

Oral Presentations  
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### Best International Abstract Award

**600 5-Aminolevulinic acid fluorescence exceeds Gd-DTPA enhanced intraoperative MRI in tumor detection at the border of glioblastoma multiforme: A prospective study based on a histopathological assessment.**

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**Introduction:** Glioblastoma multiforme (GBM) shows an invasive growth pattern extending into neural tissue beyond margins of contrast enhancement in MRI. Aim of the present study is to evaluate whether 5 aminolevulinic-acid fluorescence (5-ALA) provides an additional benefit to detect invasive tumor compared to intraoperative MRI (iMRI).

**Methods:** We prospectively enrolled 34 patients harboring a GBM with intended gross total resection. All patients had surgery using iMRI and 5-ALA guided resection following a specific protocol: First a white-light tumor resection was performed. Then, spatial location of residual fluorescence was subsequently marked. After that, an iMRI was performed and residual uptake of contrast was marked. Navigated biopsies were taken from these areas and from additional sites according to surgeons judgment. Cross tables and ROC-curves were calculated assessing performance of the imaging methods for tumor detection alone and for combined detection including infiltration zone (pathological tissue). Correlations of histopathological findings with imaging results were tested using Spearman's rho.

**Results:** 114 histopathological samples were harvested. Sensitivity for tumor detection was significantly higher ( $p < 0.001$ ) in 5-ALA (0.85) than in iMRI (0.41). Specificity was significantly ( $p < 0.001$ ) lower in 5-ALA (0.43) as in iMRI (0.70). For detection of pathological tissue 5-ALA exceeded iMRI in specificity (0.80 vs. 0.60) and sensitivity (0.91 vs. 0.66) significantly ( $p < 0.001$ ). Imaging results of iMRI and 5-ALA did not correlate significantly. Only 5-ALA showed a significant correlation with final histopathological diagnosis of specimen and with typical histopathological features of GMS.

**Conclusions:** Imaging results of 5-ALA and iMRI are significantly different at the border zone of GBMs. 5-ALA has a higher sensitivity and a lower specificity for tumor detection than Gd-DTPA-enhanced iMRI. For detection of infiltrating tumor 5-ALA is superior to Gd-DTPA-enhanced iMRI concerning both sensitivity and specificity. Thus, additional use of 5-ALA to iMRI might be beneficial to maximize extend of resection.

**601 Prospective, Multicenter Assessment of Acute Neurologic Complications following Complex Adult Spinal Deformity Surgery: The Scolio-RISK-1 Study**

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**Introduction:** The neurologic complication rate following complex adult spinal deformity surgery (ASD) has not been ascertained in any prospective, multicenter, observational study. Here, we compare preoperative lower extremity motor scores (LEMS) to 6 month postoperative scores.

**Methods:** 276 complex ASD patients from 15 sites worldwide were enrolled in this prospective, multicenter observational study. Diagnoses included primary coronal and/or sagittal deformity  $< 80^\circ$  ( $n=78$ ), congenital deformity ( $n=13$ ), revision deformity requiring osteotomy ( $n=107$ ) and/or patients undergoing a 3-column osteotomy (3-CO) ( $n=202/276$ , 73% all patients). There were 186 females (67%) and 90 males (33%) with a mean age of 57.7 years (range, 18-85). The patients had ASIA neurologic exams preoperatively, at discharge (D/C), and 6 weeks and 6 months postoperatively.

**Results:** 207/276 (75.0%) patients had normal LEMS preoperatively (Preop NML group) while 69 (25.0%) had some motor weakness (Preop ABNML group, mean  $43.8 \pm 7.6$ ). At hospital D/C, 6 weeks and 6 months postoperatively, there were statistically significant declines in LEMS in the Preop NML group ( $48.91 \pm 3.51$ ,  $p < 0.05$ ;  $49.03 \pm 3.29$ ,  $p < 0.05$ ;  $49.36 \pm 2.84$ ,  $p < 0.05$ ), while there was no LEMS change in the ABNML group at hospital D/C ( $43.67 \pm 8.33$ ,  $p=0.977$ ), 6 weeks postoperatively ( $44.98 \pm 8.05$ ,  $p=0.182$ ), but an improvement at 6 months postoperatively ( $47.02 \pm 6.28$ ,  $p < 0.05$ ). Overall, 23.1% of patients experienced worsening of their LEMS at hospital D/C, 17.8% at 6 weeks postoperatively, and 10.7% at 6 months postoperatively. Older age at time of surgery was a risk factor for deterioration in LEMS postoperatively (mean, 56.8 without vs. 61.7 with decline,  $p=0.0057$ ).

**Conclusions:** The Scolio-RISK-1 Trial documented the acute lower extremity motor weakness complication rate of 23.1% at hospital D/C, 17.8% at 6 weeks postoperatively, and 10.7% at 6 months postoperatively following complex ASD surgery. This neurologic complication rate should be considered the Gold Standard in complex ASD procedures due to the prospective, multicenter nature and strict protocols followed.

### 602 A Novel Phase 1/2A Study of Intraparenchymal Transplantation of Human Modified Bone Marrow Derived Cells in Patients with Stable Ischemic Stroke

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**Introduction:** No treatment exists to restore lost brain function after stroke. Animal studies demonstrate that brain transplantation of SB623, a human modified bone marrow derived stromal cell, after experimental stroke can improve neurologic outcome. This clinical study is the first North American trial of intraparenchymal transplantation of bone marrow derived cell therapy for chronic stroke patients.

**Methods:** This is a two center open-label safety, dose escalation feasibility study. Stereotactic transplantation targets the subcortical peri-infarct area. Inclusion criteria include 18–75 yo, 6–60 mos post subcortical MCA ischemic stroke, mRS 3–4 and NIHSS < 7. Safety endpoints include WHO toxicity scale, MRIs and clinical follow-up to 2 years. The primary efficacy endpoint is European Stroke Scale (ESS) at 6 mos; secondary efficacy measures are ESS, NIHSS, Fugl-Meyer, mRS, cognitive scores and FDG-PET.

**Results:** Eighteen patients were treated (6 each with 2.5M, 5M and 10M cells. Follow-up is < 6 mos in 16 pts and < 12 mos in 12 pts. There were 3 serious adverse events (SAEs) related to the surgery, but not to the cells (seizure, subdural hematoma, pneumonia) and 2 SAEs unrelated to either surgery or cells (UTI, delayed new neurologic symptoms). Cytokine levels, HLA antibody levels, and PBMC function were unchanged. NIHSS, ESS, Fugl-Meyer all show a significant benefit in neurologic outcomes. Two patients showed remarkable improvement in their motor function within 24h of surgery, effects which have been sustained during follow-up (20 and 5 mos). These were the only 2 patients with new FLAIR lesions (DWI neg) in the motor cortex that resolved at 2 mos.

**Conclusions:** This open-label clinical study indicates that intraparenchymal transplantation of human modified bone marrow derived stromal cells in chronic stroke patients is safe, feasible and results in improved neurologic function. Larger studies will be initiated to further assess clinical efficacy.

## Stryker Neuro-Oncology and Young Neurosurgeons Abstract Award

### 603 Mesenchymal stem cell exosomes enhance glioma stem cell viability and stemness via delivery of microRNA

Javier Figueroa (Richmond, TX); Tal Shahar, MD; Anwar Hossain, PhD; Lang Frederick, MD (Houston, TX)

**Introduction:** Although recent evidence indicates that human cancers are maintained by a population of cells with stem-like properties called cancer stem cells (CSCs), the influence of the surrounding stromal cells on the behavior of the CSCs remains poorly understood. We have recently shown that the micro-environment of human gliomas contains both glioma stem cells (GSCs) and cells that resemble human bone marrow mesenchymal stem cells (BM-hMSCs), called Glioma

Associated-MSCs (GA-MSCs). We have also shown that these GA-MSCs enhance the growth of Glioma Stem Cells (GSCs). However, the mechanism underlying the communication between GA-MSCs and GSCs has not been established. Recent studies have suggested that nano-vesicles, called exosomes, may contribute to cellular communication within the tumor niche. Therefore, we hypothesized that exosomes released by GA-MSCs may promote the growth of GSCs.

**Methods:** GA-MSC exosomes were harvested by ultracentrifugation and sucrose cushion, and analyzed by both CD63 western blot and immuno-gold electron microscopy. Both GA-MSCs and GSCs were isolated from patient tumor samples.

**Results:** Here we show for the first time that in vitro delivery of exosomes isolated from GA-MSCs significantly increased both the viability and clonogenicity of GSCs. Furthermore, in vivo xenograft implantation of GSCs, pre-treated with GA-MSC exosomes, into the brains of nude mice resulted in a greater tumor burden and a significant decrease in animal survival compared with untreated controls. These exosomes were also found to contain a wide variety of miRNA, including many which are associated with glioma. Treatment of GSCs with GA-MSC exosomes, was enough to alter the miRNA profile of GSCs, increasing the amount of these oncogenic miRNAs intracellularly.

**Conclusions:** We conclude that exosomes released by GA-MSCs represent a novel and alternative intra-tumoral communication mechanism for the exchange of miRNA, which significantly impacts the tumor microenvironment and enhances the aggressive nature of gliomas.

## Synthes Skull Base Award

### 604 Incidence of headache as a presenting complaint in over 1000 patients with sellar lesions and factors predicting postoperative improvement

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**Introduction:** Because of the high incidence of headaches and pituitary tumors, neurosurgeons are often asked to evaluate patients with benign-appearing sellar lesions and headaches without insight into whether the headache is attributable to the lesion. We sought to evaluate the incidence of headache as a presenting complaint in over 1000 patients with sellar lesions of variable pathology and to identify factors predicting postoperative improvement.

**Methods:** We conducted a five-year retrospective review of our first 1015 transsphenoidal surgeries since establishing a pituitary center of expertise.

**Results:** Of 1015 patients with sellar lesions, 340 presented with headache. Of patients with headache, 30% presented with headache as their only symptom. Patients with Rathke's cleft cysts (RCCs) had the highest percentage of headache at 60%, followed by craniopharyngioma (46%) and apoplexy (44%), while endocrine inactive and active adenomas had lower rates of headache (28-29%). Multivariate analyses revealed diagnosis (P=0.01), younger age (P=0.001), female gender (P=0.002), and recurrent lesions (P=0.04) to be associated with headache, with lesion size, suprasellar extension, and hypopituitarism not associated. Of patients presenting with headaches, 36% reported improvement of headaches at 6-week follow-up and 47% had improved at the 6-month follow-up. Multivariate analyses including associated symptoms, duration and location of headache, age, gender, lesion