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1. Experimental study on the effects of deep intracerebral hemorrhage in the rat.

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Intracerebral hemorrhage (ICH) in the basal ganglia constitutes one of the most devastating forms of cerebrovascular disease, with the majority of the survivors suffering from severe residual neurological deficits. Currently available therapy is mainly supportive, consisting in maintenance of homeostasis and treatment of brain edema. In patients with space-occupying hematomas, surgery may be beneficial to relieve the mass effect.

In order to investigate neurorestorative strategies after ICH, we have developed a model of deep ICH in the rat which mimics the clinical situation in the human by combining a striatal microtrauma with slow infusion of 30 µl autologous blood. The macroscopic observations showed that the lesion resulted in a hematoma volume of 15.2±1.5 mm3 that was significantly larger as compared to controls undergoing cannula insertion alone (0.11±0.02 mm3). The hematoma borderzone was observed to be well delineated and the perihematomal area histologically preserved. We also detected that the lesion caused a marked increase of vimentin- and OX42-immunoreactive cells in the borderzone. Rats with ICH exhibited transient spontaneous rotational asymmetry with a tendency to turn ipsilateral to the lesion side during the first 10 days and significant, irreversible deficits in the forelimb placing test. In the present study we investigated the effects of ICH on the number of tyrosine hydroxylase (TH) expressing dopaminergic neurons and on the number of total neuronal cells in the substantia nigra (SN). Immunohistochemical analyses revealed that striatal ICH resulted in a significant decrease of 45% and 15% in the number of TH-immunoreactive cells in the SN ipsilateral to the lesion at day 2 and 30, respectively. In contrast, loss in total neuronal cell numbers was less pronounced with a decrease of 20% and 5%, respectively. This result indicates that the dopaminergic nigrostriatal projection system is significantly affected by ICH in the striatum. Notably, in addition to a cell loss, ICH induced a transient downregulation of TH expression in a subpopulation of SN neurons.

In summary, due to the standardized reproduction of deep striatal ICH, the proposed model is particularly well adapted to study restorative strategies after an acute focal brain lesion and to investigate the effects on other brain regions.

2. Evaluation of metastatic brain lesions by intraoperative ultrasonography (IOUS).

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Background: Intracranial metastases are found in 20 to 30% of patients dying of systemic cancer. Intraoperative ultrasonography (IOUS) has been used as a diagnostic tool since 1970. A total of 50 patients with metastatic brain lesions were evaluated by using IOUS.

Methods: A real-time ultrasound scanner with a 3-MHz transducer was used in all cases. The tip of the ultrasound probe was placed on the intact cranial dura matter and then moved in the sagittal and coronal planes.

Results: A total of 50 consecutive patients (27 men and 23 women) with metastatic brain lesions were included in this study. The median age of the patients was 56 years ranging from 29 to 82 years. All lesions were localized and malignant characteristics were well defined by IOUS. Irregular contour, irregular contrast enhancement, necrotic parts, and perilesional edema were seen in all patients but only 18 patients showed a cystic part.

The ultrasonographic appearance of malignant cysts was as low echogenic areas. Free necrotic particles and double density were commonly present in malignant cysts. The solid component surrounding the cysts was thick. The external surface of solid parts was regular but internal surfaces facing cysts were irregular. The necrotic part of metastatic lesions was solitary in 12 patients (24%) and multiple in 38 patients (76%) and has a mixechogenic appearance. The most hypoechogenic part was commonly located in the central portion. Malignant perilesional areas were seen as two different echogenic zones. The lesions were surrounded by a first, very thin hypoechogenic zone. The ultrasonographic appearance of the second zone was hyperechogenic and was similar to that of solid tumor parts. The growth pattern of tumors was demonstrated to be of both distortive and invasive character.

Conclusion: IOUS is an excellent tool for localization of metastatic brain lesions and for detailed description of their interior. The contour of tumors, perilesional changes, the presence of cyst and necrosis and their details are the most important information. Irregular border, necrotic parts, invasive growth pattern, and dense perilesional edema can all be attributed to malignancy.

3. The Anti-inflammatory Effect of Meloxicam on Experimental Rat Femoral Artery Vasospasm.

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Aim: Cerebral vasospasm greatly influences morbidity and mortality in patients following subarachnoidal haemorrhage (SAH). Inflammation is believed to play a role in posthaemorrhagic cerebral vasospasm. Meloxicam is a nonsteroidal anti-inflammatory drug that preferentially inhibits cyclooxygenase (COX) that has an important role in biosynthesis of prostoglandins. In this study, we investigated the effect of meloxicam on rat femoral artery vasospasm using the radial wall thickness and cross luminal area as parameters under the light, scanning and transmission electron microscope examinations.

Method: A femoral artery vasospasm model in rats that described previously by Okada et al used. Twenty-four Spraque-Dawley rats randomly separated into three groups, the first one was the control group (n=8), the second one was the SAH group (n=8) and finally the last one was the SAH + meloxicam group (n=8). The rats in the treatment group (SAH + meloxicam) were given meloxicam 2 mg/kg/day for 7 days. A week later, all the animals were sacrified. After perfusion fixation, 10 mm segments of femoral arteries were removed and prepared for examinations with light microscope, scanning and transmission electron microscopes and for morphometric analysis.

Results: A statistically significant difference was detected between the scanning, electron and light microscopic findings and morphometric analysis of SAH and SAH + meloxicam group. The difference was not significant between control and SAH + meloxicam group.

Conclusion: Meloxicam treatment before vasospasm, reduces ultrastructural and morphometric vasospastic changes in the femoral arteries of the rats. These findings may strongly support the hypothesis that inflammation may play a role in one of the pathophysiologyical pathways of posthaemorrhagic cerebral vasospasm. And secondly, after clinical trials this agent may be take place in protocol of the treatment vasospasm following SAH.

4. **Benign epithelioid peripheral nerve sheath tumor (BEPNST) of the peroneal nerve presenting with acute foot drop**

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Dysfunction of the peroneal nerve usually presents with foot drop and parasthesias in the areas of sensory innervation. Peroneal nerve dysfunction is commonly seen following supracondylar fractures, knee dislocations, and proximal tibial fractures or following surgery in the area of the fibular head. A compression neuropathy can also be seen with Baker cysts, frequent leg crossing, or from the knees leaning against a sharp edge for extended periods of time.

We present a case in which the patient presented with acute onset of foot drop with pain and parasthesias located in the distribution of the peroneal nerve. The patient was found to have a perineural tumor of indeterminate pathology.

The differential diagnosis of our patient's lesion is extensive. The pathology suggests a reactive process such as fibromatosis, but other considerations such as spindle cell lipoma, low grade spindle cell liposarcoma, or a hamartomatous process cannot be ruled out completely.

This paper attempts to characterize an unusal presentation of peroneal tumor growth and reviews the histologic and pathologic differential diagnosis of such lesions.

5. Long-term Experience of Gamma Knife Radiosurgery for benign Skull Base Meningiomas

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As most of the Gamma knife reports are related only to short- or mid-term results we have evaluated the effectiveness and toxicity of radiosurgical treatment for benign skull base meningiomas in 200 patients with a follow-up of 5 to 12 years in order to define the role of GKRS for basal meningiomas and to provide further data for comparison with other treatment options.

Methods. Ninety-nine patients were treated with a combination of microsurgical resection and GKRS. In 101 patients GKRS was performed as the sole treatment option. Tumour volumes ranged from 0.38 ccm - 89.8 ccm (median 6.5 ccm) and doses of

7 Gy to 25 Gy (median 12 Gy) were given to the tumour borders at covering isodose volume curves (range: 20 % - 80 %, median 45 %).

Results. The actuarial progression-free survival rate was 98.5 % at 5 years and 97.2 % at 10 years. Passing radiation-induced oedema occurred in two patients (1 %). The neurological status improved in 83 cases (41.5 %), remained unaltered in 108 patients (54 %) and deteriorated in 9 cases (4.5 %). Worsening was transient in 7 patients (3.5 %) and unrelated to tumour or treatment in one single patient (0.5 %). Repeated microsurgical resection was performed in five patients following GKRS (2.5 %).

Conclusions. GKRS has proved to be an effective alternative to microsurgical resection, radiotherapy and Linac-based radiosurgery for adjunctive and primary treatment of selected patients with basal meningiomas. Due to the excellent long-term tumour control rate and low morbidity associated with GKRS this treatment option should be used more frequently in the therapeutic management of benign skull base meningiomas.

6. "Radical" surgery for intramedullary spinal cord tumors in pediatric patients with severe neurological deficit: is it worth to offer it?

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Introduction: "Radical" surgery for IMSCT is currently accepted as a fist-line treatment. It was shown in most surgical series that results of surgery depend on preoperative status of patient. This means, that according to contemporary information, surgery can add no advantages for patient with IMSCT with severe neurological deficit.

Methods: In 2002-2005 thirty seven pediatric patients with IMSCT were operated by author in Burdenko Neurosurgical Institute (Moscow). Our surgical goal was maximal tumor removal with functional preservation under MEP control. In cases with diffuse tumors surgery was stopped as MEP deterioration became apparent. Patients' related data were prospectively collected in formalized database. Information about surgical results in severely disabled patients was picked from database and analyzed retrospectively. Patients' functional status at last follow-up was used as a primary outcome measure.

Results: Nineteen kids were severely disabled at time of admission. Eight patients harbored McCormick score (MCC) 3 and 11 – MCC-4. Gross-total removal according to follow-up enhanced MRI was achieved in 7 patients (37%), subtotal (>80%) removal was achieved in the rest of patients. Nobody became worse after surgery or developed life-treating complications. Twelve patients (63%) improved by 1-3 points of McCormick (MCC) scale. In these 12 patients 11 (58%) became fully independent in there life. Only one patient in the group with MCC-3 did not improve (12%), but six (55%) in MCC - 4 group.

Conclusion: Attempt to perform "radical" surgery looks as attractive treatment option in our population of severely disabled patients with IMSCT. Surgery had chance to improve functional status in 58% of our patients. Taking into account that all these kid were bedridden and had progressive neurological deterioration before surgery, this improvement looks even more impressive. In our opinion, policy to withhold surgery in severe disabled pediatric patients with IMSCT can not be justified.

7. **A 'risk calculator' for Pocket PC**

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Aim: we wanted to develop a software for 'Pocket PC' to calculate the cumulative risk for adverse events e.g. life-time risk of rupture of unruptured aneurysms, risk of haemorrhage from arteriovenous malformation.

Method: The software was developed using Microsoft Visual Basic component of Microsoft Visual Studio 2005 (standard edition) on Sony Laptop computer running an updated version (SP2) of Windows XP Professional operating system. For cumulative risk to be clculated the user would need to input following variables: i. the annual risk for the adverse event, ii. the number of years. The calculation assumes that the rate of risk for the adverse is constant every year. The following formula is used to calculate the cumulative risk: Cumulative risk = 100 * (1-((100-rate of annual risk)/100) ^years).

Results: The software that was developed to calculate culumaltive risk of an adverse event was able to run on Pocket PCs (operating system: Windows CE 2003 or Windows mobile 2005) which had Microsoft Compact Framework 2.net installed.

Conclusion: Useful programs for neurosurgeons could be developed for Pocket PCs by neurosurgeons, allowing doctors to take advantage of powerful mobile computing capability offered by Pocket PCs.

8. On the difficulties in grading patients with subarachnoid haemorrhage using WFNS grading system.

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The World Federation of Neurological Surgeons (WFNS) grading system is a commonly used classification system for grading patients with subarachnoid haemorrhage (SAH). We hypothesized that the WFNS grade has an excellent inter-observer reliability in classifying patients with SAH. We wanted to test this hypothesis

Method: We distributed a questionnaire to members of our department. The questionnaire had a brief description of 5 fictional patients with SAH. Patient 1: patient with GCS 15 and right sided pronator drift; Patient 2: patient with E-4, M-6, aphasia; Patient 3: patient with GCS 15 and left sided hemiparesis; Patient 4: patient with E-4, M-6 and expressive dysphasia; Patient 5: patient with GCS 9 and hemiplegia. We requested the responders to assign WFNS grade to each of these patients. All those completed the questionnaire were of registrar grade or above.

Results: We had 13 responses. For the Patient 1, 54%, 15%, 31%, 0%, 0% thought the patient's WFNS Grade was 1,2,3,4,5 respectively. For Patient 2: 8%, 8%, 62%, 15%, 0% thought the patient's WFNS Grade was 1,2,3,4,5 respectively. For patient 3:

23%, 23%, 54%, 0%, 0% thought the patient's WFNS Grade was 1,2,3,4,5 respectively. For Patient 4: 8%, 15%, 54%, 15%, 0% thought the patient's WFNS Grade was 1,2,3,4,5 respectively. For patient 5: 0%,0%,8%, 92%,0% thought the patient's WFNS Grade was 1,2,3,4,5 respectively.

Conclusion: Our results show that WFNS grading system for subarachnoid haemorrhage can have high level of inter-observer variability.

9. Thalamic Deep Brain Stimulation in Treatment of Disabling Tourette Syndrome.

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Introduction: Tourette syndrome is a peculiar neuropsychiatric disorder characterized by motor and/or vocal tics that may result in severe disability for patients and frustration with ineffective treatment for neurologists and psychiatrists. Surgical treatment for medically intractable Tourette syndrome in the past included variety of destructive procedures, but since the introduction of deep brain stimulation 7 years ago, several reports appeared in the literature targeting various areas of the brain. In 4 patients reported up to date, bilateral thalamic DBS (centromedian nucleus, periventricular substance and VOI nucleus) was performed, and in one case each the internal capsule, internal part of the pallidum, external part of pallidum, and combination of thalamic and pallidal regions were stimulated. In all cases, symptomatic improvement was observed with decrease of frequency of both verbal and motor tics without any major side effects.

Case Description: Based on this encouraging preliminary experience, we operated on a 48 year old male with a long history of disabling Tourette syndrome. Bilateral thalamic DBS electrodes were placed aiming at CM/SVP complex (5 mm lateral and 5 mm posterior to mid-commissural point in the AC-PC plane) with subsequent internalization of electrodes to a double-channel DBS generator.

Results: Over the next 3 months, the DBS settings were gradually adjusted to control the tics. There was a consistent 70-90% decrease in frequency of both verbal and motor tics observed during monthly follow up visits (duration of follow up – 10 months). No complications related to the surgery or stimulation itself was observed. The patient returned to gainful employment.

Conclusion: Even with uniformly positive results reported so far with DBS used for treatment of Tourette syndrome, the experience is still extremely limited and uncontrolled. The optimal target location, DBS settings and exact surgical indications continue to require better definition. Our experience supports the data reported previously in showing that DBS for Tourette is feasible, safe and effective.

10. Antibiotic Impregnated Catheters for the Treatment of Neonatal Hydrocephalus.

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Introduction: Antibiotic impregnated shunts (AIS) decrease shunt infections by preventing bacterial colonization at time of surgery. There is no study which investigates the efficacy of these systems in infants less than 6 months of age.

Methods: A chart review of conducted involving pediatric patients less than 6 months of age with hydrocephalus who underwent placement of AIS components as initial treatment or following an Ommaya reservoir.

Results: 75 patients underwent 118 procedures, of which 40% had a previous Ommaya Reservoir. The average weight and gestational age at birth was 1976 grams and 32.5 weeks. The average age at time of surgery was 47 weeks. Five (15%) developed an infection, of which 90% were Gram negative organisms. 33 patients required a shunt revision surgery during the study period. No significant complications or mortality occurred from the procedures.

Conclusion: AIS systems are safe in neonates and may help decrease the incidence of Gram positive organisms in this population.

11. Robotic Micro-Neurosurgery with the Da Vinci system: a preliminary experience.

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Introduction: We describe our preliminary experience in using the Da Vinci Robot in performing microsurgery. This clinical experience was preceding by animal laboratory work with this robot and a prior experience in neurosurgical robotics with the Zeiss MKM robot and the Surgiscope.

Methods: The first patient presented with a symptomatic lipomyelomeningocele. The robotic interface was used for active fine tissue dissection and to allow experience to be gained with the instrumentation, the 3-D interface, and the endo-wrist movements.
The second patient presented with a large para-sagittal frontal brain metastases involving the falx cerebri, sagittal sinus and anterior to the motor cortex. The third patient presented with a large right parasagittal meningioma with sagittal sinus invasion and significant mass effect on the adjacent motor cortex. In both these brain cases the robotic system aided fine tumor dissection at the motor cortex junction and at the sagittal sinus.

Results: The robotic set up prolonged operative time by about 45-65 minutes. The robotic interface was intuitive for a neurosurgeon as it was similar to operative microsurgery with a magnified 3-D view. The endo-wrist system and instrumentation allowed precision and true ambidexterity in tissue dissection, with seven degrees of freedom and a tremor free operation of tools in the operative field controlled by a surgeon's hands remote from that site.

Conclusions: The use of an active robotic device with 3-D visualization and active instrumentation allows a new dimension in micro-neurosurgery and points in a future direction of overcoming the limits of the human hand .However proper training, patient selection and tool tip development is required in neurosur-

gical applications.

12. Personalised Vaccines as an adjuvant therapy for treatment of Glioblastoma: A Review

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Recent advances in molecular biology and better understanding of immune-mechanics have placed immunotherapy at the forefront of brain tumor research. Although targeting expressed antigens by a generic vaccine is attractive, it would seem more appropriate to individualize the vaccine based on the unique set of antigens or antigenic epitopes in a given patient. This allows the antitumor effector cells to display greater selectivity and potentially avoid the serious risk of autoimmune responses.

The aim of the presentation is to review the currently available information on personalized vaccines as a treatment option for glioblastoma. Various methods ranging from whole cell inoculation to specific purified peptides have been studied as ways of priming the immune system against one's own cancer. Although these models are well supported by pre-clinical studies, its clinical application is still in the early phase. The clinical studies have, apart from demonstrating the safely of brain tumour vaccines, been able to demonstrate immunological responses both peripherally and within the tumour. This is encouraging and crucial to the understanding of the complex CNS-immune interactions. However, there are other challenging issues which include the immune status of patient, the optimum route of administration and problems in manufacturing the vaccine, especially when they are patient-specific. Still, from the available evidence so far, it appears that in the appropriate subgroup of patients, when combined with other therapeutic modalities, the full potential of immunotherapy can be realized. Given the antigenic heterogeneity, both between individual patients and within the tumor itself, the strategy in future should be to tailor immunotherapies to a tumor's molecular, genomic, and immunomic status to create "customized immunotherapy".