratentorial eloquent brain tumours

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Objective

Identification of M1 motorcortex and motor-eloquent structures are essential when using cortical mapping procedures for surgery of eloquently located brain lesions. Monopolar burst-stimulation has proven reliable for mapping those structures on cortical and subcortical level. In the present study, we additionally used epidural motor mapping and compared them to the cortical motor mapping data in order to examine reliability and comparability of the epidural stimulation data.

Methods

Patients with brain lesions located in the central area of the parietal lobus presenting for primary resection with either no deficit or deficit with preserved motor function were included in this study. Before dural incision, a matrix is cut out using the craniotomy as template and perforated in 1 cm distances all over the matrix. Then the matrix is placed on the dura and monoplar stimulation is performed at all perforated locations until 15 mA or when EMG response is seen. Motor thresholds (MT) and clinical response are compared to cortical mapping data, which are obtained after dural opening and application of the matrix on the cortex. Clinical outcome, tumour location and histopathological results are collected as well.

Results

So far, 14 Patients were included. In two patients, there was one point each at which only cortical stimulation would elicit motor evoked portentials (MEPs) and two points for which only epidural stimulation elicited MEPs. Those points had a MT of 14-15mA. Epidural MT was higher at 15 points and lower at 9 points. The average difference in MT for stimulation points where both modalities worked was 1.9 mA. 10 points showed no difference in MT between epidural and cortical stimulation.

Conclusion

In the present preliminary analyses, we could show that MEPs can reliably be evoked through epidural stimulation. When compared to direct cortical stimulation, a consistent difference in MT is observed in about 2/3 of stimulated points. However, further data acquisition is required and is ongoing in a prospective study.

Neuroonkologie IV/*Neuro-Oncology IV*

J-SPNC006

Supratentorielles intraparenchymales Schwannom: Fallbericht und Überprüfung klinischer und radiologischer Merkmale

Supratentorial intraparenchymal schwannoma: case report and review of clinical and radiological features

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Objective

Supratentorial intraparenchymal schwannomas are extremely rare.

Methods

We present a case of a supratentorial intraparenchymal schwannoma and review the associated literature.

Results

A 28-year-old female presented four years before with an incidental diagnosis of a right paracentral lobule lesion. The follow up MRI characterized an enlargement of the cystic component and an enhancing nodular lesion with hypodensities ("blooming effect") on susceptibility weighted imaging. Surgery was performed with intraoperative overlay of corticospinal tractography and motor-evoked potential monitoring with direct electrical stimulation. A partial resection was performed due to a residual tumor adjacent to the corticospinal tract. Postoperatively the patient had a right hypoesthesia below D5 dermatome without motor deficits. Anatomopathological evaluation established the diagnosis of intraparenchymal schwannoma.

More than half of the cases of supratentorial schwannoma described were associated with seizures. On MRI the lesion was characteristically hypointense on T1-weighted images, had mixed-intensity on T2-weighted images, with peritumoral edema and avid enhancement with gadolinium-based contrast agent. Less than half of the cases had a cystic component or calcifications.

Conclusion

We present a rare case of a benign tumor, in which a cautious attitude was decisive to prevent a catastrophic result. Our analysis highlights the epileptogenic potential of this tumor as well as its radiological features.

Neuroonkologie IV/*Neuro-Oncology IV*

J-SBNC030

Gliosarkom - Fallbericht
Gliosarcoma - case review

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Objective

Gliosarcoma is a rare tumor of the central nervous system, corresponding to 2% of high-grade tumors. It is a tumor similar to glioblastoma, only differentiated by pathological examination.

The interest of this review is to assess how rare is this tumor in our location and to compare the histological evaluation of this tumors with gliomas.

As being a rare tumor, it is important to assess the incidence of gliosarcoma among the glial tumors in our location and to ensure our patients optimal treatment.

Methods

Medical records from the year 2015 to 2021 were collected and all cases of gliosarcoma in our service that had an anatomopathological report confirming the diagnosis were reviewed.

The patients included in this review underwent surgical resection or biopsy of the lesions, these with glial characteristics on imaging. Afterwards, their tumor samples were sent to the same analysis laboratory for anatomopathological confirmation of the sample.

Results

The cases were all analysed by microscope and run immunohistochemistry tests such as IDH mutation, ATRX, P53, MGMT metilation. In all GS, only the glial component stained strongly for glial fibrillary acidic protein (GFAP) and S-100 protein. This resulted in a bimorphic marmorate staining pattern, charateristic of this type of tumor.

Histologically, gliosarcoma is a primary neoplasm of the CNS that has both glial and sarcomatous elements. Its glial component is indistinguishable from that found in typical glioblastoma and the sarcomatous component is mostly presented as fibrosarcoma, unable to be diagnosed by morphological, clinical or radiological findings.

In this review there were 06 cases of gliosarcoma among 296 glial tumors making our incidence 2%, similar as the general data of other locations.

One of six cases needed diagnosis revision. That because on the first analyses the tumor it came as a high grade glioma, without sarcomatous elements and after histological revision, the diagnosis was then of a gliosarcoma.

Conclusion

Althought our case review took place in a single institution that primarly admits neurological and neurosurgical patients, there was no difference in the incidence of gliosarcoma in our region compared to the general data of other locations.

As histological findings for diagnosis it's necessary the presence of sarcomatous elements along with glial components. The glial components on it's own are indistinguisable from that found in typical glioblastoma and could lead to a misleading diagnosis

Abb. 1

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Überleben nach Resektion einer Hirnmetastase: Bedeutung von synchroner versus metachroner metastatischer Erkrankung

Survival after resection of brain metastasis: impact of synchronous versus metachronous metastatic disease

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Objective

Patients with brain metastasis (BM) from solid tumors are in an advanced stage of cancer. BM may occur during a known oncological disease (metachronous BM) or be the primary manifestation of previously unknown cancer (synchronous BM). The time of diagnosis might decisively impact patient prognosis and further treatment stratification. In the present study, we analyzed the prognostic impact of synchronous versus (vs.) metachronous BM occurrence following resection of BM.

Methods

Between 2013 and 2018, 353 patients had undergone surgical therapy for BM at the authors' neuro-oncological center. Survival stratification calculated from the day of neurosurgical resection was performed for synchronous vs. metachronous BM diagnosis.

Results

Non-small-cell lung carcinoma (NSCLC) was the most common tumor entity of primary site (43%) followed by gastrointestinal cancer (14%) and breast cancer (13%). Synchronous BM occurrence was present in 116 of 353 patients (33%), metachronous BM occurrence was present in 237 of 353 patients (67%). NSCLC was significantly more often diagnosed via resection of the BM (56% synchronous vs. 44% metachronous situation, p=0.0001). The median overall survival for patients with synchronous BM diagnosis was 12 months (95% confidence interval (CI) 7.5-16.5) compared to 13 months (95% CI 9.6-16.4) for patients with metachronous BM diagnosis (p=0.97).

Conclusion

The present study indicates that time of BM diagnosis (synchronous vs. metachronous) does not significantly impact patient survival following surgical therapy of BM. These results suggest that the indication for neurosurgical BM resection should be made regardless of a synchronous or a metachronous time of BM occurrence.

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Das Therapieansprechen von Patienten mit bioptisch gesicherten Glioblastomen im Alter von 80 Jahren oder älter hängt vom Methylierungsstatus des MGMT-Promoters ab

Treatment benefit in patients aged 80 years or older with biopsy-proven and non-resected glioblastoma is dependent on MGMT promoter methylation status

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Objective

Glioblastoma is associated with poor outcome in the elderly. It is especially unclear if patients in the highest age bracket, aged 80 years or older, benefit from tumor-specific therapy as opposed to receiving best supportive care (BSC) only.

Methods

Patients with newly diagnosed glioblastoma (WHO 2021), aged 80 years or older and diagnosed between 2010 and 2022 were included. Patient characteristics were assessed. Initial tumor volumes (T2 and T1 with contrast enhancement) were segmented manually. Temporal muscle thickness was measured as a surrogate for sarcopenia. Uni- and multivariate analyses were performed.

Results

The cohort comprised 76 patients, all diagnosed through stereotactic biopsy. 22 patients (29%) received temozolomide monotherapy, 23 patients (30%) were treated with radiotherapy (RT) alone and 7 patients (9%) received combination therapies. In 24 patients (32%), tumor-specific therapy was omitted in lieu of BSC. Overall survival (OS) was significantly longer in patients receiving tumor-specific therapy (in months, 5.4 vs. 3.3, $p<0.001$). Stratification according to MGMT promoter methylation status showed that OS benefit was owed to patients with MGMT promoter methylation (MGMTpos) who received tumor-specific therapy instead of BSC (6.2 vs. 2.6, $p<0.001$). Patients with unmethylated MGMT promoter (MGMTneg) did not benefit from tumor-specific therapy (3.6 vs. 3.7, $p=0.18$). In multivariate analyses, better clinical status and MGMT promoter methylation were associated with prolonged survival ($p<0.01$ and $p=0.01$).

Conclusion

Benefit from tumor-specific treatment in patients with newly diagnosed glioblastoma aged 80 years or older was dependent on MGMT promoter methylation status in our cohort. MGMTpos patients survived significantly longer with tumor-specific therapy when compared to BSC only while there was no survival benefit in MGMTneg patients. All MGMTneg patients were treated with RT and still did not benefit. This suggests a limited role for RT in elderly patients. Based on our data, RT use should be limited to combination schemes in MGMTpos patients and good clinical status. Taken together, we found that MGMT promoter status appears essential in determining which patients benefit from therapy. We therefore propose to perform tumor biopsy in all patients over 80 years with suspected glioblastoma that are not eligible for tumor resection. The decision whether to initiate tumor-specific treatment or whether BSC is more appropriate could then be made accordingly.

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Zum postoperativen klinischen Outcome von Patienten mit Hirnmetastasen und Hemiparese – eine retrospektive Analyse

Postoperative clinical outcome of patients with brain metastases causing hemiparesis – a retrospective analysis

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Objective

Brain metastases often present with neurological deficits such as hemiparesis and aphasia. With significant improvement in systemic cancer therapy, an increasing number of patients undergo surgical resection of brain metastases. Despite the significant improvement in systemic cancer therapy, the prognosis of patients with brain metastases and focal deficits is estimated to be limited. The present analysis aim to investigate to which extent surgical therapy in patients with brain metastases and symptomatic hemiparesis has an immediate and long-term positive effect on the outcome.

Methods

In a retrospective study, data of 707 patients who underwent surgery for brain metastases between 01/2006 and 12/2018 was assessed. Of this cohort, 135 patients presented with metastases located in the premotor and motor area causing hemiparesis. These patients were included in the final analysis.

Results

Seventy female patients (51.9%) and 65 male patients (48.1%) were included. The mean age of the patients was 63.8 years with a range of 23 to 87 years. Seventy/135 patients (51.9%) were diagnosed with non-small cell lung cancer (NSCLC), followed by 14 patients (10.4%) with malignant melanoma, and 12 patients (8.9%) with colorectal cancer. In 76/135 patients (56.3%), hemiparesis led to deterioration of fine motor skills and walking disability, but patients did not need support. In this group, symptoms improved in 38 patients (50%) postoperatively. Forty/135 patients (29.6%) had moderate hemiparesis that needed constant support and walking with the aid of a walker. Postoperatively, hemiparesis improved in 62.5% of patients. Nineteen patients (14.1%) had severe hemiparesis an needed constant care / were unable to walk. After tumor resection, hemiparesis improved in 10 patients (52.6%). Peri- and postoperative complications occurred in 7/135 patients (5.2%). In the 2- and 6-month follow-up and regarding patients, who were lost to follow-up, the proportion of patients with improved hemiparesis after surgery was 60%.

Conclusion

Patients with brain metastases can benefit from surgical treatment even in the presence of symptomatic hemiparesis. In advanced stages of cancer, surgical resection enables patients to be more independent in their daily activities and might contribute to an improvement of quality of life.

P185

Mittels MR-Volumetrie gemessenes Tumorvolumen als Prädiktor für die Prognose nach chirurgischer Resektion des Ependymoms und den prä-, intra- und postoperativen Verlauf.

Tumor volume measured using MR volumetry as predictor for prognosis after surgical resection of ependymoma and the pre-, intra- and postoperative course.

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Objective

Ependymoma is a rare type of cancer (incidence 500 per year in Europe) that arises from ependymal cells outlining the fluid-filled spaces. While ependymoma can occur anywhere along the neuro-axis, it is most common infratentorial (60%) typically in the central canal of the spinal cord or the ventricles of the brain (choroid plexus).

The goal of surgery is to remove as much of the tumor as possible while minimizing damage to surrounding normal spinal cord tissue. Better understanding of the long-term prognosis after various degree of resection and adjuvant therapy may help in decide upon aggressiveness of surgery.

Methods

This retrospective single-center analysis includes 150 consecutive patients who underwent ependymoma resection in the time period between 2016 and 2022. The data was collected from the patients" medical charts. Tumor volume was measured by BrainLab software program and gadoxetic acid-enhanced MRI to assess the extent of resection and the association with the long-term prognosis. Recurrence-free survival (RFS) and overall survival (OS) were estimated using Kaplan-Meier method. The Cox-proportional-hazard-model was used to evaluate clinical, pathologic, and radiologic prognostic factors.

Results

The results of the study showed that, on average, the mass of resection was above 98% of the total tumor volume. After a median follow-up of 3 years, ependymoma recurrence occurred in 7 patients (4,7%). No patient died in the follow-up period. Larger tumor volume was significantly associated with poor RFS in multivariate analysis. For predicting RFS after surgery, the optimal-cutoff of tumor volume was at 3.7 ml. A larger tumor volume than 3.7 ml was associated with poor RFS (hazard ratio (HR), 1.67, P= 0.035).

In case of radical resection deferral of radiotherapy is decided individually. 45-54 Gy is recommended for low-grade (grade II) and 54-60 Gy for high-grade ependymomas (grade III). Chemotherapy has not shown any benefit.

Conclusion

Overall, surgical resection is an effective treatment for spinal ependymoma, and the use of tumor volume-measurement using MR-volumetry can help predict RFS after resection of ependymoma. However, it is important to note that the long-term outlook for people with spinal ependymoma can vary widely, and further research is needed to better understand the factors that influence the prognosis in this patient population.

Abb. 1

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Molekulare Prädiktoren für die Wirksamkeit von Decitabin bei Meningiomen - eine Pilotstudie.
Molecular predictors for Decitabine efficacy in meningiomas – a pilot study.

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Objective

In meningiomas, recurrences after surgery or irradiation are common, and effective chemotherapeutical agents are still lacking. Previous in-vitro analyses revealed efficacy of Decitabine (DCT), a DNA methyl-transferase (DNMT) inhibitor established in the treatment of leukemia and soft tissue sarcoma, in a yet undefined subgroup of meningiomas. Therefore, we further explored DCT efficacy as well as underlying molecular mechanisms and preconditions for efficacy in primary meningioma cells.

Methods

Effects of DCT on proliferation and viability was analyzed in primary WHO grade 1 meningioma cells by Ki67 immunofluorescence staining and MTT assays, and cases were classified as drug responders and non-responders. Molecular preconditions for efficacy were analyzed using immunofluorescence for DNMT1 and five oncogenes (TRIM58, FAM84B, ELOVL2, MAL2, LMO3) previously found to be differentially methylated after DCT exposition, as well as genome-wide DNA methylation analyses.

Results

Efficacy of DCT (10µM) was found in eight (62%) of 13 meningioma cell lines 48h after drug exposition ($p<0.05$). DCT significantly reduced DNMT1 expression in all but two cell lines, and median DDNMT1 reduction 48h after drug exposition was lower in DCT-resistant (-11.1%) than in DCT-sensitive (-50.5%, $p=0.030$) cells. Rates of cell lines responsive to DCT exposition distinctly decreased to 25% after 72h. No significant correlations of the patients" age, sex, histological subtype, location of the paternal tumor, expression of Ki67, expression of DNMT1 or the analyzed oncogenes with treatment response was found ($p>0.05$, each). DCT efficacy was further independent of the methylation class (MC) and CPG island methylation of the paternal tumor.

Conclusion

In conclusion, efficacy of DCT has been confirmed in a subgroup of benign meningiomas in-vitro and is presumably mediated by inhibition of DNMT1 expression. However, neither clinical nor histological or molecular characteristics, including expression of DNMT1, and DNA methylation were eligible to predict treatment response. While effects of DCT on proliferation and viability decrease over time, impact on DNMT1 expression remains largely stable. Kinetics of drug efficacy might indicate necessity of repeated exposition and encourage further analyses.

P187

Astrozytom, IDH mutiert, ZNS WHO Grad 4: Einfluss der Resektion und Therapie in neu definiertem Tumorsubtyp

Astrocytoma, IDH mutant, CNS WHO Grade 4: Impact of Resection and Treatment Outcomes in a Newly Defined Tumor Subtype

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Objective

In 2021, the WHO classification introduced IDH mutant (IDHmut) astrocytoma CNS WHO grade 4 (A4) as a novel tumor subtype, in succession of lower-grade IDHmut astrocytoma and in distinction from IDH wildtype glioblastoma, based on a distinct clinical and molecular phenotype. So far, there is little clinical data on this tumor subtype and the best treatment strategy still needs to be defined. This study aims to describe the clinical characteristics of IDHmut A4 and to assess the impact of resection and systemic treatment on outcome.

Methods

Based on molecular work-up including DNA methylation analysis, 34 patients were (re-)classified as IDHmut A4. Clinical data, progression-free (PFS) and overall (OS) survival were assessed retrospectively. Segmentation of pre- and postoperative tumor volumes was possible in 20 patients. Statistical analysis was conducted with SPSS v29.0.

Results

Mean age was 36.4 (±11.04) years with a male preponderance (1.8:1). The most common tumor localization was the frontal lobe (70.6%). Main presenting symptoms were headaches (47%) and seizures (29%). 44.1% of tumors were initially graded as WHO grade 2 or 3 (IDHmut A2+3) and progressed to WHO grade 4, while primary diagnosis of IDHmut A4 was made in 19 patients (55.1%). Median OS and PFS was 46 and 33.5 months. Patients with primary IDHmut A4 conferred inferior OS than patients with IDHmut A2+3 at 1stdiagnosis (24 vs. 79 months; p=0.027). Contrast enhancement (CE) was observed in 80% and a T2/FLAIR mismatch sign in 65% of patients. Median preoperative volumes were 27.1cm^3 for CE and 117.1cm^3 for FLAIRtumor. Reduction of 98% of the CE tumor significantly correlated with prolonged OS (p=0.008) and PFS (p=0.014); however, increasing resection of FLAIR tumor did not improve outcome. 62% of patients received radio- and chemotherapy, whereas almost ¼ did not undergo any adjuvant therapy, mainly due to initial lower-grade diagnosis. Multivariate analysis attributed a significant effect of gender, KPS, 98% resection of CE tumor and adjuvant therapy on survival.

Conclusion

Molecularly defined IDHmut A4 confers better outcome than known from IDHwt glioblastoma, especially in those patients with lower-grade astrocytoma at 1st diagnosis. Although treatment was very heterogeneous in our cohort, the prognostic impact of extended resection and adjuvant therapy was underpinned by our analysis. Multicenter data should be collected in order to establish the best treatment strategy.

Abb. 1

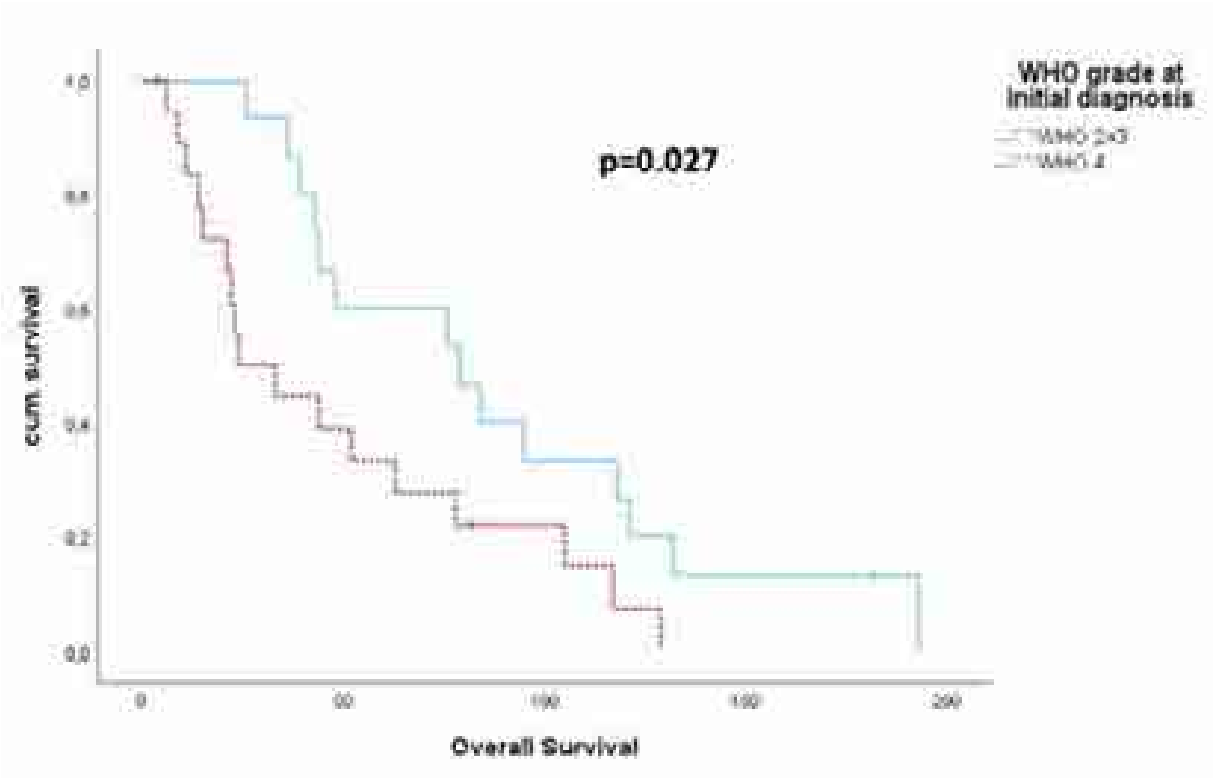
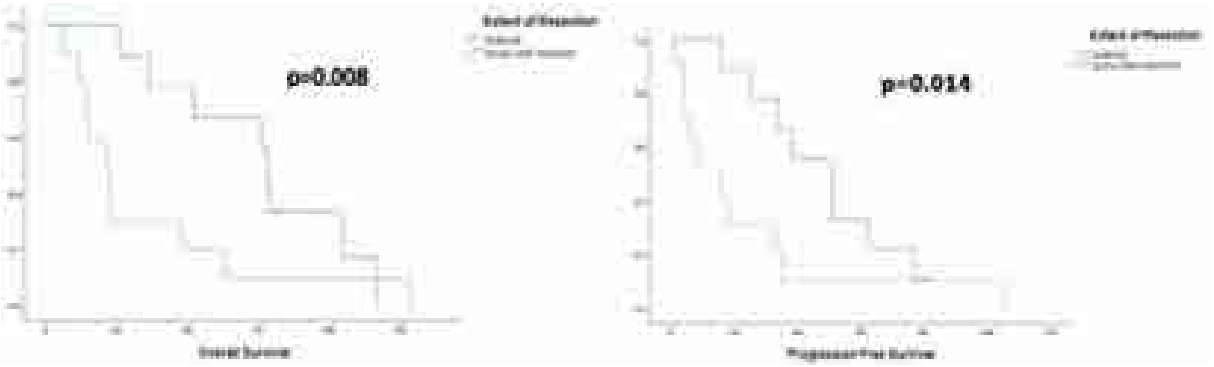

WHO grade at initial diagnosis
p=0.027
cum. survival
Overall Survival

Abb. 2


p=0.008
p=0.014

Neuroonkologie V/*Neuro-Oncology V*

P188

Implementierung von APT-basierter neuroonkolgischem Training in die neurochirurgische Assistenzarztausbildung

Implementation of entrustable professional activity-based neuro-oncology training in neurosurgical resident education

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Objective

Training in surgical neuro-oncology is, among other things, part of neurosurgery specialist training. We recently defined 70 competencies and 8 entrustable professional activities (EPA) essential for surgical neuro-oncology and to be imparted within the framework of surgical neuro-oncology training. So far, however, competences and EPA-based training concepts in operative neuro-oncology have not been integrated into specialist training in Germany.

Methods

We used a consensus-building approach to propose how skills, competencies and EPAs in surgical neuro-oncology can be imparted to neurosurgical specialist training in Germany.

Results

In total, 62 competencies and 8 EPAs for training in surgical neuro-oncology were proposed. In addition to expertise in neuroanatomy, -physiological and -pathology, diagnostics and management of tumour biology and tumour surgery, knowledge and skills in non-surgical and human basic factors are crucial. Human basic factors include skills such as adequate and clear communication, palliative care skills and constructive cooperation in a (multi-professional) team. Since neuro-oncology is an interdisciplinary field, interdisciplinary training formats, such as the DGNC or NOA courses, should be integrated into neuro-surgical training.

Here, we present a time-frame when to integrate competencies and EPAs suitable for training in surgical neuro-oncology in the 6-year neurosurgical training in Germany. The feasibility of this approach is currently evaluated at some of the author`s university hospitals.

Conclusion

The present work seeds a discussion about how to integrated competencies and EPA-based training concepts in specialty training. Finally, we contributed to create new training concepts in neurosurgery and surgical neuro-oncology.

Neuroonkologie V/*Neuro-Oncology V*

P189

Chirurgische Behandlung von Hirnmetastasen mittels intraoperativer Computertomographie (iCT) und Mikroskop-basierten Augmented Reality (AR)

Surgical treatment of brain metastases using intraoperative computed tomography (iCT) and microscope-based augmented reality (AR)

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Objective

Microscope-based augmented reality (AR) is used for improved orientation in the operative field in surgery for brain tumors, using superimposed images of segmented structures of interest in two-dimensional (2D) and three-dimensional (3D) manner. Use of AR for facilitation of resection of brain metastases (AN) in a series of patients has not been previously described.

Methods

All patients who underwent surgery for resection of brain metastases at our Department in time period 09/2016-09/2022 were included in the study. Clinical outcome in terms of postoperative neurological deficits, complications and mean survival time was evaluated, as well as neuroradiological outcome for tumor remnants and recurrence.

Results

342 consecutive patients who underwent 347 surgeries for resection of brain metastases were included in the study. The most common primary tumor was lung cancer. 108 patients underwent 109 surgeries using intraoperative computer tomography (iCT) -based registration, and 234 patients underwent 238 surgeries using fiducial-based registration. 157 patients in the non-iCT and 81 patients in the the iCT group underwent surgery using microscope-based AR. Improved navigation accuracy was noted in iCT-group ($p<0.05$). Operative time, clinical outcome and complication rate did not differ between the iCT and non-ICT as well as between AR and non-AR group. However, the use of AR improved orientation in the operative field for craniotomy planning and microsurgical resection. Segmented objects of interest in AR were tumor outline, central region and fiber tract visualization, gyri and sulci, venous sinuses, arterial vessels, as well as optic nerve and chiasm.

Conclusion

AR improves intraoperative orientation and facilitates craniotomy planning for resection of supra- and infratentorial brain metastases.

Neuroonkologie V/*Neuro-Oncology V*

P190

Falkotentorielle Meningiome: Ergebnisse nach mikrochirurgischer Resektion
Falcotentorial meningiomas: clinical outcome and volumetric follow-up after microsurgical resection

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Objective

Falcotentorial (FT) meningiomas are exceedingly rare lesions. Due to their deep seated location and their proximity to the deep venous system they present a formidable surgical challenge. We present our experience in a series of 7 patients during a 10 year period and analyze the surgical management and clinicoradiological outcome.

Methods

A retrospective analysis of 7 consecutive patients (5 women and 2 men) was conducted. We only included meningiomas originating from the anterior FT junction. Surgical approach was planned preoperatively according to the tumor extension and the displacement/involvement of the deep venous system. Clinical presentation, histological features, complications and clinical outcome were reviewed. Extent of resection and radiological follow-up was assessed with volumetric segmentation on MRI.

Results

The patients' mean age at surgery was 50 years (range 40-68 years). Preoperative hydrocephalus was evident in 3 patients and resolved after surgical resection. Most common presenting symptoms were headache and dizziness (3/7), followed by gait unsteadiness (2/7), psychomotor impairment (1/7) and hemianopia (1/7). A combined infratentorial/supracerebellar approach with an occipital transtentorial extension was utilized 4 times, while a parietal, interhemispheric approach was used 3 times. Four patients were operated in the prone and 3 in the semi-sitting position. Mean preoperative tumor volume was 43,1 cm3 (range 26-118,8). Total or near-total resection was achieved in 6 patients and subtotal resection in one instance due to firm tumor consistency and adherence to the deep venous structures. Surgical morbidity included transient hemianopia and cortical blindness in one instance, respectively. Furthermore one patient suffered a postoperative occipital hemorrhage which resulted in permanent hemianopia. Mean postoperative tumor volume was 0,9 cm3 (range 0 - 4,5). There were 6 patients with a WHO grade I meningioma and one patient with an atypical WHO grade II meningioma. Mean follow-up was 54 months (range 15-124 months). One patient with an atypical WHO grade II meningioma underwent radiotherapy and had a subsequent second surgery due to tumor progression.

Conclusion

The resectability of FT meningiomas is mainly determined by tumor adherence or encasement of the deep venous structures. Near-total safe tumor resection is possible in the majority of the cases without sacrificing major venous structures. Tumor progression is dependent on the histological subtype

Neuroonkologie V/*Neuro-Oncology V*

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Klinische und radiologische Eigenschaften der Olfactoriusrinnenmeningeome in Abhängigkeit von ihrem molekularen Profil

Clinical and radiologic features of oncogenic mutations in olfactory groove meningiomas

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Objective

Genomic studies have identified several oncogenic mutations in skull base meningiomas. Here, we sought to correlate clinical and radiologic features of olfactory groove meningiomas (OGM) with the tumor molecular profile.

Methods

We performed next generation sequencing analyses in 54 patients with OGM (37 females and 17 males) to better define the frequency of *SMO*, *AKT1, PIK3CA* and other mutations in OGM. Subsequently, the molecular results were correlated with clinical and radiographic tumor features.

Results

SMO mutations were found in 16 (29.6%) and *AKT1* mutations in 13 (24.1%) cases, while the remaining OGM harbored less common driver mutations (*PIK3CA, SUFU, TRAF7* and *NF1)* in 17 (31.5%) cases. In 8 OGM (14.8%), a driver mutation was not identified (Wild-type group, WT). The median age at first diagnosis was 64.1 years (25 -87 years), with *PIK3CA*-mutated patients representing the youngest group with 52 years (49 -78 years). The sex distribution was similar among all molecular groups (F:M = 2.1:1). Meningiomas with an *SMO* mutation presented with a tumor volume of (329.4 ± 323.0 cm3) that was non-significantly larger than *AKT1*-mutated (283.3 ± 156.2 cm3) or wild-type (330.2 ± 302.9 cm3) OGM, respectively. Tumor infiltration of the ethmoidal cells was found in 10 cases (22.2%), with the highest rate in *PIK3CA*-mutated OGM (64.8%), compared with 13.4% in *AKT1*-mutated, 30.6% in *SMO*-mutated, and 10.7% in wild-type meningiomas. In addition, tumor-associated skull base hyperostosis was common in OGM (73.5%), with the lowest frequency in the *AKT1*-mutated group (58.3%) and the highest in the *SMO* and WT- groups (91% each). The majority of cases (n= 44, 81.5%) were classified as WHO grade 1 meningioma, while the remaining 10 cases were WHO grade 2, with equal distribution among all molecular groups. Moreover, a meningothelial histology – as the dominated subtype in our cohort (72.1%) - showed no significant correlation with the molecular tumor signature. Finally, postoperative complications occurred in 10 patients (18.5%), mostly in WT-OGM (n= 5) and less common in patients with *AKT1* or *SMO* mutations (one case each).

Conclusion

Clinically actionable mutations are frequent in OGM. However, there was no association between the molecular profile and common clinical or radiologic tumor features. Therefore, preoperative prediction for an actionable mutation using clinical and radiographic data is challenging in OGM patients.

Neuroonkologie V/*Neuro-Oncology V*

P192

Zur Entwicklung eines implantierbaren Tumorrezidivdetektors
Towards the development of an implantable tumor recurrence detector

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Objective

Multiple tumor types, including glioma, are known to accumulate fluorescent agents, like protoporphyrin IX (PPIX) and this fact has been used for intra-operative demarcation of the tumor tissue. In this experimental work we investigate the possibility of creating an implantable device for early, low-cost detection of tumor recurrence.

Methods

We created custom miniaturized electronic device for generating an excitation signal at 405 nm optical wavelength and detecting the fluorescence of PPIX (~635 nm) and tested it on in vitro samples. The device comprised two light emitting diodes, a photodiode, and a microcontroller unit (MCU) with a built-in 16-bit analogue-digital (AD) converter. Its sensitivity towards fluorescence signal was tested on fluid acetone solutions in an Eppendorf tube with four different PPIX concentrations (0 – 9 ug), measured from 6 different distances (0-12.5 mm). Having passed this test, for a more realistic setup, measurements were performed on PPIX-gelatin phantoms of different thicknesses, with a pure gelatin phantom in front and behind them, to simulate brain tissue. In addition, computational simulations for inductive charging and involved heat dissipation were performed.

Results

All measurements were superposed by excitation light noise. For the distance-dependent measurements on the liquid solution, except at the distance of 0 mm, the noise closely followed a linear law (linear regression, b = 2.05, CI: 1.75 – 2.34, $p < 0.001$, R2 = 0.53) and could be reliably subtracted to obtain pure fluorescence signal. The signal itself could be modelled by power law, proportional to the square root of the PPIX concentration (linear regression, b = 10.2 – 106, depending on the distance, CI: ranging from 9.5 – 10.8 to 104 – 109, $p < 0.001$, R2 = 0.89 – 0.99, Figure 1). On the gelatin phantoms, the signal intensity depended linearly on the phantom thickness (b = 3.95, CI: 3.62 – 4.28, $p < 0.001$, R2 = 0.32, Figure 2) for the setup with the PPIX phantom in front of the pure gelatin phantom, but the empty phantom in front of the PPIX phantom had no effect on the signal (b = 0.57, CI: -3.69 – 4.83, p = 0.72, R2 = 0.0).

Conclusion

Miniaturized electronic device, suitable for implantation, can reliably detect PPIX signal in various settings. This opens new opportunities for monitoring tumor progress in the future.

Abb. 1

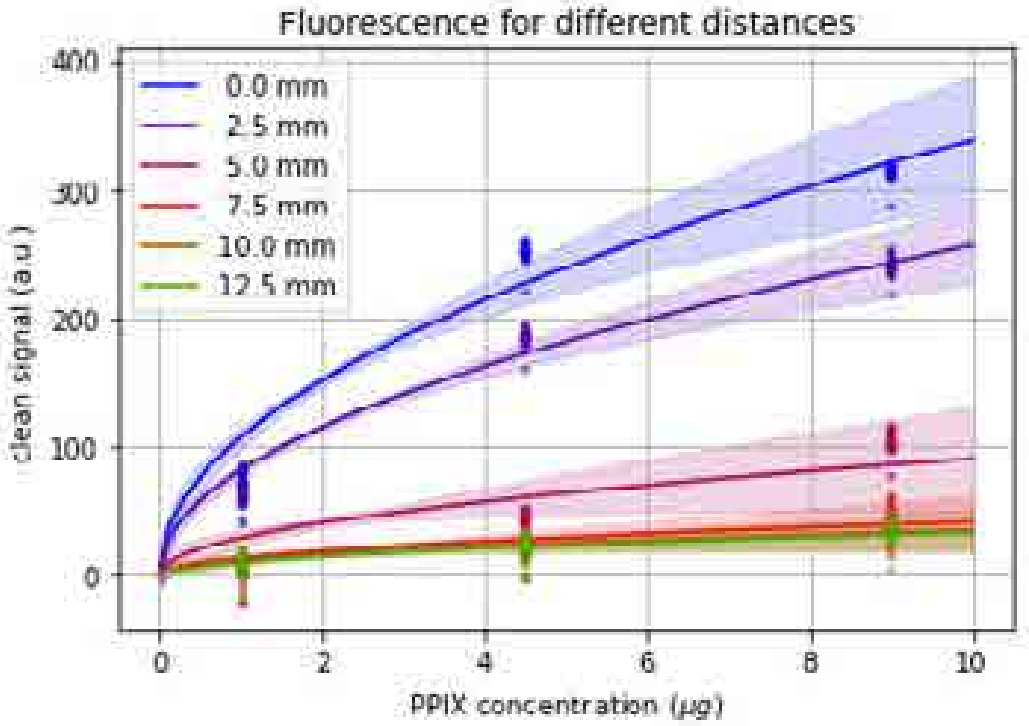
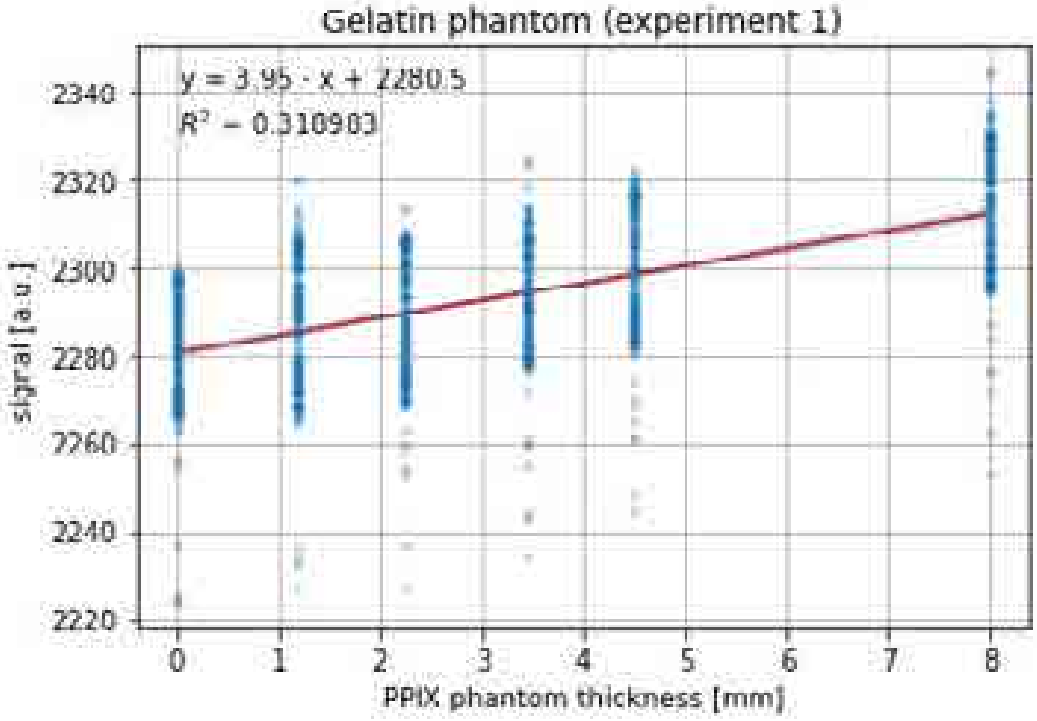

Fluorescence for different distances
0.0 mm
2.5 mm
5.0 mm
7.5 mm
10.0 mm
12.5 mm
clean signal (a.u.)
PPIX concentration (µg)

Abb. 2


Gelatin phantom (experiment 1)
y = 3.95 · x + 2280.5
R² = 0.310903
signal [a.u.]
PPIX phantom thickness [mm]

Hydrocephalus/*Hydrocephalus*

P193

Der idiopathische Normaldruckhydrocephalus: aktuelle diagnostische und therapeutische Verfahren in der klinischen Praxis in Deutschland

Idiopathic normal pressure hydrocephalus – survey on current diagnostic and therapeutic procedures in clinical practice in Germany

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Objective

Cerebrospinal fluid (CSF) shunting has become the standard treatment for idiopathic normal pressure hydrocephalus (iNPH). Nevertheless, there is still disagreement on diagnostic criteria for selecting patients for surgery and optimal shunt management. The primary aim of the present study was to provide a contemporary survey on diagnostic algorithms and therapeutic decision-making in clinical practice.

Methods

A standardised questionnaire with sections on the assessment of clinical symptoms and signs of NPH, diagnostic work-up, therapeutic decision making, and operative techniques was sent to 135 neurosurgical clinics in Germany that regularly perform shunt surgeries.

Results

Overall, responses were received from 114/135 (84%) clinics. Most responders indicated gait disturbance to be the hallmark clinical sign of iNPH (96%). Diagnostic CSF removal was utilized always or most of the time by 97 centers (86%). In 80% of centers, 30-40 ml CSF were removed for the diagnostic trial. Dynamic CSF studies were used by 15 centers only occasionally and continuous intracranial pressure monitoring by 25 centers for diagnostic purposes. Ventriculoperitoneal shunting was chosen as main CSF diversion procedure in a median estimate of 98% of iNPH patients. Overall 102 centers (93%) always or most of the time use programmable valves. 56 (51%) of the centers use antisiphon devices always or most of the times. Endoscopic third ventriculostomy was performed in only one center regulary and in another one in about half of the patients, while 64 departments never apply this method for iNPH.

Conclusion

According to the present survey, there has been a remarkable change in diagnostic criteria and surgical management of patients with iNPH over the past two decades. Further refinements are needed to address the multifold gaps and controversies concerning this still enigmatic disease.

Hydrocephalus/*Hydrocephalus*

P194

Idiopathischer Normaldruckhydrocephalus (iNPH) und Sturz im Alter
Idiopathic normal pressure hydrocephalus (iNPH) and falls in the elderly

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Objective

Falls and fall related injuries in the elderly are a major cause for serious health care problem resulting in disability, hospitalization, permanent institutional care or even death. At least 30% of adults aged over 65 years falls once a year. Risk factors for falls in the elderly are well studied and numerous. One reason could be the syndrome of idiopathic normal pressure hydrocephalus (iNPH) which remains underdiagnosed due similarities to other neurodegenerative diseases. iNPH is commonly characterized by the triad of dementia, gait and urinary disturbances which may be related to a higher risk of fall. Therefore, we hypothesized that more patients show clinical signs of iNPH who underwent a hospital treatment due to a fall than previously assumed or documented.

Methods

The clinical study investigated 94 patients in the age of 65 or older, who were hospitalized due to a fall. Inclusion criteria was the prevalence of a cranial computed tomography (CT) scan to assess the Evans-Index (EI). These patients underwent a clinical testing to examine the degree of cognitive, gait and urinary dysfunction by using the Kiefer-Scale. Based on the results of EI and Kiefer-Scale the likelihood of the presumptive diagnosis of iNPH was assessed.

Results

54 % (50/94) of elderly patients with falls showed a CT morphological enlargement of the ventricles with EI > 0.3. In the clinical examination gait disturbance was seen in 38.3 % (36/94), cognitive disorder in 36.2 % (34/94) and urinary incontinence in 42.6 % (40/94) of patients. There was a significant relationship ($p < 0.05$) among elderly patients between the prevalence of EI > 0.3 and gait disturbance (Odds Ratio (OR) = 7.74) or cognitive disorder (OR = 3.17), whereas bladder dysfunction showed no significant relationship with EI > 0.3.

Conclusion

At least one third of the elderly patients with falls meet the clinical and CT morphological criteria for iNPH suggesting that the prevalence of the disease is likely to be higher than expected. Therefore, these findings aim to create a greater awareness of iNPH, especially considering that treatment of iNPH by shunt surgery is effective with substantial improvement in up to 80 % of patients.

Hydrocephalus/*Hydrocephalus*

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Motorik, Kognition und Lebensqualität bei Patienten mit idiopathischen Normaldruckhydrozephalus – frühe Effekte einer Shuntimplantation

Motor skills, cognitive impairment, and quality of life in normal pressure hydrocephalus: early effects of shunt placement

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Objective

Traditionally clinical findings of normal pressure hydrocephalus are mainly characterized by the Hakim triad. The aim of this study was to evaluate the performance of patients suffering from idiopathic normal pressure hydrocephalus (iNPH) before and after shunt placement in a more holistic manner regarding motor skills, cognitive impairment and quality of life.

Methods

In total, 30 individuals diagnosed with iNPH as well as a healthy control group with another 30 individuals were included. The iNPH patients and the control group were matched for age, educational and morbidity. A standardized test battery for psychomotoric skills, gait, neuropsychological abilities as well as questionnaires for quality of life was applied. The iNPH group was tested prior to surgery, at 6 weeks and 3 months postoperatively. The control group was tested once.

Results

Patients showed a significantly improved performance in various items of the test battery during early postoperative follow-up. This included neuropsychological evaluation, motor skills including gait and upper motor function as well as the quality of life of the patients. Compared to healthy individuals, neuropsychological aspects and quality of life of iNPH patients improved to nearly healthy values.

Conclusion

Our findings underline that shunt surgery does not only improve the symptoms in iNPH patients but also ameliorates the quality of life to a great extent close to those of healthy individuals. This data enables an optimized counselling of iNPH patients regarding the expectable outcome after shunt surgery especially regarding cognitive performance, motor skills as well as quality of life.

Hydrocephalus/*Hydrocephalus*

P196

Die Behandlung des Pseudotumor cerebri Syndroms während der Schwangerschaft
Management of previously shunted patients with pseudotumor cerebri syndrome during pregnancy

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Objective

Pseudotumor cerebri syndrome (PTCS) is a rare disease which typically affects obese women of reproductive age. Its incidence in overweighted women between 20 to 44 years of age is almost 20 times higher than in the general population. Ventriculoperitoneal (VP) shunting is one of the preferred surgical treatments for severe cases of PTCS. There is little experience on the management of these patients when they become pregnant. Here, we report our multidisciplinary experience in this subgroup of PTCS.

Methods

Our database on PTCS was screened for patients who were diagnosed and treated with a VP shunt in our department from 2005 to 2022. Patients with PTCS who received conservative or medical treatment during pregnancy were excluded. Following pregnancy data were retrieved for each patient: onset of PTCS in relation to the pregnancy, number of pregnancies resulting to live births prior and after VP shunting as well as the delivery method.

Results

Overall 49 women with PTCS underwent VP shunting at a median age of 36,6 years. 35 patients were between 18 and 45 years at time of shunting. The median body mass index was 34 kg/cm2. A programmable valve with a default opening pressure set at 6 cmH20 (range 6-16) was implanted in all patients, in 46 with an integrated gravitation unit. 15 women had 39 births prior to shunting, while 4 women had 6 births at a median of 40,5 months after VP shunting (range 6-108). Onset of PTCS was not related to the occurrence of pregnancies. 5/6 patients had an uneventful pregnancy and a vaginal delivery. Symptoms of elevated intracranial pressure necessitating adjustment of the shunt valve were not evident in these patients. One patient experienced progressive visual loss refractory to acetazolamide treatment during the first trimester. VP shunting at 11 weeks of gestation facilitated stabilization of her visual symptoms and delivery via elective caesarian section at 35 weeks of gestation. In our series there were no peripartum cases of infection or malfunction of the shunt.

Conclusion

The complexity of PTCS during pregnancy requires a multidisciplinary approach in order to achieve optimal outcome. Our findings demonstrate that in previously shunted PTCS patients with programmable valves and gravitation units neither the occurrence of a pregnancy nor a vaginal delivery increase the risk for disease recurrence or deterioration. In severe cases, successful VP shunting during pregnancy is feasible in experienced centers and should be offered when indicated.

Hydrocephalus/*Hydrocephalus*

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Indikationen und Ergebnisse bei der Anwendung einer verstellbaren Gravitationseinheit in der Therapie des Hydrozephalus

Adjustable Gravitational Valve – Indication and Outcome

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Objective

Prevention and therapy of overdrainage are well known indications for the implantation of an adjustable gravitational valve (AGV). The reliability and safety of AGV proSA was shown in a prospective multicentre study[1]. The purpose of our prospective study was to evaluate our indications and outcome of using an AGV in hydrocephalic patients over 10 years.

1. Kehler U et al. PROSAIKA: a prospective multicenter registry with the first programmable gravitational device for hydrocephalus shunting. Clin Neurol Neurosurg. 2015 Oct;137:132-6. doi: 10.1016/j.clineuro.2015.07.002. Epub 2015 Jul 8. PMID: 26196478.

Methods

All 107 patients undergoing the implantation of an AGV (proSA) between January 2012 and December 2021 were included prospectively in a data base. Data were continuously analysed and are presented here.

Results

We implanted an AGV for 4 indications: A) Prevention of overdrainage in patients with high risk. B) Therapie of clinical and radiographic overdrainage. C) Optimization of valve adjustment in patients with iNPH in the case of lowering the opening pressure of the differential pressure valve to 2 or 0 cm water column or by exchange of non-adjustable gravitational unit to AGV. D) Patients with Idiopathic Intracranial Hypertension (IIH), empirically at high risk for orthostatic headaches related to overdrainage. Good clinical outcome, measured on the need for further surgical intervention or valve adjustment was seen in each group: A) 71%, B) 88%, C) 75%, D) 92%. In Group B overdrainage related subdural effusions under 10 mm resolved in 12 cases (92%) solely due to implantation and adjustment of the AGV (proSA). In Group C outcomes were additionally evaluated with the Black-Grading-Scale and the Kiefer-Index.

Conclusion

The use of an AGV has been well established for the prevention of overdrainage. We provide data for further indications. These include: Therapy of overdrainage and subdural effusions (Group B), Optimization of valve settings and clinical condition in iNPH patients (Group C) and inital treatment of Patients with IIH (Group D). The AGV ist safe and reliable. There were no device related shunt failures.

Hydrocephalus/*Hydrocephalus*

P198

Vorhersagekraft der quantitativen Pupillometrie bei Hydrocephalus Patienten für die Notwendigkeit der Anlage eines ventrikuloperitonealen Shunts

Predictive value of quantitative pupillometry in patients with hydrocephalus undergoing ventriculoperitoneal shunt insertion

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Objective

Hydrocephalus by its definition presumably causes significant changes in pupillary size or change in response to light associated with potential increase of the intracranial pressure. Ventriculoperitoneal shunt (VPS) insertion is so far the main stay of treatment. Emerging technologies like the quantitative pupillometry (QP) have improved clinical detection of subtle pupillary changes that may occur by CSF disorders. Therefore, the goal of this pilot study is to determine if the PLR as determined by QP can predict the presence of hydrocephalus and to evaluate how far a surgical procedure such as VPS insertion contributes to normalization of the pupil light response.

Methods

This is an on-going prospective study collecting pupillometry data from patients with intracranial pathologies. Pupillometry using the automated NPi 200® pupillometer was performed in 9 patients with clinically and radiologically confirmed normal pressure hydrocephalus (NPH). The neurological pupillometry index (NPi) ranges between 0-4.9 and quantifies the pupil reactivity with values >4.0 considered physiological. The NPi was analyzed as computed parameter before and after surgery.

Results

A total of 9 patients with a mean age of 61.6 years (SD 18.5) were analyzed. All patients presented with typical clinical signs of NPH. A CT scan confirmed the presence of hydrocephalus. The preoperative NPi was <4.0 in all patients in at least one pupil. Mean bilateral NPi were pathologic preoperatively (mean NPi 3.7 SD 0.4). All patients were opted to surgery (VPS insertion). Postoperative assessment revealed NPi a significant improvement when compared to baseline (mean NPi preoperative 3.7 SD 0.4 vs. mean NPi postoperative 4.2 SD 0.5; $p<0.05$). An amelioration of patients" clinical condition was reported in all cases after surgery.

Conclusion

This pilot study demonstrates a potential feasibility and the need for QP to help further to identify patients with hydrocephalus. Based on the current data, a significant increase of the pupillary light response was detected by the deployment of the QP after surgery. Postoperative improvement of NPi values may indicate sufficient diminish of intracranial pressure caused by CSF disorders.

Hydrocephalus/*Hydrocephalus*

P199

Abdominelle Schmerzen nach ventrikuloperitonealer Shuntanlage: Prävalenz, zeitlicher Verlauf, Einfluss auf die Lebensqualität

Abdominal pain after ventriculoperitoneal shunt: prevalence, timeline, and impact of quality of life

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Objective

The frequency of abdominal pain after ventriculoperitoneal (VP) shunt placement is still largely unknown and underreported. The aim of this study is to determine the prevalence, the course over time and the impact to quality of life.

Methods

149 patients with normal pressure hydrocephalus who underwent VP shunt placement were identified between 2020 and 2021. Data were collected by the digital patient records and by a follow-up questionnaire, to which 94 patients responded. Patients were asked about duration of pain (days to weeks, 2-12 months, >12 months), severity of pain in visual analog scale (VAS), the limitations in daily life (no limitation, barely disturbing, disturbing but tolerable, substantially disturbing), and the use of pain medication. Age, sex, and duration of surgery were documented as well. Statistical analysis was performed using logistic regression model.

Results

Overall, 39% (n=37) of patients reported abdominal pain. In 16% (n=15), pain occurred during hospitalization. 15% (n=14) reported pain for more than 12 months. The overall pain intensity was: VAS 0: 61% (n=57), VAS 1-3: 10,6% (n=10), VAS 4-6: 22.3% (n=21), VAS 7-8: 6.4% (n=6), VAS 8: 0%, after 12 months: 0: 85,1% (n=80), 1-3 2,1% (n=2), 4-6: 8,5% (n=8), 7-8: 4,26% (n=4) >8: 0% respectively. Only 7 patients used medication for abdominal discomfort. In 2.1% (n=2) abdominal discomfort was reported as substantially bothersome. There was no correlation with age or sex. With increasing time of surgery, the postoperative abdominal pain was reduced (p-value: 0.026).

Conclusion

Abdominal pain after VP-Shunt is a frequent finding (almost 40%), however, long lasting pain with a severe impact of quality of life is rare. The relation found between pain and duration of surgery remains unclear and is possibly a statistical outlier. Abdominal pain after VP-Shunt shouldn´t be neglected and further studies regarding the cause are recommended for possible improvements.

Hydrocephalus/*Hydrocephalus*

P200

Endoskopische Transaquäduktale Stentimplantation: Indikationen, neurochirurgische Technik und Resultate
Endoscopic Transaqueductal Stenting: Indications, Surgical Technique and Results

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Objective

Various endoscopic techniques for transaqueductal stenting (TAS) have been reported. Here the authors present the feasibility, and limitations of the endoscopic technique used, the achieved clinical and radiological results.

Methods

The clinical and radiological database for endoscopic TAS procedures from 01/2011 to 10/2022 was retrospectively analysed and prospectively followed. Shuntscope, Gaab scope, and flexible endoscope were used solely or in combined technique. Particular attention was given to indications, choice of endoscopic technique, its feasibility, complications, and results. Follow-up evaluation included the surgical revision rate due to aqueductal catheter misplacement or dysfunction.

Results

A total of 21 endoscopic TAS procedures were performed in 16 patients (9 adults and seven children, six female patients, and ten male patients; mean age, 27.125 years, age range 4 months to 61 years). The most common underlying pathology was an isolated fourth ventricle after shunting in 81.25%.Shuntscope-guided aqueductal stenting was considered in 11 procedures. Combined endoscopic technique with Shuntoscope and Gaab with or without flexible endoscope was used in 9 procedures. In one case, aqueductal stenting was performed under Gaab endoscope guidance exclusively. In two procedures, the transaqueductal stenting had to be abandoned, and the ventricle catheter was placed into the lateral ventricle because of unmanageable, distorted anatomical circumstances. Intraoperative surgical complications included an asymptomatic fornix contusion in three cases and discrete ependymal bleeding in 5 cases without clinical manifestation. One patient presented a transient trochlear nerve palsy. Postoperatively, 12 patients (75%) improved. Ideal transaqueductal stent placement was achieved in 78.95%. Two late revisions (9.52%) due to proximal aqueductal stent malfunction were necessary. No caterer migration was seen. The mean follow-up period was 49 months (range, 3-104 months).

Conclusion

Endoscopic transaqueductal stent placement represents a safe and low complication-rate treatment option for the selected subset of aqueductal stenosis. Shuntscope-guided trans-aqueductal stenting is a reliable endoscopic technique. The combined endoscopic technique applied in distorted intraventricular anatomy helped to overcome the shortcomings and limits of visualization of each endoscope used solely. A high rate of optimal stent placement and its long-term functionality is achievable.

Hydrocephalus/*Hydrocephalus*

P201

Chronische Kopfschmerzen nach Lumbalpunktion – kein typisches Liquorverlustsyndrom
A chronic post dural puncture syndrome without low opening pressure or altered CSF dynamics

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Objective

Chronic orthostatic headache following dural puncture is a serious condition lacking diagnostic criteria and an unambigous pathophysiological understanding. Current opinion supports the hypothesis that there should be an ongoing cerebrospinal fluid (CSF) outflow through an unsealed dural hole after a lumbar puncture. We aim to address imaging data and CSF dynamics in patients with chronic orthostatic headache following a lumbar puncture with a standardized lumbar infusion (LIT) test to test this assumption.

Methods

In a retrospective, single-center cohort study, we analyzed CSF dynamics by lumbar infusion test with resistance to CSF outflow (RCSF), lumber pressure at baseline, lumbar pressure at plateau, pulse amplitude at baseline and plateau (AMPbaseline, AMPplateau), elastance coefficient and pressure volume index (PVI). We included chronic post dural puncture headachs patients as defined by a history of dural puncture and orthostatic headache either persisting >14 days post dural puncture and/or persisting after one or more epidural blood patches.

Results

Between 04/2018 and 07/2022 we treated 77 patients with chronic post-dural puncture headache of which CSF dynamics were addressed in 24 patients. Median age was 37.5 years (IQR = 30-50). Median opening pressure during LIT was 12 cmH2O (IQR = 9 – 17). Median RCSF was 11.07 mmHg/(ml/min) (IQR = 6.96-13.57), median ICPbaseline was 9.61 mmHg (IQR = 6.94-13.81), ICPplateau was 29.88 mmHg (IQR = 22.35-37.21), AMPbaseline was 0.22 mmHg (IQR = 0.05-0.41), AMPplateau was 1.78 mmHg (IQR = 0.94-2.73, elastance coefficient was 0.17 ml-1 (IQR = 0.13-0.23) and PVI was 12.59 ml (IQR = 9.81-17.74). Neither did we find a correlation between LIT parameters and symptom duration.

Conclusion

Our results do not support the hypothesis that patients with chronic post-dural puncture headache are in a state of CSF-hypotension or have a decreased resistance to CSF-outflow.We conclude that symptoms are not readily revealed by CSF dynamics and that CSF opening pressure is not diagnostic.

Hydrocephalus/*Hydrocephalus*

P202

Prädiktoren und Variablen im Zusammenhang mit der Entwicklung eines posttraumatischen Hydrozephalus bei Patienten nach dekompressiver Kraniektomie

Predictors and variables associated with development of post-traumatic hydrocephalus in patients after decompressive craniectomy

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Objective

Decompressive craniectomy (DC) is a main domain of traumatic brain injury (TBI) treatment. Little is known about post-traumatic hydrocephalus (PTH) in patients after DC. Here, we intend to identify predictors and risk factors that are associated with PTH development after DC.

Methods

We performed a retrospective study of TBI patients who underwent DC, dividing our study cohort into two groups, patients who did not develop a PTH (Non-PTH group) and those who acquired a PTH (PTH group). We evaluated several clinical and radiographic characteristics, including the type of TBI on the initial and follow-up CT scans, ischemia, volumetric measurements of hematomas. Moreover, we assessed several trauma CT-scores as well functional outcome scores in all patients.

Results

Our cohort comprised 126 patients (93 males and 33 females) with a median age of 53 years (18-84 years). In total, 34 patients (27%) were in the PTH group. Parameters associated with a higher risk of PTH developing included brain herniation through the DC defect (PTH=82.4% vs Non-PTH=58.7%; p=0.02), a post-traumatic ischemia (PTH=70.6% vs. Non-PTH=33.7%; p<0.001), hemorrhagic contusion"s progression (PTH=47% vs. Non-PTH=18.5%; p=0.002) and a high Stockholm-CT-tSAH-Score (2-6 points) (PTH= 50% vs. Non-PTH= 19.6%; p<0.001). A modified Rankin Scale (mRS) higher than 3 points at the time of discharge after DC was significantly correlated with development of PTH (PTH=100% vs. Non-PTH=78.3%; p=0.002). In the multivariable analysis, an advanced age at the time of DC (OR 1.048; CI95% 1.012-1.085), subarachnoid hemorrhage (SAH) in the cisterns (OR 7.545; CI95% 1.477-38.544), a post-traumatic stroke (OR 5.319; CI95% 1.767-16.007), brain herniation through DC (OR 5.543; CI95% 1.449-21.199), hygroma (OR 8.131; CI95% 1.942-34.048) and hemorrhagic contusion"s progression (OR 4.386; CI95% 1.36-14.148) were independent variables associated with development of PTH.

Conclusion

Our study reveals SAH in the cisterns, advanced age, development of hygroma, post-traumatic stroke, brain herniation through the DC and hemorrhagic contusion"s progression as independent risk factors for developing PTH after DC.

Hydrocephalus/*Hydrocephalus*

P203

Gleichzeitige vs. gestufte Kranioplastik und VP-Shunt-Implantation nach Entlastungskraniektomie
Simultaneous versus staged cranioplasty and VP shunt implantation after decompressive craniectomy

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Objective

Many patients after decompressive craniectomy (DC) require both cranioplasty (CP) plus ventriculoperitoneal shunt (VPS) implantation due to secondary hydrocephalus. Both procedures are associated with a high complication risk, and the timing of these interventions remains controversial. Thus, we retrospectively compared the outcome after CP and VPS implantation as a one-step vs. a two-step procedure, as well as attempted to define an optimal timepoint of VPS implantation after CP in case of a two-step procedure.

Methods

All unilateral DC patients who received both CP and VPS in our center between 2010 and May 2022 were divided in two groups: CP with simultaneous vs. staged VPS implantation. Clinical data was retrospectively acquired from patients" records. MW-U and ChiSq tests were used in monovariate analysis, KM and Cox regression in patient overall survival (OS) assessment and ROC/AUC to define an optimal timepoint in case of staged surgery.

Results

30 patients with a mean age of 53 years (95CI 47-58) were analyzed. CP was performed on average 84 days (95CI 58-111) after DC with a mean follow-up of 33.6 months (95CI 19.2-48.1). In 14 patients (47%), a VPS was implanted simultaneously with CP, while this was performed in a delayed fashion in 16 patients (53%).

No association with the type of brain injury, patient age, pre-morbidity, implant type and laterality was found between the groups (p – n.s.). Absolute and relative mRS did not differ (p – n.s.). Mean estimated patient OS was also comparable: 15.7 years (95CI 9.3-22.0) in the simultaneously implanted VPS group vs. 14.6 years (95CI 9.1-20.1) after staged surgery (p – n.s.). There were no differences in early or late postoperative complication rates (p – n.s.). Equally high number of revisions during the hospital stay were necessary after one- and two-step procedures: CP-associated in correspondingly 3/14 and 4/16 cases, as well as VPS-associated in correspondingly 4/14 and 5/16 cases.

If VPS was implanted in the second stage, to reduce 6 months revision rate, it should had been done not later than 26 days after CP (AUC 0.9, sensitivity 1.0, specificity 0.8; p=0.05).

Conclusion

No differences in morbidity and mortality were found between CP with simultaneous vs. staged VPS implantation. Hence, simultaneous surgery as one-step procedure may be preferred. If a staged procedures is considered, VPS implantation should be performed not later than 26 days after CP.

P204

Kann die Anwendung von Kinesiotape postoperative lokale Schmerzen nach lumbalen oder cervikalen Wirbelsäulenoperationen verringern?

Can Kinesiology Taping reduce postoperative pain after lumbar and cervical spine surgery?

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Objective

Lower back pain is frequent after dorsal lumbar spine surgery and so is neck paint after cervical spine surgery. Hematoma, oedema, stretching of muscles and affection of the facet joints result in local complaints. Kinesiology Tape (K-Tape) is an adhesive elastic tape which became popular in the last decade. Its pain-reducing effect is discussed controversially. Several authors prove it for the conservative treatment of musculoskeletal disorders. There is no investigation of K-Tape in the postoperative neurosurgical pain treatment so far. In this study we investigate in how far patients who underwent spine surgery benefit from the application of K-Tape direct postoperatively during hospital stay.

Methods

A prospective randomized design was used. The pathology was limited to degenerative lumbar and cervical spine diseases and to maximal 2 segments. The taping group (T) had an adhesive Kinesiology Tape which was applied in the evening of surgery day (Fig. 1 und Fig. 2), the control group (C) did not receive the taping. The visual analog scale (VAS) was assessed preoperatively (t1), one day after surgery (t2) and at the point of discharge (t3) from hospital. The area of pain was subdivided into three regions ranging from proximal to distal (lower back/ neck (1), gluteal region/shoulder (2) and leg/ arm (3)). Additionally, the pain medication was assessed preoperatively, one day after surgery and at the point of discharge.

Results

Between June 2022 and December 2022 40 patients were included. 20 were randomized in the T and 20 in the C group. 27 patients underwent lumbar surgery, 13 anterior cervical discectomie and fusion (ACDF). Mean difference of VAS in the K group between t1 and t3 was 3.95. Mean difference of VAS in the C group between t1 and t3 was 1,55 The difference of the mean VAS between the T and the C was significant with 0,002 at the day of admission.

Conclusion

K-Tape is an application which is simple to use and has practically no side effects. It reduces postoperative pain under consideration that the observation is only in the short term (2-3 days after surgery).

Abb. 1

Abb. 2

Wirbelsäule II/*Spine II*

P205

Lebensqualität und funktionells outcome nach der Resektion von spinalen Meningeomen
Quality of life and functionality after resection of spinal meningiomas

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Objective

Resection of juxtamedullary meningiomas can be demanding and little is known about the quality of life (QOL), the functionality of these patients, as well risk factors that influence a better outcome.

Methods

Patient"s outcome was assessed by established questionnaires such as short Form Survey-36 (SF-36), Oswestry Disability Index (ODI) and Neck Disability Index (NDI), as well as by postoperative physical examination at our academic neurosurgical department.

Results

39 patients completed the questionnaires. Most of the patients (69.2 %, N=27) reported very good postoperative conditions in the ODI and NDI (score < 10). Overall QOL was comparable to results of the normal healthy population. Favorable functional and neurological outcome was associated with mild preoperative symptoms (McCormick scale 1 and 2; P<0.05). Unfavorable outcome occurred in those patients that displayed severe preoperative deficits (McCormick scale > 4) and in those suffering from other medical diseases.

Conclusion

Resection of spinal meningiomas results in the majority of the cases in a favorable outcome. Our results indicate that tumor resection in early stage of the disease may lead to a better outcome.

Wirbelsäule II/*Spine II*

J-SBNC032

Idiopathischer vorderer thorakaler Rückenmarksbruch - ein Fall beziehen
Idiopathic Anterior thoracic spinal cord herniation - a case relate

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Objective

We describe a very rare case of Anterior thoracic spinal cord herniation (ATSCH) of Idiopathic origin, with a 63 years old female patient presenting herself in our department with a progressive gait disturbance for about 6-7 years, without any relevant medical history. ATSCH was first described in 1974, by Wortzman et al1, and since then few but increasing numbers of cases worldwide have been described. Gold standard treatment of ATSCH is neurosurgical intervention, with a reduction of the herniated spinal cord and correction of the dura defect. With neurosurgical treatment most of the patients achieve a stabilization or improvement of the symptoms.

Methods

A 63 years old female patient presented herself in our outpatient department with a progressive gait disturbance for about 6-7 years. The patient did not have any relevant medical history of trauma, infection, surgery or signs of a congenital disorder of the thoracic spine. An MRI with CSF-Flow was requested confirming the suspicion of an idiopathic ATSCH. Since the patient had progressive neurological deficits the indication for surgical treatment with closure of the defect was given.

Results

The surgery then was performed through a posterior approach with T5/T6 laminotomy and intraoperative neurophysiological monitoring. After the midline opening of the dura mater the spinal cord was visualized. Under continuous electrophysiological monitoring the spinal cord was carefully mobilized with visualization of a large dural defect through which the spinal cord was herniating (figures 01 and 02). To close the defect we decided to perform a duraplasty with bovine pericardium. Patient had a satisfactory postoperative evolution, there were no new associated deficits and during the follow-up she presented improvement of previous symptoms.

Conclusion

ATSCH is a very rare entity and rarely diagnosed, with most dural defects reported in literature located ventrally at the thoracic spine level. Spinal cord herniation can be divided into such causes as pressure erosion, trauma, discal extrusion, congenital disorder, inflammatory process.3 Here we described a case of anterior thoracic SCH through a dural defect. The treatment is eminently surgical, with favorable outcomes.

Abb. 1

Abb. 2

Wirbelsäule II/*Spine II*

P206

Symptomatik, Diagnostik und chirurgische Therapie des primären Tethered-Cord-Syndroms bei Erwachsenen.
Symptomatology, diagnostic and surgical treatment of primary tethered cord syndrome in adult patients.

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Objective

Tethered cord syndrome (TCS) is a stretch-induced dysfunction of the spinal cord because of anatomical restriction of normal spinal cord movement or hypoxia of distal structures. Tethered cord may be congenital or secondary. We present a case series on this rare syndrome in the adult population and address treatment indication, surgical technique, and clinical outcome.

Methods

Adult patients who were treated for TCS at our institution between 2009–2022 were retrospectively identified. Medical records and imaging data were reviewed. The analyses included symptoms leading to the diagnosis, imaging characteristics, surgical technique, intraoperative neuromonitoring, complications and clinical outcome. Patients with a history of perinatal surgery for spina bifida were excluded.

Results

Twenty-six adult patients with TCS were identified. Mean age at presentation was 39±14 years. 73% were female. The most frequent symptom was sensory deficit of lower extremities followed by back pain, urinary incontinence, and motor deficit in 69%, 62%, 42% and 31% of the patients, respectively. 50% of the patients had an occult tethered cord that could only diagnosed with MRI in prone position. 42% had a lumbar intradural lipoma and 8% had spina bifida occulta. Surgical treatment consisted of cutting the filum terminale in patients with occult tethered cord and detethering as well as complete or partial resection in patients with spinal lipoma. Intraoperative neuromonitoring included electromyography of the muscles of lower extremities with electrical bipolar stimulation of the cauda equina at an intensity of 1 to 3 mA to identify the filum terminale. The main postoperative complication was cerebrospinal fluid leakage which occurred in 4 patients (15%). Average follow-up was 129 weeks. In patients with preoperative deficits, motor weakness improved in all of them (100%), sensory deficit in 61% and urinary incontinence in 55%. Occult tethered cord was associated with a better postoperative recovery of sensory deficits comparing to patients with lipoma, p = 0,017. Otherwise, no significant difference was found between the two patient groups.

Conclusion

Occult tethered cord was the most frequent cause of tethered cord syndrome in our adult patient cohort, followed by spinal lipoma. Surgical treatment with intraoperative neuromonitoring led to symptom relief in the majority of the patients with a low risk profile.

Wirbelsäule II/*Spine II*

P207

Der posterolaterale epidurale supra-C2-Nervenwurzel Zugang (PESCA) für Biopsie des Dens axis

Posterolateral epidural supra-C2-root approach (PESCA) for biopsy of lesions of the odontoid process

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Objective

This study aims to describe the posterolateral epidural supra-C2-root approach (PESCA), which might be a good alternative to the transoral, anterolateral, and other posterolateral approaches for biopsy of lesions of the odontoid process (OP) and retro-odontoid region.

Methods

For PESCA, the patient is positioned under general anesthesia in prone position. In case of an osteolytic lesion with fracture of the OP, an x-ray is performed after positioning to verify anatomic alignment. In the first step, in case of instability and compression of the spinal cord, a craniocervical fusion and decompression is performed (laminectomy of the middle part of the C1 arc and removal of the lower part of the lateral C1 arc).

The trajectory is immediately above the C2-root (and under the upper rest of the lateral part of C1 arc). Even if the trajectory is narrowed, it is possible to perform PESCA without relevant traction of the spinal cord. The vertical segment of V3 of the VA at the level of C2 is protected by the vertebral foramen and the horizontal part of V3 is protected by the remnant upper lateral part of the C1 arc (in case of normal variants).

Results

Three patients were included in the study (mean age: 67 years, range 58-72 years). The pathological examination of the masses showed in the first and the third case a spondylodiscitis of the OP (microbiological analysis of the probe of case 1 revealed Corynebacterium striatum and of case 3 staphylococcus aureus) and in the second case calcium pyrophosphate crystals (in addition to the clinical symptoms, especially neck pain, the diagnosis of ´crowned dens syndrome´ was made).

The lesions were treated in the first and third case with antibiotic therapy and in the second case with NSAIDs, colchicine and steroids. In all of our patients the pathological findings were the key to the successful treatment.

All three patients recovered well from surgery. 6 months after surgery, the patients did not manifest any neurological symptoms.

Conclusion

PESCA might be a good choice for biopsy of selected lesions of the OP in same sitting procedure after craniocervical stabilization and decompression.

Wirbelsäule II/*Spine II*

P208

Degenerative zervikale Myelopathie: Chronisches Trauma führt zu chronischen Veränderungen von Angiopoetin II, einem endogenen angiogenen Mediator im Liquor. Hinweise auf eine verlängerte Angiogenese?

Degenerative cervical myelopathy: Chronic trauma leads to chronic alterations of Angiopoetin II, an endogenic angiogenetic mediator in CSF. A notice for extended angiogenesis?

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Objective

Endogenous immune mediated angiogenesis is a component of secondary spinal cord injury in patients with degenerative cervical myelopathy (DCM). Aim of this study is to identify alterations of the proangiogenic protein Angiopoetin II (ANG II) in the cerebrospinal fluid (CSF) in patients with chronic spinal cord injury (SCI) compared to a control group.

Methods

Pre- and postoperative patients with DCM (n=49; 21 female; mean age 62.9±11.28) and indication for surgery were included. CSF samples were taken pre- and postoperatively between 3-5 months. A control group of patients (n=45; 17 female; mean age 61.06±14.54) with abdominal aortic aneurysm (AAA) requiring surgery was established. AAA patients received a CSF drainage for intrathecal pressure monitoring, samples were taken preoperatively. The neurological status of all participants was evaluated prior surgery including NDI and mJOA. Controls with any neurological deficit or history of neurological diseases were excluded. Samples were examined by ELISA testing. Protein-concentrations of ANG II in CSF (pg/ml) were analyzed.

Results

Both groups did not differ in terms of age and gender distribution. Groups differed regarding their neurological status (mJOA: DCM 10.96±3.1, AAA 17.28±1.26, $p<0.001$; NDI: DCM 40.2±21.1, AAA 6±8.3, $p<0.001$, and in preoperative ANG II concentration: DCM 276±90, AAA 463±240, $p<0.001$). 3 months after surgery ANG II values were almost unaltered in DCM patients, compared to preoperative values (277±65, $p=0.998$). Subgroup correlation analysis of clinical data showed no significant differences in concentrations of ANG II.

Conclusion

In patients with DCM concentrations of ANG II lower than in controls were found pre- and persistent postoperatively. These results correspond probably to immune mediated secondary harm in chronic spinal cord injury. Chronically reduced angiogenetic activity could be a relevant part of DCM pathogenesis and secondary harm mechanisms to the spinal cord. However, due to a missing correlation with clinical outcome data, the question of the role of angiogenesis on symptom relief or persistence remains elusive.

P209

Intraoperative MEP-Verbesserung als elektrophysiologischer Marker für klinische Besserung nach chirurgischer Dekompression bei polyneuropathischen Patienten mit zervikaler degenerativer Myelopathie

Improvement of intraoperative motor evoked potentials might predict early recovery in polyneuropathy patients after surgical decompression of cervical degenerative spinal myelopathy

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Objective

Intraoperative motor-evoked potential (MEP) improvement during surgical decompression of cervical degenerative spinal myelopathy (DSM) has been shown to correlate with postoperative neurological recovery. Patients with combined polyneuropathy (PNP) and DSM have a variable prognosis following decompression of the cervical spinal cord. The aim of this study is to determine the role of intraoperative MEP monitoring during dorsal decompression for DSM in PNP patients and its correlation with postoperative neurological improvement.

Methods

Patients were screened for PNP by a neurologist. Transcranial electrical stimulation was performed to elicit MEP during surgery for DCM. Bilateral osteoligamentous decompression via (partial) hemilaminectomy (OLD) was performed in the sitting position. MEP threshold levels were assessed separately at the beginning and at the end of the surgery in the muscle groups corresponding to nerve roots at the level of or distal to decompression. Clinical outcome was measured using the modified Japanese Orthopedic Association (mJOA) score preoperatively and at discharge.

Results

12 PNP and 36 non-PNP patients underwent surgery for DSM. There was a non-significant trend towards a lower occurrence of early clinical improvement in the PNP group in comparison to the non-PNP group (45.4% vs 72.2% respectively, $p = .14$). In contrast, the evolution of MEP threshold variation was comparable in both groups (63.6% vs 58.3% respectively for general MEP improvement $p > .99$).

Conclusion

As PNP is associated with altered motor cortex connectivity, electrophysiological variations in PNP patients after surgical DSM decompression could constitute early manifestations of subclinical improvement. Long-term data concerning this patient collective is needed.

Wirbelsäule II/*Spine II*

P210

3D-C-Arm-Scan-gesteuerte navigierte perkutane transpedikuläre Plazierung von Gentamycin-PMMA-Kugelketten nach perkutaner Fusion bei progredienter oder rezidivierender Spondylodiszitis

3D-C-arm-scan navigated percutaneous transpedicular targeted placement of Gentamycin-PMMA-beads-chain during percutaneous fusion surgery in case of progressive or recurrent spondylodiscitis

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Objective

Spondylodiscitis (SD) is a potentially life-threatening bacterial infection with a morbidity rate of more than 7% and a high recurrence rate.

This study aims to describe the 3D-C-arm-scan-navigated percutaneous transpedicular targeted placement (3DnavP) of Gentamicin-PMMA-beads-chains (GBC) in case of progressive or recurrent SD.

Methods

For 3DnavP, the patient is positioned under general anesthesia in the prone position. In the first step, a small incision for exposure of one spinal process is performed. The patient"s reference array is fixed on the spinal process.

A 3D-C-arm-scan (Ziehm 3D) for spine navigation registration (Brainlab) is performed under apnea after preoxygenation. Percutaneous transpedicular fusion is performed above and below the spondylodiscitis under spine navigation and x-ray.

After percutaneous fusion surgery, the percutaneous transpedicular punction with the targed of the infection focus is performed with the vertebra access device using the bevel tip needle (Joline) under spine navigation and x-ray. The trajectory is angled through the caudal part of the posterior pedicle and the upper part of the anterior pedicle. A Kirschner wire (K-wire) is inserted into the trajectory. A vertebra introducer device (Joline) is inserted into the target following the track of the K-wire. A gentamicin-PMMA-beads-chain (Septopal) is inserted into the target through the vertebra introducer device under x-ray guidance.

Results

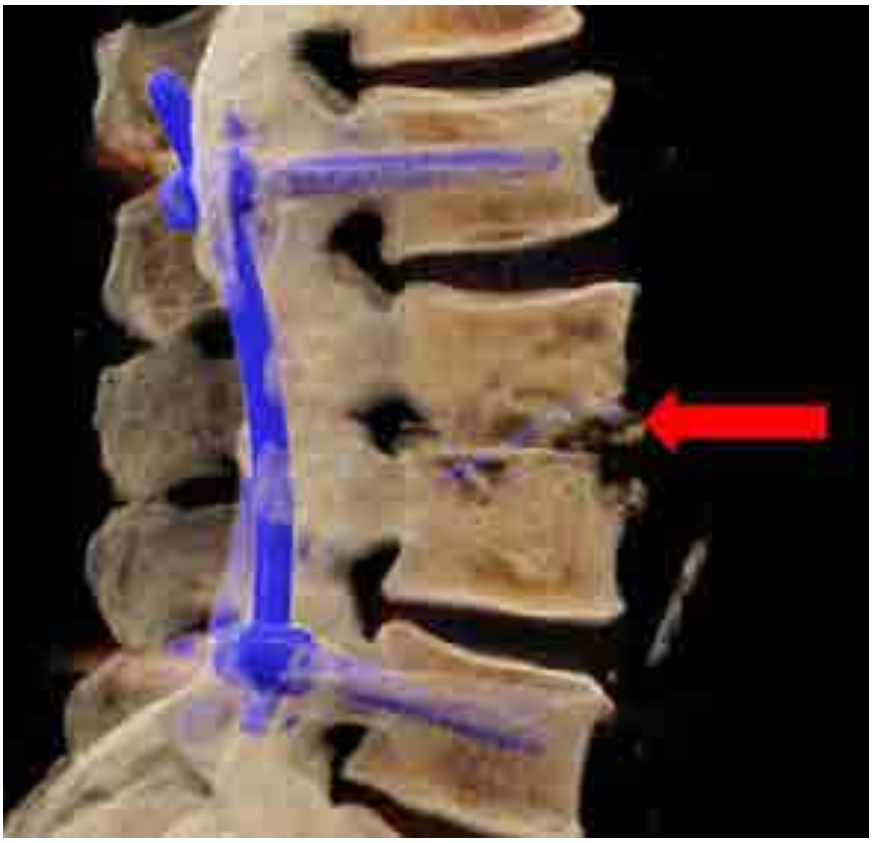
The postoperative CT scan revealed a proper positioning of the screw (Gertzbein–Robbins grade A) and the antibiotic sphere chain.

At follow-up examination 4 months after surgery, the patient had no neurological symptoms and no pain. The C-reactive protein level was normal.

Conclusion

3DnavP of GBC might be a good choice for targeted local antibiotic therapy in cases of spondylodiscitis and an alternative to open approaches. It combines the advantages of 3D-C-arm-scan guided navigation regarding the accuracy and targeted placement, percutaneous transpedicular surgery regarding minimal invasiveness, and the advantages of local antibiotic therapy regarding high local antibiotic dose.

Abb. 1



Wirbelsäule II/*Spine II*

P211

Ambulante parenterale Antibiotika Therapie (APAT) bei Wirbelsäuleninfektionen
Intravenous antibiotic treatment in patients with spinal infections in the outpatient setting: a feasibility study

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Objective

Spondylodiscitis, spinal empyema and deep postoperative wound infections require a long-term intravenous antibiotic treatment. To prevent an extensive hospital stay, the treatment can be performed in self-sufficient patients in an outpatient setting. Current literature supports its advantages, but there is a lack of data regarding patients suffering from spine pathologies. We hereby investigate the feasibility and benefits of the outpatient antibiotic treatment in spinal infections.

Methods

We prospectively enrolled all patients eligible for the outpatient antibiotic treatment in our neurosurgical department from 2019-2022. We assessed inflammation markers, the clinical status and the length of hospital stay as well as the readmittance rate and treatment failures.

Results

In total, we included 27 patients. We enrolled patients suffering from deep wound infections (40%), spondylodiscitis (18%) and patients suffering from low grade implant infections (29%). In 22 patients we were able to identify specific bacteria causing the infection (mostly Staphylococcus aureus). Median length of hospital stay was 9 days, median length of the antibiotic intravenous treatment was 4 weeks (range 2- 16 weeks). In total, we were able to provide 649 days of intravenous antibiotic treatment in the outpatient setting. The readmittance rate was 7%.

Conclusion

Outpatient antibiotic treatment presents a valid treatment alternative for independent neurosurgical patients requiring long-term intravenous antibiotics for spinal infections. All but two patients were successfully treated and described a high contentedness with the outpatient treatment.

Wirbelsäule II/*Spine II*

P212

Die Knochendichte des 2. Halswirbels gemessen anhand von Hounsfieldeinheiten einer Computertomographie - eine Datenanalyse von 198 Patienten

Bone density of the second cervical vertebra measured using Hounsfield units of computed tomography

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Objective

Die Densfraktur Typ II nach Anderson und d´Alonzo ist eine der häufigsten Frakturen der oberen Halswirbelsäule. Insbesondere bei älteren Patienten mit einer verminderten Knochendichte kommt dieser Frakturtyp häufig vor. Das Ziel der Arbeit war es, die Knochendichtewerte mittels Hounsfield-Einheiten (HU) in den einzelnen Abschnitten des zweiten Halswirbels zu bestimmen. Des Weiteren sollte überprüft werden, ob zwischen den einzelnen Abschnitten geschlechts- oder altersbezogen Unterschiede der Knochendichte bestehen.

Methods

Die Studie ist eine monozentrische retrospektive Datenanalyse von 198 erwachsenen Patienten, die eine Polytrauma-Computertomographie mit Kontrastmittel in einem Zeitraum zwischen dem 01.01.2020 und dem 31.06.2021 in einem Klinikum der Maximalversorgung erhielten. Gemessen wurden die HU mit einem elliptischen Messfeld in drei verschiedenen Lokalisationen: Dens axis, Übergangbereich und Wirbelkörper. Die gemessenen HU wurden mithilfe einer validierten Formel in Knochendichtenwerten umgerechnet (QCT-Wert = 0.71 × HU + 13.82).

Results

Es gab einen signifikanten statistischen Unterschied der Knochendichtewerte in den verschiedenen Regionen des 2. Halswirbels (302,79 vs. 160,08 vs. 240,31mg/cm³, p<0,001). Im Bereich des Wirbelüberganges wurden statistisch signifikant niedrigere Werte im Vergleich mit den anderen Bereichen gemessen (160,08 mg/cm³, p<0,001). Die gleiche Abnahme der Knochendichtewerte fiel zwischen Dens axis zum Corpus des zweiten Wirbels auf, mit einer weiteren Abnahme zum Übergangsbereich des Wirbels. Das war ebenfalls beim Vergleich der Geschlechter auffällig (p< 0,001).

Die Knochendichtenwerte nahmen im Allgemeinen mit dem Alter in allen Abschnitten ab. Es bestand eine eindeutige Abnahme der Werte nach einem Alter von 50 Jahren, sowohl bei Männern als auch bei Frauen (p < 0,001).

Conclusion

In der Untersuchung der Knochendichte des 2. Halswirbelkörpers fiel auf, dass zwischen dem Dens axis und dem Corpus ein Übergangsbereich bestand, bei dem statistisch signifikant niedrigere Knochendichtwerte bestanden. Dieser Knochenbereich stellt sicherlich eine Prädilektionsstelle für Frakturen des zweiten Halswirbelkörpers dar. Die weiteren gewonnenen Daten der einzelnen Wirbelabschnitte können hilfreich sein, um einen besseren präoperativen Plan vor einer Instrumentierung zu entwerfen.

Abb. 1

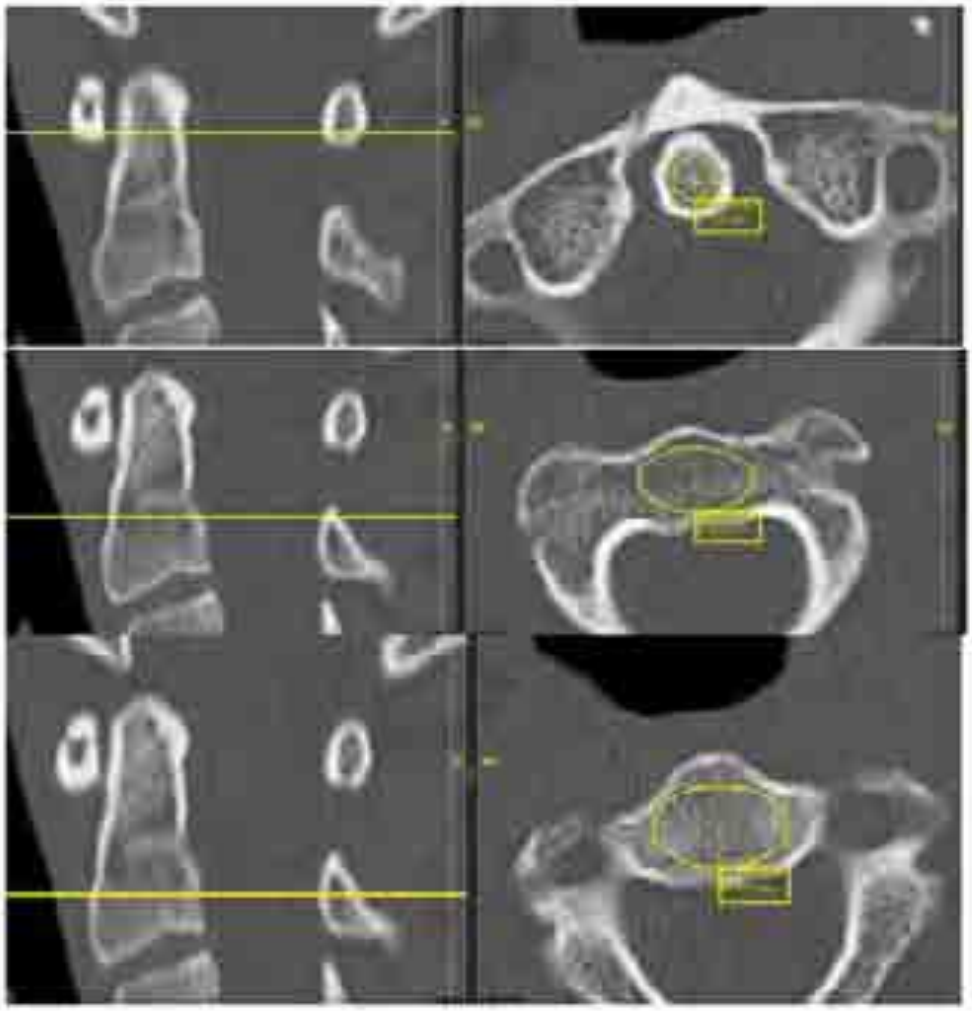

Abbildung 1: Bestimmung der HU des HWK2 Wirbelkörpers in 3 Lokalisationen: Dens axis, Übergangbereich und Wirbelkörper

Abb. 2

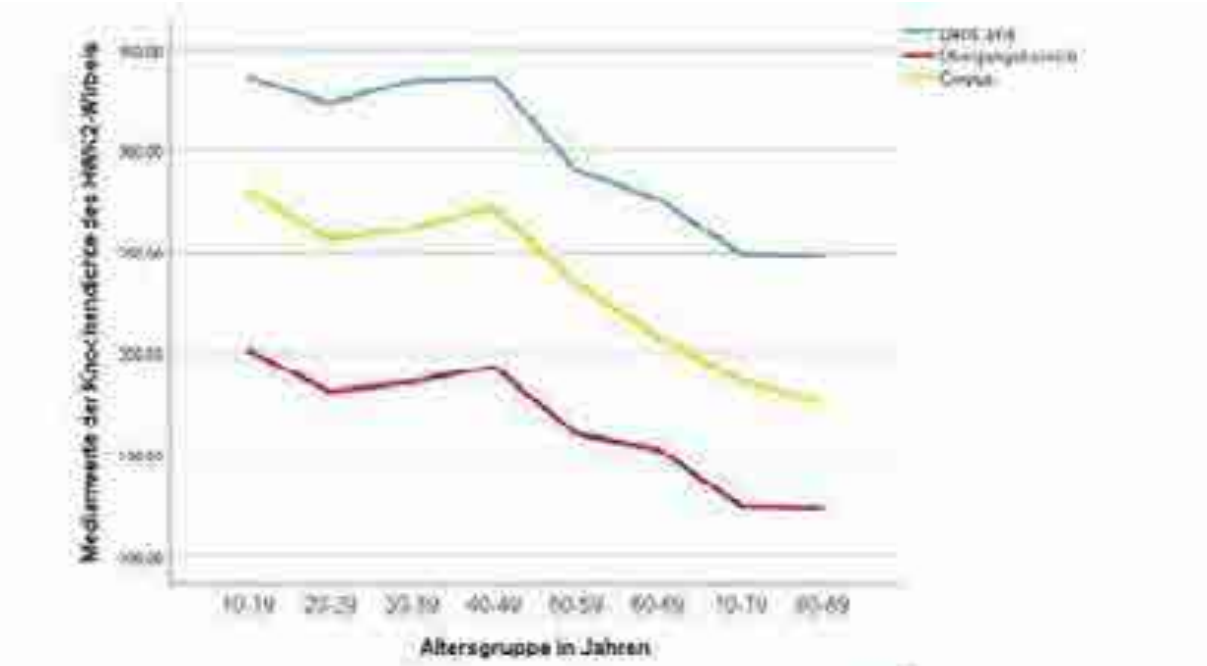

Abbildung 3: Knochendichtewerte aller Patienten im Bereich von Dens axis, Übergangsbereich und Corpus je nach Altersgruppe

Wirbelsäule II/*Spine II*

P213

Die Knochendichte der gesamten Wirbelsäule gemessen anhand von Hounsfieldeinheiten einer Computertomographie - eine Datenanalyse von 200 Patienten

Bone density of the cervical, thoracic and lumbar spine measured using Hounsfield units of computed tomography

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[1]Universitätsklinikum Jena, Klinik und Poliklinik für Neurochirurgie, Jena, Deutschland

Objective

Die Bewertung der Knochendichte hat heutzutage aufgrund des zunehmenden Patientenalters eine große Bedeutung. Gerade in Hinsicht auf die operative Stabilisierung der Wirbelsäule ist die Beurteilung der Knochendichte wesentlich für die Therapieentscheidung. Das Ziel der Arbeit war es, die trabekulären Knochendichtewerte mittels HU in den Wirbelkörpern der Halswirbelsäule, Brustwirbelsäule und Lendenwirbelsäule zu erfassen.

Methods

Die Studie ist eine monozentrische retrospektive Datenanalyse von 200 Patienten, die eine Polytrauma-Computertomographie mit KM in einem Zeitraum zwischen dem 01.01.2020 und dem 31.06.2021 erhielten. Grundliegende Informationen sowie die HU und die Knochendichtenwerte der Wirbelkörper von HWK3 bis LWK5 wurden erfasst. Gemessen wurden die HU mit einem elliptischen Messfeld in drei verschiedenen Lokalisationen innerhalb des Wirbelkörpers: unterhalb der Deckplatte, in der Mitte des Wirbelkörpers und oberhalb der Grundplatte. Die gemessenen HU werden mithilfe einer validierten und publizierten Formel in Knochendichtenwerten umgerechnet (QCT-Wert = 0.71 × HU + 13.82)

Results

Der Mittelwert des Alters des Patientenkollektivs betrug 47,05 Jahre. Es gab einen signifikanten statistischen Unterschied zwischen den Knochendichtewerten der Hals-, Brust- und Lendenwirbelsäule ($p<0,001$). Die Knochendichte sank statistisch signifikant von kranial nach kaudal ab: die medianen Knochendichtenwerte der Halswirbelsäule waren höher als die Knochendichtewerte der Brustwirbelsäule (228,67 vs. 169,31 mg/cm³; $p<0,001$), die medianen Knochendichtewerte der Brustwirbelsäule waren höher als die Knochendichtewerte der Lendenwirbelsäule (169,31 vs. 149,69 mg/cm³; $p<0,001$). Im Bereich der unteren Halswirbelsäule (HWK6 und HWK7) waren die Werte statistisch signifikant niedriger als die Werte der oberen Halswirbelsäule ($p< 0,001$).

Conclusion

Diese Daten der einzelnen Wirbelsäulenabschnitte können unter anderem hilfreich sein, einen besseren präoperativen Plan vor einer Instrumentierung zu entwerfen. Die Knochendichte verschiedener Wirbelkörper kann ebenso wichtig für die Medizinproduktindustrie sein, die die Instrumente wie Schrauben und Implantate entwickeln muss. Diese Medizinprodukte müssen speziell für die lokalen anatomischen Verhältnisse verschiedener Wirbelsäulenregionen und deren Knochendichte angepasst sein.

Abb. 1

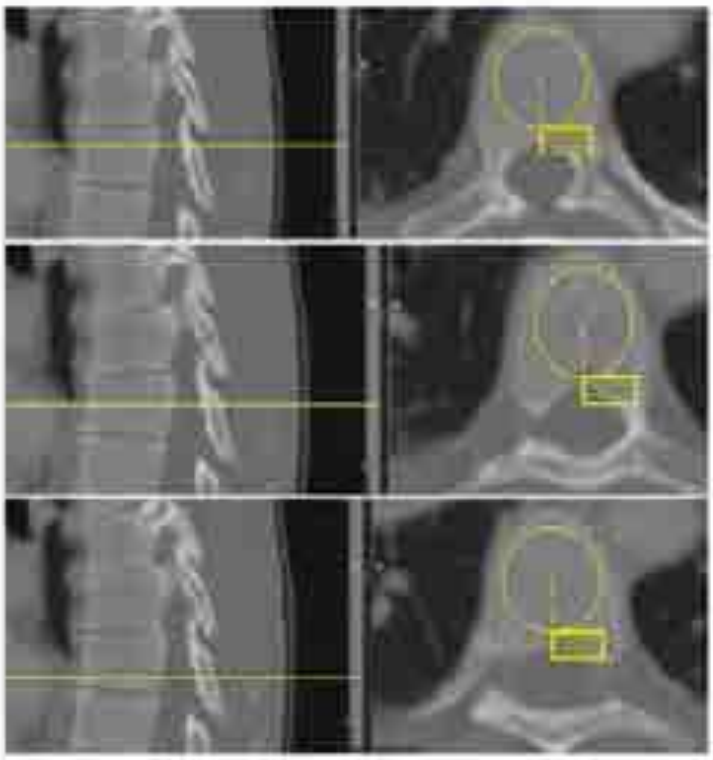

Abbildung 1: Bestimmung der HU eines thorakalen Wirbelkörpers in 3 Lokalisationen unterhalb der Deckplatte, in der Mitte des Wirbelkörpers und oberhalb der Grundplatte anhand eines Computertomographie mit Kontrastmittel

Abb. 2

Abbildung 2: Medianwerte der Knochendichte von den Wirbelkörpern aller Patienten in mg/cm³

Wirbelsäule II/*Spine II*

P214

Therapie rezidivierender Iliosakralgelenksschmerzen: ultraschallgesteuerte autologe Injektionen mit plättchenreichem Fibrin

Therapy of recurrent sacroiliac joint pain: of ultrasound-guided autologous platelet-rich fibrin injections

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Objective

Low back pain (LBP) is a common problem with enormous socioeconomic and medical consequences. In up to 30% of LBP-cases pain originates from the sacroiliac joint (SIJ). In many patients symptoms relapse despite multiple minimally invasive interventions such as infiltrations with corticosteroids and severely reduce the patient"s quality of life. Platelet rich fibrin (PRF) is an autologous biomaterial that is easily prepared from the blood of patients with a high concentration of platelet growth factors. Its regenerative and anti-inflammatory properties led to its wide utilization in maxillofacial, orthopedic and plastic surgery. This study retrospectively analyzed the effects of PRF infiltration in a series of patients where symptoms relapsed despite previous multiple corticosteroid injections.

Methods

A series of 13 patients (3 men and 10 women; mean age, 54 years) with verified chronic relapsing bilateral SIJ-irritation despite multiple prior corticosteroid injections (range: 1-4) were referred to our institution for treatment. PRF was prepared after collecting 120 ml of blood from each patient and was then percutaneously injected in the the sacroiliac ligaments under ultrasound guidance. Numeric Pain Related Scale (NPRS) and Roland-Morris Disability Questionnaire (RMDQ) evaluated the efficacy of the treatment for an average follow-up period of 3 months after the intervention.

Results

Mean pain scores were significantly reduced at one month after treatment (NPRS, 5±1; RDQ, 11±3) and this was generally maintained throughout the observation period(3 months after treatment: NPRS, 3±1, RDQ; 3±2). Following treatment, no patient experienced adverse events.

Conclusion

Ultrasound-guided autologous platelet rich fibrin injections appear to be a safe alternative to alleviating relapsing pain that originates in the sacroiliac joints. Our results revealed a statistically significant reduction in SIJ symptoms compared to standard corticosteroid injections. More clinical studies are needed to validate our results.

Epilepsie/*Epilepsy*

P215

Epilepsiechirurgie bei fokaler Epilepsie – Langzeit-Outcome und Lebensqualität nach Läsionektomie
Epilepsy Surgery in Focal Epilepsy – Long-term Outcome and Quality of Life after Tailored Lesionectomy

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Objective

In pharmaco-resistant focal epilepsy, surgical resection of the epileptogenic focus is crucial for therapeutic success. The aim of the present study is to investigate long-term epileptological outcome and changes in disease-related quality of life following tailored epilepsy surgery in a large patient population.

Methods

Overall 311 adult patients with 321 surgeries were retrospectively included, who underwent tailored lesionectomy between 2000-2016 (mean age at surgery: 36 years, male/female n=171/140) and who had classified follow-up (of which 60% >5 years, median 6.6 years). The follow-up period ranged from 2000-2021. Anatomically, 54% of lesions were located temporal, 34% frontal, and 12% elsewhere. Lesionectomy was exclusively performed in 87%, with additional hippocampectomy in 10% and with multiple subpial transection (MST) in 3%. Underlying pathologies included focal cortical dysplasia (28%), cavernomas (21%), gliosis (16%), gangliogliomas (8%), dysembryoplastic neuroepithelial tumors (6%) among other pathologies. Data were collected on pre/postoperative findings, neurological/neuropsychological status, perioperative complications, and long-term epileptological outcome. In addition, statistical analysis highlighted possible predictive factors for long-term favorable postoperative outcome.

A subgroup (n=41 of 100 consecutively included adult patients with surgery between 2011-2016) was additionally questioned about their quality of life in epilepsy using the validated questionnaire QOLIE-31 (Cramer et al, 1998), in which the condition immediately before surgery and the current condition were queried and compared.

Results

Long-term epileptological outcome (range 0.25-20 years, median 6.6 years) was Engel 1a/ILAE 1 in 62%, Engel 1 in 70%, and 18% experienced relevant improvement (Engel 2-3/ILAE2-4). Surgical complications required surgical revision in 6.9% of cases. Postoperative non-calculated neurological deficits were permanent in 4.4% of cases. Quality of life was significantly ($p<0.0001$) improved by epilepsy surgery, with the mean score achieved on the QOLIE-31 increasing from 42.9 to 81.0 points (scale 0-100).

Conclusion

Tailored epilepsy surgery allows effective disease control and permanent seizure freedom even in the long-term course. Including the patients" perspective, the surgery itself is perceived as tolerable compromise and allows patients to achieve a significantly improved quality of life in the long term.

Epilepsie/*Epilepsy*

P216

Outcome bei epilepsiechirurgischen Eingriffen bei Temporallappen-Epilepsie: Läsionelle versus nicht-läsionelle Pathologien. Unsere aktuellen single-center Erfahrungen

Outccome in temporal-lobe epilepsy surgery: lesional verus non-lesional pathologies. a recent single-center experience

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Objective

Surgical treatment has been proven successful for patients suffering from medically refractory temporal-lobe epilepsy. Herein, we present the results of our recent temporal lobe surgical series comparing patient outcomes with lesional versus non-lesional pathology.

Methods

All patients who underwent surgical treatment for medically refractory temporal-lobe epilepsy at our institution between 2015 and 2019 were included and analyzed. Altogether, 70 patients received surgery for medically refractory temporal-lobe epilepsy with a median age of 36.3 years (range: 2,5 – 63.3) at time of surgery and a median postoperative follow-up of 36.5 months. Median age of seizure-onset was 15.5 years (range: 0 – 49).

Results

Temporal-lobe lesions on preoperative MRI were detected in 79%, of which mesial temporal sclerosis represented the most common one (n=35, 64%). Most frequently performed procedures were anteromedial temporal-lobectomy including amygdalahippocampectomy (64%), followed by trans-sylvian selective amygdalahippocampectomy (25%). Favorable surgical seizure-outcome (ILAE-Outcome-Scale (IOS) = 1 or 2), was achieved in 68%. In patients with IOS = 3 or less, a reduction of anticonvulsive drugs was achieved in 26%. Patients with detected lesions on MRI achieved favorable seizure-outcome in 71%, compared to 53% in patients with no temporal-lobe lesions. At one-year follow-up, contralateral quadrant-anopia was the most prevalent detected morbidity, which was observed in 10 cases (14%). Overall complication rate was 7% with no persistent neurological deterioration. No surgical-site infections were reported.

Conclusion

Temporal lobe epilepsy surgery is a safe and effective treatment method for patients with temporal lobe epilepsy, either lesional or non-lesional. Nevertheless, our results confirm that patients with lesional pathology have far better seizure outcomes compared to non-lesional patients.

Epilepsie/*Epilepsy*

P217

Die funktionelle Organisation des supplementär motorischen Areals – eine Untersuchung basierend auf direkter kortikaler Stimulation mittels subduraler Plattenelektroden in Epilepsiepatienten

The functional organization of the supplementary motor area revisited - a study based on direct cortical stimulation in epilepsy patients with subdural grid electrodes

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Objective

The supplementary motor area (SMA) is a complex brain region with inhibitory and excitatory motor function. Surgery in this region can be associated with neurological deficits, which are difficult to predict due to great symptom variation and duration. To understand the role of the SMA in motor and non-motor functions for more adequate prediction of postoperative deficits, we aimed to study the functional organization of the SMA region by direct electrical stimulation in alesional epilepsy patients with implanted subdural grid electrodes for invasive EEG monitoring purposes.

Methods

Patients with medically refractory epilepsy, who underwent invasive diagnostic EEG monitoring with subdural grid electrodes located in the frontal lobe were included in this retrospective cohort study. Monopolar direct cortical stimulation via electrode contacts was performed with simultaneous video EEG recording. Stimulation phenomena were evaluated and categorized into positive motor/negative motor responses of the respective extremities, speech impairment as well as other induced phenomena. Analysis of anatomical location of electrode contacts using preoperative MRI was performed.

Results

Nine-teen patients were included with a total of 481 electrode contacts within the SMA region. 301 stimulation results were analyzed. Motor phenomena occurred in 207 stimulated contacts (68.8%), while 28% of those phenomena were negative motor responses. Analysis of the location of motor responses showed a significant correlation of affected body part within the anterior-posterior (anterior: upper extremity, posterior: lower extremity; $\rho = 0{,}53$; $p \leq 0{,}01$) as well as medial-lateral axis (medial: lower extremity, lateral: upper extremity; $\rho = 0{,}37$; $p \leq 0{,}01$).

Conclusion

In the present study we provide further evidence for a distinct anterior-posterior as well as medio-lateral somatotopic order of the SMA region based on direct electrical stimulation. These data serve as a substantial adjunct to existing literature and can aid neurosurgeons in planning of resective procedures within the SMA region.

Epilepsie/*Epilepsy*

P218

3D-Topographie von epilepsiechirurgischen Resektaten als Schnittstelle zwischen MRT-Traktographie und zellulärer Analyse neuronaler Netzwerke

3D topography of epilepsy tissue as an interface between MRI tractography and cellular neural network analysis

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Objective

Cortical tissue resected during epilepsy surgery provides a unique opportunity to study the human neocortex at the cellular level, contributing to important insights into the functional and molecular architecture of the epileptogenic tissue. Technical advances in cellular electrophysiology and molecular biology enable detailed analyses, leading to a better understanding of epilepsy mechanisms. Independently, data are regularly collected by electrophysiological (EEG, ECoG) and imaging studies (MRI including diffusion tensor imaging followed by tractography) as part of preoperative diagnosis. Integration of such cellular findings with information from diagnostic electrophysiology and imaging is necessary to accelerate translational advances. In this study, we aim to establish a workflow to match cellular electrophysiological properties of resected epilepsy tissue with imaging and tractography data from patients using a time-of-flight (TOF) based 3D camera.

Methods

Preoperatively, temporal lobe epilepsy patients (n=5) received cranial MRI imaging (including DTI). Resected tissue was scanned with a TOF-based 3D camera (Basler blaze). A 3D dataset of the resected tissue was generated from the images (CloudCompare), which was fused with the preoperative MRI data (BrainSuite21a). Following the scan, acute brain slices were obtained from the cortical tissue and examined at the cellular level.

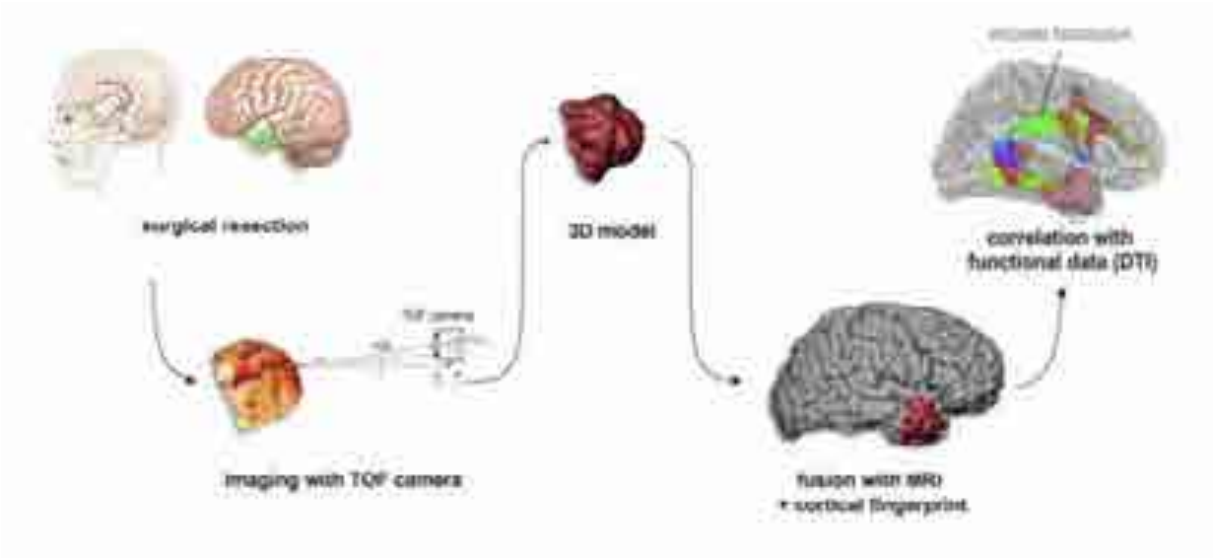
Results

3D scans of resected tissue allow exact fusion with preoperative MRI datasets. Furthermore, electrophysiological data from examined pyramid cells can be matched onto the 3D coordinate system. We demonstrate the feasibility of a surgical workflow allowing the integration of cellular electrophysiology and tractography data (Fig. 1).

Conclusion

In this proof-of-concept study, we established the technical workflow for a "cortical fingerprint" allowing the integration of cellular data with clinical electrophysiological data (EEG, ECoG) and imaging modalities (MRI). Thus, this method represents an important translational interface towards a more complete analysis of patient-specific neuronal networks.

Abb. 1


surgical resection
3D model
correlation with
functional data (DTI)
imaging with TOF camera
fusion with MRI

Epilepsie/*Epilepsy*

P219

Lokalisation epileptischer Foci mittels MEG Node Degree im Vergleich zum invasiven EEG
Epileptic focus localization using MEG node degree compared to invasive EEG

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Objective

Current evidence shows that interictal resting state MEG (rsMEG) contains subtle alterations of network characteristics. Such changes may add complementary information to the workup of epilepsy surgery in patients with pharmacoresistant focal epilepsies. In the presented study, we investigate node degree (ND), a graph-theoretical parameter of functional connectivity, in relation to the seizure onset zone (SOZ) determined by invasive EEG (iEEG).

Methods

rsMEG from a consecutive series of 50 adult patients with pharmacoresistant focal epilepsies were analyzed retrospectively. Inclusion criteria consisted of invasive EEG and MEG evaluation as part of the presurgical workup. Exclusion criteria were unclear SOZ or low-quality MEG data preventing routine evaluation.

Per patient, 10 minutes of rsMEG data were subjected to whole brain, all-to-all connectivity analysis using imaginary part of coherence. Thresholded graphs were described using ND and parcellated using the Automated Anatomical Labeling (AAL) atlas. Results were compared to the SOZ in iEEG.

Results

All frequency bands except for alpha showed significantly higher maximum ND (mND) values inside the SOZ compared to outside (ratios 1.11-1.20, alpha 1.02, not significant (ns)) on a lobar and sublobar level (1.13-1.38, all significant, except gamma 1.02). Area-under-the-curve (AUC) values for identification of the SOZ (sublobar level) were 0.58-0.78 ($p < 0.05$).

Conclusion

MEG ND is significantly related to SOZ in iEEG, especially especially in delta, theta and beta bands. In contrast, alpha and gamma ND show limited associations. Node degree may aid focus localization for presurgical evaluation of epilepsy surgery.

Epilepsie/*Epilepsy*

J-SBNC035

Behandlung des Lennox-Gastaut-Syndroms: Vergleich zwischen Kallosotomie und Vagusnervstimulation in einer systematischen Übersichtsarbeit mit Meta-Analyse

Lennox-Gastaut Syndrome management: Callosotomy vs Vagal Nerve Stimulation comparison in a systematic review with meta-analysis

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Objective

Lennox-Gastaut syndrome (LGS) is a severe drug-resistant epileptic syndrome. Palliative treatments such as corpus callosotomy (CC) and vagus nerve stimulation (VNS) have emerged as treatments to reduce the number of seizures in patients. The aim of this study is to compare the effectiveness of CC and VNS in patients with LGS studied in the last 30 years.

Methods

We conducted a systematic review with meta-analysis and collected papers from PubMed (MEDLINE), Ovidsp, Web of Science, and Cochrane Library data bases. The articles analyzed were published between January 1990 and December 2020. Keywords were chosen based on internal and external validation in the PubMed data base (the analysis is available in the Supplementary Data Supplementary Appendix). Prospective or retrospective case reports ($n \geq 2$), case series, cohort studies, or case-control studies involving patients with LGS were included in the analysis. We selected studies that had no age or sex restriction and that provided data on seizures before and after treatments. Studies not written in English, published without peer review, or not indexed in the data bases were excluded. Other exclusion criteria were the absence of seizure data and the impossibility of extracting this information from the studies. To analyze the results, we used the random-effects model based on the assessment of heterogeneity (I^2 statistics) in two scenarios. In scenario 1, we assessed the incidence of patients with a seizure reduction ≥ 50%; in scenario 2, we assessed the incidence of patients with a seizure reduction > 0%.

Results

Of the 7418 articles found using the keywords, 32 were considered eligible. Of these, 18 articles were on VNS (175 patients) and 14 on CC (107 patients). For scenario 1 (seizure reduction ≥ 50%), CC had an incidence of 65% (95%CI, 37%–94%), with an I^2 value of 82.7%; VNS had an incidence of 34% (95% CI, 11%–57%), with an I^2 value of 80.7%. For scenario 2 (seizure reduction >0%), CC had an incidence of 80% (95% CI, 58%–100%), with an I^2 value of 84.7%; VNS had an incidence of 64% (95% CI, 38%–89%), with an I^2 value of 90.8%. There was an overlap of confidence intervals, with no statistical difference between the treatments in both scenarios.

Conclusion

Our analysis of LGS showed that the CC and VNS treatments are significantly beneficial to reducing seizures, without superiority between them.

Epilepsie/*Epilepsy*

J-SBNC036

Ausstrahlen mehrerer Transektionen allein für refraktäre Epilepsie
Radiating multiple transections alone for refractory epilepsy

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Objective

Multiple subpial transections (MST) represent a technical option of surgical treatment for patients with epileptogenic foci located in eloquent cortical areas. They could be performed in addition to other surgical techniques or alone. We report the clinical results of 10 patients who received as single MST surgery with a minimal follow-up of 5 years.

Methods

The authors studied all patients who underwent a surgical intervention between 2007 and 2019 for refractory epilepsy. Among them,20 had radiating MST (rMST) as the only surgical treatment with a follow-up of at least 5 years. They were 4 female patients and 6 male patients, with average age 28.5 year old (5 year old to 42 year old). The causes of epilepsy were Rasmussen encephalitis two cases, glioma in eight cases, subacute sclerosing panencephalitis in two and eight cases with focal dysplasia in eloquent area (one of them with Landau Klefner syndrome). The MST technique was described according to the number of transections performed and the Brodmann areas (BAs) involved. Any MST-related complications were registered and followed up. Clinical outcome was described in terms of seizure suppression or reduction according to the Engel modified classification.

Results

The effect on function was reviewed in 20 cases; only 40 cases were evaluated with respect to seizure control, since a follow-up period of 5 years or more (5 to 12 years) is required before conclusions can be drawn. Multiple subpial transection was applied to the precentral gyrus in 10 cases, the postcentral gyrus in two, Broca"s area in 6 (1 with syndrome of Landau Kleffner), and Wernicke"s area in two. With respect to function, the major finding was that none of the 10 patients has suffered a clinically significant behavioral deficit (although subtle deficits could be detected by careful neurological examination). Complete control of seizures has been obtained in 12 (60%) of the 20 cases evaluated. None of the patients developed recurrent seizures consequent to progressive disease unsuspected before operation.

Conclusion

Our series demonstred a complete resolution of crisis in only 60% of the cases after a long follow up different from the initial results with 80% of seizure free. We have only one case in our series with 5 year old boy who was harboring of Landau Kleffner and recovered completely his speech after MST.

Epilepsie/*Epilepsy*

P220

Einfluss von Dauerlicht auf die Expression von Inflammasomen und ihren Bestandteilen im Hippocampus
Influence of constant light on the expression of inflammasomes and their components in the hippocampus

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Objective

Chronodisruption refers to a disruption of the circadian system that can have detrimental effects on health. Chronodisruption is considered to lead to dysregulation of the immune system, contributing directly to the pathogenesis of neurodegenerative changes. Disturbed circadian rhythms in the CNS can lead, among other things, to impaired hippocampal functions. The role of PRRs in this process is intensively discussed. The best-known PRRs include NOD-like receptors (NLRs), which are important components of inflammasomes. Inflammasomes represent intracellular protein complexes that mediate the production and release of pro-inflammatory cytokines after activation. They have already been described in some neurodegenerative diseases, which also show chronodisruptive concomitant symptoms.

Methods

First, general condition and differential blood counts were examined. Furthermore, astrocytes and microglia were stained and analysed by immunohistochemistry to investigate the effect of LL on glial cells. Subsequently, qRT-PCR and Western blot were used to investigate the expression of the following inflammasomes at RNA and protein levels: NLRP1b, NLRP3, NLRC4, AIM2 and their components - ASC, Casp1 and IL-1β, IL-18.

Results

The 14-day constant light exposure induced a marked chronodisruption in the mice, manifested by altered period length, phase shift and reduced rhythm stability. On a systemic level, no influence on weight gain or on the number of leucocytes could be detected. No activation of astrocytes and thus no astrogliosis could be detected in the hippocampus. However, the increased IBA1 immune response suggests activation of microglia by continuous light. The qRT-PCR studies revealed that gene expression of active *Casp1* and *AIM2* was significantly reduced in LL mice. In contrast, protein expression of Casp1 and NLRP1b was significantly increased in the LL group.

Conclusion

The results of our study suggest that acute chronodisruption leads to a pro-inflammatory response in the hippocampus of mice. These results are also of great importance for humans, as in modern 24/7 society we are increasingly exposed to non-physiological light stimuli during the night, which can trigger chronodisruption. Further studies are to clarify the complex relationship between chronodisruption and the activation of the immune system in the CNS and investigate to what extent the findings obtained in mice can also be transferred to humans.

Epilepsie/*Epilepsy*

P221

TGF-β aktivierte kinase 1 ist in mikroglia nach experimenteller epilepsie aktiviert und trägt zur epileptogenesis bei

TGF-β Activated Kinase 1 (TAK1) is activated in microglia after experimental epilepsy and contributes to epileptogenesis

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Objective

Increasing evidence suggests that inflammation promotes epileptogenesis. TAK1 is a central enzyme in the upstream pathway of NF-κB and is known to play a central role in promoting neuroinflammation in neurodegenerative diseases. Here, we investigated the cellular role of TAK1 in experimental epilepsy.

Methods

To explore the role of TAK1 in epilepsy, C57Bl6 and transgenic mice with inducible and microglia-specific deletion of Tak1 (Cx3cr1CreER:Tak1fl/fl) were subjected to the unilateral intracortical kainate mouse model of temporal lobe epilepsy (TLE). Immunohistochemical staining was performed to quantify different cell populations. The epileptic activity was monitored by continuous telemetric electroencephalogram (EEG) recordings over a period of 4 weeks.

Results

Immunofluorescence staining of phosphorylated TAK1 in combination with the astrocyte marker S100b and the microglial marker Iba1 was performed at different time points. TAK1 activation was not observed in S100β-positive astrocytes. TAK1 was activated predominantly in microglia at an early stage of kainate-induced epileptogenesis. Fewer alterations in microglial morphology (hypertrophic cell bodies and processes) were observed in TAK1 KO animals compared to their control littermates. Iba1 immunoreactivity was also significantly reduced on the ipsilateral side of TAK1 KO mice than on the ipsilateral and contralateral side of Cre-negative littermates 5 dpi. The number of Iba1-positive cells was also significantly lower in TAK1 KO mice than in Cre-negative littermates. Tak1 deletion in microglia resulted in reduced hippocampal reactive microgliosis and attenuated chronic epileptic activity without affecting the severity of *SE*.

Conclusion

TAK1-dependent microglial activation contributes to the pathogenesis of chronic epilepsy.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P222

Welche Projekte zur tiefen Hirnstimulation werden durch die Deutsche Forschungsgemeinschaft (DFG) derzeit gefördert?

Which deep brain stimulation projects are funded by the DFG (Deutsche Forschungsgemeinschaft)? A current account

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Objective

Deep brain stimulation (DBS) is a surgical neuromodulation technique with an increasing range of therapeutic indications. An assessment of the current work in this field is warranted to determine the current status and its development. Here we aimed to identify active studies sponsored by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) and the involvement of different disciplines.

Methods

Active DBS projects funded by the DFG were extracted via the GEPRIS database by using the search terms "deep brain stimulation", "tiefe Hirnstimulation" and "Tiefenhirnstimulation". Projects were categorized by investigated disorder, brain target, study design, population, topic, name of head researchers and their respective specialty.

Results

From a total of 86 DFG-funded projects related to DBS, 46 active DFG-funded projects were identified. Despite a general shift to conditions other than movement disorders, most active DFG-funded projects were related to movement disorders (n=66). Studies focused commonly on imaging and/or electrophysiology (n=50) and the development of stimulation techniques and adaptive technologies (n=11). Most studies were performed in a clinical context in humans (n=43). The majority of projects were submitted by neurologists (n=34).

Conclusion

Our overview of current DBS-related trials funded by the DFG provides insight into the current status of DBS research in Germany. Furthermore, we may foresee the impact of new brain targets, indications and techniques. Astonishingly, only a small part of research grants was attributed primarily to neurosurgeons.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P223

Auswahlkriterien für implantierbare Pulsgeneratoren für die Tiefe Hirnstimulation – Ergebnisse einer weltweiten Befragung

Choice of Implantable Pulse Generators for Deep Brain Stimulation – results from a global survey

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[3]Haukeland University Hospital Bergen, Neurochirurgie, Bergen, Norwegen
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Objective

The success of deep brain stimulation (DBS) treatment depends on several factors, including proper patient selection, accurate electrode placement, and adequate stimulation settings. Another factor that may impact long-term satisfaction and therapy outcomes is the type of implantable pulse generator (IPG) used: rechargeable or non-rechargeable. However, there are currently no guidelines on the choice of IPG type. The present study investigates the current practices, opinions, and factors DBS clinicians consider when choosing an IPG for their patients.

Methods

Between December 2021 and June 2022, we sent a structured questionnaire with 42 questions to DBS experts of two international, functional neurosurgery societies. The questionnaire included a rating scale where participants could rate the factors influencing their choice of IPG type and their satisfaction with certain IPG aspects. Additionally, we presented four clinical case scenarios and asked participants if they would recommend a rechargeable IPG in each case.

Results

Eighty-seven participants from 30 different countries completed the questionnaire. The three most relevant factors for IPG choice were "existing social support", "cognitive status", and "patient age". Most participants believed that patients valued avoiding repetitive replacement surgeries more than the burden of regularly recharging the IPG. Participants reported that they implanted the same amount of rechargeable as non-rechargeable IPGs, and 20% converted non-rechargeable to rechargeable IPGs. Half the participants estimated that rechargeable is the most cost-effective option.

Conclusion

This present study shows that the decision-making of the choice of IPG is very individualized. We identified the key factors influencing the physician's choice of IPG. Compared to patient-centric studies, clinicians may value different aspects. Therefore, clinicians should rely not only on their opinion but also counsel patients on different types of IPGs and consider the patient's preferences. Uniform global guidelines on IPG choice may not represent regional or national differences in the healthcare systems.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P224

Funktionelle Verbesserung von Patienten mit Parkinson-Syndrom durch eine individualisierte Rehabilitationstrainingssoftware

Functional improvement of patients with parkinson syndroms using an individualised rehabilitation training software

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Objective

People with Parkinsonian disorders require a special attention regarding physiotherapy and consistent movement training to perserve a certain amount of mobility. To adress the problems of staff shortage and rising incidence of the diseases, a computer software was invented that might serve as an additional home-based extension to conventional physiotherapy.

Methods

The trial took place in a rehabilitation centre and the training program that was set up to be investigated over three weeks while UPDRS-III and Clinical measurements were performed before and after. 74 patients were included and randomised between one control group (CG) and two intervention groups that received training sessions two times (IG1) or five times per week (IG2). Using the markerless Microsoft Kinect® camera, participants controlled a digital avatar with their own body movements.

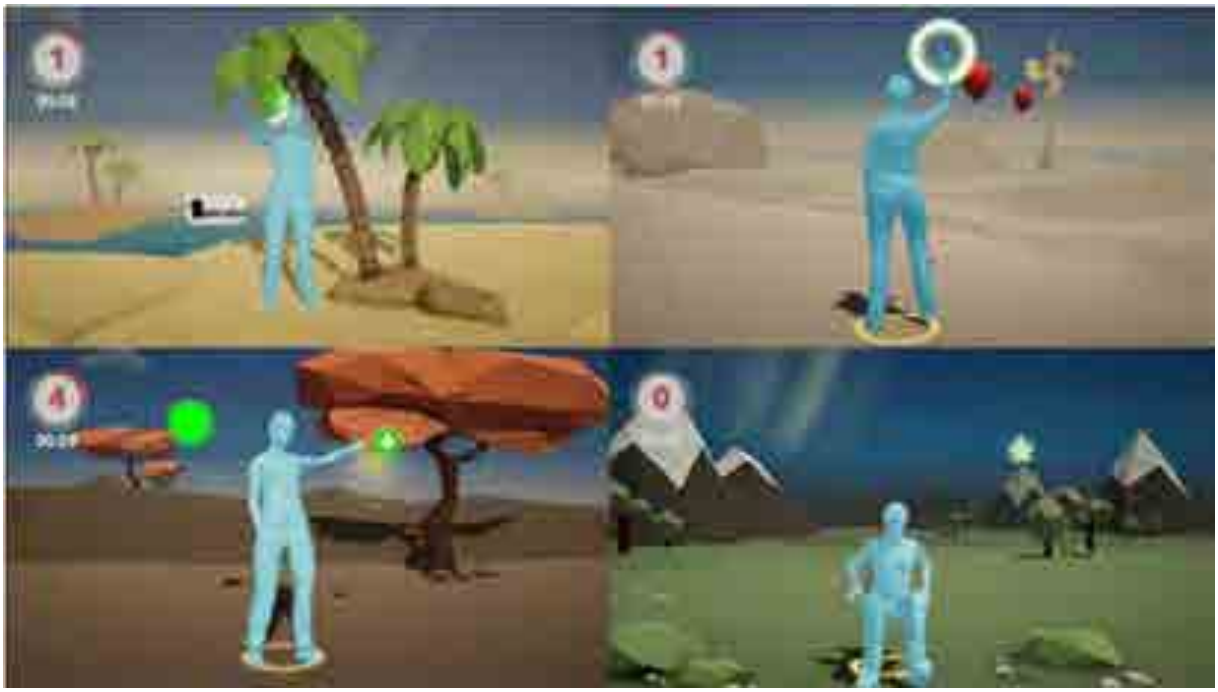
Results

All groups improved in UPDRS-III pre and post intervention whereas reduction rates were higher for IG1 (-10.89%) and IG2 (-14.04%) than for CG (-7.74%). Differences between the groups were not significant (p-values CG/IG1 0.225, CG/IG2 0.347). Growth rates for the arm abduction angle were significantly higher in IG1 (11.6%) and IG2 (9.97%) than in CG (1.87%) (P-values CG/IG1 0.006, CG/IG2 0.018), as was the 5-steps-distance (CG 10.86%; IG1 24.5%; IG2 26.22%; p-values CG/IG1 0.011, CG/IG2 0.031).

Conclusion

The study shows the beneficial effects of computer-based training and substantiates the assumption of a similar impact in a home-based setting. The utilised software is feasible and meets with the patient"s approval. Group dynamics seem to have an additional supporting effect for improving mobility.

Abb. 1



Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P225

Symptomatisches Peri-Elektroden-Ödem nach THS-Implantation bei Essentiellem Tremor
Symptomatic peri-lead edema following deep brain stimulation for essential tremor

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Objective

Deep brain stimulation is a well-established treatment for movement disorders over decades with a beneficial risk profile. Idiopathic delayed onset peri-lead edema is a poorly understood postoperative complication, with varying incidences from 0.4% to 39%.

Methods

Here we present the case of a 71-year-old female patient with essential tremor who underwent bilateral DBS of the ventral intermediate nucleus and developed immediate postoperative anarthria with an early peri-lead edema.

Results

The 71-year-old female patient diagnosed with disabling refractory essential tremor since 2009 and no other relevant comorbidities underwent standard bilateral VIM-DBS with directional leads in 2022 at our institution with no peri-procedural sequels. In the evening after surgery, the patient presented with complete anarthria. Immediate CT scan revealed no alterations and regular lead placement. Follow-up CT-scans on days 2 and 5 showed profound peri-lead edema while clinical impression was unchanged. Tremor symptoms were completely suppressed with stimulation-off. Peri-operative antibiotics were discontinued, and a corticosteroid pulse dose over three days was administered. MRI scan on day 8 confirmed T2-hyperintense edema around the track of the leads with tiny bleeding around the tip of the right lead, but no evidence of infarction. Speech production slowly improved after one week and was still recovering 3 weeks postoperatively. After four months, initial symptoms have vanished with favorable tremor control stim-on and associated moderate dysarthria and ataxia. In our cohort of 22 patients symptomatic with peri-lead edema (4.5%), there were only two with early onset within 24 hours after surgery.

Conclusion

Symptomatic delayed peri-lead edema has been reported as a rare complication of DBS surgery. Common symptoms include confusion state, seizure or headache. Here we report a rare case of immediate complete anarthria following bilateral VIM-DBS with an associated early peri-lead edema. While most edemas appear later than 72 hours, mostly at one to two weeks after surgery, occasionally acute appearance has been described. The use of corticosteroids is controversial, while long term prognosis is mostly favorable with or without treatment. Increasing awareness of the phenomenon with varying reported numbers of affected patients and prolonged hospitalization warrants future investigation.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P226

Aseptisches perifokales Elektrodenödem - Klinische Evaluation und Behandlungsoptionen
Aseptic perifocal lead oedema – clinical evolution and management options

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Objective

Temporary post-surgical oedema after implantation of deep brain stimulation (DBS) systems is a hardly understood phenomenon. In the last 6 years, it has been reported in increasing numbers and, in part, also with permanent sequels.

Methods

491 DBS operations were analyzed and each patient was investigated by an early post-surgical CT and examined clinically in the early postoperative phase up to demission, usually between day 7 and 14 after surgery. Stimulation activation was mostly performed on Day 1, rarely Day 2 or 3. Patients with significant pneumencephalus underwent a second early CT at 6 to 10 days.

Results

A peri-focal lead oedema was identified by CT in 30 patients (6.1%) (8 female), mean age 61.4 years (range 35.2 to 78.2 years); the targets were GPI in dystonia in 5, VIM in tremor in 5 and STN in Parkinson"s Disease in 20 patients. In 8 patients, the oedema remained asymptomatic and was detected only in a second post-surgical CT for control of initial pneumencephalus. In 22 patients (4.3%), the oedema was clinically symptomatic, by apathy and mood changes in 4 patients, by aphasia or other neurological deficit in 8 patients, by a single epileptic fit in 4 patients, by repeat epileptic fits in 5 patients. Among symptomatic patients, 10 were affected unilaterally and 12 bilaterally, presenting between day 1 and 19, on average 8.6 days, and accounting for altogether 34 symptomatic hemispheres, caused by 4 ring leads (0.9%) and by 30 directional leads (5.6%). In 1 asymptomatic and in 14 symptomatic patients a three-days-intravenous therapy with Methyl-Prednisolone at 250 to 500mg (rarely 1,000mg)/ day, was followed mostly by fast clinical improvement. In 6 patients, after a generalized epileptic fit, levetiracetam was started. Four patients needed temporary intermediate care. Except for one patient who developed a secondary infection, complete remission was noted within 3 weeks to 2 months in all the other patients.

Conclusion

Peri-focal lead oedema mostly develops between the 6th and 14th post-surgical days and may remain silent. Since the introduction of directional leads, similar to other centers, we have noticed higher incidences, at an earlier stage and to a more severe extent, including neurological deficits like aphasia, hemiparesis and epileptic fits. The most important challenge is the identification of patients at those clinical risks.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P227

Topografische Anatomie der subthalamischen Region
Topographic anatomy of the subthalamic region

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Objective

The topographical anatomy of the subthalamus is still not fully understood; however, the structures of this area have long been important targets of deep brain stimulation (DBS) with the indication of movement, but also in psychiatric disorders. Despite the clinical significance, only a few study aimed the detailed investigation of this region using cadavers since its original description in the late 1800s. The aim of our study was to provide an accurate topographical depiction of the subthalamic region to promote effectiveness and safety of DBS.

Methods

Ten in formalin fixed human cadaveric brains (20 hemispheres) were involved in this study. The cadavers were donated with educational and research purpose to the institute of the first author. 19 hemispheres were dissected from medial to lateral according to Klingler´s fiber dissection method. One hemisphere was prepared for histological examinations. Serial slices were cut and stained with neurofibril silver impregnation according to Krutsay. Polarized light was used during the evaluation to increase the contrast between the individual fiber bundles. Constrained spherical deconvolution tractography was performed on 50 healthy subjects (100 hemispheres) of the S500 dataset of the Human Connectome Project using the Mrtrix software (version 3.0). The results of the tractography were correlated with the macroscopical and histological findings.

Results

The following structures of the subthalamus were dissected on all specimens: the fasciculus retroflexus, the red nucleus, the ansa lenticularis, the ipsi- and contralateral cerebello-rubro-thalamic tract, the thalamic fasciculus, the lenticular fasciculus, the subthalamic nucleus (STN), the substantia nigra and the anterior part of the external globus pallidus (GPe). The GPe was identified as a relay station between the STN and the prefrontal cortex. A discrete fiber bundle originating from the ventral tegmental area and entering in the anterior limb of the internal capsule and coursing in the direction of the prefrontal cortex could not be identified using fiber dissection.

Conclusion

The topographical anatomy of the subthalamus was characterised for the first time using a combination of fiber dissection, histology and tractography. As a relay station with important limbic functions, the GPe should be considered as a DBS target in the treatment of psychiatric disorders.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P228

Automatische Segmentierung des Nucleus Subthalamicus – Einfluss der zugrundeliegenden MRT – Modalität
Automatic Segmentation of the Subthalamic Nucleus – Influence of MRI Modality

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Objective

With the availability of automatic segmentation methods, imaging-based visualization of target structures in deep brain stimulation (DBS) such as the subthalamic nucleus (STN) became a valuable addition to preoperative planning of optimal lead localization, intraoperative visualization of target structures and postoperative programming by visualizing target structures in spatial relation to implanted leads. Multimodal automatic segmentation in contrast to many other approaches incorporate information of different magnetic resonance imaging (MRI) submodalities. However, its effect on segmentation results has not yet been investigated.

Methods

3D data of ten healthy volunteers was prospectively acquired at a 3T MRI (Trio, Siemens, Erlangen, Germany) equipped with a 12ch Rx-coil including a T1-weighted (T1w), T2-weighted (T2w), fluid-attenuated inversion recovery (FLAIR) and a susceptibility weighted (SWI) data set. To evaluate the effect of different combination of modalities, for each volunteer eight subsets were generated including only the T1w image set, or the T1w image set in combination with one further, two further or all three other data sets. For all subsets, rigid image fusion (Brainlab, Munich, Germany) was performed with the T1w image set as root data set. Afterwards, automatic segmentation was performed using the Anatomical Mapping Element (Brainlab, Munich, Germany).

Results

Whereas the STN volume varied between different volunteers, the STN volume across the different sets of multimodal image data showed only small differences with a mean standard deviation of 0.010 cm^3 for the left and 0.009 cm^3 for the right STN. The intersection of subset-dependent automatic STN segmentation results revealed a mean volume of 0.057 ± 0.022 cm^3 (49.67 ± 18.48 %) in relation to a mean STN volume of 0.116 cm^3 for the left STN and a mean intersection volume of 0.054 ± 0.011 cm^3 (45.07 ± 10.02 %) in relation to a mean STN volume of 0.119 cm^3 across all multimodal segmentations. Visual inspection of all cases revealed a further prominent shift of STN segmentations along the cranio-caudal axis.

Conclusion

The spatial location of automatically generated STN segmentations varies depending on the included imaging data, and thereof can affect preoperative planning of optimal DBS leads location, intraoperative visualization in relation to electrophysiological measurements and postoperative image guided programming.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P229

Medianus SSEP Aufzeichnungen von DBS Elektroden in verschiedenen subkortikalen Strukturen zur Bestimmung des Ursprungs der N18 Welle

Recording of median nerve somatosensory evoked potentials from DBS electrodes in various subcortical targets to determine the origin of the N18 wave

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Objective

The different peaks of somatosensory evoked potentials originates from a variety of anatomical sites in the central nervous system. The origin of the subcortical N18 has been studied under various conditions, but its exact generator is still unclear. While it has been claimed to be located in the thalamic region, other studies indicated a generator below the pontomedullar junction. Here, we scrutinized and compared SSEP recordings from median nerve stimulation through DBS electrodes implanted in various subcortical targets.

Methods

We studied 24 patients with dystonia, Parkinson disease, and chronic pain who underwent quadripolar electrode implantation for chronic deep brain stimulation and recorded median nerve SSEPs from globus pallidus internus (GPi), subthalamic nucleus (STN), thalamic ventral intermediate nucleus (Vim), and ventral posterolateral nucleus (VPL) and the centromedian-parafascicular complex (CM-PF).

Results

The largest amplitude of the triphasic potential of the N18 complex was recorded in Vim. Bipolar recordings confirmed the origin to be close to Vim electrodes (and VPL/CM-PF) and less close to STN electrodes. GPi recorded only far field potentials in unipolar derivation.

Conclusion

Recordings from DBS electrodes located in different subcortical areas allow determining the origin of certain subcortical SSEP waves more precisely. The subcortical N18 of median nerve SSEP - to its largest extent - is generated ventral to the Vim in the region of the prelemniscal radiation / Zona incerta.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P230

Tiefe Hirnstimulation bei Hemidystonie: eine Metaanalyse mit individuellen
Deep brain stimulation for hemidystonia: a meta-analysis with individual patient data

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Objective

Deep brain stimulation (DBS) is now well established for the treatment of dystonic movement disorders. There is limited data, however, on the efficacy of DBS in acquired hemidystonia, which is a very rare disorder. This meta-analysis aims to summarize the published reports on DBS for hemidystonia of different etiologies, to compare different stimulation targets, and to evaluate clinical outcome.

Methods

A systematic literature review was performed on PubMed, Embase and Web of Science to identify appropriate reports. Further, secondary sources were screened systematically. The primary outcome variables were the improvement in the Burke-Fahn-Marsden Dystonia Rating Scale movement (BFMDRS-M) and disability (BFMDRS-D) scores for dystonia.

Results

Twenty-two reports (39 patients; 22 with pallidal stimulation, 4 with subthalamic stimulation, 3 with thalamic stimulation, and 10 with combined target stimulation) were identified. Mean age of surgery was 27.25 years. Mean follow-up time was 32.93 months. An overall mean improvement of 40% in the BFMDRS-M score was achieved, which was paralleled by a mean improvement of 41% in the BFMDRS-D score. There was a wide variability in outcome in the BFMDRS-M score ranging between 0% and 94% improvement. When considering a 20% cut-off for improvement, 23/39 patients (59%) would qualify as responders.

Conclusion

Based on the results of the current analysis, DBS can be accepted as an effective treatment for hemidystonia. The posteroventral lateral GPi is the target used most often. More research is needed to understand the variability in outcome and to identify prognostic factors.

Funktionelle Neurochirurgie III/*Functional neurosurgery III*

P231

Morphometrische Gehirnanalyse von Patienten mit Zwangserkrankung unter Tiefer Hirnstimulation anhand der Schwere der Erkrankung und des klinischen Verlaufs

Morphometric brain analysis of obsessive-compulsive disorder patients treated with deep brain stimulation based on disease severity and clinical outcome

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Objective

Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder characterized by intrusive thoughts (obsessions) and repetitive routines or mental rituals (compulsions). Standard therapy involves psychotherapy and pharmacotherapy, mainly consisting of serotonin reuptake inhibitors. Deep brain stimulation (DBS) can be considered for therapy refractory OCD. In a recent meta-analysis 66% of OCD patients treated with DBS were considered as full responders. In the past, several biomarkers have been analyzed as potential predictive factors for clinical improvement. In this retrospective analysis, we aimed to identify morphometric biomarkers that could correlate with disease severity and clinical outcome after DBS.

Methods

We retrospectively analyzed the clinical outcome of 45 OCD patients treated with DBS at our department. All patients received bilateral electrodes in the nucleus accumbens/anterior limb of the capsula interna (Nacc/ALIC). T1 sequences of preoperative MRIs were used for morphometric analysis. Voxel-based morphometry analysis of the subcortical structures was carried out using cat12 SPM12-toolbox. For the voxel-based analysis of the cortical surface, FreeSurfer was used. Clinical improvement of the patients was measured using the Yale-Brown Obsessive-Compulsive Scale (YBOCS) before the surgery and after one year of DBS.

Results

There was a moderate correlation between the preoperative YBOCS and the cortical thickness in the right medial orbitofrontal cortex (OFC) ($r = 0.22$), the right insula ($r = -0.25$), the right transverse temporal gyrus ($r = 0.23$) and the left temporal pole ($r = 0.21$). None of these correlations were statistically significant. There was a moderate positive correlation between the clinical improvement measured on the YBOCS and the cortical thickness in the left caudal middle frontal gyrus ($r= 0.23$), the left rostral anterior cingulate gyrus ($r = 0.21$), the right lateral OFC ($r = 0.21$) and the left medial OFC ($r = 0.30$). The correlation between the clinical improvement and the cortical thickness in the left OFC was statistically significant ($p = 0.045$).

Conclusion

We found a significant positive correlation between improvement on the YBOCS after DBS and the cortical thickness of the left OFC. A correlation between the clinical improvement of the patients and the size of the Nacc, as reported on previous studies, could not be shown in our cohort.

Komplikationen, Monitoring und Trauma/*Complications, monitoring and trauma*

P232

Prospektive Diagnosestellung eines Delirs bei neurochirurgischen Patienten
Prospective diagnosis of delirium in neurosurgical patients

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Objective

Delirium (DL) poses an acute threat and has a negative impact on the clinical outcome of patients. The overall delirium incidence is 10-24% and as high as 37- 46% in postoperative patients due to general anesthesia, longer hospital stay and further risc factors, especially in elderly patients. Studies on patients with cerebral diseases show an even lower incidence of 12-26%. We therefore assume that DL is underdiagnosed in neurosurgical patients and that screening needs to be optimized.

Methods

We conducted a prospective study. Patients over 50 years of age who underwent surgery under general anesthesia were included. We divided our patients into two groups. In one group, the CAM-ICU-Score (CIS) was collected daily to determine whether delirium was present. In the other group, no scoring method was used and the interpretation whether delirium was present or not was made by the medical staff. We only included patients on a normal ward. Differences in baseline data and risk factors between the two groups were analyzed using chi-square test. Furthermore, we correlated established risk factors with the occurrence of DL in all our patients using two-tailed Pearson´s correlation.

Results

Sixty patients were included so far. Five patients developed a DL, the incidence is 8.8% (3) in the group with CIS and 7.7% (2) in the group without score (p=.948). DL occurred on average on day 2 after surgery (range 0-6). There was no significant difference between the 2 groups with regard to age, sex, and admission diagnosis. In addition, we did not find significant differences concerning risk factors (neurologic, psychiatric and general medicine history, medication, social factors [mobility, hearing, vision], the duration of surgery and length of postoperative ICU stay).

Analysis of risk factors for the occurrence of DL show that the use of sedative drugs correlated significantly with DL (p=.004). Use of antiarrhythmic drugs (p=.05), cardiac (p=.068) and liver disease (p=.089) showed a relatively low but not significant p-value.

Conclusion

Up to date, we could not demonstrate that the use of the CAM-ICU score in neurosurgical patients facilitates the diagnosis of DL, which may be due to the low number of cases. Regardless, there were few significant associations between the occurrence of DL and classic risk factors, indicating that different rules may apply to neurosurgical patients and that diagnosis of DL is challenging.

Abb. 1

		CAM-ICU SCORE N=34	NO SCORE N=26	LEVEL OF SIGNIFICANCE
AGE		71,3 y	70,8 y	p=0.602
GENDER	FEMALE	16	14	p=0.822
	MALE	18	12	
ADMISSION DIAGNOSIS	CEREBRAL	17	9	p=0.233
	SPINAL	17	17	
DELIRIUM		3	2	p=0.948

Table 1 Baseline characteristics

Komplikationen, Monitoring und Trauma/*Complications, monitoring and trauma*

P233

Postoperative Überwachung auf Intensivstation nach elektiven Kraniotomien; wie viel Monitoring ist erforderlich?

Postoperative monitoring on ICU after elective craniotomies: how much monitoring is required?

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Objective

In most neurosurgical departments, patients undergoing elective craniotomy for intracranial surgery routinely are postoperatively monitored on an intensive or intermediate care unit(ICU;IMC). The Covid-19 pandemic has required this valuable resource and especially ICU beds are re-allocated. A guideline for an efficient and reasonable monitoring duration for neurosurgical procedures respectively is missing. The aim of this study was to evaluate occurrence of complications in the early postoperative phase to re-define the monitoring algorithm after elective craniotomy.

Methods

Data acquisition was conducted as a single-center retrospective analysis. Patients undergoing elective craniotomy from 2018-2021 were included. Demographic data, diagnosis, American Society of Anaesthesiologists(ASA)-score, Charlson comorbidity index(CCI), duration of surgery, blood loss, complications(hemorrhage, respiratory failure, decline of neurological status), as well as type and duration of monitoring were analyzed.

Results

486 consecutive patients(213 men and 273 women)with a mean age of 60.04 years(SD=14.19) were included. 274(56.4%) patients underwent microsurgical resection of extra-axial, 184(37.9%) of intra-axial tumors, and 75(15.4%)procedures were infratentorial. Median of ASA was 3, of CCI was 3 and of Frailty score was 14.39 patients experienced a postoperative incident that required intensive care treatment. 8 of these patients needed an emergent revision surgery. The mean time to incident was 8h(SD=5.9h). Sex, age, and tumor type did not influence the risk for complications.Independent predictive factors for postoperative complications were ASA(p=0.003) increasing by 124%/ASA grade (CI95%=1.3-3.8); operating time(p<0.0001) increasing by 0.8% risk/minute (CI95%=1.0-1.1), and CCI(p=0.09, 13.2% risk increase/point (CI95%=0.9-1.3)). The threshold of operating time causing a higher risk was 200 min(Youden-Score 0.35).The selected collective of patients for postoperative monitoring on ICU had a 21-fold(CI95%=3.03-164.8) higher risk of complications.

Conclusion

In this study the principle of assigning a postoperative ICU bed already seems to be efficient. In the majority of cases a dense monitoring beyond 8 hours doesn"t seem to be necessary. Considering comorbidity and surgery-associated complications to identify high-risk patients, a more precise algorithm with an earlier transfer to the normal ward should be established apart from the undisputed gold standard of ICU monitoring.

P234

Digital integriertes, telemetrisches Vitalparametermonitoring – Postoperatives Sicherheitsnetz zur automatisierten Erkennung kritischer Ereignisse auf Normalstation

Digitally integrated, telemetric vital sign monitoring – Postoperative safety net for automated detection of critical events on the regular ward

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Objective

The immediate detection and response to surgical complications is one of the main challenges of early postoperative care. Against this background, the present study describes our experience during the pilot phase of implementing a new telemetric monitoring system for routine postoperative vital sign monitoring on a regular neurosurgical ward.

Methods

The vital signs of postoperative neurosurgical patients were continuously assessed for 12-24 hours on the regular neurosurgical ward after transfer from the recovery room using a telemetric, finger-sensor-based monitoring system (MASIMO, Irvine, California, USA). Overall, 12 mobile monitoring units were available for 44 beds and all postoperative patients were eligible. The system has Bluetooth and WiFi integration and connects to a mobile pager-alarm system and stationary monitoring console installed on the ward. Vital signs and their limits for alarm initiation were: (1) heart rate (40 vs. 130bpm), (2) body temperature (35 vs. 40°C), (3) blood pressure (sys.: 90 vs. 160mmHg; dia.: 50 vs. 110mmHg), and (4) oxygen saturation (<85% for more than 15 sec).

Results

Between June and December 2021, 214 patients (male: 110, female: 104) with a median age of 58 years (IQR 42-70) and a mean hospital stay of 6 days (IQR 4-10) were monitored. This represented 13% of 1646 patients that underwent surgery during that time period in 2021. Surgery types included 108 cranial (50 tumor, 20 vascular, 14 hydrocephalus, 24 other), 90 spinal (65 degenerative, 7 tumors, 2 vascular, 16 other), and 16 peripheral nerve procedures. Among the monitored cohort, no acute clinical deterioration event and no vital sign-related alarm occurred. Overall, 30 sensor alarms due to interrupted data transmission to the central monitoring console, in-house WiFi connectivity issues and finger-sensor or Bluetooth malfunctions were documented. The main reasons for the high patient inclusion gap and alarm documentation gaps were perceived added workload and lack of familiarity with the new technology.

Conclusion

Routine implementation of telemetric vital sign monitoring on a regular neurosurgical ward is feasible but faces the challenge of alarm management and acceptance of the technology by the staff, which is mirrored by the large inclusion gap of operated patients. Systematic training and automatic data integration into the hospital information system could help facilitate acceptance through education and a reduction of the general documentation workload.

P235

Postoperative Routine CT-Untersuchungen nach elektiven Kraniotomien zur Resektion von Meningeomen: notwendig oder entbehrlich?

Routine postoperative CT scans after elective craniotomies for resection of meningeomas: necessary or dispensable?

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Objective

Postoperative CT scans are performed routinely after elective craniotomies for tumor resection to detect possible complications early. In most instances, these scans may show unspecific postoperative findings (air, etc.) but have no consequences otherwise. To obtain such scans patients need to be transported to the CT unit and they cause extra costs. We therefore investigated, which preexisting factors or which circumstances seen in these CT scans could lead to consequences like surgery or special treatment on the ICU.

Methods

We retrospectively investigated the postoperative CT scans and clinical data of all adult patients, undergoing an elective craniotomy for surgery of supratentorial meningeomas over a 1-year period. CT scans were routinely obtained 6 hours after surgery. We reviewed all radiological and medical records of these patients.

Results

We identified 53 patients with a mean age of 61 years (range 28-84 years) at the time of surgery for supratentorial meningeomas, and 6 patients with a mean age of 57 (range 33-77 years) for infratentorial meningeomas. CT scans did not show pathological findings except in one instance. In one woman with a convexity meningioma on the right, postoperative air in the operation field was noted, and she suffered from an unspecific malaise and mild aphasia. This patient had a second CT to control for reduction of air trapping.

Conclusion

Our study shows that routine postoperative CT scans provide only little information after surgery in asymptomatic patients. Considering the declining capacity in ICU capacities, qualified nursing staff, and the costs of CT imaging the question arises whether there is a real need for early postoperative routine CT imaging in this group of patients.

Komplikationen, Monitoring und Trauma/*Complications, monitoring and trauma*

J-SPNC007

Arachnoidalzyste der hinteren Schädelgrube nach einem Schädel-Hirn-Trauma
Posterior fossa arachnoid cyst following traumatic brain injury

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Objective

To report a case of an adult male patient with a past medical history of traumatic brain injury in the previous year that presented with intracranial hypertension secondary to a post-traumatic arachnoid cyst of the posterior fossa.

Methods

A 20-year-old male was admitted to the emergency department with subacute-onset worsening headaches, unsteadiness of the gait and vomiting. His exam was remarkable for gait ataxia and dysmetria. He had a past medical history of a left suboccipital craniectomy for subdural and left sided cerebellar contusion evacuation following a traumatic brain injury one year ago. He had been discharged 2 weeks later and his post-operative course had been uneventful with a rapid return to school. The current computed tomography scan and magnetic resonance showed a cystic lesion, measuring 30 x 30 x 25 mm - transverse x posterior anterior x cephalocaudal axes, located on the right cerebellar hemisphere, with non-enhancing walls and associated edema, causing marked compression of the IV ventricle and supratentorial hydrocephalus.

Results

The patient was positioned prone and a right suboccipital craniotomy was performed. The dura was opened, the lesion was exposed and cyst fenestration to the subarachnoid space was done successfully. The cyst wall was biopsied. No mural nodule was found. A watertight closure of the dura mater was done, and the bone flap was placed back. The postoperative magnetic resonance showed no complications. The postoperative period was uneventful with rapid clinical improvement in the first days after the surgical procedure. The patient was discharged home 5 days later. The neuropathological analysis revealed an arachnoid cyst. At 6-month follow-up the patient shows no signs of disease recurrence with resumption of his normal activity.

Conclusion

Herein we depict a rare case of a post-traumatic posterior fossa arachnoid cyst that presented with intracranial hypertension, treated with a single surgery with fenestration of the arachnoid cyst allowing communication with the subarachnoid space and resolution of the hydrocephalus, with no need for cerebrospinal fluid diversion techniques.

P237

Analyse des Komplikationsmanagements nach Operationen in der hinteren Schädelgrube
Analysis of complication management after surgery in the posterior fossa

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Objective

Complication after surgery in the posterior fossa, defined as CSF-leakage, wound healing disorder or infection, is a well-known problem. The aim of this retrospective study was to outline the complications associated with surgery in the posterior fossa (PF) and to review the optimal complication management.

Methods

To evaluate complications and outcomes of surgery in the PF, we reviewed 619 patient files and analyzed 36 patients (5.82%) suffering complications (surgeries between 2018 and 2022). Data collected for analysis included patient demographics, surgical procedure measurements, postoperative complications and their management.

Results

Out of 36 patients with complications, 19 (52.8%) patients were males. The median age was 56.2years (ranged 2–87years). Indications for the initial surgeries were tumor extirpation (17), decompression due to cerebellar infarction (7), infratentorial bleeding (10) and Chiari-Malformation (2). In total, 99 surgeries were performed, while 21 patients underwent one revision surgery (RV), 7 patients underwent two RVs, 6 patients underwent three RVs, and 2 patients underwent more than three RVs. The leading cause for a revision was CSF-leakage (30.3%) followed by wound healing disorders (14.1%). Due to infection of the operation site, 14 patients underwent 21 RVs. Of these, 6 successful RVs were treated only with passive pressure drainage with intermittent antibiotic irrigation (28.6%). Regarding CSF-leakage, the combination of a ventricular-peritoneal shunt (VPS) with duraplasty (DP)(41.7%) was the most effective method for a successful RV. In 13 of the successful RVs, a DP was used with the most common combination of muscle patch, fibrin sealant and Tachosil™ (23.1%) or muscle patch only (13.3%). A lumbar drainage was placed in 5 successful RVs, always in combination with DP (13.9%). Fascia lata was also used in 5 successful RVs (13.9%), 2 of which in combination with VPS (5.5%). The initial surgery duration did not directly correlate with the number of revisions needed (median operation time: 218min).

Conclusion

The management of complications after surgery in the posterior fossa remains a difficult challenge for neurosurgeons. Our Study showed a significant value in using a combination of VPS with different DP techniques. Therefore, VPS should be taken into account early for the planning of surgical treatment in revision cases.

Komplikationen, Monitoring und Trauma/*Complications, monitoring and trauma*

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Risikofaktoren für Wundinfektionen bei Glioblastompatienten
Risk factors for surgical site infections in glioblastoma patients

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Objective

Surgical site infections (SSI) after craniotomy are leading to an increased morbidity and mortality and higher costs. Furthermore, they are associated with a longer hospital stay, which is particularly unfavorable in glioblastoma patients due to a limited life expectancy. Risk factors for SSI have already been described for craniotomies in general. However, hardly any data exist for glioblastoma patients. Premature postoperative irradiation is a considered risk for SSI, but no valid data are found on this. This was the purpose of investigating our patient collective.

Methods

We performed a retrospective analysis of all patients who underwent craniotomy with histological evidence of a glioblastoma between 2012 and 2021. Cases with open biopsy and tumor removal (GTR,STR) were included. Patients who underwent stereotactic biopsy were excluded. Age, gender, duration of surgery, diameter of the trepanation, postoperative radiation with interval, postoperative chemotherapy, highest blood glucose level, previous surgery, ASA score, foreign material introduced, redon drain, ventricular opening and length of stay in hospital were recorded and analyzed. The need for surgical revision due to infection was counted as an SSI.

Results

A total of 177 patients could be recorded, of which 14 patients (7.9%) suffered an SSI. These occurred after a median of 45 days. The group with SSI tended to include more men (57.1%) and more pre-operated patients. In addition, foreign material and a Redon drain had been implanted more frequently and the ventricle had been opened more frequently in patients with SSI, without this being significant. Surprisingly, significantly fewer patients with SSI had been irradiated. Other factors like age, length of hospital stay, ASA score, diameter of trepanation, duration of surgery, highest blood glucose level or chemotherapy were very similar in both groups

Conclusion

The results make it possible to better assess the risk of SSI in glioblastoma patients. Patients with previous surgery, introduced foreign material, redon drain and opening of the ventricle may have the highest risk for SSI. However, because none of these factors was significant, this does not justify a less radical approach to surgery involving opening a ventricle, implanting foreign material, or inserting a Redon drain. The suspected role of irradiation was not observable, so that a rapid chemoradiation should be performed to achieve a good oncologic outcome.

Abb. 1

	SSI	No SSI	P value	Test
Number	14 (7.9%)	163 (92.1%)		
Female	6 (42.9%)	102 (62.6%)	0.163	Fisher
Age	59 +- 11	63 +- 11	0.1802	t-Test
Hospital Stay	18 +- 9	21 +- 10	0.2156	t-Test
Interval SSI	45 +- 41			
Previous-Surgery	7 (50.0%)	46 (28.2%)	0.1253	Fisher
Chemotherapy	10 (71.4%)	105 (64.4%)	0.7758	Fisher
Irradiation	8 (57.1%)	131 (80.4%)	**0.034**	Fisher
Interval Irradiation	22 +- 14	23 +- 9	0.9507	t-Test
Highest Blood Glucose Level	13 +- 4	13 +- 5	0.9381	t-Test
ASA Score	2 (0-2)	2 (0-2)	0.9302	Fisher
Foreign Material	10 (71.4%)	95 (58.3%)	0.4057	Fisher
Redon drain	6 (42.9%)	59 (36.2%)	0.7736	Fisher
Ventricle opening	6 (42.9%)	54 (33.1%)	0.558	Fisher
Diameter of trepanation	65 +- 17	64 +- 18	0.7318	t-Test
Duration of surgery	267 +- 120	258 +- 87	0.7932	t-Test

P239

Einfluss der postoperativen Thromboseprophylaxe auf thrombembolische Ereignisse bei Patienten mit Meningiomen und Glioblastomen

Influence of postoperative thromboprophylaxis management on thrombembolic events of patients with meningiomas and glioblastomas

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Objective

Thrombembolic events after brain surgery are serious side effects. In this study, we investigate, whether the use of certoparine, enoxaparine and enoxaparine combined with pneumatic stocks differ in the incidence of thromboembolic events (TE) after tumor resection of a meningioma or a glioblastoma.

Methods

In a retrospective analysis, 600 patients after tumor resection of a meningioma or glioblastoma (surgery between 02/01/2017 and 30/06/2022) were evaluated for symptomatic TE like deep vein thrombosis (DVT), pulmonary embolism (PE). Patients received a thromboprophylaxis either with certoparine (n=336) (group 1), enoxaparine (n=81) (group 2) or enoxaparine combined with pneumatic stockings (n=183) (group 3) postoperatively. The influence of risk factors (diagnosis, duration of surgery or intraoperative blood loss) were evaluated for every group.

Results

After tumor resection of meningiomas/glioblastomas in 600 patients, 29 TE occurred (incidence: 4.83%). The incidence of both DVT and PE was significantly higher ($p<0.001$) in group 2 (11.1% for DVT; 9.9% for PE; 14.8% for TE) vs. group 1 (3.0% for DVT; 3.0% for PE; 3.9% for TE) and group 3 (2.2% for DVT; 1.1% for PE, 2.2% for TE). In a final multivariate binary logistic regression, these findings were confirmed for the use of enoxaparine with a hazard ratio (HR) of 4.6 (CI 1.750-12.031; $p=0.002$) for DVT, a HR of 2.6 (CI 0.96-7.1; $p=0.060$) a HR of 3.6 (CI 1.53-8.36; $p=0.003$) for the combination of DVT and PE. There was no significant difference between group 1 and 3.

Patients older than 65 years had significantly more PE (5.4%) than younger patients (1.6%) ($p=0.011$). Further, the duration of surgery seems to be a determining factor for the occurrence of PE postoperatively (1.7% <200min vs. 5.5% >200min; $p=0.019$). More than 200ml intraoperative blood loss (2.3% <200ml vs. 4.9% >200ml; $p=0.106$), diagnosis (glioblastoma 4.4% vs. meningioma 2.2%; $p=0.132$) and gender (male 4.1% vs. female 2.6%; $p=0.365$) showed differences in the incidence of PE without any significance.

Conclusion

Tumor patients (meningioma/glioblastoma) treated with enoxaparine alone have a significant higher risk for TE compared to treatment with certoparine or the combination of enoxaparine with pneumatic stocks. Further, duration of surgery (>200min) and the age of patients (>65 years) have a significant impact on the risk of postoperative TE.

P240

Lagerung autologer Knochendeckel im Ultratiefkühlschrank - ist dies noch zeitgemäß ?

In-house deep-freezer preservation of autologous bone flaps after decompressive hemicraniectomy – still appropriate in 2022?

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Objective

After decompressive hemicraniectomy (DHC), skull fragments (SF) are regularly stored in dedicated ultra-freezers for later reimplantation (RI), usually after 3-6 months. As the underlying conditions warranting DHC are often life-threatening, many patients either do not survive until RI or are lost to follow-up, leading to the accumulation of SF. It is unclear, what percentage of SF undergo RI, and when SF could potentially be discarded.

Methods

We retrospectively reviewed the documentation on our ultra-cold storage freezer for SF from 07/2010 to 12/2022. Only patients with DHC were included and age at DHC, sex, time from DHC to reimplantation, and time from DHC to discarding the SF were extracted. Data are descriptively presented, patients with/without RI are statistically compared, and medicolegal pitfalls are discussed.

Results

From 07 / 2010 until 12 / 2022, SF from 492 DHC patients were stored in the dedicated -80°C storage freezer. The majority of those patients were male (270M, 222F), with a mean age of 53 ± 19 y. 141 patients (29%) underwent RI of the SF, 25% (122) of the SF were discarded, and 229 (46%) were still stored at the time of evaluation. Thus, routinely storing SF in-house has led to the inadvertent creation of a biobank, which falls under strict legal regulation.

The mean time from DHC to RI was 134 ± 111 d; 89 % of the patients were reimplanted less than six months after DHC. However, reimplantation of stored SF exposes the surgeons to liability for the viability, sterility, and proper storage of the grafts, posing a significant medicolegal risk. In contrast, SF were discarded after a mean duration of 979 ± 533 d following DHC, resulting in avoidable costs for the maintenance of a dedicated ultra-cold freezer.

Patients undergoing RI were significantly younger (54±17 vs. 49±15 y, p=0.025) and patients aged 70 and above generally had a significantly lower probability of RI (4%). Allogeneic cranioplasties fabricated from novel materials with fibrovascular integrative features and no risk of bone resorption -especially relevant for younger patients- might be a good alternative.

Conclusion

Less than a third of explanted SF are reimplanted following DHC, predominantly in younger patients. Considering the medicolegal risk of in-house biobanking and the in-time availability of novel allogeneic cranioplasties, default storage of bone flaps after DHC may no longer be a sensible modus operandi.

Komplikationen, Monitoring und Trauma/*Complications, monitoring and trauma*

P241

Erzeugung neuer Neuronen aus Astrozyten durch Lentivirus-vermittelte Überexpression von Ascl1 in vitro als mögliche neue Behandlungsoption für traumatische Hirnverletzungen

Generation of new neurons from astrocytes in vitro by lentiviral vector-mediated overexpression of Ascl1 as a potential new treatment option for traumatic brain injury

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Objective

Traumatic brain injury leads to loss of neurons, astrogliosis, and subsequent glial scar formation, further limiting the low regenerative abilities of the central nervous system. By converting emigrating astrocytes to functional neurons, we aim to potentially limit the negative effects of astrogliosis while generating new neurons to restore function in the damaged areas. This current study investigates the *in vitro* capabilities of converting astrocytes into neurons using the overexpression of Ascl1 as a basis for *in vivo* translation.

Methods

Primary cell culture from rat pub cortex astrocytes was established by separating different cell types with shaking incubation. The purified astrocyte cell culture was then transduced with a custom-designed set of four different lentiviral vectors, introducing an overexpression of the transcriptional factor Ascl1 coupled to a TetOn system as well as enabling the identification of successfully transduced astrocytes by expression of the fluorescent protein BFP-HA Tag under the control of a GFAP promoter. Further lineage tracing of the transduced astrocytes was done by GFAP-driven Cre recombinase expression and following flipping of the double-floxed fluorescent protein mScarlet which is then expressed in the cell under the neuron-specific Synapsin promoter. Cells were fixed after 7 and 14 days and further investigated by immunofluorescence staining and phenotypically assessed by confocal microscopy.

Results

A primary cortex astrocyte culture could be successfully established, as confirmed by the expression of GFAP and Sox 9. Using molecular cloning and HEK Lenti-X cells, the custom-designed set of lentiviral vectors was successfully produced. The transduction of primary astrocytes with the lentiviruses was supported by TransDux and medium change from DMEM complete to NPC culture medium. After 7 and 14 days, a conversion of the astrocytes to neuron-likeke cell type could be confirmed by the co-expression of the mScarlet fluorescent protein and neuronal markers such as Doublecortin (DCX).

Conclusion

The generation of neurons from cortex astrocytes via Ascl1 overexpression seems to be feasible in vitro. Our vector system allowed the assessment of the conversion progress and transduction efficiency at any given time point. Therefore, these data could be the foundation for future in vivo trials investigating the therapeutic potential of Ascl1-mediated astrocyte-to-neuron conversion after experimental TBI.

P242

Exosomen von neuronalen Vorläuferzellen fördern das Wachstum von Neuriten in vitro
Neuronal precursor cell derived exosomes promote neurite outgrowth in vitro

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Objective

Inhibition of neurite outgrowth because of secondary injury processes after spinal cord injury (SCI) is associated with reduced functional recovery. Neuronal precursor cell (NPC) transplantation has shown promising effects on neuroregeneration, potentially mediated by their secretome. We thus aimed to isolate, characterize, and utilize NPC-derived exosomes (NPC-exos) to promote neurite outgrowth on a PC12 cell model *in vitro*.

Methods

Primary NPCs were extracted from the subventricular zone (SVZ) of 14-day-old rat embryos and cultured until passage four. NPC-exos were then isolated by three-step differential ultracentrifugation and filtration (0.22 µm), followed by quantification with nanoparticle tracking analysis (NTA) and bicinchoninic acid protein assay (BCA). To verify the exosomal identity of the vesicles, transmission electron microscope (TEM) and western blot with multiple exosomal markers were used. NPC-Exos were extensively characterized by mass spectrometry and ingenuity pathway analysis (IPA). To evaluate their promotive effects on neurite outgrowth, different concentrations of NPC-exos were applied to an induced PC12 cell culture. The length and quantity of the neurites were assessed using immunofluorescence staining and relative fluorescence units (RFU) analyses and statistically compared.

Results

Primary cell culture of purified rat NPCs could be successfully established and characterized by Nestin expression in absence of NeuN-, GFAP-, and Olig2-expression. After isolation, NPC-exos were verified via the markers CD63, CD81, and TSG101 in western blot analysis and by an average size of 141±7nm in NTA. In addition, their typical cup-shaped morphology was confirmed by TEM. Proteomic analysis indicated significant enrichment of the proteins Syntaxin 1B, Netrin-1, and Integrin β-1, which play an important role in axon guidance signaling and neurite outgrowth. Induced PC12 cells treated with different concentrations of NPC-exos revealed a dose-dependent significant effect of the vesicles on the quantity and elongation of neurites in vitro.

Conclusion

NPC-exos, carrying enriched neurite outgrowth and axon guidance-related proteins, strongly promote the outgrowth of neurites in a PC12 cell model *in vitro*. Thus, NPC-exos might be a potential non-cell-based treatment option for neuronal regeneration after SCI, which should be further assessed.

P236

Welche Risikofaktoren beeinflussen signifikant den Therapieerfolg neurochirurgischer Patienten mit einer Alkoholkonsumstörung?

Which risk factors significantly influence outcome of neurosurgical patients with alcohol use disorder?

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Objective

Every year approximately 10 million people worldwide suffer traumatic brain injury leading to hospitalization or mortality. Both chronic alcohol abuse and acute alcohol intoxication increase the risk of developing traumatic brain injury. Approximately 30%-64% of persons are involved in trauma yearly due to alcohol abuse. Alcohol use disorder as a predictor of outcome in neurosurgical patients and the definition of pre- and postoperative risk factors have been sparsely addressed so far. This study aims to improve the understanding of the effects of alcohol use disorder in the context of neurosurgical therapy.

Methods

This study included patients admitted to our level 1 trauma center with a traumatic brain injury and alcohol use disorder from January 1, 2010, to December 31, 2018. Univariate and multivariate analyses were performed to identify risk factors for a poorer outcome, which was assessed by the Glasgow Outcome Score.

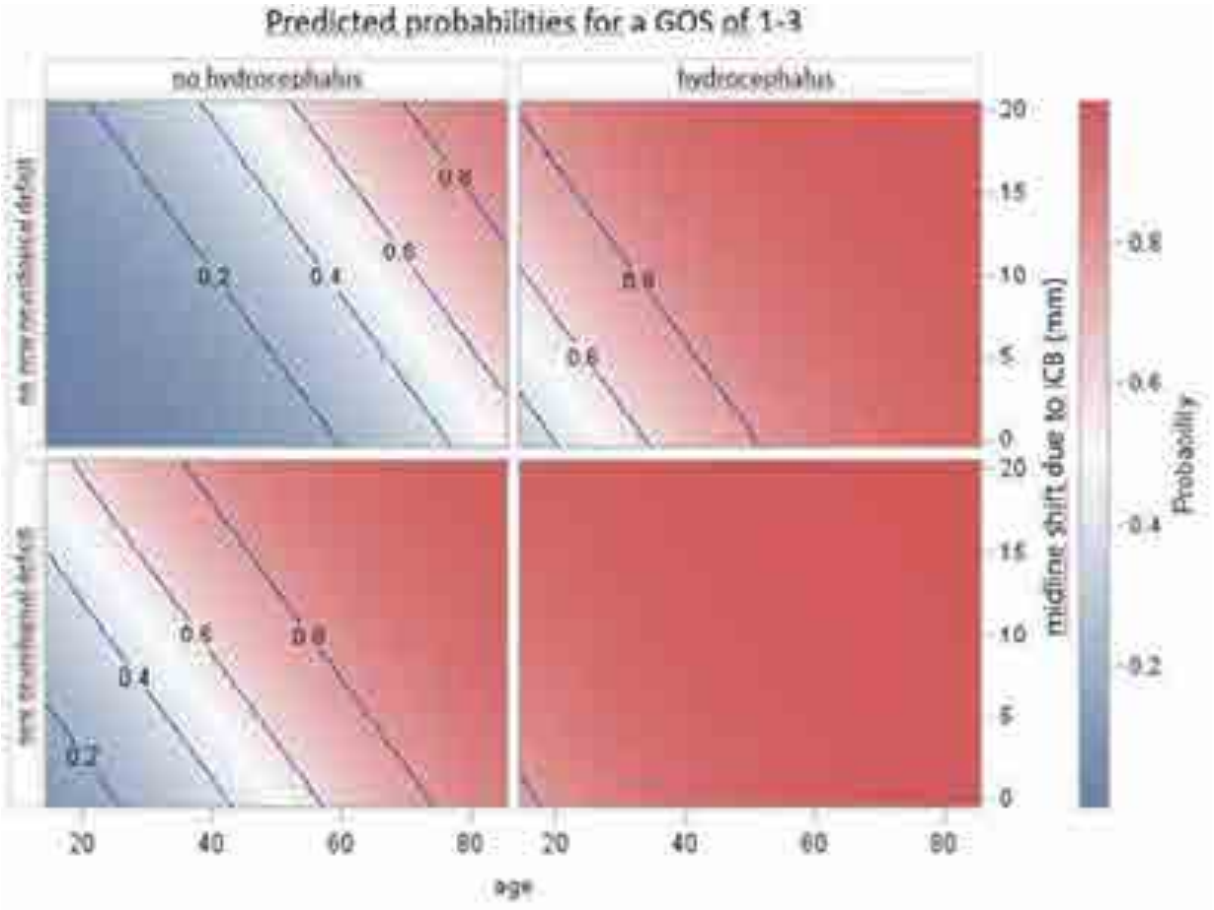
Results

Of the 197 patients included, 156 (79%) were male and 41 (21%) female with a median age of 49 years (range: 16-84 years). The median blood alcohol concentration on admission was 2.00 per mille (range: 0.10-4.74). In multivariate analyses, age (OR: 0.95, 95%CI: 0.92-0.97, p<0.001), the occurrence of a new neurologic deficit (OR: 0.14, 95%CI: 0.06-0.36, p<0.001), the development of hydrocephalus (OR: 0.04, 95%CI:0.00-0.38, p=0.005) and CT-graphic midline shift due to intracerebral hemorrhage (OR: 0.90, 95%CI:0.83-0.97, p= 0.008) emerged as significant predictors of a worse outcome (GOS 1-3). The level of blood alcohol concentration correlated significantly with the occurrence of seizures (p= 0.009).

Conclusion

The measurement of blood alcohol levels in patients with traumatic brain injury should be performed with a low level of suspicion and the self- or other history of these patients should include questions regarding alcohol use disorder. Most notably, the development of hydrocephalus, age, midline-shift on CT due to intracranial bleeding and the development of a new neurological deficit should be considered as potential risk factors for a worse outcome and need for extended rehabilitation programs. With increased alcohol levels, the occurrence of seizures should be kept in mind.

Abb. 1


Predicted probabilities for a GOS of 1-3
no hydrocephalus
hydrocephalus
midline shift due to ICB (mm)
Probability
age
0.2
0.4
0.6
0.8
20
40
60
80
0
5
10
15

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P243

Untersuchungen zum Stellenwert von digitalen und virtuellen Tools in der modernen Lehre für Neuroanatomie

Analysis of the Value of Digital and Virtual Tools in Modern Teaching of Neuroanatomy

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Objective

The field of neurosurgery requires the highest level of knowledge in applied neuroanatomy. One of the greatest challenges in training medical students and neurosurgeons is the teaching of 3D-dimensional competence concerning topographical relationships in the CNS. The foundation for understanding functions and topography is based on preclinical teaching. In the context of the Corona pandemic, classical teaching has been questioned in medical education regarding its role in the future. In this study, we address the value of digitalization and VR (virtual reality) in the teaching of neuroanatomy.

Methods

10 medical students (7 female, 3 male) of the preclinical segment were offered virtual teaching over a period of one semester in addition to classical teaching on models and cadaver plastinates: Using digitally prepared presets on the anatomy table, M1 relevant structures ("Physikum", equivalent to USMLE Step 1) in neuroanatomy were visualized in a targeted manner. Implementation of the supplementary teaching was exclusively digital: Onboarding was via QR code and teaching was given at a virtual dissection table ("Anatomage"). A performance evaluation survey was used to investigate the level of knowledge and expectations prior and after the tutorial.

Results

Our questionnaire evaluated the perfomance as followed: 1= high performance/very likely, 5= low performance/very unlikely. Evaluations have revealed the following: The usage of "Anatomage" for self-study prior to our tutorial was estimated poorly (4,4 points). The level of knowledge in neuroanatomy was rated with 3,6 points. Post tutorials both ratings increased: Using virtual tools for self-study was now rated with 1,8 points and the level of knowledge 1,5 points. In general, teaching with digital features was universally accepted with an 1,3 rating.

Conclusion

Using a digital scalpel on a virtual cadaver, dissection steps can be peformed repeatedly at will and anatomical relationships can be individually designed. The brains of body donors can be virtually displayed together with vascular and surrounding structures. Our virtual teaching shows that a majority of the students have improved with regard to topographical competence. The use of customizable, digital tools will continue to grow in modern teaching and will pave the way for innovation in educational institutions. In conclusion, we propose this method should also find its way into the anatomical training of young neurosurgeons.

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P244

Detaillierte Rekonstruktion der Sylvischen Fissur für das mikrochirurgische Simulationstraining
Dissecting the Sylvian fissure: Reconstruction of a realistic model for microsurgical education

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Objective

The correct microsurgical dissection of the Sylvian fissure (SF) is an important technique in neurosurgery requiring considerable expertise and technical skills acquired through years of experience and rigorous training. Especially different configurations of the SF according to Yasargil and the stiffness of the brain constitute major challenges of the microsurgical dissection. However, the incorporation of simulators into the neurosurgical curriculum remains a challenge due to their lack of realism, high acquisition costs or complex and time-consuming production processes. The aim of this work is to develop and evaluate a highly realistic yet cost-effective and easily reproducible synthetic model of the SF for effective microsurgical training purposes.

Methods

Using freeware, segmentation and high-detail reconstruction of patient's skull, brain and cerebral arteries from CT and MRI datasets were produced. The models were sliced into replaceable, adjustable parts that were printed using a desktop 3D-Printer. Based on rheological tissue characterizations, a mixture of candle gel and silicone was used to cast high-detailed models of the SF with emphasis on mimicking the tactile properties of a stiff angry brain and relaxed brain parenchyma and arachnoidea (Figure 1, 2). Furthermore, five different configurations of the SF according to Yasargil were constructed (MG Yasargil; 1984). Eight medical students and two experienced neurosurgeons were recruited. Participants' performances and the effectiveness of the model were assessed using the objective standardized assessment criteria (OSAACS) for aneurysm clipping. Each participant evaluated the simulator's realism and usefulness scored on a 5-point Likert scale.

Results

All participating students showed a rapid and significant improvement in surgical anatomy and accuracy. All participating neurosurgeons deemed the phantom as highly realistic and effectiv in simulating the most important aspects of the surgical strategy.

Conclusion

We were able to demonstrate that developing a high-fidelity phantom of the sylvian fissure for the realistic simulation and training of one of the most challenging neurosurgical procedures is achievable in a timely manner and without extensive investments. Apart from aneurysms of the middle cerebral artery, our model can be modified to train the correct opening of the Sylvian fissure for multiple intracranial pathologies, including distal basilar artery aneuryms as well as suprasellar and insular pathologies.

Abb. 1

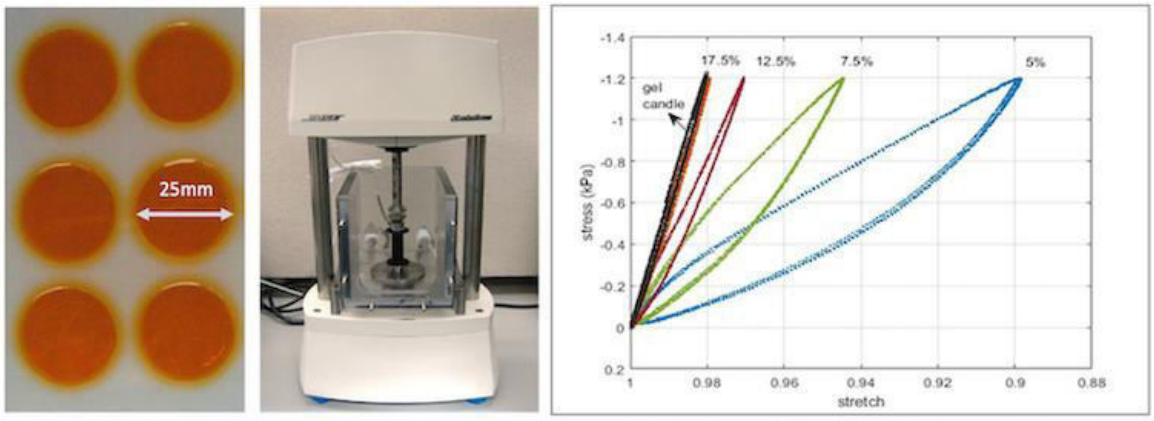

Fig. 1: Left: Agarose mold for preparation of 260 bloom gelatin and candle gel samples executed on a Bose Electroforce System (middle). Right: results of the 3-cycle compression tests

Abb. 2

Fig. 2: Segmentation and 3D reconstruction of the Sylvian fissure, Sylvian fissure and aneurysm model.

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P245

Grenzen der neurochirurgischen Ausbildung überwinden: Ein neuer Ansatz in der praktischen Simulation von Ventrikulostomien

Overcoming Barriers in Neurosurgical Education: A Novel Approach to Practical Ventriculostomy Simulation

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Objective

In the high-risk speciality of neurosurgery, traditional teaching methods often fail to provide young residents with the proficiency needed to perform complex procedures in stressful situations, with direct effects on patient outcome. To overcome this growing barrier in neurosurgical education, additional teaching methods besides the established methods are required. Physical simulators provide hands-on training in a more controlled environment. However, the adoption of simulators into a training curriculum remains a challenge due to high acquisition costs, complex production processes and lack of realism. One of the first and most important procedures performed by residents is the placement of an external ventricular drain (EVD). Our aim was to build and evaluate a highly realistic yet cost-effective, reusable and customizable physical ventriculostomy simulator as an effective training tool for young neurosurgeons.

Methods

Whole brain and skull segmentation and reconstruction from patients' MRI and CT scans were executed using freely available software. The reconstructed files were printed using a desktop 3D-Printer. A negative silicone form of the anatomical brain model was molded for the casting process. Based on rheological characterizations of brain tissue, gelatin in various concentrations was used to cast tactilely realistic brain models with life-like physiological properties (Fig.1). Six neurosurgeons and six medical students took part in the study. After succesful cannulation (Fig. 2) participants were asked to evaluate the simulator in respect to realism, haptics, tactility, and general usage, scored on a 5-point Likert scale. Participants' performances and the simulator's efficacy were assessed using the objective structured assessment of technical skills (OSATS) tool (JA Martin et al., 1997).

Results

The methods demonstrated in this work enabled us to create a cost-effective and easily reproducible EVD simulator with realistic haptic feedback characteristics for neurosurgical teaching, training, and preoperative planning. We saw a rapid and significant improvement of accuracy among novice medical students. All participants deemed the simulator as highly realistic, effective and superior to conventional training methods.

Conclusion

We were able to demonstrate that implementing a high fidelity simulator for one of the most common neurosurgical procedures in neurosurgical training and daily practice is achieveable in a timely manner and without extensive investments.

Abb. 1

Fig. 1: A, B: simulation of cerebrospinal fluid flow; C, D: Simulation setup.

Abb. 2

Fig. 2: Placements of external ventricle drains through Kocher's and Frazier's points.

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P246

Verbesserung der Genauigkeit mit augmented Reality während der Anlage von externe Ventrikeldrainage(IMAGINER): Machbarkeitsstudie

IMproving Accuracy with auGmented Reallty during placement of exterNal vEntricular dRains (IMAGINER): A feasibility study

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Objective

Placement of a ventricular catheter (i.e. external ventricular drain, EVD) is a common and essential neurosurgical procedure. In addition, this procedure is one of the first procedures performed by young neurosurgeons. With or without surgical experience, placement of an EVD, using anatomical landmarks, can be difficult with the potential risk for inaccurate catheter placement. Repeated corrections always imply the risk of avoidable complications. Augmented Reality (AR) could provide a useful guide and improve the accuracy of drain placement, especially in patients with acute pathology leading to displacement of anatomical structures. We therefore performed a feasibility study using AR in EVD placement procedures performed in a human cadaver model.

Methods

20 medical students performed the EVD placement procedure with a Cushing´s ventricular canula on the right, and on the left side. The canula was placed according to landmarks on one, and with the assistance of AR (Microsoft Hololens 2). With AR a planned trajectory was displayed in the field of view which has to followd with the canula. Subsequently, the actual position of the canula was assessed with the help of a CT with 1mm layer thickness. The bony structure as well as the left and right canula positions were registered to the CT with the planned target point before the placement procedure. The software Cloudcompare was applied for the registration and the evaluation of accuracy.

Results

EVD placement using AR was easily applied by medical students. The predefined target point (ventricle) was struck with both techniques. However, it could be shown that the scattering radius of the target point reached with AR (12 mm) could be reduced by more than 54% compared to the puncture without AR (26 mm) and this represents a doubling of the puncture accuracy.

Conclusion

This feasibility study specifically showed that the integration and use of augmented reality helps to achieve more than double the accuracy in the placement of ventricular catheters. Due to the easy availability of these new tools and the intuitive handling, we see great potential in using this new option.

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P247

Eine Pilotstudie der Verwendung von Mixed Reality mit Head-mounted Geräten in einfachen neurochirurgischen Praxis verwenden für unerfahrene Ärzte.

A Pilot Study for Unexperienced Medical Doctors using Mixed Reality with Head-mounted Devices in Simple Neurosurgical Practice

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Objective

Mixed reality is increasingly integrated in the medical field. However, this technology was tagged with high-tech association and sophistication and thus, is not yet widely applied routinely. This pilot study is aimed to evaluate the feasibility, time, and cost requirements of simple mixed reality applications with head-mounted devices (HMD) in neurosurgical practice, even for unexperienced medical staff.

Methods

A neurosurgeon with mixed reality and HMDs experience and a medical student without any respective experience participated in this study. Five MRI data sets were acquired from 5 healthy volunteers for mixed reality applications. Clinical relevant major arteries were considered to simulate a simple clinical scenario. The medical student was trained for 45 minutes, on how to conduct the mixed reality display in HMD using raw MRI data sets. Time costs were recorded for both of the participants. The mixed reality scenarios were evaluated by an experienced neurosurgeon, based on the artery definition. Time of every procedure were evaluated using the students´ t-test. A statistical difference was defined as $p < 0.05$. The unexperienced participant was interviewed after the tasks relating to the technical impression.

Results

Both participants could successfully conduct all of the mixed reality applications individually. The 45-minute training was sufficient for simple scenarios with HMD using raw MRI data sets. There were no statistical differences in time costs in most of the processing procedures, such as data loading and saving, and projection in HMD ($p> 0.05$). The unexperienced participant needed, however, a longer time for fine adjustment of the segmented arteries (Mean 28.6 vs 16.2 minutes, $p<0.05$). The defined arteries could be all successfully identified through HMD by the third person and no major differences were detected.

Conclusion

The application of mixed reality using HMD was a simple, time-efficient technology, which could be acquired in a short time training and may also be applied in more complicated scenarios.

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P248

Nützlichkeit von patientenspezifischen 3-dimensional gedruckten Modellen und gemischter Realität für die Patientenaufklärung und chirurgische Planung für die intrakranielle Aneurysma-Chirurgie: vorläufige Ergebnisse. *Usefulness of patient-specific 3-dimensionally printed models and mixed-reality for patient education and surgical planning for intracranial aneurysm surgery: preliminary results.*

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Objective

3-dimensional printed model (3DM) allows for haptic feedback and thus may become a planning instrument for optimal clip selection in unruptured IAs. In this prospective trial, we aimed at 1) evaluating the accuracy of 3DM for presurgical selection of the proper aneurysm clips and 2) their potential to reduce temporary clipping time and clip repositioning when comparing to a historical matched cohort.

Methods

A hollow, semi-elastic 3DM of the patient"s neurovascular anatomy and surrounding skull base was generated from convectional imaging data. A standardized questionnaire was used to evaluate the accuracy of the latter compared to 3DM with regard to the intraoperative findings by means of correct clip selection, depiction of parent vessels, and adjacent perforators. In a matched cohort of 73 patients with unruptured IA not planned 3DM beforehand, we compared the time of temporary clipping and need for clip repositioning.

Results

In eleven consecutive patients, 13 IAs were clipped. Patients" mean age was 61 years (range, 39-78 years). The 3DM allowed adequate depiction of the IAs, parent vessels and adjacent perforators <1mm in all patients. Intraoperative clip application was correct as selected with the 3DM in ten (77%) IAs, compared to conventional imaging in 2 (15%) IAs (p=0.01). Intraoperative angiography revealed complete IA obliteration in all but one (8%) patient. Compared to the matched cohort, the use of 3DM reduced the time of temporary clipping significantly, namely from 9.2 ± 5.4 min to 4.2 ± 4.1 min, p=<0.001. No significant changes in the number of clip repositioning was noted; namely in 11 (21%) IAs without preoperative 3DM planning vs. 7 (29%) IAs with preoperative 3DM planning (p=0.56).

Conclusion

The novel 3D model allows for adequate haptic feedback, optimal selection of the surgical approach, best clip configuration with regard to the intraoperative findings and completeness of occlusion in the majority of patients with significant reduction of temporary clipping time. The 3D model might become a valuable planning tool to attain a safe and complete obliteration of unruptured IAs.

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P249

Intraoperative augmentierte Realität in der hinteren Schädelgrube
Intraoperative augmented reality in the posterior fossa

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Objective

Augmented reality (AR) is established as a useful intraoperative tool in the non-invasive visualization of individual anatomical parameters in the operating microscope. In this study we examined the feasibility of the implementation of AR in the resection of tumors in the cerebellopontine angle (CPA) and cerebellum.

Methods

20 patients with non-acoustic tumors were recruited. All of them underwent microsurgical resection. In 10/20 cases microscope-based AR was performed, while in the rest of patients navigation was not applied. Integration of AR into the operative view was evaluated. Intraoperative ultrasound was registered with image guidance data and navigation update was performed by the coregistration of cranial nerve topography and semiautomatic segmentation of the underlying neurovascular relationships.

Results

11 hemangiolastomas, 3 pilocytic astrocytomas, 2 endolympathic sac tumors, 2 epidermoid cysts, one trigeminal neuroma, one glossopharyngeal neuroma were successfully resected. Gross total resection was achieved in all cases. AR was able to delinate the intraoperative individual anatomy of the tumors and corresponding neurovascular structures with high accuracy in 10/20 patients. With the image processing tool of navigation update and intraoperative ultrasound the preoperative MRI data could be adjusted to the current microsurgical state by defining reference structures such as the brainstem, cranial nerves and vasculature.

Conclusion

We herein show, that microscope-based AR for the resection of posterior fossa tumors supports the intraoperative orientation and especially enhanced surgical safety corresponding to the functional integrity of cranial nerves and adjacent vasculature at the surface of the brainstem. With the tool of navigation update referring to robust structures such as the brainstem, cranial nerves and vessels the intraoperative image guidance and AR can enhance the intraoperative visualization tool. We herein show, that microscope based AR supports microsurgical orientation and training.

Innovative Lehrtechniken in der Neurochirurgie/*Innovative teaching in neurosurgery*

P250

Eine Globale Studie über die unterschiedlichen Bildungsmöglichkeiten für Medizinstudierende durch die Teilnahme an neurochirurgischen Kongressen in Abhängigkeit von sozioökonomischen Faktoren

Global Prospective Study on Different Training Opportunities for Medical Students Attending Neurosurgical Congresses Dependent on Socioeconomic Factors

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Objective

Medical students education varies widely depending on numerous factors like country of study or personal background. Participation in international congresses could provide students with equal educational opportunities and access to networks, regardless of their background. With this study we want to assess socioeconomic differences of medical students attending international congresses and the effect on medical student careers in the field of neurosurgery.

Methods

For the evaluation, we collected data through anonymous baseline data from congress registrations, the abstract center, and two surveys designed to assess the student experience before and after the congress. We included medical students planning to attend a neurosurgical conference for medical students. Questions considered socioeconomic background, prior experience with congresses, and knowledge assessment via Likert scales 1-5 (1 no experience, 5 much experience). Analysis was performed using GraphPad Prism.

Results

Baseline data showed that female participation was higher (52.6%) than that of males. The evaluation of the abstracts showed that the proportion of submissions by women was also higher with 58.9%. In addition, women acquired higher rankings in presentation format. The congress was attended mainly by students from Europe (Germany 26.3%, Romania 19.3%, Spain 15.8%). Students with a relative in the field of medicine, rated their knowledge higher (4.00), compared to those without one (2.90). Among the respondents, 72.7% reported having attended over 80% of the lectures and 87.3% attended over 80% of the workshops. With 96.5%, almost every participant confirmed that their knowledge and skills had improved due to the congress and their participation.

Conclusion

Through our analysis, we highlighted different opportunities for medical students depending on country of study, family background, and gender. Congresses can help to even these differences and create opportunities to compensate for deficits. In contrary to current assumptions, we emphasized that the highest number of participants were female, and women also represented with the most scientific contributions. This must be used to counteract the current imbalance among neurosurgeons by supporting female medical students early on in their career. Due to the high number of participants in lectures and workshops, we illustrated the high interest in neurosurgical congresses by medical students.

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Die Rolle von Studierenden in der Forschung - Ergebnisse einer deutschlandweiten Analyse und mögliche Strategien zur Förderung studentischer Beteiligung in der Forschung

The Role of Students in Neurosurgical Research - Results of a German-wide Analysis and Potential Strategies to Facilitate Student Participation in Research

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Objective

In recent years, there has been a growing appreciation of the importance of evidence-based medicine, which requires clinical skills as well as a deep understanding of research. Nonetheless, the teaching of research skills still constitutes a small part of the medical curriculum. Thus, students who are interested in developing these skills often have to do so through extracurricular opportunities, for example through getting involved in medical research. In this study, we investigated the participation of students in neurosurgical research in Germany and the different strategies, which may be employed to facilitate this.

Methods

In order to gain a comprehensive picture, we developed two surveys, one for medical students and one for neurosurgeons, using Google Forms. The student survey was distributed to all medical faculties in Germany and included items about demographic data and previous research experience. Likert scales (1 - low, 5 - very high) were used to assess interest in research, neurosurgery, and neurosurgical research. Neurosurgeons were asked their interest in research, current project ideas, and experience in working with students. Analysis was performed using GraphPad Prism version 9.4.1..

Results

The questionnaires were answered by 169 students from 34 universities and 30 neurosurgeons from 17 hospitals, respectively. 71.0% of the students are either interested (4) or very interested (5) in extracurricular research and 73.9% have a high (4) or very high (5) interest in neurosurgical research. Currently, only 26% of respondents are involved in a research project. Amongst the neurosurgeons, 93.3% are interested in doing research besides clinical practice (4: 13.3%, 5: 80%), with 41.4% participating in a clinician scientist program. 96.7% of the neurosurgeons had at least one research project, which they are currently unable to execute due to time constraints; 46.7% of the respondents have ≥ 4 such projects. Of the neurosurgeons, 66.7% are currently collaborating with students on research projects.

Conclusion

The results show a high level of interest and availability on the students' and an abundance of research ideas and willingness to collaborate on the neurosurgeons' part. To benefit both sides and to support research projects in general, collaborations between students and neurosurgeons should be facilitated. One possible solution could be the establishment of a research platform to facilitate communication and to encourage student participation in research.

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