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ABSTRACTS

Intramedullary mass lesions – function directed surgery

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Recent advances of electrophysiological monitoring allow for safe surgery within the spinal cord.

We have evaluated our series over the past 8 years to determine the effects of monitoring and to establish in how many cases the surgery was altered and directed by the electophysiological findings.

In a period 2005-2012 total of 77 patients with various intramedullary pathologies were operated. The dominant lesions were ependymomas followed by astrocytomas and cavernomas. This series was compared to earlier series of 29 patients in whom electrophysiological monitoring was not used.

The radicalism of surgery increased from 30 to 70%. In general clinically the patients remained the same as preoperativelly in both groups. In 29 patients the steps and techniques of surgery was changed according to MEP and D wave findings during the procedure.

Conclusions: Thanks to MEPs and D wave are highly sensitive and specific in outcome prediction.

The better the preop neurological findings the better the outcome.

Monitorability depends on preop findings.

The outcome depends on intraop monitoring.

The surgeon must be able to change the surgical strategy whenever the warning is announced by the electrophysiologist.

Any surgery of the spinal cord should be performed with intraop monitoring

Posterior fossa meningiomas

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Posterior fossa meningiomas are deemed to be difficult lesions. However, this seems to be true for certain tumors only.

Series of 123 posterior fossa meningiomas operated in a period 1998-2011 was reviewed and divided into various location groups and related to the extent of surgery and neurological outcome.

Overall MM rate was 5,7% and overall S1 and 2 resection was 73%. The tumours were finally divided into two groups only – A. anterior to the cranial nerves (n=63) and B. posterior to the nerves (n=60).

MM rate in group A was 9,5% with some minor morbidity in another 23,6%. In the group B MM rate was 1,7% with zero minor morbidity. S1 and 2 resection was achieved in 73% of patients in group A and in 95% of patients in group B.

In conclusion surgery should be offered to all patients with tumors located posterior to the cranial nerves. In patients with tumors located anterior to the nerves other treatment modalities should be considered.

Anterior fossa midline skull base meningiomas – preservation of N.I function

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Using a standard anterior skull base approach for olfactory groove meningioms does not allow preserving the function of the first cranial nerves. Series of 67 meningiomas located in the midline skull base of anterior fossa was reviewed. The tumours growing from posterior (sellar) or from the side (sphenoid wing, clinoid) and reaching the cribriform plate were excluded. In the years 1998-2002 total of 21 such cases were treated. All the tumours were approached via anterior midline and in neither case the first nerve has been preserved. There was 0 mortality and 9% minor morbidity. Anosmia was present in all patients. Since 2003 we have preferred pterional approach to these tumors. In a period 2003 - 2011 we have treated 46 patients. The overall mortality was 4% and minor morbidity 4%. In 17 surgeries anterior midline cranitomy was introduced, in 3 endoscopic endonasal route was used, and in 26 pterinal approach was introduced.

We were able to preserve at least some smell in 19 patients (41%). The best results were achieved in pterional craniotomy group – 50% smell preservation and 85% Simpson 1 and 2 resections.

The major advantage of pterional approach, apart from potential contralateral n.I preservation, is early exposure of important structures in the sellar region and early CSF drainage. The potential of endonasal endoscopic approach is yet to be established. Anterior subfrontal approach is reserved for the tumours reaching the most anterior parts of the anterior fossa and for the extra large tumours.

The role of stereotactic biopsy in the management of infiltrative and multicentric cerebral gliomas

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Diffuse and multi-centric growth-pattern of glioma precludes the gross-total resection of these tumors and represents the main cause of the poor outcome of the patients. Therefore, stereotactic biopsy is an alternative option for the management of these types of tumors. The authors present their experience in 102 cases of stereotactic biopsies performed for infiltrative, multicentric and deep-seated cerebral gliomas.

One hundred and two patients with infiltrative, multicentric and deep-seated cerebral gliomas admitted in our clinic between November 2008 and February 2013 were included in this study. All patients underwent the stereotactic biopsy according to the standard protocols. Stereotactic and neuroimagistic tools used for these procedures included the Leksell stereotactic system and the software: Stereotactic Planning System (SPS), NTPS 8.2. The histopatological results (according to World Health Organization (WHO)

classification) were: 66 cases of glioblastomas (grade IV) (64,7%), 7 cases of anaplastic astrocytomas (grade III) (6,9%), 14 cases of grade II diffuse astrocytomas (13,7%), 7 cases of grade I astrocytomas (6,9%), one case of grade II oligodendroglioma (0,09%), 3 cases of anaplastic oligodendrogliomas (grade III) (2,9%), one case of grade I ganglioglioma (0,09%), one case of anaplastic ganglioglioma (grade III) (0,09%), and 2 cases of anaplastic ependymomas (grade III) (1,9%). In 32 cases (31,4%) the immunohistochemistry has been performed in order to obtain an accurate histopathological result. In this series, the early postoperative mortality was 0%, with no cases of clinically significant hemorrhages after biopsy procedures. Temporary increase of neurological deficits has been noticed in 9 patients (8,8%).

In conclusion, image-guided stereotactic biopsy represents now a safe and accurate diagnostic method for infiltrative and deep-seated cerebral gliomas, which can favorably infl uence the therapeutic management of the patients.

Key words: Stereotactic biopsy, infiltrative gliomas, immunohistochemistry.

New trends in treatment of elderly patients with high-grade glioma

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Background: optimal treatment for elderly patients with high-grade glioma is not well defined. They are often excluded from multimodal approach due to concerns of increased morbidity due to poor performance index and associated diseases. We present our results in treatment of patients over 65 years with different type of high grade gliomas. The primary end point was overall survival. Some data of recent clinical studies that will perhaps change the treatment decision for these patients will be presented.

Patients and methods: 65 patients, with a median age of 69 years, have been treated between 2005 and 2010 in our Institution. Female/male ratio was 37/28. Histological type was: glioblastoma multiforme (GBM) 44 patients (66.6 %), anaplastic astrocitoma 7 patients (10.61 %), oligoastrocitoma grade 3 in one patient (1.54%). Other histological types were less frequent representing 13, 86%. Surgery was performed in all patients: complete resection in 50 patients (76.9%), subtotal resection in 13 patients (20%), and 2 biopsies (3.1%). Postoperative 3D conformal radiotherapy was performed with two different type of fractionation: a) standard fractionation: TD= 40-60 Gy, mean dose 56 Gy; and 2) hypofractionation: TD= 3-45 Gy, mean dose 32 GY. Concomitant and adjuvant chemotherapy with Temozolomide was done in 33.33% of patients, concomitant radiochemotherapy only in 22.75 % of patients and 37.88% of patients performed radiotherapy alone. At the beginning of postoperative treatment 58.4% of patients had Karnofski index (KI) > 70. Main associated diseases were high blood pressure, cardiovascular diseases, diabetes.

Results: Overall survival at 36 month was 13% (CI: 7%-25%) with the worst survival for patients with GBM (8%). Toxicity during radiotherapy was measured after

RTOG scale and generally was 0-1 (6.07% of patients) with no significant difference between the two type of fractionation.

Conclusions: The number of patients in our study was small, but study show that elderly patients could be treated with radio-chemotherapy without major toxicity. Hypofractionated radiotherapy was well tolerated and could be a good option in order to shortening the treatment time for these patients. Important decision factors for treatment type must be KI and the status of associated diseases.

Supratentorial low grade glomas latest developments in diagnosis and treatment

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Introduction: Low grade gliomas (LGG) are slow growing tumors. The aim of the treatment is to simultaneously combine an optimal resection by preservation of functional integrity with correct grading of tumor malignancy and the adequate adjuvant therapies in order to achieve a long survival, with a good postoperative quality of life. There are some important questions regarding LGG: What is the delimitation of LGG? What are the therapeutical decisions: observation, surgical removal or biopsy? Does surgical removal alone ever cure LGG? If recurrences appear, is another surgery recommended? What is the efficiency of radiotherapy and chemotherapy in LGG recurrences? What are the indications of Gamma Knife Surgery (G.K.S.)?

Material and methods: Our experience in a series of 160 adult patients with supratentorial LGG, operated over a period of 11 years (January 2002- December 2012) is presented, focusing on the newest achievements in the diagnostic of gliomas (neuroimaging, immunohistochemical analysis of tumor specimens), surgical treatment (intraoperative electrophysiology) and adjuvant therapies (oncological protocols).

The preoperative diagnosis was based on 1T MRI images. Microsurgical resection was performed in all cases: total removal 79 cases (49,3 %), partial removal 81 cases (50,6 %), with no perioperative mortality. The outcome at 6 months (GOS) showed: good recovery in 135 cases (84,3%), moderate disability in 21 cases (13,1%), severe disability in 4 cases (2,5%). The follow-up period ranged between 12 months and 9 years with a medium range of 4,5 years. The histological grading was assessed by classical pathologic examination and showed: fibrilary astrocytomas in 102 cases, oligodendriogliomas in 26 cases, oligoastrocytomas in 21 cases, dysembryoplastic neuroepithelial tumor in 5 cases, protoplasmic astrocytoma in 4 cases, ganglioglioma in 2 cases.

In our data at 5 years postoperative we find: 11 lost patients, recurrences to grade III-IV in 49 cases, regrowth grade II-III in 53 cases, 47 cases remain in evidence (grade II).

The total number of regrowth-recurrences is 102 (63,8%). It's very important to perform a check-up MRI every 6 months.

LGG causing long-standing and medically refractory epilepsy are more likely to be associated with multiple epileptogenic foci, therefore intraoperative electrocorticography was used for tailoring the resection, together with intraoperative localization of central sulcus using somatosensory evoked potentials in tumors localized around the central area. Intraoperative electrophysiological monitoring was performed in 31 cases.

Because actually, the final diagnosis requires immunohistochemistry and also, study of the molecular biology of these tumors is an important step for understanding the genesis and biological behavior of these diseases, in the last years of the study we have performed also immunohistochemical analysis of the tumor specimens. We have studied in order to identify, quantify and compare, in a series of 37 cases of glioma surgical specimens (low grade and high grade gliomas), previously classified concerning their histological grade (WHO), the following immunohistochemical markers: Ki-67 proteins and PCNA (markers of the cellular proliferation), p53 (product of the tumor suppressor gene TP53), CD 34, VEGF, VEGFR2, bFGF (markers for angiogenesis).

Surgical specimens were immunostained for p53 (Clona DO-7, Biogenex USA); Ki-67 (MIB-1; 1:50, DAKO- Glostrup, Denmark) and proliferating cell nuclear antigen (PCNA; 1:10, PC10 Dakote). Proliferative activity (nuclear immunostain) was measured.

P53 immunoreactivity was positive in all grade III and IV gliomas, and in 50% of low grade gliomas. With a median of 12% and 24% for MIB-1 and PCNA respectively, for all neoplasms in the study, the mean percentage positive nuclear area for MIB-1 and PCNA was 3.06% and 13.11% in low-grade (II) astrocytomas, 14.34% and 29.68% in highgrade (III) astrocytomas, and 18.77% and 44.11% in glioblastoma multiforme (grade IV).

One-way analysis of variance showed a significant correlation between the histological grade and MIB-1 and between the histological grade and PCNA. Isolated cases of low grade gliomas with high MIB and PCNA percentage were noticed.

CD34, VEGF, VEGFR2 and bFGF expression were determined by immunohistochemistry (CD34, Clone Q band, Immunotech; VEGF, sc-152, Santa Cruz Bioth.; VEGFR2, sc-7269, Santa Cruz Bioth; bFGF, bFGF88, Biogenex). Immunoreactivity for CD34 was positive in all types of the tumors. Immunoreactivity for VEGF, VEGFR2 and bFGF was seen in both endothelial cells and tumor cells, with increased levels in more aggressive tumors, comparing with normal tissue where immunoreactivity was present only in endothelial cells.

Conclusions: LGG could be treated only surgically. We advocate the idea, that patients with LGG and medically refractory epilepsy, may undergo tailored resections.

Incompletely resected tumors may be managed with irradiation in the tumor bed, or by observation alone. Proliferation in gliomas, measured as MIB-1 and PCNA, correlates significantly with histological grade, providing useful additional information for diagnosis evaluation of the tumor recurrence susceptibility. Angiogenesis markers could indicate the invasiveness tendency of the tumor. Correlated with the proliferation markers, they express the agressive tendency of the tumor and consequently, the prognosis. As

a result, the correct treatment and prognosis of the case could be evaluated, especially in LGG where the indication of radiotherapy is debatable.

Despite the optimism associated with prognostic in LGG, these tumors usually recur, having a higher grade of malignancy. We consider that new, even more aggressive treatment protocols are needed for their management.

Key words: low grade gliomas, supratentorial, microsurgery, intraperative electrophysiology, immunohistochemistry, neuro-oncology, Gamma Knife Surgery (G.K.S.)

Treatment of brain metastases with cyberknife robotic radiosurgery

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Objectives: CyberKnife robotic radiosurgery is a potentially effective treatment strategy for brain metastases, including large or multiple lesions.

Aims of study: To evaluate efficacy and toxicity of Cyberknife robotic stereotactic radiosurgery (SRS) alone or in combination with whole brain radiotherapy (WBRT) in the treatment of metastatic brain lesions.

Case report: We retrospectively reviewed data of patients with brain metastases who underwent CyberKnife SRS at the University of Messina, ITALY between July 2007 and February 2013

Material and methods: In the study, we included 252 patients with 343 lesions with >18 months follow up. Recursive partitioning analysis (RPA) was used to categorize clinical status of patients. Treatment planning was obtained on CT and contrast-enhanced MRI. The clinical target volume (CTV) adopted was the gross tumor volume (GTV) plus an isometric margin of 1-2 mm. Follow up examinations were carried out 2-6-12 months after SRS, then yearly.

Results: Follow-up ranged 18-50 months. All patients were treated in single fraction, median tumor volume was 1.9 cc (range 0.06-22.9 cc), median dose was 20 Gy (range 11-24 Gy), median isodose 80% (range 60-90%). 55/252 patients were lost to follow up. Median survival at 1 and 2 years were 63% and 55% respectively. One and two years local disease control were 84% and 62% respectively. Median survival was 14, 7.6 and 4.8 months for RPA class 1, 2 and 3 respectively. 80% of the patients treated with SRS only were alive at 40 months versus 43% of the patients treated with SRS plus WBRT. Patients who had been treated for lesions â‰¤ 2.5 cm who survived at 24 months were 78%versus 43% of the patients with lesions > 2.5 cm. Early and late neurological effects were recorded in 17% of patients located in eloquent brain areas.

Conclusions: Our results confirm the efficacy of Cyberknife stereotactic radiosurgery in the treatment of brain metastases. Best results were obtained in patients in RPA class 1, with lesions of â‰¤ 2.5 cm and in patients without or with controlled extracranial disease. Furthermore, the preliminary data of this study suggest that the combination SRS with WBRT adds no benefit over SRS alone for oligo-metastatic patients.

Brain tumor related seizures

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Approximately 4% of all seizures are secondary to brain tumors. Seizures are the onset symptom in about 20-40 % of patients with a brain tumor diagnostic and about 20-45% of these patients will present a type of seizure during the course of the disease.

Objectives: The objective of our study was to analyse all cases of patients with a brain tumor diagnostic during a thirty nine month period, observing the incidence of seizures, seizure type, the relation of the seizure with the tumor type, the moment of the diagnostic and the treatment applied.

Aims of study: We were interested to create a clear picture of the relation between brain tumor and seizures in our Neurological Unit from Emergency County Hospital Cluj.

Case report: The study has a retrospective design, including a number of 112 patients with a brain tumor, admitted from January 2010 to March 2013.

Material and methods: We analyzed brain tumor patients, grouping them according to demographical date, onset of seizure in relation with the moment of diagnostic, seizure type, tumor type and the antiepileptic treatment applied. Results: From the 112 brain tumor patients included in this study, 76 patients (64.3%) never developed a seizure, 26 patients (23.2%) presented a seizure before the diagnostic and 21 patients (18.75%) developed seizures after the diagnostic was established. Most of the cases were meningiomas (27.67%) and astrocitomas (24.1%). 56% of the pacients suffered from primary generalized seizures and 31.3% suffered from partial motor seizures. 41 pacients were submitted to monotherapy and 7 patients received dual AED therapy.

Conclusions: Our results demonstrated once more that seizures are a major complication of brain tumors, the management of these patients being particularly difficult.

Angiogenesis in gliomas and plasma levels of vascular endothelial growth factor (vegf) and basic fibroblast growth factor (bFGF)

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Objectives: Glioma progression and patient's survival is strongly dependent on the development of a new vascular network that occurs primarily by angiogenesis. The knowledge of the plasma detectability of distinct angiogenic factors in patients with brain tumours is very limited.

Aims of study: The purpose of the study was to evaluate the plasma levels of the angiogenic factors Vascular Endothelial Growth Factor (VEGF), and Basic Fibroblast Growth Factor (bFGF) in patients with brain tumours.

Material and methods: Plasma samples of 25 patients with histologically confirmed intracranial tumours, divided in 2 groups- Group I (gliomas- glioblastoma multiforme, WHO grade IV, n=6; astrocytoma, WHO grade II-III, n=4;

astrocytoma, WHO grade I, n=4) and Group II (meningiomas, n=11), were analyzed. Group III (the control group) included 10 clinically healthy patients. The plasma concentrations of the examined angiogenic factors were evaluated by highly specific enzyme-linked immuno sorbent assays (ELISAs).

Results: Median levels of VEGF and bFGF in plasma were significantly higher in patients with high-grade gliomas as compared with patients with low-grade gliomas or meningiomas. The serum levels of the investigated angiogenic factors demonstrated correlation to tumour grade and vascularity.

Conclusions: Despite the limited number of patients, our data suggest that the plasma levels of VEGF and bFGF correlate with the tumour type and grade. The levels of the angiogenic factors in the plasma correlate with the degree of tumour vascularity. The plasma detectability of the individual angiogenic factors seems to depend at least partly on the tumour type as well as on tumour progression.

The value of microRNA as a prognostic factor in high grade gliomas

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Objectives: MicroRNA (miRNA) is a class of highly conserved, single-stranded, noncoding small RNAs. After maturation, they entry into the RNA interference pathway and regulate gene expression on the post-transcriptional level by inhibiting the translation of protein from mRNA or by promoting the degradation of mRNA. Many studies have shown that miRNAs control cell proliferation, differentiation, and apoptosis in different types of cells.

Aims of study: The purpose of the study was to evaluate the expression of a miR cluster in high grade glial tumours.

Material and methods: Tumour samples (n=20) of high grade gliomas neurosurgically treated in our clinic were simultaneously fixed in formalin for histological analysis and refrigerated to -80°C in RNALater(Ambion). After the isolation of pure and intact total RNA from the samples, the expression of the miR cluster was investigated by RT-PCR.

Results: The histological examination confirmed the glial character of the tumours and demonstrated their high-grades according to the WHO classification. The molecularbiological analysis validated the existence of the examined miR cluster.

Conclusions: The miR cluster was expressed in high grade gliomas. The correlation between the expression levels and the histological grade and patients' survival could be valuable for identifying new biomarkers predicting the behavior of theses tumours. MicroRNAs may be clinically useful as prognostic biomarkers.

Intracranial meningiomas-an overview

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Introducere: Intracranial meningiomas represent the second most frequent type of cerebral tumors encountered in

neurosurgical practice. Despite being characterized as benign tumors, the risks of recurrence or malignant transformation last for a lifetime. Based on our surgical experiences, we wish to illustrate that, aside from the histopathological type or subtype, two other factors independently infl uence the risk of recurrence of these tumors: the tumor resection ratio and its location.

Material and methods: Our retrospective study is based on the experience of the main author, encompassing 688 locations of intracranial meningiomas encountered in 657 patients (some patients with multiple meningiomas) requiring 817 surgical interventions (including recurrences). In our practice, intracranial meningiomas accounted for 22,9% out of the total of 3004 cerebral tumors surgically treated by the same author between 01.01.2000 and 31.12.2012. We present some surgical key point for different location and analyze the recurrence rate of meningiomas in relation to tumor location, World Health Organization (WHO) grading and gender and tested the statistical significance by using the Chi square test.

Results: 597 cases with documented total macroscopic ablation met the inclusion criteria for statistical analysis. Out of these, 83 cases were recurrences (13.9%), which had a median recurrence period of 3 years. 65% of the recurrences had a non skull base location, the most frequent cases being parasagittal and falcine meningiomas (35%), followed by convexital recurrences (30%). When analyzing the risk of recurrence in the case of parasagittal and falcine meningiomas, we found an Odds Ratio (OR) of 1.92 (CI [1.17, 3.17]), p=0.008) compared to other locations. The risk of having a skull base meningioma recurrence was 1.41 (CI [0.85, 2.29], p=0.15). The OR for recurrences in WHO grade II-III meningiomas was 3.3 (CI [1.73, 6.29], p=0.0001). We also found an OR of 1.31 (CI [0.82, 2.1], p=0.24) for tumor recurrence in male patients.

Conclusion: Considering that total ablation was noted in all of the tumors taken into calculation (Gross Total Removal GTR, Simpson grades I and II), we clearly demonstrated that falcine and parasagittal meningiomas tend to recur, the risk of recurrence being almost twice greater compared to other locations. In addition, our study shows that there is a significant association between WHO grade II-III meningiomas and recurrences, the risk of recurrence being 3 times greater when harboring aggressive types of meningiomas.

Key words: intracranial meningiomas, surgery, recurrences, locations.

Cerebral gliomas-resuming a surgical experience

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Introduction: The cerebral glioma category includes numerous histopathological types with varying peculiarities considering evolution, diagnosis, imaging and treatment. Therefore, encompassing them within a single presentation might prove hazardous. In spite of their differences, all these tumors share, apart from their ultrastructural origin, two major similarities: their fatal evolution in large

majority of the cases and the principles of surgical treatment. This is why we are attempting to highlight some of the elements concerning the role of neurosurgery in the treatment of cerebral gliomas, with particularities regarding histopathological types, location, surgical strategy and results.

Material and methods: The presented retrospective study is based on the experience of the first author (Prof. Dr. Florian) of 997 gliomas operated between 01.01.2000 and 31.12.2012, accounting for 33,18% out of the total of 3004 tumors operated within the same interval. 311 cases of HGG and 224 cases of LGG met the inclusion criteria for multivariate statistical analysis in order to define the role of radical surgery in multimodal glioma treatment.

Results: High-grade gliomas (HGG) represent 59,87% (597 cases) of all cerebral gliomas: anaplastic astrocitomas (25.7%), glioblastoma multiforme (65.5%), high-grade oligodendrogliomas (5.8%) and high-grade ependimomas (3%). From a total of 400 LGG cases (41,13% of all gliomas) pilocytic astrocitoma represent 23,5% (94 cases), Grade II gliomas (astrocitomas, mixed glioams) represent 44,5% (178 cases), oligodendrogliomas 10,7% (43 cases) and ependimomas (grade I and II) 15,25% (61 cases). 121 of all glioma operated cases (12,13%) where at the pediatric age, the majority being represented by LGG (83,47 %). Gross total removal (GTR) was achieved in 86% of HGG and in 88% of LGG. In HGG, at 24 months follow-up, the median survival was 12 months with GTR and only 6 months with STR. The improvement of the KPS scale is significantly higher ($p < 0,05$) in patients with LGG in whom gross total removal of the tumor was achieved.

Conclusions: The age and type of surgery were prognostic factors that had significantly infl uenced the survival rate at 12, 18 and 24 months for patients with HGG. In LGG extent of removal independently infl uences the outcome, but no correlation with malignant transformation could be established. Radical surgery must be the goal in multimodal treatment of cerebral gliomas.

Risk versus benefit criteria of the microsurgical treatment for recurrent glioblastomas

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Glioblastoma is the most common primary intra-axial tumor of the central nervous system with a poor outcome, despite the multidisciplinary approach which consists in surgery, radio- and chemotherapy. The rule is recurrence, which usually occurs between 6 and 12 months after primary treatment. There are divergent opinions regarding the management of the glioblastoma recurrence. While some authors support the surgical resection of tumor recurrences, others prefer the palliative oncological treatment.

The authors of this study present a case series of glioblastoma recurrences – 185 cases (143 patients), operated in our clinic between 1998 and 2012 by the senior author. The majority of patients (119 cases) underwent one operation for recurrences, 18 patients have been operated for two times, 6 patients for three times and 3

patients for four times. The surgical mortality in this series was 1,1 % (2 cases) and morbidity (new neurological deficits postoperatively) was 9,7% (18 cases). The medium survival time for recurrent glioblastoma was 6.5 months. The authors analyzed the risks and potential benefits of the microsurgical treatment for glioblastoma recurrences and tried to identify some preoperative criteria which predict a better postoperative outcome. Therefore, the authors correlated the postoperative results (mortality, morbidity and the medium survival time) with the following preoperative parameters: age, tumor location (dominant or nondominat hemisphere), tumor volume and extension (lobar, multilobar, and bilateral), mass effect with midline shift, Karnofsky preoperative score and associated diseases. Authors identify several preoperative criteria which were predictive for a better outcome in the microsurgical treatment of glioblastoma recurrence: age<70 years, location in non-dominant hemispheres, extension in one lobe, Karnofsky preoperative score>70.

In conclusion, tumor resection should be considered for the majority of the patients with glioblastoma recurrences especially in those cases with age<70 years, tumor location in non-dominant hemispheres, non-infiltrative growth pattern of reoccurrence and symptoms related to tumor mass-effect. The goals of surgery for glioblastoma recurrences are tumor debulking, prolonging survival and family and social reinsertion. Careful selection of the patients, based on analysis of several specific preoperative criteria (age, location, mass-effect, Karnofsky score), is important in order to obtain a better outcome and a good quality of life.

Key words: Recurrent glioblastoma, prognostic criteria, mortality, morbidity

Paraneoplastic sensory neuronopathy – and the cochrane study results

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The classic paraneoplastic neuropathy is subacute sensory neuropathy (SSN). Other types of peripheral neuropathy in cancer occur but are less well characterized This review is based on cancer related PNS, and deliberately omits paraproteinemic neuropathies, as they are conventionally discussed as a separate entity.

A Cochrane review discussed the therapeutic options in paraneoplastic neuropathy (Cochrane reviews:Treatment for paraneoplastic neuropathies - 2012) and came to the conclusion that presently no convincing therapies are available.

Objectives: Paraneoplastic neuropathies occur in different types and tumor associations. The most characteristic syndrome is subacute sensory neuronopathy, which is usually a sensory ataxic neuropathy. Motor involvement is discussed , and has been found in about 30 % in the EUROPNS study. Other types of neuropathies as sensory neuropathy, sensorimotor neuropathy, infl ammatory neuropathies have been reported in singular cases, but have not been consistently reported.

Aims of study: The aim of the Cochrane review was the effect of tumor treatment or therapy of paraneoplastic neuropathy.

Case report: The Cochrane Neuromuscular Disease Group Specialized

Register, CENTRAL (2012, issue 1), Medline January 1966-2013), EMBASE (January 1980- 2013) and LILIACS (January 1982- 2013) was searched for „paraneoplastic neuropathy“ and “treatment”. The following key words were used in conjunction with “treatment” and “therapy”: paraneoplastic neuropathy, paraneoplastic subacute sensory neuronopathy, paraneoplastic sensory ganglionopathy, paraneoplastic sensory neuropathy, paraneoplastic sensory motor neuropathy, paraneoplastic motor neuropathy, paraneoplastic immune-mediated neuropathy, paraneoplastic polyradiculoneuropathy, paraneoplastic multiplex mononeuropathy, paraneoplastic autonomic neuropathies.

Studies were accepted when other causes of cancer associated neuropathy had been ruled out and the diagnosis was based on symptoms, signs and NCV studies. All types of interventions as surgery, radiotherapy, chemotherapy, immune-modulating (corticosteroids, IVIg, plasmapheresis, immunosuppressants), supportive care and physiotherapy were considered. The treatments could be use alone or in combination. We evaluated stabilization or improvement versus worsening of disability after treatment. The data were analyzed according to two categories of treatments: tumor and immunemodulating treatment.

Results: Paraneoplastic neuropathies are rare and for this reason quality controlled studies on their treatment are diffcult to conduct. Most of the evidences is based on uncontrolled studies, case reports or expert opinion. In our search we found suffcient information on treatment of paraneoplastic neuropathy in 70 case reports, 12 case series (defined as a study with more than 3 patients), and 17 papers based on expert opinion. Two categories of treatment were distinguished: tumor treatment and immunemodulatory treatment.

Tumor treatment: In the case series a total number of 315 patients with peripheral neuropathies were reported. The total number of treated patients is not known, but we found that 26 patients improved with tumor therapy among eight of whom also received immunotherapy. From the analysis of cases reports we found that 49 out of 70 patients received cancer treatment and 36 patients improved of whom 6 had also immunomodulatory treatment. In the case reports patients who improved after tumor treatment had heterogeneous tumors and neuropathy. The types neuropathies were: subacute sensory neuropathy (SSN), sensory motor neuropathy, sensory neuropathy, infl ammatory demyelinating neuropathy, and other entities in single cases.

IVIG: From the analysis of the studies, cases series and case reports we identified 43 patients who improved or stabilized with IVIG. This hast to be considered with care as the duration of the IVIG treatment, the ranking of improvement and detailed information on concomitant tumor treatment was soften missing.

Plasmapheresis (PE): directly removes antineuronal antibodies of other factors from the circulation. Concerns in the use of PE in cancer patients involves the possibility that it will increase chemotherapeutic drugs clearance, once tumor treatment has been initiated. PE is not often used as a therapeutic approach for paraneoplastic neuropathy. We found 8 patients with paraneoplastic neuropathy which seemed to be responsive to PE treatment.

Steroids: are generally recommended for their effects on immune mediated disorders. We found 18 patients which had improved or stabilized after steroids. Limitations in understanding their efficacy comes from the fact that steroids were given at different dosage and schedules.

Immunosuppressants: There is concern that the use of immunosuppressants in cancer patients favors tumor growth or enhances toxicity of cancer therapies. To date, however, this hypothetical concern has not been properly evaluated. Cyclophosphamide, azothiaprine, often in combination with steroids have been used, but no recommendations can be given based on our analysis.

Conclusions: In conclusion the most promising treatment option is the identification and treatment oft he underlying tumor. The impact of the immunotherapy on paraneoplastic peripheral neuropathy is still unclear The reasons are the low number of patients treated, the combination of several interventions, and the concomitant cancer treatment. Moreover treatment experience is based mainly on case report, small case series or open labeled studies while randomized prospective studies are missing.

Cancer around the brain

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Objectives: Neurooncology is concerned with direct and indirect effects of cancer on the nervous system. The main clinical focus is intraparenchymatose diseases as primary brain tumors and brain metastasis. In addition meningeal involvement by cancer and extraparenchymatous tumors as meningioma. In addition to metastasis also toxic, metabolic, infectious and paraneoplastic have to be considered.

Types of tumor spread: Cancer can metastasize into the cavernous sinus, dura, calvaria, the base of the skull, cavities as nasal sinus, orbit and also into tissues as the skin, and the soft tissue of the neck, where nerves can be affected by compression, invasion and rarely solid nerve metastasis.

The complications of cancer in and around the skull are more heterogeneous then the well defined intraparenchymatouse metastasis and are usually a diagnostic, as well as a therapeutic challenge.

Aims of study: The aim of this review is to define the mechanisms, sites and treatment of cancer metastasis occurring in the adjacent structures of the skull, and neck.

Material and methods: The review is based on a selected literature research aiming at the key words of the surrounding structures of the brain, skull , in particular the base of the skull and neck. Own experience, based on observations and practical experience is added.

Mechanisms: Nerves are can be damaged by cancer via compression, invasion and also by effects of treatment as surgery and radiotherapy. The particular mechanisms of nerve invasion have been classified into invasion, intranerval metastasis and antero- and retrograde spread. In solid tumors, the invasion of peritumoral nerves is considered as a bad prognostic factor.

Results: Primary brain tumors: Usually primary brain tumors as glioma do not metastasize outside of the brain. The observations in the past years have shown, that metastasis, either to the lung or spinal seeding may be more often than previously expected. The invasion of adjacent structures as the meninges, the cavernous

sinus and the cranial nerves have been observed. Interventions as biopsies can seed the tumor and induce skin metastases.

Brain metastases: several studies are ongoing to identify the best treatment of intracerebral metastasis. Recent years have shown, that due to improved systemic tumor treatment also cerebral metastases occur in cancer types as prostate or intestinal cancers, which previously had been considered unlikely.

Meningeal involvement as meningeal carcinomatosis occurs in several cancer types and several studies have elaborated treatment, depending on the tumor type. The invasion or isolated metastasis into the dura, with or without osseous involvement occurs in several cancer types.

Although meningioma is often considered as typical in neuroimaging, rarely also metastasis can appear as a meningioma mimick. Local extracerebral tumors can also compress the venous sinus.

The base of skull metastasis can appear at several sites, and are usually classified according to the topography into orbital, parasellar, middle fossa, jugular foramen and occipital. They can be local or infiltrating invasive. Local pain, often in combination with cranial nerve involvement are the typical presentations.

Within the skull not only the cavities as the orbits and sinus can be the side of cancer, but also mucous membranes and the skin. Propagation of cancer via retrograde spread has been demonstrated.

The spread of cancer outside of the skull, in particular of ENT tumors, or metastasis can present with local pain syndromes, often projecting to the skull, cranial nerve lesions, and also compression and invasion of blood vessels.

Conslusion: The spread of cancer in structures around the brain, in the skull and neck is important in clinical neurooncology and usually no standardized treatment schedule is available. The lesion of nerves and nerve plexus is often associated by a combination of local pain and peripheral nerve damage. Although the morphological patterns of nerve invasion have been described the pathophysiologic mechanisms need to be further elucidated.

Molecular targeting of glioblastoma: new experimental perspectives

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Several candidate genes for resistance of human glioblastoma cell lines towards erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor, have recently been proposed. In the current study, we sought to examine the antiproliferative effect of additionally inhibiting two of these candidate resistance gene products, i.e., RAC1 and SMO, on glioblastoma cell lines with erlotinib-sensitive, somewhat responsive and resistant phenotypes. Glioblastoma cell lines selected to represent the erlotinibsensitive, somewhat responsive and resistant phenotypes, respectively, were grown in 96-well plates and exposed to erlotinib, HhAntag (an inhibitor of SMO) and NSC23766 (an inhibitor of RAC1) in various combinations and concentrations. After 10 days of continuous exposure, inhibitory concentration 50 (IC50) values were determined using a cytotoxicity assay, and drug combination effects (i.e., synergism, additivity, or antagonism) were calculated using the Bliss equation.

Antiproliferative synergism among erlotinib, HhAntag and NSC23766 was observed for the combination of erlotinib with either HhAntag or NSC23766 as well as for the combination of all three agents in both the erlotinb-sensitive and – to a lesser extent – in the somewhat responsive cell line. Importantly, in the erlotinib-resistant cell line, combinations of erlotinib plus HhAntag or NSC23766 or both acted antagonistically. In a system of human glioblastoma cell lines with sensitive, somewhat responsive and resistant phenotypes, this study is the first to identify erlotinib combined with inhibitors of RAC1 and SMO to synergistically inhibit proliferation in a priori erlotinib-sensitive and somewhat responsive cell lines. These results strengthen the role of multi-targeting approaches in the development of more effective therapies for glioblastoma. The antagonistic action of erlotinib, HhAntag and NSC23766 in the erlotinib-resistant cell line is counterintuitive and requires further clarification. Taken together, combinations of targeted agents may act differentially depending on the glioblastoma cell phenotype.

Cerebral metastases

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Objectives: Brain metastases are common, occurring in 20-40% of cancer patients and contributing to 20% of annual cancer deaths. Brain metastases are particularly common among patients with non-small cell lung cancer (NSCLC), even at the time of diagnosis, accounting for approximately 18-64% of all brain metastasis diagnoses. Overall prognosis of patients with brain metastases is limited, but has been shown to vary significantly, based on factors such as tumor histology, number of lesions, patient age and performance status.

Material and methods: We present our experience in brain metastases treatment. We analyzed retrospectively a series of 70 patients with cerebral metastatic involvement admitted to our department during 2011-2012. We present the particularities of our series in terms of demographics, attitude at admission, therapeutic options, surgical results, and subsequent management.

Results: 32 patients underwent surgery, the rest being submitted to oncology for systemic treatment. Reasons for surgery included: solitary lesion with good general status, diagnosis, lesions that posed a vital risk. We discuss particular cases with rare localization or with atypical presentation and pathology findings

Conslusion: Our review of the recent experience in the management of cerebral metastasis suggests, in accordance with the other published reports, that patients with neurometastatic disease represent a very polymorphic group. The decision making process has to be highly individualized for each case and should be a team effort, including neuroradiologists and oncologists.

Gliadel and MGMT methylation: is there a correlation with patient's prognosis?

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Clinical protocols combining local chemotherapy and concomitant radiochemotherapy have shown improvement of survival for patients with newly diagnosed malignant glioma. Histomorphological diagnosis is the most valuable tool for the classification of human tumors, but provides insufficient information concerning of therapy response. On the other hand, genetic data becomes more and more important. Our aim is to determine chromosomal alterations as well as the methylation status of MGMT, p15 (CDKN2B) and p16 (CDKN2A) in order to analyse their infl uence on survival time, radioand chemotherapy response.

In our trail 72 Glioblastoma patients were included, divided in two treatment groups: group A (36 patients) treated according the EORTC-Study and group B (36 patients) treated also according the EORTC-Study but receive additional local chemotherapy with Gliadel.

Promoter hypermethylation of MGMT, p15 and p16 and CGH analysis were performed as described in standard protocols.

Univariate cox regression showed prolonged survival time of patients with tumors harbouring deletions on chromosome 9p and 10q under chemotherapy treatment (p=0.0042). No significant effect was observed for gains on chromosome 7p.

Promotor methylation MGMT in tumor tissue was not associated with prolonged overall survival (p=0.46). Promotor hypermethylation of p16 was also not correlated with prolonged overall survival (p=0.821), whereas p15 showed significant differences between both groups (p=0.0684).

Although these results needs to be confirmed in larger series and under different treatment conditions, our retrospective study underlines that the tumor suppressor gene p15, involved in cell cycle control, can act as an attractive candidate for therapeutic approaches in glioblastomas.

Prognosis of meningiomas in the 1970s and today

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Objectives: The benefit of the current strategy for diagnosis (computer tomography and magnetic resonance imagine) and treatment (microsurgery, microscope, endoscope) of meningiomas, in contrast to the standard treatment in use before CT- and MR-imaging and the microsurgical era, has not yet been determined.

Aims of study: Our new planning/navigation system has been designed with practical necessity for easy modification with minimum cost. Accordingly, the support for new ideas from surgical side is possible with a simple but accurate realization.

Material and methods: A retrospective

statistical analysis was performed for 1349 patients with meningiomas who underwent surgery at the Neurosurgical Department of the Saarland University between 1965 and 2011.

Results: There were no major differences in symptomatology, tumor localization, and number of surgical procedures. The mean time until tumor diagnosis was significantly shorter after 1985. A significant better prognosis for patients operated after 1980 with regard to the postoperative duration of recurrence free survival could be revealed.

Conslusion: Based on the results of this study, the time from diagnosis to treatment have been remarkably reduced within the last 30 years. Also the overall prognosis for patients with meningiomas has changed from the 1960s until today. Thus, the introduction of modern diagnostic modalities and surgical procedures has improved the outcome in patients with meningiomas signicifantly.

Management of neurologic manifestations of primary brain tumors: the role of the neurologist

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The comprehensive care of patients with brain tumors involves a multidisciplinary team of specialists. Neurologists serve as valuable members of this team and bring a unique perspective to this approach.Complications in patients with brain tumors can result from the tumor itself (e.g., seizures), from treatment directed at controlling tumor growth (e.g., fatigue), or from treatments directed at controlling symptoms (e.g., corticosteroids). Seizures are the presenting sign in roughly 15-50% of patients diagnosed with gliomas. Levetiracetam is beneficial in patients with brain tumors with >50% reduction in seizure number in 20/25 brain tumor patients, but there is no role for seizure prophylaxis in patients with newly diagnosed brain tumors. The risk of deep venous thrombosis (VTE) and pulmonary embolus is high for patients with brain tumors, especially gliomas. In general, pharmacologic anti-coagulation after the peri-operative period has not been recommended for cancer patients. Therapeutic anticoagulation for patients with VTE is widely accepted for at least 3 months after first thrombosis, and can be considered for longer periods in patients who are good medical candidates.Thrombolytic therapy for VTE, is contraindicated in patients with intracranial malignancies. Improvements in MRI over the past two decades have increased awareness of spontaneous intratumoral hemorrhage within malignant gliomas. The risk of symptomatic intracranial hemorrhage during treatment has become an area of interest as anti-angiogenic treatments have become available. Glucocorticoids are a mainstay of therapy for the cerebral edema associated with brain tumors. Decadron is the preferred glucocorticoid due to its long half-life and low mineralocorticoid activity, but other corticosteroids may also be used. Although these drugs are often required to treat increased intracranial pressure in patients with brain tumors, these drugs should be weaned as soon as possible to minimize side events. Hydrocephalus can develop as a late complication of treatment. The development of new headaches or a significant worsening of baseline headaches

should prompt an evaluation for hydrocephalus. Diversion of CSF is the standard treatment for hydrocephalus. While some superficial infections can be treated with antibiotics alone, many will require surgical drainage with intensive post-operative antibiotics. Pneumocystic jiroveci (PCP) pneumonia is a well-recognized complication of patients with brain tumors. Prophylactic bactrim is safe and effective; alternatively dapsone or pentamidine. Fatigue directly affects quality of life by diminishing a patient's ability to fully participate in personal, social, educational, and work related activities. Exercise remains the most reliable treatment for this common problem. Cognitive decline predicts tumor progression and may precede tumor progression by months.Behavioral interventions, such as cognitive behavioral therapy and compensatory strategies (e.g., keeping lists), are important tools . In addition, stimulants such as methylphenidate may improve cognitive dysfunction related to subcortical white matter changes. Palliative care focuses on supporting the patient's physical, psychological, and social needs and is aimed at maximizing quality of life for patient's and their families.

Spinal ependymoma up to date

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Ependymomas are lesions with a moderate cell density, originating from the ependymal lining of the central canal of the spinal cord, ependymal cell clusters in the terminal filum, or from ependymal rests left during embryonic development. The pathophysiologycal mechanism it is traditionally thought to be an oncogenetic event that transforms the ependymal cells phenotype. There are studies that suggest that epigenetic silencing of tumor suppressor genes, through DNA methylation, is an important mechanism in the pathogenesis of ependymomas. The benign pathological nature of these tumours poses great difficulty in their early diagnoses and management. However, their compressive rather than infiltrative nature makes them amenable to surgical resection and the role of adjuvant radiotherapy and chemotherapy is still debated. Despite previous research, prognostic factors for ependymoma remain relatively controversial. Given the variety of localisation for this rare disease, the establishment of protocols for diagnostic or management is still a challenge. This paper proposes an updated overview regarding this challenging pathological entity.

Introduction / Objective / Objectives: Ependymoma represent a relatively broad group of glial tumours which share a common origin from differentiated ependymal cells lining the ventricles of the brain or the central canal of the spinal cord. There are only about 230 spinal ependymomas diagnosed each year in the United States, yet they constitute the most common type of primary spinal cord tumors. Owing to the rarity of the disease, the literature regarding ependymomas in adults is scarce and limited to retrospective series. Thus, the level of evidence regarding therapeutic strategies is low and universally accepted guidelines are lacking. This broad group of glial tumors pose special problems regarding diagnostic and in many cases diagnostic is delayed. The patients with

ependymoma of the filum terminale due to the difficulty of diagnosis are occasionally wrong labeled as psychosomatic or hypochondriac. Given the rarity of the disease there are no generally established management protocols, for operative treatment the general principles of surgery of the spinal cord tumors apply. After operative management 50% of patients with ependymomas experience immediate postop worsening in terms of sensory disturbances due to posterior column retraction. The benign pathological nature of these tumours poses great difficulty in their early diagnoses and management. However, their compressive rather than infiltrative nature makes them amenable to surgical resection and the role of adjuvant radiotherapy and chemotherapy is still debated. Despite previous research, prognostic factors for ependymoma remain relatively controversial.

Aim / Aims / Aims of study: The objectives of this paper are to present the actual knowledge level about the subject, offer an integrative update based on the newest studies, draw common lines for possible future protocols and identify new research directions.

Case report / Design / Background and aims: Ependymomas are classified based on the morphologic phenotype (cellular, papillary, tanycytic, clear cell, pigmented and epithelioid, giant cell ependymoma) or on the WHO tumour grading as it follows: low grade (grade 1 or 2), or high grade (grade 3 or anaplastic). Compared with intracranial ependymomas, spinal ependymomas are less prevalent, occur in a younger population, and exhibit a better prognosis. The fourth decade of age seems at most risk and the sex distribution is equal although some studies report a slight male prevalence. In the lumbosacral region, ependymomas are most commonly associated with the conus medullaris and cauda equina, but can also occur extradurally in the sacrum, presacral tissues, or subcutaneous tissues over the sacrum, extradural epedymomas are extremely rare entities. The clinical presentation can broadly vary according to location. Diffuse dull pain constantly increasing due regional impediment of venous outfl ow is worse at night or upon awakening. When contact with nerve roots the pain becomes of a burning or fulgurant character and may irradiate radicularly. Tactile and pain sensation are usually affected first because of the central topography of these tumors. Motor deficits and pathological refl exes are also depending on the tumor location. MRI is the radiological exam of choice, either for surgical planning or to rule out differential diagnosis. Current efforts being made to identify the pathophysiology of this disease suggest that epigenetic silencing of tumor suppressor genes, through DNA methylation, is an important mechanism in the pathogenesis of supratentorial and spinal ependymomas. There appears to be a consensus for radiation therapy in cases of subtotal resections of intradural tumors although the role of adjuvant therapy in subtotal resection is controversial.

Patient and methods / Material and methods / Methods / Purpose: This paper is based on the review of relevant literature on spinal ependymoma. The latest studies converge to some key points usefull in helping the clinician to establish the best therapy option for each case.

Results / Result: One interesting aspect of ependymoma is the pathophysiological mechanism; one theory assumes that ependymal cell rests arise from the

coccygeal medullary vestige, a remnant of the dural part of the terminal filum that involutes during embryonic development. Others authors assume that these ependymal rests occur as a result of incomplete closure of the neural arch. Ependymoma has been characterized at the DNA copy number and mRNA expression levels and was associated with an increase in expression of genes encoding for proteins involved in methylating DNA. Genes involved in the control of cell growth and death and the immune system including members of the JNK pathway seem to play an important role. Genetic and transcriptional differences between tumors arising in different locations have been described. Studies report that members of the c-Jun N-terminal kinase (JNK) signaling pathway; MAPK10 and MAP3K1 display hypermethylation in spinal ependymoma but they are not specific. CD99 monoclonal antibody could differentiate between ependymomas and nonependymal tumors, and so act as a marker but was of no consequence in determining the variant type or degree of histologic aggressiveness. In some studies is reported that over two thirds of the patients had experienced symptoms for more than 6 months before diagnosis. Also patients who had tumors involving the spine had symptoms for a significantly longer time than patients who had ependymomas involving the brain. Dissemination evidence of ependymoma cells into the cerebrospinal fl uid CSF fl uid examination is a key factor in staging, prognosis, and treatment and allthough intradural ependymomas can spread throughout the CNS they are not likely to metastasize outside it. A neuro-axis MRT study is recommended to rule out tumor dissemination. The optimal treatment for intramedullary spinal tumors is controversial. Current therapeutic options include surgery, radiation therapy, chemotherapy, or a combination of these modalities. Stereotactic radiosurgery for intramedullary spinal tumors is feasible and safe in selected cases. Resection and conventional radiation therapy are associated with potential morbidity and so there is no optimal treatment established. Some studies suggest that radiation therapy among adults might be somewhat deleterious to survival. Age at diagnosis appears to be a strong predictor of the outcome of those patients according to some authors, tumor histology was more infl uential in adults than children, and complete resection was the most effective treatment option, regardless of age.

Conclusion / Conclusions: Multicentric studies could be a solution for getting a better insight on the spinal ependymoma complex problematic. For small tumors with no or little neurological deficit there is a tendency for conservative management with multiple follow up imaging studies. Even if the diagnostic is not histologically established the conservative strategy is more often adopted in clinical practice due to the high risks correlated with the operation. For high cervical lesions the indication for surgery is even more difficult given the possible complications of spinal injury caused by the operation. Adequate knowledge of anatomy and the correct use of microsurgical techniques allow total resection of some tumors with minimal morbidity and maximum functional recovery. There are no studies focused on fl uorescence assisted microsurgical extirpation for spinal ependymoma. Cranial ependymomas are often being

administrated a fl uorescent substance preceding the operation in order to allow a better demarcation of the tumor intraoperatively. A possible practical study direction can be establishing if fl uorescence is an efficient means to improve postoperative outcome for extended intraspinal ependymomas.

Clinical behavior and outcome of optic pathway gliomas in children

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Background: Tumorsof the optic pathways comprise 4-6% of pediatric intracranial tumors and may have a more aggressive course in younger children.

Methods: In the present study we retrospectively reviewed the clinical characteristics, treatment and outcomes of 15 children diagnosed with optic pathway gliomas (OPG) between 2000 and 2010.

Results: The age range of the children at diagnosis was 11 months to 17 years (mean 8.1 years). The male/female ratio was 8/7. Presentation included: decline in visual acuity (53%), headache (27%), proptosis (13%) and seizures (7%).Forty per cent of the children with OPG had neurofibromatosis type 1 (NF1). Treatments included various combinations of surgery, chemotherapy and radiation. Biopsy was not performed in two cases. Five children were treated with chemotherapy alone, three with radiotherapy, threewith combined treatment, while four children were observed. After a median follow-up of 6 years, 12 patients are alive with stable disease.

Conslusion: Despite the benign histology of optic pathway gliomas, its biological behavior is unpredictable. Because of difficulties in defining progression and generally variable natural history the most favorable management of optical pathway gliomas is still controversial. Association of NF1 is a favorable prognostic factor, these tumors tended to be less aggressive in NF1 patients.

Aspects of microsurgical treatment of craniospinal, cervico-medullary and cervical intramedullary tumors

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Surgical removal of intrinsic medullary tumors still make a challenge at any level of the spinal cord including the cauda equina, because of the risk inherent with surgical manipulation. This risk is even more enhanced within the cervical, cervicomedullary region.

Patient material: In the period between 1985 – 2005 we operated 216 cases of intramedullary lesion with different pathologies (108 ependymomas, 58 astrocytomas, 14 hemangioblastomas, 15 cavernomas, the others less frequently occurring pathologies), and 50%, 108 affected the cervical spinal cord, as well. Within the cervical group two subgroups could be differentiated: cervico-medullary and high cervical, and low cervical, cervico-thoracic group, roughly in two third-one third proportion, considering the frequency of occurrence.

Surgical strategy and techniques: Only well

delineated, circumscribed tumors could be operated radically, and with good success. Contrast enhanced MRI was the most important factor in predicting operability. Radical removal was avoided in cases of diffuse, infiltrative tumors, instead decompression, biopsy, and radiotherapy was done. At surgery bony exposure was kept at minimum, using a wide spectrum of minimally invasive approaches and standard microsurgical techniques were applied. In the high cervical group special postoperative intensive care was needed due to respiratory and lower cranial nerve problems. Rehabilitation was also necessary in most of the cases.

Results: Outcomes were measured according to the McCormick classification. According to our follow-up survey, most of our patients are still alive, if the underlying pathology permitted. The longest survival is 20 years, 18 had died on various reasons.

Conclusion: Surgery should be done as soon as possible, in spite of the risks, since quality of life depends on the preoperative state. Therefore, we adopted an aggressive surgical strategy, and gros total removal was the goal to be achieved. Radiotherapy was applied depending on histology, and rehabilitation was followed after radical surgery.

The brain tumour patient and caregiver: what is important for the journey?

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Brain tumours are one of the most devastating of diagnoses. Whether benign or malignant, primary or secondary, they strike at the very core of who a person is, affecting not only physical abilities, but an individual's cognitive and psychosocial aspects as well.

One of the most notable things about brain tumours is that they intersect three major disease areas: cancer, neurological disease and rare disease.

Brain tumours are no respecter of race, religion, sex, age or geography. They strike people around the globe indiscriminately, and present a formidable enemy in any language.

Brain tumour patients and their caregivers face many medical, social and psychological challenges.

But there are also other challenges for brain tumour patients and their caregivers beyond the medical ramifications – political and financial challenges which impact on each and every person on this journey.

This presentation will include a discussion of these challenges as well as observations from the "coalface" as the speaker brings to the topic her own personal experiences as a caregiver to her young adult son Colin who was diagnosed with a grade two astrocytoma in 2004 at age 24 and passed away seven years later, in 2011, at age 32 from a glioblastoma multiforme. This presentation will also focus on the role of brain tumour patient support organisations and the brain tumour caregiver.

Intracranial hemangiopericytomas lack typical cytogenetic and epigenetic features of meningiomas and gliomas

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Objective: Intracranial hemangiopericytomas (cHPC) are rare tumors of mesenchymal origin with a high proclivity towards recurrence and extraneural metastasis. Total tumor resection is the main treatment of choice due to its radiochemical resistant nature. Considering the paucity of reports dealing with the tumor genetics and epigenetics of cHPC and the still ongoing debate over their histological standing, we examined a series of 9 cHPC for known important meningioma and glioma specific cytogenetic and epigenetic aberrations.

Methods: In a total of nine histopathologically confirmed cHPC, this study evaluated the promoter methylation status of MGMT, p15(CDKN2B), p16INK4A, TIMP3 and NDRG2 genes which have been shown to be epigenetically altered in gliomas and meningiomas, respectively. Typical numerical chromosomal aberrations reported in gliomas and meningiomas were investigated using two-color fl uorescent in situ hybridization (FISH) on touch-preparations with locus specific probe pairs detecting 1p36/22q11, 14q24/18q21, and 9p21/10q23. Additionally, conventional comparative genomic hybridization (CGH) was performed to access genomic imbalances.

Results: All studied cases presented with an unmethylated status of the MGMT, p15 and TIMP3 promoters. One specimen was encountered with positive methylation signal for p16 in methylation specific PCR analysis. Direct bisulfite sequencing for NDRG2 revealed only in 1 of 6 cases a moderately elevated average methylation degree. In FISH analyses, disomy for all targeted chromosomal regions was found in 5 of 9 studied cHPC specimens; in two tumors an oligocellular clone with hemizygous loss of 10q23 was detected. In one other specimen, virtually all nuclei harbored a hemizygous deletion of 9p21. One further cranial hemangiopericytoma was characterized by a tetraploid mainline with slight sidelines that contained trisomies of 9p21 and 10q23. CGH analysis showed a chromosomal imbalance in all nine specimens involving loss and or gains of partial or complete chromosome segments. The one cHPC specimen that presented with positive methylation for p16 harbored the hemizygous deletion of 9p21 with corresponding loss of chromosome 9p in CGH.

Conclusions: This work shows that cHPC obviously lack glioma and meningioma specific epigenetic and molecular cytogenetic lesions, further providing evidence that cHPC represent a distinct tumor entity with different genetic features. These present findings prompt one to speculate on the possible role of the inactivation of p16INK4a, and deletions on chromosome 9p in the underlying tumorigenesis of a subgroup of cranial hemangiopericytomas.

Controversies in pathological bone fracture of the spine

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New imaging technologies offer for neurosurgeons important preoperative and postoperative data for spinal fractures. It is possible now to make the differential diagnosis for pathological bone fracture, to distinguish the tumoral from osteoporotic fractures. The new MRI techniques we

currently use in Neurosurgical Clinic, County Hospital Timisoara are: diffusion weighted image(DWI) and spectroscopy (H-MRS) MRI SPECTROSCOPY â€“ can evaluate intra-lesional components (metabolites). Offers the opportunity for establishing differential diagnosis (infl ammatory, tumoral, osteoporosis) DIFFUSION WEIGHTED IMAGING (DWI)-is using the water diffusivity properties; the ADC coeffcient is very different in osteoporotic comparing with tumoral fractures, helping in differential diagnosis. Acquisitions are made with 1,5 T MRI, SIEMENS, Avanto. We have examined 15 pacients with pathological bone fracture of spine: 10 osteoporotic and 5 neoplasic fractures. 13 pacient needed surgery and we have anatomo-pathological examination for this patients.. Conclusions: Using new imaging technologies we can , with 86% sensitivity of this methods, to establish the metabolic lesional components. Our study make the differential diagnosis in pathological bone fractures using diffusion and MR spectroscopy.

Introduction: New imaging technologies offer for neurosurgeons important preoperative and postoperative data for spinal fractures. It is possible now to make the differential diagnosis for pathological bone fracture, to distinguish the tumoral from osteoporotic fractures. The new MRI techniques we currently use in Neurosurgical Clinic, County Hospital Timisoara are: diffusion weighted image(DWI) and spectroscopy (H-MRS)

Aim: To evaluate if it is possible now to make the differential diagnosis for pathological bone fracture, to distinguish the tumoral from osteoporotic fractures.

Case report: We have examined 15 patients with pathological bone fracture of spine: 10 osteoporotic and 5 neoplasic fractures. 13 patient needed surgery and we have anatomo-pathological examination for this patients.

Material and methods: MRI SPECTROSCOPY â€“ can evaluate intra-lesional components (metabolites). Offers the opportunity for establishing differential diagnosis (infl ammatory, tumoral, osteoporosis) DIFFUSION WEIGHTED IMAGING (DWI)-is using the water diffusivity properties; the ADC coefficient is very different as value in osteoporotic comparing with tumoral fractures, helping in differential diagnosis.

Results: Using new imaging technologies we can, with 86% sensitivity of this methods, to establish the metabolic lesional components of bone fractures of spine.

Conclusion: Our study succeed to make the differential diagnosis in pathological bone fractures using diffusion (DWI) and MR spectroscopy MR techniques.

Cerebral metastases-preoperative diagnostic, possible or not?

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New development in imaging technologies brings for neurosurgeons important preoperative and postoperative prospects for intracranial lesions and especially for cerebral metastatic disease evaluation. The new MRI techniques we currently use in Neurosurgical Clinic, County Hospital Timisoara are: DTI (diffusion tensor imaging), DWI(diffusion weighted imaging), cerebral spectroscopy, SWI (susceptibility weighted imaging),

cerebral perfusion(PWI) DTI (diffusion tensor imaging)- MRI techniqueapplication is useful for localizing white mater tracts in relation with intracranial lesions, MRI SPECTROSCOPY â€“ can evaluate intra-lesional components (metabolites). Offers the opportunity for establishing differential diagnosis (ischemic, infl ammatory, tumoral). In tumor pathology it is used to establish tumoral grading, and to differentiate the metastatic from primary cerebral tumors. SWI (susceptibility weighted imaging) - a very new sequence in MRI which evaluates magnetic properties of blood, iron and other structures. Now it is used for diffuse axonal injuries, micro bleeds, angiogenesis in tumors, venous angiomas (slow fl ow vessels). Acquisitions are made with 1,5 T MRI, Avanto in â€oeNeuromed â€oe Diagnostic Image Center Timisoara. Conclusions: Using new imaging technologies we can , with 95% sensitivity and 91% sensibility of this methods, to establish the metabolic lesional components. Our study tries to make the difference in cerebral lesional evaluation of primary cerebral tumors from metastatic cerebral lesions.

Introduction: New development in imaging technologies brings for neurosurgeons important preoperative and postoperative prospects for intracranial lesions and especially for cerebral metastatic disease evaluation. The new MRI techniques we currently use in Neurosurgical Clinic, County Hospital Timisoara are: DTI (diffusion tensor imaging), DWI (diffusion weighted imaging), cerebral spectroscopy, SWI (susceptibility weighted imaging), cerebral perfusion (PWI).

Aim: Our study tries to make the difference in cerebral lesional evaluation of primary cerebral tumors from metastatic cerebral lesions.

Case report: Our study is made for 30 patients with secondary cerebral tumors.

Material and methods: Acquisition is made with 1,5 T MRI in â€oeNeuromed â€oe Diagnostic Image Center Timisoara. Used MRI techniques are: DTI (diffusion tensor imaging) - MRI technique-application is useful for localizing white mater tracts in relation with intracranial lesions, MRI SPECTROSCOPY â€“ can evaluate intra-lesional components (metabolites). Offers the opportunity for establishing differential diagnosis (ischemic, infl ammatory, tumoral). In tumor pathology it is used to establish tumoral grading, and to differentiate the metastatic from primary cerebral tumors. SWI (susceptibility weighted imaging) - a very new sequence in MRI which evaluates magnetic properties of blood, iron and other structures. Now it is used for diffuse axonal injuries, micro bleeds, angiogenesis in tumors, venous angiomas (slow flow vessels).

Results: Using new imaging technologies we can, with 95% sensitivity and 81% specificity of this methods, to establish the metabolic lesional components.

Conclusion: Using new imaging technologies we can, with 95% sensitivity and 81% specificity of this methods, to establish the metabolic lesional components. Our study tries to make the difference in cerebral lesional evaluation of primary cerebral tumors from metastatic cerebral lesions.

Follow-up in operated and non-operated low grade gliomas

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The follow-up in low grade gliomas can be accomplished in very good condition establishing protocols for each category of cases: operated and non -operated patients. In our clinic we have a 5 years followed -up 150 low grade gliomas: 85 operated, 65 non -operated. The protocol in this moment is :in first year, every 3 months conventional cerebral MR, in 2-nd and 3-d year every 6 month conventional MR, after that every year conventional cerebral MR. In every year we have a imaging neurodiagnose MRI made with spectroscopy, diffusion, perfusion and swi. Those protocols brings better results in this low grade gliomas follow-up. We can appreciate that by following this protocol. We can see the moment when this gliomas turn into high grade and we appreciate the moment of recurrence in post surgical cases.

Introduction: The follow-up in low grade gliomas can be accomplished in very good condition establishing protocols for each category of cases: operated and non -operated patients.

Aim: The aim of our study was to share our experience in this diffcult follow -up of low grade gliomas.

Case report: In our clinic we have in 5 years followed-up 150 low grade gliomas: 85 operated, 65 non-operated. The protocol in this moment is: in first year, every 3 months conventional cerebral MR, in 2-nd and 3-rd year every 6 month conventional MR, after that every year conventional cerebral MR.

Material and methods: In every year we have a neurodiagnostic imaging MRI made with spectroscopy, diffusion, perfusion and swi.

Results: Our results were good, better than before this period of non protocoled follow up in low grade gliomas.

Conclusion: We can appreciate that following this protocol we can see the moment when this gliomas turn in high grade, and to appreciate the moment of recurrence in post surgical cases.

Common igs planning support for frame-based stereotaxy and frameless navigation

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Our Vister3D system is a new prototype of planning platform for frame-based and frameless stereotactic interventions which integrates most important elements of image guided navigation. According to general opinion, the frame-based systems have the advantage of proven clinical utility and instrument carriage with a high degree of mechanical stability and accuracy. Frameless methods are more complex, but also very fl exible, and have already many applications in general neurosurgery. In general, comparisons until now have been limited between different planning platforms and different surgical sessions, utilizing commercial neuronavigation systems. Vister3D planning platform integrates calculations for arc-based stereotactic frames (Riechert-Mundinger and MHT, Freiburg, Germany) into frameless neuronavigation environments. The system communicates with Polaris-

type cameras (Northern Digital Inc, Canada); registers surgical space to diagnostic images and visualizes tracked devices in volumetric and surface views. During frame-based stereotaxy, rigid reference system (marker plates) with recognizable landmarks in images, are used to align stereotactic space with imaging volume. The integrated platform is supported by detailed data parsing (for DICOM and NIFTI images, as well as archive studies), CT-MR fusion algorithm (with subvolume targeting) and different 3D visualizations. The system is designed to determine the geometrical overlap of targeting, carried out, either in stereotactic space of the arc-based frame, or in moving reference space of the navigation platform. The main challenge in comparison is to have computations of identical rules for both environments. Therefore, Vister3D uses strictly 3D-based algorithms to get projection transform between any two coordinate spaces, that guarantees full transparency between frame-based and frameless techniques.

Objectives: The main motivation of this work is to develop a common IGS (image-guided surgical) platform which is suitable for sharing surgical planning data in frame-based stereotaxy and frameless, navigated brain surgery. The comparison until now has been based on planning with different platforms and review of associated variables of both techniques. In biopsy the final outcomes are compared by pathology diagnostic accuracy and (in electrode placement as well) immediate post-operative CT imaging. The eligibility of frameless technique depends on target size, anatomical location, with an ongoing debate on un-quantifiable variables which ultimately infl uence technique selection (anesthesia, size of craniostomy, diagnostic yield, etc).

Aims of study: Our new planning/navigation system has been designed with practical necessity for easy modification with minimum cost. Accordingly, the support for new ideas from surgical side is possible with a simple but accurate realization.

Case report: Vister3D is usable for planning target and entry positions for DBS electrodes and sampling parameters along the path of biopsy needle. After graphical planning the surgeon can proceed with frame-based stereotaxial intervention or frameless navigation technique. The frameless method can be turned into different tracking modes supporting diagnostic needs during surgeries (tumor resection support, 3D localization of features, etc).

Material and methods: In our approach, common IGS platform integrates fusioned CT and MR images and standard 3D planning tools for target trajectory. The electrode placement or biopsy techniques include Riechert-Mundinger or MHT (Freiburg, Germany) stereotactic frames. The IGS platform is able to calculate parameter settings for these frames with a newly developed algorithm providing for 3D transforms between diagnostic space, stereotactic space and patient local reference (AC-PC). Moreover, the platform communicates with Polaris Spectra and Vicra optical tracking devices (Northern Digital, Inc.) and registers surgical space to diagnostic data. Alignment tests of frame-based and frameless geometries are possible: 1/ Static: calibration procedures have been used to find the origin and axes direction of the arc-based system within the frameless reference. By collecting samples

from the frame geometry (with the pointer of navigation system), statistical calculation gives an estimate for location/orientation of stereotactic space within the frameless environments. 2/ Dynamic: display/refresh polar coordinates for actual position of navigated device. The actual navigated position has been registered in CT volume and projected into stereotactic space using the registration transform of stereotactic space. After it, - if the tracked device crossed distance of planned entry from the arc-surface, the device tip has been set as target position, and the cross point used as entry point and the polar settings continuously updated with these points.

Results: Vister3D now is routinely used in planning trajectories for DBS electrode placement and biopsy sampling. Number of frame-based stereotactic surgeries performed by the system now is close to 50. The planning procedure is very straightforward and easy to follow, thanks to the hierarchical workfl ow implemented in the system. The subvolume-targeted CT-MR fusion is found usable in finding the most accurate MR registration when compared to fusion with the whole volumes. Stereotactic planning of target trajectory can follow steps known in the frame-based technique (finding the polar settings for DBS electrode or biopsy needle in frame reference), or can use the interface for frameless neuronavigation system. These results have been compared, and in some cases the electrode movement was detected by optical tracker and displayed with frame-based, planned data. In this tracking mode, the system converted the actual location/orientation of device into polar coordinates and, in parallel, visualized the model in CT volume. The difference between the planned and actual polar settings was tested. This difference proved to be very sensitive to the device calibration accuracy (i.e. the transform from tool sensor space to device coordinate space).

Conclusions: Novel 3D algorithm has been implemented for frame-based stereotactic planning, which follows the rules known in frameless neuronavigation. This approach could help in a unified treatment of both techniques and can make the interpretations (at least) computationally transparent. Direct comparison of surgeries using frame-based stereotaxy with sensor tracking approach is possible with this development. Critical issue is the device calibration i.e. the accuracy of transform between the DBS electrode or biopsy needle geometry and the attached sensorâ€™s space. Further work is needed to explore more meaningful applications of the system.

Cauda equina cavernoma:clinical case prezentation and rewieu of the genetic findings

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Objectives: To present an rarely encountered case, diagnosed and operated in the Neurosurgery Department of Pitesti of a patients with cauda equina cavernoma, which is the 15th worldwide case cited in the literature.

Material and methods: We present differential diagnosis in terms of clinical

and imaging, and surgical technique approached and post-operative results. It is about 60 years old patient hospitalized for it atrocious lumbar pain, paravertebral muscle contraction associated with bilateral lombosciatica, relatively poorly systematized, installed after a heavy lifting exercise. Simple X-ray orients us toward disc pain,highlighting a pinched L5-S1 disc space and posterior osteophytes at this level. We performed a lumbar spine CT highlighting an area of spontaneous hiperdensitay apparently intradural, at L4, followed by MRI showing a well defined formation in T1 hipersemnal with areas of hemosideria located at the cauda equina level. We intervened surgically, ablation being performed entirely under the operator microscope of a purplish tumor, well defined, with diameter about 1.5 cm, developed between ponytail roots at L4 level Complete clinical remission after surgery.

It is a benign hamatom with vascular origin, occurring forms involving sporadic or familial forms of vascular malformations with autosomal – dominant transmission. Etiology is unknown.In sporadic forms that implies a solitary cavernoma a contributinf factor that could induce cavernomas is radiotherapy. Family forms involving two or more cavernoame occur in 50% of Hispanic patients and 10-20% in the Caucasian population. We identified mutations in 3 genes, with diferent loci 15:

1. CCM 1 on chromosome 7q 21.2, KRITI-1 gene increases endothelial proliferation;

2. CCM2-15-p13 on chromosome 7p, MGC 4607 gene-role in the cellular response to osmolar insults. Togheter with gene located on p 38 MAPKs give signals for modeling and vascular maturation;

3. CCM3 on chromosome 3q25.2- -q27, the gene that encodes 212 amino acids 10 PDCD with role in apoptosis (a small muscle cells). In our case we didnt had the possibility to perform genetic studies.

Conclusions: Cavernoimas found at the cauda equina lelvel is exceptional, this beeing only the 15th case publied in literature Clinical symptoms include sphincter disturbances, motor and sensitivity acusses, our case having a totally atypical symptomatology. In our opinion, acute symptoms of the disease were caused by intratumoral bleeding, confirmed by histopathological examination. In terms of surgery our approach is through 2-level laminectomy, opening dura mater and cavernoma dissection grom cauda equina roots.

Treatment of peripheral nerve tumors - multidisciplinary approach

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Objectives: Peripheral nerve tumors are relatively rare lesions. Most of these tumors are benign lesions built from the neural sheath cells: Schwann cells, perineurial cells and fibroblasts.

Aims of study: Aim of this paper is to present and analyze results of treatment of peripheral nerve tumors of all patients treated in our clinic during last ten years.

Case study: In this study, we included all patients treated in our Clinic, during last

ten years, who have been admitted for surgical treatment of peripheral nerve tumor. Relevant data about every patient, diagnostic procedures, course of treatment and outcome, has been collected through detailed analysis of 39 patient histories.

Material and methods: We analyzed demographic data, clinical presentation (occurrence of pain and paresthesia as symptoms, neurological deficit – quantified in six-grade system (M0-M5 and S0-S5 respectably), localization, size of the lesion, used diagnostic procedures, pathohystological type of tumor, and finally, treatment of choice for each case.

Results: Analysis showed that there was slight gender predominance (53.8% female, and 46.2% male). Over half of all patients (61.6%) were treated in six months to one year after first symptom occurred. Most common tumor of peripheral nerves is schwannoma (66.7%). Method of choice was microsurgical resection. In about 80% of all threated patients, after surgery, baseline function was preserved or improved.

Conclusions: Clinical presentation, diagnosis, indication for specific type of treatment for peripheral nerve tumors are still actual debate topic. However, all collected data show that individual and multidisciplinary approach is necessary in treatment of these tumors.

Low grade gliomas – how to deal with

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Introduction: Low grade gliomas represent a relative frequent part of the tumoral pathology of the CNS, with a highly potential to recurrence and progression. We wanted to determine the prognostic factors associated with these two possibilities of evolution.

Material and methods: We have retrospectively analyzed the cases of low grade gliomas from the 3rd neurosurgical department at Clinical emergency hospital "Prof. Dr. N. Oblu" Iasi from the last 5 years, 2008 -2012

Results: Low grade gliomas represent 15 to 20 % of CNS tumors and aff ects mostly the young adults, 50% of our patients having ages between 20 and 40 years, with a slightly male predominance M:F ration 1,31:1. The most common presenting symptom was represented by seizures 70% of cases, the most frequent cerebral lobes were the frontal 46% and insular lobes 31%. 3 or more lobes were involved in only 17% od cases. Contrast enhancement was observed in half of the cases comprised in our series and 31% presented a mixt structure of the tumor, solid and cystic component or solid with calcifications. 97% of the cases underwent surgical resection as a first line treatment with a rate of gross total resection of 41%. Adjuvant treatment after surgery was used in 8 cases, with equal distribution between combined RxT+CHT and RxT alone. The median follow up period was, and during this period we had 27% recurrences 11 cases from which 7 cases presented malignant transformation. The treatment of recurrences was represented by in 63% and RxT in 27% of the cases.

Conclusions: LGG represent a relative frequent pathology, with a better prognostic compared with their counterparts (high grade gliomas), but with a real potential of recurrence and progression (gross total

resection being often difficult to achieve) facts that emphases the need for a close and rigorous follow up which sometimes can be difficult and which sometimes puts the neurosurgeon in a difficult position with regard to further treatment decisions.

Gamma-knife radiosurgery in brain metastases

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Introduction: At least 12-13% of cancer patients develop symptomatic brain metastases and this figure is likely to rise as diagnostic technologies improve, allowing additional occurrences to be identified. With no treatment, patients with symptomatic brain metastases usually die within two months of diagnosis. However, early diagnosis and vigorous treatment, while rarely curative, may lead to a useful remission of neurological symptoms and enhance the quality of a patient's life, as well as, prolong survival. Given the number of cases, the question arises, how many of these cases are appropriate for Gamma-Knife Radiosurgery?

Material and methods: Indications for Gamma-Knife Radiosurgery in Brain Metastases are presented in relation with their location (deep seated or in eloquent areas) and their pathology. Comparisons to alternative treatments (radiosurgery versus surgical resection, radiosurgery versus whole brain radiotherapy) and various combined indications (surgery, whole brain radiotherapy and radiosurgery) are reviewed using well established predictive factors regarding the clinical benefit for the patients with brain metastases, as part of an evidence-based clinical practice guideline.

Results: Brain metastases are excellent targets for Gamma-Knife Radiosurgery.

This treatment has an important role in the management of patients with metastatic brain tumors. The authors present their experience, as well as studies from across the world, which have shown its eff ectiveness in treatment of brain metastases. Local control provided by radiosurgery for the management of metastatic brain tumors in any brain location exceeds 85% on average. There is also a cost-effectiveness analysis of the economic impact of stereotactic radiosurgery for patients harboring brain metastases and improvement of the quality of life for these patients.

Conclusions: Brain metastases constitute a significant disease burden and have major impact on morbidity and mortality. This presentation reveals the relative merits of stereotactic radiosurgery, whole brain radiotherapy and open surgery, which have to be used alone or in combination for the treatment of patients with brain metastases. Treatment aims to provide disease control with a good quality of life, although prolonged survival may not be always be achieved.

The effect of ferite nanoparticles on brain tumours in vitro

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One factor contributing to the poor response to the therapy of brain tumour

patients is the limitation of conventional drug delivery systems. Recently, magnetic nanoparticles received enormous attention as new tools for drug delivery in cancer treatment. The aim of this study was to analyse the toxic effect of ferite nanoparticles in vitro, in order to evaluate their biological compatibility as drug support in brain tumour tratment. For this reason, we used two brain tumour primary cell cultutes: glioblastoma GB3B cells and astrocytoma AC1B cells. As a normal control, we used human fibroblast HDF cells. The cells were exposed to 0,25 ug/ml, 0,5Aμg/ml 1 ug/ml ferrite nanoparticles and the proliferation rates were evaluated 24, 48 and 72 hours, after the treatment. Statistical analysis revealed that no significant effect of ferrite nanoparticles treatment was induced on malignant or normal cell lines used in this study (pï€¾0,05). In conclussion, our results showed that ferite nanoparticles, did not cause significant cytotoxicity in brain tumour cells and encourage the use of these compound as drug carrier in brain cancer treatment Grant support: 134/2011 UEFISCDI Romania

Multiple functional image-guided resection of cerebral low grade glioma

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Objectives: Early and extensive resection of low-grade gliomas (LGGs) may lead to better patients survival. Nevertheless, resection of LGGs is often limited by extensive involvement of functional brain areas. We describe the surgical management of patients with tumors at risk due to their diffuse nature and relationships with functional neural tissue.

Material and methods: The use of multimodal neuroimaging, including routine MRI for intraoperative neuronavigation, functional MRI with speech and motor mapping, diffusion tensor imaging and tractography, and CT/MR perfusion, is described in preoperative evaluation of LGGs.

Navigated Transcranial Magnetic Stimulation (nTMS) was performed to map the motor cortex. Intraoperative motor mapping and monitoring were performed in a consecutive series of patients.

Tumor removal was performed through a transsylvian approach for insular lesions, and through a trans-sulcal approach in stimulation-confirmed noneloquent areas for all other lesions. Resection was continued until neuronavigation-evidenced normal white matter or cortical or subcortical stimulation revealed functional areas.

Results: Gross-total resection was achieved in 78% of cases, as assessed by postoperative MRI. Over the average follow-up duration of 24 months, no patient experienced tumor progression or recurrence. No patient experienced new deficits at the long-term follow up. Intraoperative mapping and clinical results demonstrated that pre-operative planning using multimodal neuroimaging and nTMS reliably identifies distribution of tumor, eloquent brain structures and their relationships.

Conclusions: Significant resection of diff use LGGs is possible, even in presumed eloquent neural tissue, without necessarily causing permanent neurological deficits. Individualized preoperative neuroimaging evaluation, with pre- and intraoperative speech and motor mapping, is an essential tool in achieving a good outcome.

Genetic heterogeneity in gliomas

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Gliomas display a wide range of histopathological features and biological behavior, and an inherent tendency to progress to a highly malignant phenotype. Molecular- and cytogenetic studies revealed that different grades of gliomas correlate with specific genetic alterations. Glioblastomas, the most malignant form of gliomas, may develop de novo (primary glioblastomas) or through progression from low-grade or anaplastic astrocytomas (secondary glioblastomas).

To analyze the genetic heterogeneity, we performed different cytogenetic methods considering their methodic limitations. Cell culture analysis may be biased by clonal selection artifacts. Homogenized tissue lacks control over the tissue composition and permits contamination of the tumor specimen with preexisting and reactive nonneoplastic tissue. Moreover, gliomas exhibit a diffuse infiltrating growth pattern into normal brain so that no tumor area contains a uniform cellular composition. In order to evaluate an intratumoral genetic heterogeneity we performed FISH investigations and microdissection analysis in paraffin-embedded glioma tissue and correlated the cytogenetic data with the histomorphology of the given tumor areas.

Low-grade astrocytomas most often showed normal karyotypes, by conventional cytogenetic methods. However, we were able to identify numerous alterations in low-grade astrocytomas, especially in areas with a gemistocytic appearance. Primary glioblastomas and secondary glioblastomas showed consistant as well as different genetic findings, which correlate partial with the histomorphological features of the investigated areas. Our results provide clear evidence of inter- and intratumoral genetic heterogeneity in gliomas independent of the applied method. In order to develop genetic prognostic criteria, the distinct genetic heterogeneity of these tumors has to be considered.

Preoperative surgical planning with probabilistic fibre tractography

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Deterministic tractography are primarily based upon streamline algorithms where the local tract direction is defined by the major eigenvector of the diffusion tensor (white matter tractography). On the other hand the probabilistic tractrography uses the anisotropy of water to generate probabilistic maps of connectivity between brain regions and it may draw fibers into the grey matter. In the last decade numerous software was made to process Diffusion Tensor MRI data and the application of tractrography has become more and more widespread in the neurosurgery. In this paper, we present our experiences and future opportunities of preoperative planning of brain surgery with the aid of probabilistic fibre tractography. In the course of our work we used 3T 32 directions diff usion-weighting and high resolution T1 MR Images, FMRIB Software Library (FSL 5.0) and 3D Slicer software. At the surgical planning of the brain tumours in the delicate regions we visualized eloquent intact tracts in vivo to avoid them. This method is widely used for visualization of corticospinal tract pathway in the surgery of central region tumours. In

addition, we used tractography maps for surgery of tumours in the vicinity of language-related regions and improving the stereotactic targets of Deep Brain Stimulations in movement disorders. The fibre tractography help to understand for the neurosurgeons the advantages and disadvantages of approaches in order to most benefit from pre-surgical mapping.

Objectives: Deterministic tractography are primarily based upon streamline algorithms where the local tract direction is defined by the major eigenvector of the diffusion tensor (white matter tractography). On the other hand the probabilistic tractrography uses the anisotropy of water to generate probabilistic maps of connectivity between brain regions and it may draw fibers into the grey matter. In the last decade numerous software was made to process Diffusion Tensor MRI data and the application of tractrography has become more and more widespread in the neurosurgery.

Aims of study: In this paper, we present our experiences and future opportunities of preoperative planning of brain surgery with the aid of probabilistic fibre tractography.

Material and methods: In the course of our work we used 3T 32 directions diffusionweighting and high resolution T1 MR Images, FMRIB Software Library (FSL 5.0) and 3D Slicer software.

Results: At the surgical planning of the brain tumours in the delicate regions we visualized eloquent intact tracts in vivo to avoid them. This method is widely used for visualization of corticospinal tract pathway in the surgery of central region tumours. In addition, we used tractography maps for surgery of tumours in the vicinity of language-related regions and improving the stereotactic targets of Deep Brain Stimulations in movement disorders.

Conclusions: The fibre tractography help to understand for the neurosurgeons the advantages and disadvantages of approaches in order to most benefit from pre-surgical mapping.