

1st Regional Congress of Neurosurgery in the Danube-Carpathian Region

Neurosurgical Controversies

26th - 27th May 2011

ABSTRACTS

Predictive outcome factors by open surgery in intracranial aneurysms (IA). An experience of 628 cases

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Background: The intracranial aneurysm (I.A.) has a prevalence between 0,2-7,9% in the literature. The variability depends of hospital referral, neuroimaging findings and autopsy pattern. The pathology of intracranial aneurysms is a dominant element in neurosurgical activity, because of the multiple preoperative and management problems.

IA affect mainly the active age (40 and 60 years old) and the male sex. Generally the incidence in USA is 10-28/100.000 (official data).

The etiology of IA may be: congenital, (aneurysms appear due to a defect of the muscular layer of the arterial wall), arterial hypertension, neoplastic disease, atherosclerosis, inherited diseases, trauma, infection (mycotic an.), unknown causes. In all the cases of aneurysm ruptures, some of the following are incriminated as risk factors: cigarette smoking, alcohol excess, life stress.

The cerebral circulation must be evaluated in totality and aneurysms in

particular and the accuracy management is necessary for limitation of important lifethreatening complication (rebleeding and ischemic stroke).

Material & Methods: The authors present a study about 628 consecutive operated patients with intracranial aneurysms, operated in first Neurosurgical Department between 1997- December 2010 – 14 years - (40 children and 588 adults). Most cases (286 case - 45,5%) were between 41 and 50 years old. Male is the preponderent sex - 427 cases (68%) (2,1 : 1). The symptoms were dominated by: headache (98%), stiffneck (94%) and focal neurologic deficit (71%) etc. Most patients were Hunt and Hess grade II (230 cases, 36,7%) and Hunt and Hess grade 3 (97 cases, 15,4%) at admission. The associated pathology was: systemic arterial hypertension (471 cases, 75%) and obesity/hypercholesterolemia (214 cases, 34,1%), ischemic cardiopathy (100 cases,16%), diabetes melitus (100 cases,16%), chronic alcoholism (82 cases,13%), ischemic stroke (75 cases,12%), atrial fibrillation (63 cases, 10%), miscellanea (88 cases, 14%, anticoagulant therapy).

The main investigations were: CT scan, DS angiography. Actually, the most important were 3D DS Angiography and 3D CT AngioCT.

The common localization of intracranial aneurysms was the anterior communicating artery 183 cases (29,1%); the other locations

were: medium cerebral artery 157 cases (25%), posterior communicating artery 107 cases (17%), internal carotid artery 84 cases, (13,3%), basilar top artery cases 21 (3,3%) and vertebral artery 11 cases (1,8%). Multiple aneurysm represent in our data 65 cases (10,3%).

All cases were operated, as soon as possible after the subarachnoid hemorrhage (SAH) and IA angiography diagnosis. "Early surgery" eliminates the risk of re-bleeding and facilitates the treatment of vasospasm which peak is between 6-8 days post SAH.

From all complications two are very critical for life and morbidity: aneurysm rebleeding and cerebral ischemia.

The authors present by personal experience the outcome predictive factors : age (up to 65 and under 5 years) associated pathology (arterial hypertension 491 cases (78,1%)), obesity and hypercholesterolemia 214 cases (38,3%), ischemic cardiopathy 107 cases (17%), diabetes mielitis 11 cases (16%) and so on, subarachnoid hemorrhage diffusion (according to the Fisher scale), aneurysm particularities – number, shape, size, association with AVMs, aneurysm timing of operation, brain relaxation (hyperventilation and CSF drainage) aneurysm rerupture, peroperative vasospasm, ICU facilities, possibilities of coiling treatment, early neuroprotection and neurorehabilitation.

The Glasgow Outcome Scale (GOS) in our data (at 6 months postoperator) shows: good recovery 421 cases (67%), moderate disability 148 cases (23.5%), severe disability 31 cases (4.9%), persistent vegetative state 7 cases (1.1%), death 21 cases (3.4%).

Conclusions: IA represents an important neurosurgical challenge. Also IA by the rupture and complication is the real lifethreatening diseases. Clinical features are dominated by SAH & neurological signs

(Hunt and Hess scale-1968, was perfectly useful).

Complete vascular exclusion is the treatment of choice by open microsurgical approach or endovascular embolization.

The important measures to avoid rebleeding and cerebral ischemic stroke in intracranial aneurysms are perfect evaluation and early approach, perfect aneurysm dissection and neuroprotective measures (pre, intra and postoperative). Neuroprotective agents – useful to avoid cerebral ischemic stroke The timing of aneurysm surgery is one of the key of avoidance lifethreatening complication.

Recent diagnostic and therapeutic management of gliomas with special emphasis on 3T intraoperative MR (239 cases)

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Brain gliomas are the most frequent primary brain tumors. They include a variety of histological subtypes and diagnostics is based on histological classification which relies on morphological findings in the tumor tissue. The treatment is still complicated and not as successful as one would expect. However, in last years new diagnostic and treatment methods were introduced. In nonrandom chromosomal aberrations and gene mutations were found in last decade. As a one of first steps in tumorigenesis mutation of IDH1/2 was revealed in low-grade gliomas. Duplication of BRAF gene was found in pilocytic astrocytomas. New chemotherapeutic agents are constantly put in trials, temozolomide has become the "golden" standard in the treatment of

malignant gliomas. The extent of resection of glioma seems to be a very important factor in progression-free and overall survival not only in high-grade but also in low-grade gliomas.

Methods: Since April 2008 the image-guided surgical suite is routinely used for glioma surgery. The suite is directly connected with 3.0T MR scanner (GE) by rail-based transfer system (Maquet) and capable to perform intraoperative MR examination (iMRI). A consecutive series of 213 patients undergoing surgery with iMRI is presented. All patients signed an informed consent for iMRI examination. Patient's head is fixed in 3.0T MR compatible headholder. Surgery may be interrupted according to neurosurgeon decision at any moment and iMRI is then performed. The iMRI takes about 15-20 minutes depending on the MR examination protocol.

Results: Since April 2008 to December 2010, 213 glioma patients underwent 239 surgeries (200 resections, 38 stereobiopsies, 1 tumor cyst puncture) with iMRI. We have performed a prospective study to evaluate the safety and efficacy of iMRI in this consecutive series. In 101 patients the radical resection was intended and it was achieved in 80 (80%). Unexpectedly, in the group of non-intended radical resection in 10 cases of 99, radical resection was achieved. In total in 90 of 200 cases the tumor was radically resected (MR radicality), in 45% of all resections. In comparison with our older series the radicality ratio doubled (from 22% in 2006 to 45% in 2010). iMRI changed the surgery strategy in 25% of all cases, the resection continued after the iMRI. The goal of resection was achieved in 177 surgeries, in 23 cases the resection could have been more extensive by retrospective analysis. Mortality in the series was 2,9% (7 patients), most common cause of death was

haematoma (5 cases). Morbidity was 26,7% (64 patients – any kind of complication) but serious worsening was observed only in 7,1% (17 patients.). Total MM was thus 10% (9 haematomas, 15 neurological worsenings).

Conclusions: One of the new “most challenging” tools in gliomas seems to be intraoperative MR examination. It is a valuable method for gliomas, efficient and safe. In our experience the resection radicality increased more than twice with iMRI. The morbidity/mortality rate is slightly higher in our series, but still acceptable.

Treatment of supratentorial low-grade gliomas: surgical versus conservative

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The management of low grade glioma is one of the most controversial areas in clinical neuro-oncology. There are numerous communications outlining the difficulties in management of these lesions. Indeed, the principal questions about their management remain unanswered. However, the concept of management of low grade gliomas is not unitary but much more a composite of different challenges depending on the clinical presentation, signs, neuroradiology, perspectives of neurologists, the opinion of the neurosurgeon, and perhaps most importantly, the aspirations of the patient. It is true therefore that in many patients there will be a dilemma about what is considered optimal management since there is no good evidence base to underpin any single management undertaken. Conversely, however, there are many groups of patients with various low grade gliomas in whom management decisions

are made more easily and pragmatically. In this presentation, the current approaches to different low grade gliomas presenting with different symptom complexes in different regions of the brain will be reviewed and the rationale for decision making discussed.

Under the recent World Health Organization classification of primary intracranial tumors, low grade gliomas would encompass grade I and grade II neuro-epithelial tumors. The more common grade I tumors are pilocytic astrocytoma, dysembryoblastic neuro-epithelial tumors (DNET), pleomorphic xantho-astrocytoma (PXA), neurocytoma, and ganglioglioma. The more common grade II tumors include astrocytoma, oligodendroglioma, and mixed oligoastrocytoma. This spectrum of neuropathological entities is important since the grade I tumors generally can be cured by surgical excision and their symptoms very often alleviated. In turn, with the grade II tumors, these are generally incurable but have median survival times of > 5 years. Tumors with oligodendroglial components generally do better than astrocytomas.

Basically, there are three treatment options for a low-grade glial tumors: surgery to remove the tumor, radiation therapy to shrink the tumor, observing the tumor to monitor changes until treatment is necessary. Low-grade gliomas tend to grow very slowly and may not cause any signs or symptoms for years. Because of this, simply monitoring the tumor with scans is a very reasonable approach. In such cases, treatment is delayed until the tumor appears to be growing or gives rise to problems.

Tumor location plays a key role in determining treatment. If the tumor is in a critical area, surgery will be a challenge and may cause significant and permanent brain

damage, in these cases surgery also becomes a branching point in the therapeutic algorithm. Special care is needed for the identification of eloquent in the surgery of tumors located near speech-eloquent or primary motor brain areas, along with special techniques of removal. Usually, when the tumor can be safely removed, surgery is considered to be the best treatment.

30 – 40 % of pediatric primary brain tumors are low grade glioma. Their annual incidence is calculated to be 10 –12 per 1.000 000 children under the age of 15 years in western countries. These tumors occur at all ages with a mean age at diagnosis or operation between 6 and 8 years. Therefore, special reference is made to the management of pediatric cases.

Glioma surgery and neuronavigation - are there any controversies?

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Aim: The purpose of the current study was to analyze prospectively the effect of neuronavigation on some intraoperative neurosurgical parameters at intracranial gliomas and to specify the indications for the application of neuronavigation in glioma cases.

Material and Methods: The study included 58 patients with cranial gliomas treated neurosurgically with neuronavigational assistance. Seven of the patients, who underwent biopsy as a standalone procedure (1 case through burr hole and 6- following craniotomy), were analyzed separately as well as one case with a

mesencephalic glioma, treated neuroendoscopically, was discussed in a neuroendoscopy group. The accomplished study on the rest 50 cases was prospective, evaluating the neuronavigational impact on the parameters: “skin incision”, “craniotomy”, “anatomical orientation”, “dissection guiding”, “tumour localization”, “assessment of the extent of resection” and “duration of surgery”. The patients were examined and followed-up in a standard manner.

Results: In the series, by means of neuronavigation, the gliomas were removed gross totally in 26 cases, subtotally- in 13 and partially- in 11. No any procedure-related morbidity and mortality were identified. In the cases with gross total tumour removal the navigation was evaluated as particularly useful for determination of the border tumour-edematous brain tissue and for localization of potential tumour residuals. At the patients with subtotally and partially excised tumours, the preoperatively planned volume of surgical activity was accomplished. Thus, the navigational guidance was assessed as necessary exactly for determination of the borders of the marked for extirpation volume of the tumour, in order to avoid the eloquent brain zones and the relevant neurological deficit.

Conclusion: In the resection of brain gliomas the neuronavigation optimizes the surgical approach, outlining their interrelations to the skull landmarks and to the neighboring critical neurovascular structures. In consequence, neuronavigation may improve the early surgical results by precise localization, reliable dissection guiding and increased radicalism. The neuronavigational guidance, as a rule, is indicated in glioma cases because of its versatile benefits.

Arguments in favor of intraoperative ultrasonography in gliomas

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Intraoperative ultrasonography is a means of investigation in real time, widely available, relatively inexpensive and non-constraining. It is used to localize subcortical and deep lesions, define tumor margins, evaluate the tumor resection and determine the surgical complications. The transducer can be put into practice repeatedly within different stages of the operation. Color and power Doppler B-mode sonography offers the possibilities of intraoperative control of neurosurgical procedures, recognition of tumor vascularisation, which thus helps avoiding unnecessary bleeding and preserves the vessels in contact with the tumor. Ultrasonography estimates the unclear boundary between the tumor and brain edema, and comes in the aid of operative approach's planning. The quality of ultrasonography improves with newer technologies, higher frequencies.

The major drawback of ultrasonography is that it cannot be applied in order to acquire images through substances of high density (bone).

Why the current standard multimodal treatment failed? The glioma stem cells paradigm

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Objective: Angiogenesis is an important prognostic factor associated with tumor growth and progression. Starting from personal clinical observations in some cases of re-intervention for recurrence in patients

treated with temozolomide (TMZ), regarding to the development of particular aspects of angiogenesis, specific tumor angiogenic characteristics were investigated, to identify the most suitable prognostic factor in generating multimodal therapy protocols.

Material and methods: Fresh tumor biopsies were processed for obtaining established cell lines and for development of a three dimensional (3D) functional angiogenesis assay in fibrin-gel matrix supplemented with serum-free growth medium, in presence of TMZ and anti-angiogenic or pro-angiogenic factors (bevacizumab, sunitinib, VEGF, EGF and PDGF). Chemosensitivity for TMZ of isolated tumor cells was determined by MTT test. Genes implicated in angiogenesis were evaluated at mRNA level by real-time PCR in tumor tissue and peritumoral tissue as control: VEGF, PDGF, TNF- α , ICAMs, CTGF, EPCR. Microvascular density (MVD) was also determined using a protocol adapted after Weidner's method.

Results: In 14 established cell lines, tumor cells tested by MTT assay shown sensitivity for TMZ in 60% of cases. Spontaneous angiogenesis was observed in most of the tumor explants tested and the development and spreading of capillary structures were enhanced in presence of TMZ in 11 from 19 cases (57.8%). MVD values varied between 22-130, with a median value of 83.6. Enhanced angiogenic potential in 3D model was correlated in 4 cases with higher MDV results (MDV>90) (21%) and in 5 cases with an increased expression of pro-angiogenic genes(26%). Higher levels of VEGF and PDGF mRNA were observed in 47% of tumors.

Conclusions: A great individual variability was observed in tumor cells sensitivity to TMZ and in angiogenic potential of GM,

suggesting that these processes are controlled by multiple factors, mainly by the presence of growth factors such as VEGF and PDGF, but in correlation with other variable local factors from the vascular niche. TMZ enhanced angiogenesis in some tumors, probably by selection of cancer stem cells. A complex evaluation of each tumor can indicate the best choice of further therapy.

Individualized treatment strategies in pediatric low-grade gliomas (microsurgery vs stereotactic biopsy and brachytherapy)

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Objective: In search for optimized treatment conditions for children with WHO grade I and II gliomas not accessible to complete resection, brachytherapy (BT) has been proven to be beneficial. BT with temporary Iodine-125-seeds provides precise radiosurgical planning sparing surrounding normal tissue. The results in 29 pediatric cases treated with BT after partial tumour resection or with BT alone, are presented.

Methods: 15 boys and 14 girls were included in the present study. Mean age at the time of BT was 9 years. Tumour location was hypothalamic/suprasellar in 9, lobar in 8, deep in 6, within the brainstem in 4, and in the cerebellum in 2 children. Histology revealed 18 pilocytic astrocytomas, 9 fibrillary astrocytomas, one ependymoma and one ganglioglioma. Partial resection with subsequent BT was performed in 12 cases, 17 tumours were stereotactically biopsied and implanted with Iodine-125-seeds.

Results: Mean follow-up time was 33

months. Ten tumours showed complete regression 6 to 40 months after seed implantation, tumours decreased in size in 18 children 2 to 16 months after BT. Two children developed space occupying radionecrosis which had then to be resected leading to neurological improvement. One boy died due to tumour progression of his WHO grade II astrocytoma. Twelve children even experienced an improvement of their previous neurological deficits.

Conclusions: Brachytherapy is a safe and effective method even in the younger patient group under 3 years of age. Microsurgery in combination with BT or BT as single treatment provides excellent surgical outcome, good tumour control and low morbidity.

New Facts on Epidemiology and Prevention in Traumatic Brain Injury in Germany

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Introduction: The purpose of epidemiology is disease control and prevention. A review of the data published on the epidemiology of traumatic brain injuries (TBI) reveals that the data of almost all studies are drawn from local or regional series. Nationwide data are rarely available. In Germany, there has been a nationwide mortality register since 1898 and since 1994 all hospitals provide data on all admissions. In addition, the whole country is divided in trauma centres which provide data since 1995.

Methods: All head injuries between 1972 and 2009 were analysed according to ICD-9 and after 1998 according to the updated ICD-10. The data were provided by the Federal Bureau of Statistics. The data of

hospitalized cases and fatal cases were correlated with population data to calculate incidences and mortality rates. Age-group specific data as well the specific situation after the reunification were also available and analysed.

Results: The incidence rate of fatal head injuries in Germany decreased continuously from 27.2/100 000 in 1972 to 8.3/100000 in 2006. The mortality is highest inside the group older than 75 years. After the reunification in 1989 the number of fatal head injuries showed a temporary increase till 1994. The number of patients treated in-hospital increased from 266 944 in 1995 to 316 573 in 2006.

The majority of hospitalized patients suffered minor head injuries.

There is an increase in the number of vehicles and motorcycles on German roads and highways (in 2002 over 53 Millions vehicles and 3.6 millions motorcycles), but a marked decrease of severe traffic accidents.

The number of surgical procedures is highest in the age group 70 till 75 years.

Conclusions: Analysis of the data of all German hospitals reveals surprising views of incidence, morbidity and mortality rates of head injuries in this country.

Rapid changes in motorization during the reunification period cause an increase of severe head injuries.

Prevention by laws and technical standards are very important.

Less head injuries caused by traffic accidents occur due to the increasing age of the population. But with increasing age more severe accidents occur at home.

Seven years experience in 3D custom-made implants for craniofacial bone defects reconstruction

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Background and objectives: The posttraumatic or postoperative cranio-facial bone defects have functional and esthetical impairments among involved patients that can not be underestimated. For this reasons reconstruction of cranio-facial defects, a step in multimodal rehabilitation treatment, is mandatory. In the last years, the development of rapid-prototyping technologies offers the possibility of reconstructing some of the bone defects with custom-made craniofacial implants from alloplastic materials. This paper present our seven years experience in using these modern technologies.

Material and method: Different bone defects of neural or visceral skull were morphological and functional rehabilitated using custom-made implants of polymethylmethacrylate or polyethylmethacrylate-hydroxyapatite. The implants were produced by three-dimensional modeling, rapid-prototyping and casting into silicone-rubber molds.

Results: Produced for each specific case, the custom-made implants adapted perfectly into the bone defects, assuring an excellent morphological and functional rehabilitation. Due to the preoperative modeling, the time spent into the operation was significantly decreased. There were no adverse effects to the materials used. The process of producing custom-made craniofacial implants still involves an expensive technology which limits their use to complex cases but the future will expand the use of these technologies to ordinary cases.

Conclusions: The possibility of producing custom-made implants opened a new era in the reconstructive surgery of the craniofacial area. Despite of some disadvantages linked to the high costs of production, the advantages of their clinical use proved to be multiple.

Surgery of the tumours of the third ventricle, our attitude

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Neural structures composing the walls and the floor of the third ventricle participate at important functions, first of all maintenance of the homeostasis, memory mechanisms and visual functions. Gradual involvement of the structures by enlarging tumour may be compensated for a certain time period. Surgical manipulation with damaged neural structures during exposure of the tumour and its removal may cause serious worsening of the patient's condition. Therefore in past the main goal of surgery was biopsy and reopening or shunting the cerebrospinal fluid spaces.

Improvement of imaging diagnostic methods and microsurgical techniques enabled to reach almost any region of the brain without causing permanent neurological deficit. Sufficient exposure of the tumour and its relationships with surrounding structures may thus be reached. Surgeon thus can determine optimal extent of surgery and under favourable anatomical conditions may remove the tumour radically without jeopardizing the patient. In our series of more than one hundred patients this could be reached in two thirds of them with surgical mortality below 3%. The extent of tumour resection varied according to the location of the tumour and its histological nature.

In our series we did not include patients with the tumours located predominately inside the lateral ventricles extending into the cavity of the third ventricle through a dilated foramen of Monro or the patients with the tumours growing within the lateral wall of the ventricle, i. e. in the thalamus (paraventricular tumours). According to the relationships of the tumour to the ventricular cavity and to its floor three types of lesions were distinguished: basal tumours (intraventricular or extraventricular craniopharyngiomas, gliomas) occupying predominately basal part of the ventricle involving its floor, oral tumours (colloid cysts, gliomas) occupying predominately superior part of the ventricular cavity sparing the ventricular floor, and caudal tumours (pineocytomas, pineoblastomas, embryonic cell tumours, gliomas) growing in the posterior part of the ventricle.

During the resection of the basal tumours we made every effort not to damage the optic chiasm and the hypothalamus. The goal could be achieved by choosing an appropriate surgical approach and the optimum extent of

tumour resection: a) a part of a craniopharyngioma involving the hypothalamic structures within the floor and the walls of the third ventricle was left alone, b) anterior part of basal gliomas infiltrating the chiasm was not resected; only posterior-superior part of the tumour which occluded the third ventricular chamber and not infiltrated its lateral walls was removed.

The most endangered structure during removal of the oral tumours is fornix. Care must be taken to preserve it in order to avoid severe memory disturbances. Whenever possible we avoided manipulation with both halves of the fornix; we always try to remove the tumour through one foramen of Monro and use the other only for assessing the completeness of resection if necessary. Oral gliomas did not involve the ventricular floor and could be safely completely resected in majority of patients.

The most favourable anatomical conditions from surgical point of view were encountered in patients with caudal tumours which could be removed radically in a great majority of patients including those with gliomas.

Controversies in craniopharyngiomas. Total or partial removal?

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Objectives: Craniopharyngiomas (CPH) are benign slow-growing intra-cranial calcified tumors, preponderant in children. CPH expand in the pituitary stalk axis, from the sphenoid body to the third ventricle. MRI improves the anatomical location, the tumor diagnosis and the

operative strategy. Microsurgery represents the main treatment option in spite of major difficulties. The goal of this study is to analyze the outcome of a series of 122 CPH cases of pediatric population, treated surgically.

Methods: Authors performed a retrospective analysis of 122 consecutive children (0 – 16 year old) with CPH diagnosed and operated at the “Bagdasar-Arseni” Clinical Hospital, Bucharest, during a period of 20 years (1991 – 2010).

In this cohort of children, males were slowly preponderant (64 boys and 58 girls), affecting predominantly the age group 7 – 10 y.o. (49 cases – 40.2%). Clinical features consisted of visual impairment (85 cases – 69.6%), endocrine dysfunction (99 cases – 81.3%) and increased ICP syndrome (82 cases – 67%). Visual and endocrine symptoms prevailed. Headache, was frequently encountered – 106 cases (86.6%). Hydrocephalus was present preoperatively in 31 cases (25,4%) and was dealt with VP shunt before definitive tumor therapy in 15 cases (12.3%). The essential neuroimaging findings is actually MRI. No DSA investigation was carried out routinely.

Pathology: the adamantinous type was preponderant in children (111 cases–91.1%). All the cases were followed up during a period going from 6 months to 15 years.

In our series, in children, the most frequent location of CPH was the suprasellar retrochiasmatic region (89 cases – 73.2%). Pathologically, combined forms (cystic forms with calcifications) are prevalent: 65 cases (53.6%). A personal craniopharyngiomas grading scale was presented.

In children, surgical approach was adapted to the tumor location: bilateral subfrontal (42 cases–34.4%), unilateral frontal (26 cases–21.4%), and pterional (24

cases–21.4%), followed by midline interhemispheric (21 cases–16.9%), transcallosal (3 cases–2.7%) and combined (6 cases–5.3%). Actually, the fronto-lateral and pterional approach were preponderant surgical strategy both in children and adults.

Results: In children: the total removal of the CPH was the goal of the surgery, but this was achieved in only 65 cases (54.4%), because of the risk of functional impairment or possible operative mortality. In 11 cases (8.9%) we performed near-total resection, in 41 cases (33.9%) partial resection, and 5 cases (4.1%) were biopsies. We performed biopsy with cyst evacuation only on giant, extremely compressive forms, in which the tumor collapse was accompanied by cardiac bradycardia. Hydrocephalus was present in 32 cases (26.2%). No intraoperative death occurred. In the first month, there were 6 deaths (4.9 %), due to hypothalamic injury, in each case total removal having been attempted.

The real recurrences occurred in 22 cases from 66 cases of total removal (33.3%); tumor regrowth was noticed in 44 cases (77.2%) from a total of 57 cases with remnant tumor (near-total, partial and biopsies).

The actual treatment target the cystic craniopharyngiomas which is prevalent on children. In this situation, have tried: catheter on cyst and evacuation of the cyst in omaya reservoir, which is needle periodically; chemotherapy with Bleomycin intracystic with disadvantages of allergy to this drug and multiple adherent, intracystic application of isotope of: Phosphorus-32; Rhenium-186; Yttrium-90 completely prohibited today and finally application of interferon alfa with some good results. The procedure consists in intracystic catheter placed by: 1.single burr hole using neuronavigation, 2. endoscopically, 3.

Positioning by craniotomy or 4. subcutaneous Ommaya reservoir (3,000,000 IU/day for 12 days) + cyst fluid aspiration.

Gamma Knife Surgery (GKS) was performed in 7 cases in children, all with recurrences, but the results remain disputable because the tumoral chist pression asked a surgical approach.

Neuropsychological assessments revealed no altered IQ at individual level. The Intracranial Hypertension (ICP) and the tumor localization determine attention deficits. Extended tumor localization determines the deficient mental control and the apathy. The recurrent tumors determine psychological dysfunction: attention, memory and the orientation. The depression is dependent by age old of the patients and the QOL is dependent by the tumor localization. Psychosocial reinsertion is affected by memory dysfunction, medium moodiness and the forceless Ego. A good rehabilitation recorded in 50% patients who underwent counseling before neurosurgical interventions.

Conclusions: Surgical treatment remains the main option, but the important number of complications, regrowths and recurrences prove the necessity of a multidisciplinary approach: microsurgery, radiosurgery and endocrinological treatment. Total or partial removal depends on the tumoral volume and hypothalamic adherences. Actually the authors advocate for partial removal with adjuvant therapies. The adamantinomas type was very important in recurrences and regrowths of CPH. Also, the authors present a CPH scale which facilitates the perfect location, surgical approach and outcome in this kind of tumor.

Orbital exenterations - actual point of view

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Purpose: To determine the clinical indications and surgical approaches in the orbital exenterations.

Methods: Retrospective case review of 46 exenterations performed in Cluj County Emergency Hospital, Romania, 1990 and 2011. Reviewed data indications for exenteration, histopathologic diagnosis, and recurrences on follow-up.

Results: Secondary intraorbital spread of malignant adnexal tumors was the most common indication for exenteration (24 of 46). Among these, the site of the primary neoplasm was the eyelid in 18 cases. Exenteration was total in 10 cases, subtotal in 7 cases, and extended in 28 cases and bilateral in 1 case. In 5 cases, a dermis-fat graft was used for socket reconstruction; 3 cases were allowed to granulate spontaneously, subtotal exenteration prosthesis in 12 cases, Ti dynamic mesh in 39 cases. The average healing time was 21 weeks, (range, 4–6 months) for spontaneous granulation, and 6 weeks (range, 4–8 weeks) for dermis-fat grafts, 2 weeks in exenteration prosthesis and Ti dynamic mesh. Survival of the patients in the first year after exenteration (43 of 46) 93,4%. Long term follow up 11 recurrences (23,9%). 13 patients (28,2%) died in the first 5 years after exenteration for aggressive tumors.

Conclusions: The first year is the most important period for follow-up of local recurrences, but systemic examination is needed for the longer follow-up. The exenteration prosthesis and Plastia with dynamic mesh significantly reduce the healing time and ameliorate the aesthetic aspect.

New diagnostic techniques in developmental abnormalities of cerebral venous evolution - SWI (susceptibility weighted imaging)

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DVA (developmental venous anomalies) are congenital cerebrovascular anomalies.

This pathology was detected since new imaging techniques have developed, techniques in which slow flow vessels and any trace of hemosiderine can be seen.

This new technique is called SWI (susceptibility weighted imaging).

Our study is a preliminary study of 44 cases with different types of venous angiomas, with different situations, types and clinical manifestation.

We detected also the presence in the same time of 30% cases of associated cavernous angiomas.

Examination was made with SIEMENS-1,5 T AVANTO MR, we used: T1-TSE 2 D, T1 MPRAGE 3 DWE with gadolinium, T2 TSE, T2 FLAIR, SWI.

Conclusions: The development of new MR techniques allows to detect this new pathology of DVA, to evaluate the complexity and the treatment of this cerebral vascular anomalies.

Clip or Coil: Treatment of MCA-Aneurysms after ISAT

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After the ISAT-Study a substantial change of aneurysm treatment away from clipping towards coiling was observed. However, the long-term results concerning the clinical outcome do not show an

advantage but a higher rebleeding rate in the coil group.

We evaluated our middle cerebral artery-aneurysms from 2007 to 2010: 105 Patients were treated, 58 were admitted with a subarachnoid hemorrhage. Clinical results in the clip group were favorable although not showing statistical significance. Mortality rate in the Clip- group with SAH was 9% respective 25% in the Coil-group. No mortality in unruptured MCA aneurysms was observed in either group.

The microsurgical approach for MCA-aneurysms is also after ISAT a very good approach and seems to be superior in many cases. However, in every case, an individual approach should be discussed by the vascular team – independent to any vanity - to realize the best result for the patient.

Aneurysm treatment in Europe: An internet survey

Bradac Ondrej

Introduction: Aneurysm (AN) treatment appears to differ from country to country and even from centre to centre. We therefore decided to conduct a survey, better to understand 'state of the art' aneurysm treatment in Europe.

Aims: Primary aim was to understand the roles of clipping and coiling in aneurysm treatment.

Design and Methods: An interactive form was sent to major European neurosurgical centres. The responses relating to AN location, status (ruptured/unruptured) and treatment modality were divided with regard to the volume of cases and centres geographical location.

Results: Responses were received from 99 European centres. Main finding was that clipping was used significantly more often in Eastern Europe than in the rest of Europe to treat ruptured ANs of anterior

circulation (median 90% AComAANs in Eastern vs. 30% in rest of Europe, 100% of MCAANs vs. 70%, 90% PComAANs vs. 30%, 80% ICAANs vs. 20%). Almost all ruptured ANs across all locations are treated actively. The treatment of unruptured aneurysms of anterior circulation is similar. The median relating to observed unruptured ANs across the Europe was 10%. Posterior circulation ANs are treated predominantly by coiling, regardless of aneurysm status or geographical location. The average number of coilers vs. surgeons per centre was 2.5:3.0 in Western, 1.9:3.6 in Southern, 1.9:4.3 in Eastern and 2.7:3.1 in Northern Europe.

Conclusions: The way in which intracranial aneurysms are treated appears to correlate with the economic development of European countries. It is probably also affected by the lack of experienced coilers in Eastern Europe.

New endovascular treatment options for intracranial aneurysms based on flow dynamics and flow related biology

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The clinical benefits of endovascular treatment for intracranial aneurysms have been proved by multiple studies. Although the endovascular approach provides better clinical outcome, its long-term stability is inferior as compared to open surgery. Until recently, all endovascular techniques were entirely based on the mechanical obstruction of the aneurysm cavity as it is seen on angiographic images. Treatment plan was purely based upon the geometry and the underlying hemodynamic

conditions were not taken into consideration. In order to design more effective treatment methods, better understanding of the disease process is inevitable. With the combination of modern imaging technology and computer science, the local flow dynamics can be studied in vitro in real human aneurysms. It is well known, that intracranial aneurysms grow at arterial sections exposed to high hemodynamic load. Computed Fluid Dynamics (CFD) simulation demonstrates that the most important hemodynamic factor in aneurysm initiation is high wall shear stress (WSS) and even more importantly high spatial WSS gradient. Inside the aneurysms, high WSS areas seem to induce further aneurysm growth, while low WSS sections are prone to wall degeneration and may lead to rupture.

Understanding of the local hemodynamics initiated the development of new therapeutic methods. Instead of attempting a mechanical obstruction while leaving the surrounding flow dynamics unchanged, these techniques aim to modify to local flow conditions in a way that favor aneurysm thrombosis. For sidewall and fusiform aneurysms, intravascular flow diverters are now regularly used and achieve a rate of over 90% thrombosis in large and giant aneurysms at 6 months and 1 year. Further, this technique makes the aneurysms to collapse, effectively alleviating mass effect and compression syndromes. For bifurcation aneurysms, intrasaccular flow diverters are being developed that demonstrates promising early results in clinical application as of today.

Conclusion: understanding the interaction between flow and biology may help to develop treatment techniques that achieve true arterial reconstruction and high long-term stability.

Brainstem cavernomas treated microsurgically and radiosurgically

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The purpose of this retrospective study was to compare the long-term outcome of brainstem cavernomas after microsurgical or radiosurgical treatment in our institution.

Microsurgical resection of a CM was performed in 21 patients and 26 patients had been treated by gamma knife surgery. All cavernomas of the RS group were deep seated. Following the classification of Schefer and Valavanis most lesions were classified as Type II (11.55%) and Type I (6.30%). The most common localization was pons (50%), followed by thalamus (30%). Neurological improvement was found in 66% after microsurgery (MS) and 50% after Gamma knife radiosurgery (GK), unchanged in 11% after MS 25% after GK. Deterioration occurred in 22% after MS and in 25% after GK. One patient died after rebleeding after GK treatment. Reduction of bleeding rates was achieved in both groups ($p < 0.001$) and neurological improvement was also found in both groups applying the modified Rankin scale (0.9 after surgery and 0.5 after radiosurgery).

Conclusion: Our experience shows, that brainstem cavernomas can be treated with low morbidity and mortality. During a long-term follow-up both, microsurgery and Gamma Knife Radiosurgery, are effective to reduce significantly the rebleeding rates.

Predictive outcome factors by open surgery in intracranial aneurysms (IA). An experience of 628 cases.

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Background: The intracranial aneurysm (I.A.) has a prevalence between 0,2-7,9% in the literature. The variability depends of hospital referral, neuroimaging findings and autopsy pattern. The pathology of intracranial aneurysms is a dominant element in neurosurgical activity, because of the multiple preoperative and management problems.

IA affect mainly the active age (40 and 60 years old) and the male sex. Generally the incidence in USA is 10-28/100.000 (official data).

The etiology of IA may be: congenital, (aneurysms appear due to a defect of the muscular layer of the arterial wall), arterial hypertension, neoplastic disease, atherosclerosis, inherited diseases, trauma, infection (mycotic an.), unknown causes. In all the cases of aneurysm ruptures, some of the following are incriminated as risk factors: cigarette smoking, alcohol excess, life stress.

The cerebral circulation must be evaluated in totality and aneurysms in particular and the accuracy management is necessary for limitation of important life-threatening complication (rebleeding and ischemic stroke).

Material & Methods: The authors present a study about 628 consecutive operated patients with intracranial aneurysms, operated in first Neurosurgical Department between 1997 - December 2010 - 14 years - (40 children and 588 adults). Most cases (286 case - 45,5%) were between 41 and 50 years old. Male is the preponderant sex - 427 cases (68%) (2,1 : 1). The symptoms were dominated by: headache (98%), stiffneck (94%) and focal neurologic deficit (71%) etc. Most patients were Hunt and Hess grade II (230 cases, 36,7%) and Hunt

and Hess grade 3 (97 cases, 15,4%) at admission. The associated pathology was: systemic arterial hypertension (471 cases, 75%) and obesity/hypercholesterolemia (214 cases, 34,1%), ischemic cardiopathy (100 cases, 16%), diabetes melitus (100 cases, 16%), chronic alcoholism (82 cases, 13%), ischemic stroke (75 cases, 12%), atrial fibrillation (63 cases, 10%), miscellaneous (88 cases, 14%, anticoagulant therapy).

The main investigations were: CT scan, DS angiography. Actually, the most important were 3D DS Angiography and 3D CT AngioCT.

The common localization of intracranial aneurysms was the anterior communicating artery 183 cases (29,1%); the other locations were: medium cerebral artery 157 cases (25%), posterior communicating artery 107 cases (17%), internal carotid artery 84 cases (13,3%), basilar top artery cases 21 (3,3%) and vertebral artery 11 cases (1,8%). Multiple aneurysm represent in our data 65 cases (10,3%).

All cases were operated, as soon as possible after the subarachnoid hemorrhage (SAH) and IA angiography diagnosis. "Early surgery" eliminates the risk of re-bleeding and facilitates the treatment of vasospasm which peak is between 6-8 days post SAH.

From all complications two are very critical for life and morbidity: aneurysm rebleeding and cerebral ischemia.

The authors present by personal experience the outcome predictive factors : age (up to 65 and under 5 years) associated pathology (arterial hypertension 491 cases (78,1%)), obesity and hypercholesterolemia 214 cases (38,3%), ischemic cardiopathy 107 cases (17%), diabetes melitus 11 cases (16%) and so on, subarachnoid hemorrhage diffusion (according to the Fisher scale), aneurysm particularities – number, shape, size, association with AVMs, aneurysm timing of operation, brain relaxation

(hyperventilation and CSF drainage) aneurysm rerupture, peroperative vasospasm, ICU facilities, possibilities of coiling treatment, early neuroprotection and neurorehabilitation.

The Glasgow Outcome Scale (GOS) in our data (at 6 months postoperator) shows: good recovery 421 cases (67%), moderate disability 148 cases (23.5%), severe disability 31 cases (4.9%), persistent vegetative state 7 cases (1.1%), death 21 cases (3.4%).

Conclusions: IA represents an important neurosurgical challenge. Also IA by the rupture and complication is the real lifethreatening diseases. Clinical features are dominated by SAH & neurological signs (Hunt and Hess scale-1968, was perfectly useful).

Complete vascular exclusion is the treatment of choice by open microsurgical approach or endovascular embolization.

The important measures to avoid rebleeding and cerebral ischemic stroke in intracranial aneurysms are perfect evaluation and early approach, perfect aneurysm dissection and neuroprotective measures (pre, intra and postoperative). Neuroprotective agents – useful to avoid cerebral ischemic stroke The timing of aneurysm surgery is one of the key of avoidance lifethreatening complication.

Controversies in ruptured aneurism timing

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Aneurismal subarachnoid hemorrhage was and still is in our days a subject of large debate and controversies. Historical periods in this field evolved from controversies: surgery – conservative treatment, macrosurgery – microsurgery, delayed surgery – early surgery, open approach –

endovascular approach.

Hunt and Hess scale was created to differentiate class of patients suitable for early surgery in anesthetic and surgical conditions offered in the 70's. Despite initially aged patients and high score patients were considered for delayed surgery, during the next years technical advances in more and more hospitals modified this limit toward an early aneurismal occlusion.

In this paper we analyze 170 ruptured aneurisms operated on in a period of 24 months (01.01.2009 – 31.12.2010). The analyses criteria were: time of admission, time of surgery, H&H grade, aneurism position and morphology, associated hematomas or hydrocephalus, age, associated medical conditions, especially HBP, complications and results.

Only 50% of the patients were submitted to an early surgery (first 3 days after rupture).

The reason of delayed surgery was in range: delayed admission, high clinical grade, medical comorbidities, age of the patient.

The protocol changed during these two years toward a more active attitude especially concerning early surgery in elderly people.

Our hospital protocol together with endovascular treated cases and the literature review are also emphasized.

Mini-invasive instrumented stabilization of lumbar and thoracolumbar spine

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Minimally invasive spine surgery (MISS) represents a growing collection of

surgical techniques that allow surgeons to perform spinal procedures through smaller incisions. The primary goal of MISS is to limit damage to the soft tissue envelope of the spine, thereby diminishing postoperative pain and allowing an earlier return to normal activities. Other advantages of MISS include reduced blood loss, shorter hospitalization and quicker rehabilitation. MISS procedures generally depend in part on the use of specialized surgical equipment including operative microscopes, endoscopes, cannulated screw technology, tubular retraction systems, fiber optic lighting and image guidance technology. It is an important not to compromise the goals of the surgical procedure when performing a MISS approach. As with traditional spinal surgery, adequate decompression of the neural elements and meticulous preparation of a spinal fusion bed should be achieved.

The objective of our study was to compare the efficacy of three techniques of instrumented transforaminal lumbar interbody fusion (TLIF) in the treatment of low grade degenerative instability of lumbar spine.

We conducted a prospective study with mean follow up 26 months. Eighty-five patients (39 men and 46 women) were enrolled into study. Twenty-seven patients (group 1) were treated by standard median approach with subperiosteal separation of muscles and 38 by two paramedian Wiltse transmuscular incisions (group 2). Interbody fusion was done by unilateral insertion of cage after total or partial resection of facet joint. Screws were inserted according the method advocated by Weinstein in both groups. Twenty patients (group 3) were instrumented by percutaneous screw system a way for interbody fusion was done through tubular retractor. Decompression of spinal canal

was done by one side partial hemilaminectomy and undrecutting of opposite side. Operation time, blood losses, number of complications, accuracy of pedicle insertion were evaluated. Post operative pain profiles were measured each day during the first week after surgery by Visual analogue scale (VAS). VAS and Oswestry disability index (ODI) were filled during outpatient controls 6 weeks, 3 and 6 months, one and two years after surgery. Overall patient's satisfaction and fusion were assessed 2 years after surgery.

There were no significant difference in operation time among these three groups ($p > 0.05$). In group 2 and 3 blood losses were less significantly compared to group 1 ($p < 0.05$). First week post operative pain profile measured by VAS was significantly different for groups 2 and 3 compared to group 1. ($p < 0.05$) Patients from group 2 and 3 were less painful and no significant difference between these groups were found. No significant difference in values of VAS and ODI were found during the rest of follow up. Overall satisfaction was without any significant difference among the groups after two years of follow up. ($p > 0.05$)

We have concluded that - long term clinical and radiological results after instrumented TLIFs in degenerative lumbar spine instability are not related to extend of surgical approach. Less invasive technique can offer more convenient pain profile during the first days after surgery. Less invasive instrumented TLIF looks to be viable alternative to standard techniques in treatment of low grade lumbar spine instability.

After familiar adoption of MISS technique on the field of the degenerative lumbar spine instability we have decided to explore potential of MIS in the treatment of other pathologies. In the next pilot study we

treated 15 patients with thoracolumbar fractures type A, according AO classification). We observed one screw malposition, without any clinical consequences, no other periprocedural complication, no wound complication, no hardware failure and no loss of correction during one year follow up.

MISS technique was used in the treatment of couple low back pain cases from the posterior approach and as additional posterior instrumentation after anterior procedure too.

Finally, after five years lasting experience with MISS, we can conclude that low grade slips on the lumbar spine, thoracolumbar fractures type A or B, low back caused by DDD, some spinal tumors and inflammations could be recommended for this treatment. Complex deformities, thoracolumbar fractures type C and high grade slips still present suboptimal indication.

Controversies in anterior cervical discectomy

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Herniated cervical disc is still a subject of acute controversies to our days.

In our hospital we are routinely doing two different kinds of surgery by two different teams which are among the authors.

One attitude is microsurgical simple discectomy and osteophytes resection. The other attitude consists in discectomy and instrumentation, most often with intracorporeal polymeric cages. We analyze 30 consecutive cases operated on with the first protocol and 30 consecutive cases operated on with the second protocol.

Symptomatology, imaging aspect, cervical stability evaluated through flexion-

extension radiography, post-operative immobilization, complications and outcomes were evaluated for all these cases.

A bias consisting in applying the protocol with implants exists because all the cases with instability were treated by this method but this condition was met in only two cases.

We present illustrative cases and surgical videos.

No significant differences were observed between the two groups with a two month post-operative control.

Some literature data are also reviewed.

In our experience the two procedures seem to be equivalent in short term results and seem to be a personal preference of the surgeon.

Treatment options in recurrent high-grade gliomas

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Glioblastoma is the most common malignant primary brain tumor in adults. The current standard of care is maximal safe neurosurgical resection followed by radiation treatment to the involved brain with concurrent and adjuvant temozolomide. Despite aggressive treatment, local tumor recurrence or progression develops in most patients in less than 1 year. There are limited options for salvage therapy: re-operation (if possible and clinically appropriate); re-irradiation (if no other options or small volume recurrence); local therapy in conjunction with re-operation or investigational therapy); chemotherapy; targeted therapy

(i.e., bevacizumab) or investigational therapy. There is a heterogeneous population at recurrence: 15% of patients are not able to receive further treatment, 9% refuse further treatment, 13% will receive second surgery or radiotherapy but not systemic therapy and 52 % progressed and will receive subsequent systemic therapy. The results of these different treatment options are poor: OS between 6, 9 and 7 month with 6-months PFS between 9 and 19%. Prospective studies, investigational therapies, best in clinical trials, are needed for these patients with poor neurological status and reduce expectance of life.

Alternative approaches to adjuvant chemotherapy for WHO grade III and IV malignant gliomas

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Introduction: Malignant gliomas remain one of the most devastating disease known to man and affects more than 17.000 patients in the United States alone every year. This malignancy infiltrates the brain early in its course and makes complete neurosurgical resection almost imposible. Recent years have brought significant advances in tumor biology, including the discovery that many cancers, including gliomas, appear to be supported by cells with stem-like properties. In the current study we have investigated the effects of combining metformin or arsenic trioxide with the temozolomide-based standard treatment-of-care chemotherapy.

Materials and methods: The subjects of the current study were eight patients with newly diagnosed high-grade gliomas,

operated at the Department of Neurosurgery - Clinical University Emergency Hospital from Cluj Napoca. Tumor tissue cultures were performed, characterized using immunofluorescence microscopy and PCR analysis for CD133, CD90, GFAP, Nanog, SOX2, Neurofilament and ALDH1 and the sensitivity to metformin, EGF and temozolomide tested. Microvascular density assay was performed on the tumor samples. Low concentrations of arsenic trioxide or metformin were added in culture and cell proliferation was assessed.

Results: Seven of the eight cases had a positive correlation between the number of the endothelial cells, the phenotype of the isolated tumor cells and the response to adjuvant chemoradiotherapy. The isolated tumor cells had a stem-like behaviour being resistant to conventional drugs. In most cases there was no statistical significant difference between temozolomide alone and temozolomide plus EGF arms, but there was an important difference between temozolomide alone and temozolomide plus metformin arms in six of the cases. Low concentrations of arsenic trioxide also lead to morphologic differentiation, with fewer stem cells in G0 state and differentiation-associated cytochemical features, like increased sensitivity to cytostatic drugs and radiotherapy.

Conclusion: New drugs and targeted molecular therapies are important for future therapeutics, but sometimes we must not exclude drugs already used in the clinic that might have notable results. Such is the case in the current paper, where exposure before conventional postoperative chemoradiotherapy for glioblastoma increased treatment efficacy. Further in vivo experiments on laboratory animals and analysis of absorption rate and side effects are required.

Hormonal impact on malignant glial tumors

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Background: Glial tumors comprise about 40% of all the primary Central Nervous System tumors, out of which Glioblastoma Multiforme (GBM) represent one half. The way these tumors are influenced by the hormonal status of the patient is still an unknown, although numerous suppositions have been made. Estrogen has been shown to have a stimulatory effect through the ER- α , although some studies suggest its protective role, oxytocin and progesterone have been considered to have an antiproliferative effect while prolactin inhibitors could be a metamorphic therapy for GBM. Populational studies show a smaller incidence for high grade gliomas (HGG) in the female population. Our purpose was to assess the way the hormonal status of female patients could influence the behaviour of HGG.

Material and method: Our study was divided in two. The first part was a retrospective study on 113 cases of HGG from the Neurosurgical Department of Cluj County Emergency Hospital. Cases were analysed to find differences between appearance, clinical behaviour and evolution of HGG in active hormonal female patients, and other patients. The other part was an in-vitro study on two lines of GBM cells and one tumor stem cell line that were cultivated and treated with doses of: 1ng/ml estrogen, 2,2ng/ml Oxytocin, 25ng/ml progesterone, 1ng/ml bromocriptin, 1,5ng/ml testosterone, and

then. Proliferation rate was analysed using MTT assay.

Results: The incidence of HGG cases in female patients <51y in our group was the smallest(17,69%). HGG appeared 7 and 8y earlier in male patients versus female patients. The clinical symptoms evolved slowest (14.45weeks) in female patients<51y. Reccurence occurred in this grup in a median time of 18.28 months vs.9.85 months in female patients >51y. Median survival was significantly different between female patients under and over 51y ($p<0.05$), but not significantly different vs. male patiens<51 y. The 24 hours MTT assay for the GBM cell culture showed the smallest rate of proliferation for estrogen and the highest for testosterone, progesterone had a smaller proliferative effect than the controll culture, and the other hormones had a more intense proliferative activity. In the stem cell cultre all hormones had a proliferative activity close to the control.

Conclusion: Hormones could influence the growth pattern of HGG and their clinical evolution. Our study suggests that hormones could be a factor that improve the way these tumors evolve in the female population, but that survival is only influenced by the patient's age.

From internal to external validity in RCTs

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The last decade has been very fertile in the development of both neurosciences and evidence based medicine (EBM), even if sometimes they did not go hand in hand.

Evidence based medicine is a concept that tries to build clinical decisions based on

empirical knowledge collected from randomized control trials (RCTs). RCTs were designed in order to avoid systematic sampling errors.

Randomised controlled trials (RCTs) and systematic reviews are the most reliable methods of determining the effects of treatment.

Clinicians have to make decisions about individuals, and how best to use results of RCTs and systematic reviews. This has generated considerable debate.

They key issue remains to what extent the overall results of trials can properly inform decisions at the bedside or in the clinic.

RCTs must be internally valid (i.e., design and conduct must keep to a minimum the possibility of bias), but to be clinically useful the result must also be relevant to a definable group of patients in a particular clinical setting; this is generally termed external validity, applicability, or generalisability.

As we can see from the genomic, transcriptomic and proteomic studies of post lesional regulations, the biological reality of the nervous system is extremely complex and rather individualistic (neurotrophicity, neuroplasticity and neurogenesis responses).

Therefore, due to patients' heterogeneous responsivity in clinical practice, the approach of neurorehabilitation should be more individualistic, with better chances to manage complex situations.

This presentation will analyze the concepts of internal and external validity of RCTs and why RCTs model is difficult to be applied to neurorehabilitation clinical trials.

Wrong side in neurosurgery

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A very important problem of bioethics in surgery in general and in neurosurgery as our concern is wrong side surgery.

This kind of mistake is more common in specialties where patients are operated immediately and in departments with a big number of interventions, like orthopedics but in neurosurgery also this kind of mistake has been reported. In US alone there are 1,300 to 2,700 wrong-site procedures annually in neurosurgery.

In order to address this problem, the neurosurgical departments need guidelines to prevent wrong-site surgery.

These guidelines should include to verifying the surgical procedure to be performed, marking the surgical site in advance; taking a “time out” immediately prior to starting the operation, during which team members verify that they’ve got the right patient, and Confirming that medical records and scans are not reversed and match the marked surgical site.

This preoperative check-up of the operative field should be performed by at least two doctors.

It is also indicated that a ct scan or MRI should be performed immediately postoperative to confirm the correct cure of the pathology.

Wrong side surgery even just an incision without the craniotomy represents a serious mistake and should be avoided

New versus classic in brain protection and recovery

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The old concept that neuroprotection means suppressing pathophysiological processes, the idea that a single mechanism molecule might be effective in clinical practice are obsolete today, and represents the root cause of failure.

The effects of etiological agents on the brain traditionally are conceived as a linear sum of independent pathophysiological processes (excitotoxicity, inflammation, apoptosis-like, oxidative stress, misfolding protein, etc.) generating the pathways of pathological cascades in acute and chronic disorders.

The pathway approach has produced a very detailed understanding of molecular changes in the postlesional brain but it possesses blind spots that are critically related to the failure of pharmacological neuroprotection treatment in neurodegenerative disorders.

This is due to the simplistic way of understanding the neurobiological processes supporting brain protection and recovery and pathophysiological mechanisms. The failure of modifying disease therapies in many pathological conditions is measuring the failure of the reductionistic approach to the problem.

Every lesion in the nervous system initially triggers an endogenous neuroprotective reaction followed by an endogenous repair process, combining neurotrophicity, neuroprotection, neuroplasticity and neurogenesis, overlapping and acting under genetic control to generate endogenous defense activity (EDA) which continually counteracts pathophysiological processes - damage mechanism (DM).

All these biological processes are initiated and regulated by biological molecules.

Neurotrophic factors are probably the best example in this respect. They are acting in a pleiotropic neuroprotective way against pathological cascades.

The same molecules, due to a complex genetically regulated process, are able to regulate further on neurotrophicity, neuroplasticity and neurogenesis as well. Therefore, they have not only pleiotropic neuroprotective activity but also multimodal mechanism of action.

Beside the concept and therapeutical effects of pleiotropic multimodal molecules, this presentation will give an overview on particular aspects about new randomized controlled trials in the field.

Long-term effect of thalamic and subthalamic deep brain stimulation on motor symptoms of Parkinson's disease

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We report the long-term effect of unilateral and bilateral thalamic (VIM-DBS), and bilateral subthalamic deep brain stimulation (STN-DBS) on patients with Parkinson's disease (PD).

52 consecutive patients with severe „on-off” fluctuation underwent CT-guided stereotactic impantation of model 3389 electrodes and Kinetra or Activa PC (Medtronic Inc) neurostimulator systems with mean follow-up of 47.6 ± 25.1 (13-114) months. Additional 19 tremor-dominant patients had unilateral and 11 patients had bilateral Vim-DBS with a mean follow-up of 43.5 ± 14.8 (14.2-101.4) months and 29.5 ± 8.2 (14.1-45.2) months respectively. Clinical evaluation included

Hoehn-Yahr stage (H-Y), Unified Parkinson's Disease Rating Scale (UPDRS), and the Schwab and England scale for activity of daily living (S&E). The drug therapy follow-up was based on Levodopa equivalent daily dose (LEDD). The bradykinesia was quantitatively measured with passive marker-based analyser of motions (PAM) with a computer based scoring system, The proximal movements assessed with the pointing test (PT) and the distal movements with the finger tapping test (FTT). The tremor was measured with PAM and computerized digital spiral drawing test (DSDT).

After STN-DBS the „off” state H-Y stage showed a 32%, the S&E an 86%, the tremor an 80%, the rigidity a 52.5%, the bradykinesia a 46.5%, and the fluctuation a 48.3% improvement. The ON dyskinesia was reduced by 76.5%. The LEDD was 553 ± 453 mg and 32% lower than at the baseline. The PT score was measured in 24 patients in medication „off” state StimOFF and StimOn, and improved significantly ($P=0.001$) and uniformly on the left side from 0.52 ± 0.28 to 0.84 ± 0.39 , and on the right side from 0.50 ± 0.27 to 0.85 ± 0.35 . The FTTS significantly ($P=0.001$) improved from 3.8 ± 3.0 to 11.0 ± 8.9 on the left side and from 4.1 ± 3.5 to 12.6 ± 9.0 on the right side.

Unilateral Vim-DBS showed a 84.3% improvement on tremor score, and had a long lasting effect. In long-term, the reduction of improvement on rigidity and bradykinesia was observed. The changes of axial symptoms were minimal or could not be observed. Bilateral Vim-DBS showed an 82.9% of tremor, a 41.7% of rigidity and a 29.3% of bradykinesia improvement. In long-term the postural stability, gait and speech remained without significant changes in both StimOFF and StimON

conditions. The LEDD increased by 7% to 318 ± 282 mg after unilateral Vim-DBS, and increased by 10% to 461 ± 109 mg after bilateral Vim-DBS.

PAM tremorometry showed a reduction of rest tremor by 94% and postural tremor by 90%. DSDT showed a 76.2% regression of kinetic tremor on the contra-lateral to surgery side. Frequency domain had trend to change toward physiologic values.

Based on the clinical scales and quantitative measurements, STN-DBS, in both short and long-term, substantially alleviates all main motor symptoms of PD. Vim-DBS, according to the clinical scales and quantitative measurements, is highly effective in tremordominant PD patients equally for both unilateral and bilateral tremor.

The endovascular therapy of the cerebral aneurysms as an alternative to neurosurgery. The first 132 endovascular treated cerebral aneurysms

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Introduction: Since May 2005 we started to treat the intracranial aneurysms endovascular way as an alternative minimum invasive to the classic neurosurgery treatment.

Methods: An all-inclusive retrospective review of every patient who underwent coils embolization (stent or balloon assisted included) of saccular aneurysms from May 2005 to April 2011 was performed.

Goals: We studied the patients' demographics, clinical presentation, aneurysm size and configuration, type of coils used for embolisation, the percentage of compaction and recanalization

(especially in patients that presented with subarachnoid hemorrhage), the immediate complications due to our procedure.

Results: A total of 123 patients (49 men and 64 women) and 132 aneurysms were treated. A total of 108 patients (41 men and 55 women) underwent follow-up femoral cerebral angiograms (mean follow-up was 25 months and the longest was at 37 months). 6 patients required intra-arterial abciximab or integrilin due to thrombus formation. 4 patients had aneurysm rupture while the coil was being advanced. 12 patients were treated during vasospasm peak. 8 patients had recanalization at 12 months follow-up.

Discussion: The average hospitalization period was 4 days (between 38 days and 1 day). There is a close relation between Hunt and Hess scale score before the treatment and post interventional neurological status. The vasospasm due to subarachnoid hemorrhage, although treated endovascular, remains a threatening of the patient's neurological status.

Conclusions: Treatment of cerebral aneurysms with endovascular embolization with coils is a safe and durable option. The risk of recanalization or rerupture in our cohort is small compared to series that have been published elsewhere. Larger series of patients treated with this method may support better our evidence.

Clipping aneurysms- some arguments in favor of surgery

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Objective: Our objective is to determine the value of the surgical treatment in experienced hands compared to the literature data regarding open-surgery, and the endovascular strategy in incidentally discovered intracranial aneurysm.

Material and methods: We designed a retrospective study based on our series of 49 cases with H&H 0 and 1 of intracranial aneurysm out of the total of 458 patients who underwent open-surgery for intracranial aneurysms.

Results: During a fourteen years' period, from the total of 458 cases treated by the authors for aneurismal pathology, 49 patients underwent open-surgery for non-ruptured intracranial aneurysms, in all cases definitive clipping being achieved. We reviewed the results using the Karnofsky Performance Status Score and Glasgow Outcome Scale, and we correlated these with the general and neurological status at admission, aneurismal localizations, associations, morphology and intra-operative particularities. From our series of 49 patients admitted with Hunt & Hess grade 0 and 1a, 83.7% were neurologically intact after surgery; only one patient was classified as GOS 3 immediately post surgery. In general, the outcome depended on the general status, age, the localization and the morphology of the aneurysm, associated aneurysms and co-morbidities.

Conclusions: Our results and comparisons show that open-surgery is in the most cases a very viable, if not the best option in the treatment of incidentally discovered intracranial aneurysms, conditioned by the fact that the surgical team must be an experienced one, and there must be an optimal collaboration between the surgeon, anesthesiologist and neurologist.

Aneurysm clipping vs coil occlusion is still a controversies

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Background: The aneurysmal subarachnoid haemorrhage (SAH) is one of the most devastating disease whose management still raises a lot of

controversies between neurovascular specialists. The actual standard treatments in the last decade are both surgical clipping of the aneurysm neck and aneurysm sac occlusion with detachable coils.

The objective of this study is to weigh evidence for the efficacy of endovascular coiling compared with microsurgical clipping in patients with aneurysmal subarachnoid haemorrhage.

Methods: We retrospectively reviewed the charts, procedural reports and imaging of patients who underwent surgical clipping or embolization for cerebral aneurysms in two medical centers between January 2004 and December 2009. In one center clipping is the standard procedure and embolization is in the other one. The all patients and procedural dates were statistically analyzed and correlated.

Results: The study group include 297 patients with coil occlusion and 406 patients treated by microsurgical clipping. The basic characteristics of patients in treatment groups were close in terms of location and size of aneurysm, severity of bleeding and clinic evaluation on various scales. Hypertension and EKG modifications (25.4%) were the most commonly risk factor. 9% patients were Hunt and Hess grade I, 21% grade II, 42% grade III, 25% grade IV, and 3 grade V. 8% patients to endovascular group and 1.2% to surgical group show aneurysm repermeabilization. The periprocedural technical complication rate associated with coiling was 7.2% vs 9.5% with clipping. Follow-up angiographic results were better with clipping, as total aneurysm occlusion was 91.3% vs 67.6% with coiling. The incidence of clinic vasospasm was 20.4% with coiling vs 25.4% with clipping, whereas the incidence of shunt-dependant hydrocephalus was 5% higher in embolization group.

Conclusion: Continuous improvement of practical experience and a good selection of patient based on optimal criteria correlated with the rapidly evolving of treatments technology will definitely determine a better outcome results in patients treated for aneurismal SAH, in the near future.

The usefulness of intraoperative microvascular Doppler sonography in cerebral aneurysm surgery

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Aims: To evaluate the usefulness of intraoperative microvascular Doppler sonography (MDS) in cerebral aneurysm surgery.

Material and methods: For 28 patients (12♂, 16♀, mean age 59.5 years) who underwent surgery for the treatment of 34 intracranial aneurysms, MDS with 16- and 20-MHz microprobe (tip 1mm & 2mm) was used before and after clipping, to confirm the complete obliteration of the aneurysm. Postoperative angiography was performed to assess the complete occlusion of the aneurysm and the patency of adjacent

vessels. The findings of MDS were analysed and compared with the postoperative angiography.

Results: The 1-mm microprobe was able to insonate all vessels of the circle of Willis and their major branches; furthermore, perforating arteries were reliably insonated. The mean duration of MDS investigations was 5.3 minutes. For 7 patients (20,5%), MDS exposed parent artery or branching artery stenosis or occlusion and guided the immediate adjustment of aneurysm clip placement. In addition, MDS demonstrated that 4 out of the 34 aneurysms failed to be completely occluded (11,7%). In two cases, a repositioning of the clip was performed and in the other two cases a second clip application became necessary for the complete occlusion of the aneurysms. There were no complications of microvascular Doppler probe use.

Conclusions: Intraoperative MDS is a safe, instantaneous, effective, reliable, and cost-effective method for documenting the patency of parent vessels, arterial branches, and major perforators and the complete occlusion of cerebral aneurysms. This technique can be reliably used, in many instances, instead of intraoperative angiography for the surgical treatment of aneurysms.