Phenytoin reduces 5-ala mediated fluorescence in glioblastoma cells

Christopher Steele

Johnathan Lawrence  
*Northern Michigan University, jolawren@nmu.edu*

Richard A. Rovin  
*Marquette General Hospital*

Robert J. Winn  
*Northern Michigan University*

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ST-001. PHASE 1 TRIAL OF A RETROVIRAL REPLICATING VECTOR (TOCA 511) IN RECURRENT HIGH GRADE GLIOMA - PATIENTS DEMONSTRATES THE IMPORTANCE OF REAL-TIME MRI-GUIDED DELIVERY FOR DOSE-RELATED EVALUATION OF SAFETY AND EFFICACY

Manush Agah1, Michael A. Vogelbaum2, Douglas J. Jolly3, Joan M. Robbins3, Derek Osterra4, Carlos E. Ibanez3, Harry E. Gruber5, Noriyuki Kasahara4, Krystof Bankiewicz6, Timothy F. Cloughesy7, Susan M. Chang1, Nicholas Butowski1, Santosh Kesari5, Clark Chen7, Tom Mikkelsen8, Derek Ostertag3, Carlos E. Ibanez3, Harry E. Gruber5, Noriyuki Kasahara4, Joseph Landolfi9, E. Antonio Chiocca10,12, J. Bradley Elder10, Greg Foltz11, and the duration of Toca FC.

As a result, real-time MRI-guided delivery was introduced using Toca 511 in-stead release 5-FC (Toca FC) were investigated in 25 HGG patients to date. Levels, escalated by half logs, the mode of administration and the use of extended release 5-FC (Toca FC) were investigated in 25 HGG patients to date. Treatment at all dose levels has been well tolerated. Post-treatment resection in two patients showed viral protein and DNA and RNA sequences including the CD gene, suggesting viral spread and persistence. MRI and clinical improvements were also occasionally observed. Virus was initially delivered via a brain biopsy needle and placement in the tumor was predicted using conventional neuro-navigation. Immediate MRI after injection of Toca 511 showed with gadolinium we observed inconsistent delivery of Toca 511 to tumor. As a result, real-time MRI-guided delivery was introduced using Toca 511 in infusion with a stopped-tip cannula. Using this approach, delivery into as many as 4 locations of up to 3 ml of Toca 511 at flow rates of up to 30 μL/min has been achieved without reflux. In a tumor biopsy from a patient who received 1 ml of Toca 511 and subsequent Toca FC, we observed tumor selective vector transduction and expression by PCR and RT-PCR with concomitant tumor necrosis. At higher Toca 511 doses, significant MRI changes consistent with tumor regression were observed post-Toca FC dosing. Completion of this study is planned, including dose escalation of Toca 511 and increasing the dose and duration of Toca FC.

ST-002. ENDOCYTIC PITUITARY TUMOR SURGERY: THE LEARNING CURVE

Amjad Anaziz, Christopher Taylor, Jennifer Kosty, Lee Zimmer, and Philip Theodosopoulos; University of Cincinnati, Cincinnati, OH, USA

INTRODUCTION: Endoscopic endonasal pituitary surgery is increasing utilized and is being passed on to the next generation of neurosurgeons. This approach can be technically challenging due to lack of 3 dimensional visualization, increased operative working distance and novel/different instrumentation. We present our experience with the exclusive endoscopic endonasal approach over the last 10 years. METHODS: We performed a retrospective review of patients who underwent an endoscopic endonasal pituitary tumor resection between 2003-2012 by a single neurosurgeon (group A) with the second half of patients (group B). RESULTS: A total of 240 patients with adequate follow up were included in the study. Average patient age in both groups was 31 years. F:M ratio in both groups was 1.15:1. In Group A 53.8% had a GTR and 44.2% had a STR. In Group B, 59.2% had a GTR and 40.8% had a STR. The rate of new post-operative pituitary dysfunction was 18.3% in Group A and 15% in Group B. The rate of diabetes insipidus was 12.5% in group A and 3.3% in group B (P < 0.01). The rate of post-operative CSF leaks was 3.3% in Group A and 2.5% in Group B. CONCLUSION: The 2 dimensional view, increased working distance and novel instrumentation can result in a steep learning curve for endoscopic pituitary surgery. Increased experience should result in improved patient outcomes, particularly a decreased rate of diabetes insipidus.

ST-003. FACIAL NERVE PRESERVATION SURGERY FOR LARGE VESTIBULAR SCHWANNOMAS: FUNCTIONAL AND TUMOR CONTROL OUTCOMES

Amjad Anazi, Eric Gantwerker, Myles Pennak, and Philip Theodosopoulos; University of Cincinnati, Cincinnati, OH, USA

OBJECT: Large vestibular schwannomas pose a unique challenge of achieving surgical cure while maintaining normal facial nerve function. Facial nerve preservation surgery, defined as preserved function at the cost of residual tumor when adherent to the facial nerve or root entry zone, is a novel idea. We present our experience and evaluate functional outcomes and extent of resection. METHODS: We performed a retrospective review of patients treated surgically by a single surgeon team (PVT, MP) for large (Koos & 4) vestibular schwannomas between 2003-2012. We review the extent of resection, post-operative hearing and facial nerve function. We separated the patients into groups based on extent of resection (gross total, near-total and subtotal) and evaluated the tumor control rate and functional outcome. RESULTS: A total of 56 patients were included in the study. Four patients had radiation treatment to their tumors prior to surgery. 18 patients underwent a resection and 38 underwent a translabyrinthine approach. Hearing was preserved in 1 of 5 (20%) GTR patients, 0 of 2 NTR patients and 1 of 3 (33%) STR patients. Good facial nerve function (HBI & II) was achieved long term in 17 of 20 (85%) GTR patients, 11 of the 12 (92%) NTR patients and 22 of the 24 (92%) STR patients. Only the GTR group had HB IV or worse facial nerve function (3 patients). Long term tumor control was 100% for GTR, 92% for NTR and 83% for STR. 9 STR patients and 1 NTR patient received postoperative radiation therapy. Average follow-up was 33 months. CONCLUSION: Facial nerve preservation surgery is associated with increased chance of long term good facial nerve outcome. The rate of tumor progression following STR is 17%.

ST-004. NASAL CAVITY MALIGNANCIES INVOLVING THE SKULL BASE: IS THERE A ROLE FOR ENDOSCOPY?

Amjad Anazi, Sanjeev Grewal, Philip Theodosopoulos, and Lee Zimmer; University of Cincinnati, Cincinnati, OH, USA

OBJECT: The role of endoscopy in the resection of malignant lesions remains controversial. Such malignancies are traditionally resected through transcranial approaches and any skull base involvement is addressed through transcronic or combined approaches. We present a series of patients with nasal cavity malignancies involving the skull base treated with purely endoscopic or endoscopic-assisted resections and offer an algorithm to assist in the appropriate selection of these patients. METHODS: We retrospectively reviewed the charts of patients with malignant nasal cavity lesions involving the skull base resected utilizing nasoendoscopic approaches. RESULTS: A total of 9 patients were included in the series. M:F ratio was 3:5. Average age at time of surgery was 52 years. Pathology included Esthesioneuroblastoma, sarcoma, SNUC, melanoma, adenoscarcoma and myofibriloblastic tumor. 2 patients (22%) had intra-orbital extension and 1 patient (11%) had pterygopalatine or infratemporal fossa extension. All patients had skull base involvement, 5 (56%) of which had intradural extension. 6 patients (67%) underwent a purely endoscopic resection and 3 patients (36%) had a combined approach. 6 (67%) patients had a GTR and 3 (33%) patients had subtotal resection. Average EBL was 780 ml. 67% of patients retained olfaction post-op. Average follow-up was 25 months. 6 (67%) underwent post-operative adjuvant treatment. Complications included 2 post-op CSF leaks. CONCLUSION: Nasal cavity malignancies involving the skull base can often be difficult to resect. Open transcranial approaches are effective, but can be associated with significant morbidity. We believe that endoscopic and endoscope-assisted techniques offer a more innovative and safer alternative for the management of many of these lesions in appropriately selected patients.
**ST-005. SURGICAL RESECTION FOLLOWING PRIMARY RADIATION TREATMENT FOR VESTIBULAR SCHWANNOMAS: DOES RADIATION IMPACT SURGICAL OUTCOMES AND EXTENT OF RESECTION?**

Amjad Anaziz, Myles Pensak, and Philip Theodosioupolos; University of Cincinnati, Cincinnati, OH, USA

OBJECTIVE: With the advent of highly focused delivery of radiation, an increasing number of vestibular schwannomas are being treated this way. A minority of these patients will fail this management strategy and require subsequent treatment. Early studies have shown poor post-operative facial function presumably due to radiation-induced fibrosis and adhesions to surrounding neurovascular structures. We present our experience with salvage surgical procedures following failed primary radiation treatment for vestibular schwannomas.

METHODS: We performed a retrospective review of patients with unilateral vestibular schwannomas who underwent resection following failed primary radiation treatment. No patient had prior surgery for the same lesion and NF2 patients were excluded. We present patient demographic information, preoperative radiation treatment modality and preoperative facial nerve function. We review operative approach, pathology, extent of resection, facial nerve function, tumor control and complications.

RESULTS: 5 patients with vestibular schwannomas previously treated with radiation underwent surgical resection. 3 patients received prior SRS and 2 patients received prior fractionated radiotherapy. Average time between radiation and surgery was 42 months. No patients had serviceable hearing prior to surgery. All patients underwent a translabyrinthine approach. A gross total resection was achieved in 4 patients (80%), and a subtotal resection in 1 patient (20%). 3 patients (60%) had a good (HBI & II) post-operative facial nerve function. One patient (20%) had a HB IV facial nerve palsy. Pathology revealed WHO I vestibular schwannoma in all patients. No patient had post-operative tumor progression with an average of 27 months follow up.

CONCLUSION: Vestibular schwannomas that have failed primary radiation can present a difficult treatment dilemma to the surgeon. Although radiation effects can increase the potential for post-operative cranial nerve dysfunction and decrease the likelihood of achieving gross total resection, surgical resection with modern surgical technique is a safer and more effective than what earlier data would suggest.

**ST-006. ENDOSCOPIC SURGERY FOR INTRAVENTRICULAR AND PARAVENTRICULAR TUMORS**

Yoshiki Arakawa1, Yoo Kang2, Daiki Murata1, Ko-ichi Fujimoto1, and Naoyuki Minami1; 1Department of Neurosurgery, Kyoto University Graduate School of Medicine, Kyoto, Japan; 2Department of Neurosurgery, Ohno Memorial Hospital, Osaka, Japan

BACKGROUND: Endoscopic management for the ventricular lesions has been widely applicable according to instrument’s development. In ventricular and paraventricular tumors, endoscopic biopsy has been less invasive and safer standard surgery. Here, we report our technique to resect intraventricular tumors with endoscopy. PATIENTS AND METHODS: Between 2007 and 2012, 40 patients with intraventricular tumors have been received endoscopic treatment. Our endoscopic system constitutes MINOP Modular Neuroendoscopy System (Aesculap), VISERA Pro video system with HD camera (OLYMPUS) and Navigation system (BrainLAB). Approach to lateral ventricle is performed through frontal craniotomy, in 3 cm diameter. The field exchange technique is composed of the dry field with evacuated CSF and the wet field with artificial CSF filled in.

RESULTS: Tumor resection was accomplished in 12 patients. 2 patients received prior SRS and 2 patients received prior radiotherapy. Average time between radiation and surgery was 42 months. No patients had serviceable hearing prior to surgery. All patients underwent a translabyrinthine approach. A gross total resection was achieved in 4 patients (80%), and a subtotal resection in 1 patient (20%). 3 patients (60%) had a good (HBI & II) post-operative facial nerve function. One patient (20%) had a HB IV facial nerve palsy. Pathology revealed WHO I vestibular schwannoma in all patients. No patient had post-operative tumor progression with an average of 27 months follow up.

CONCLUSION: Vestibular schwannomas that have failed primary radiation can present a difficult treatment dilemma to the surgeon. Although radiation effects can increase the potential for post-operative cranial nerve dysfunction and decrease the likelihood of achieving gross total resection, surgical resection with modern surgical technique is a safer and more effective than what earlier data would suggest.

**ST-007. ORBITAL METASTASES AS PRIMARY CLINICAL MANIFESTATION OF LUNG CANCER: CASE REPORT AND LITERATURE REVIEW**

María Blaga, Maurizio Paulis, Giuseppe Orunesu, and Salvatore Serra; Department of Neurosurgery, San Francisco Hospital, Nuoro, Sardinia, Italy

INTRODUCTION: Orbital metastases are an infrequent etiology of adult proptosis; approximately 3–7% of orbital biopsies have demonstrated a metastatic tumour, and this diagnosis is often unexpected. Between 2% and 5% of cancer patients will develop an ocular or orbital metastasis. In 25% of these, it is the presenting sign of malignancy. Frequently, this presents a diagnostic challenge and represents a poor prognosis. METHODS: A 50-year-old man presented with swelling of the eyelid margin, local pain and proptosis of his right eye. Past medical history was unremarkable and the patient took no medications. A CT scan revealed extensive bony destruction of the orbital roof and anterior skull base. A right frontoorbital approach was used for total removal of the osteolytic tumor. RESULTS: A simple thorax x-ray reveals aletectomy on the lower left lobe and via a bronchoscopy we found an endobronchial mass. We obtained a biopsy and the resulting diagnosis was a spinocellular carcinoma, confirming that the originating tumor for the orbital metastasis. Histopathological and cytological study confirmed the diagnosis of an orbital metastases associated with abscess. Postoperative MRI demonstrated a total removal of the tumour. Three months after surgery the patient’s condition is deteriorating and currently is receiving palliative care. CONCLUSIONS: An ophthalmologist must keep in mind that in the event of proptosis and/or ptosis with a history of cancer should be evaluated for orbital metastasis. Prognosis can be poor, and thus treatment is sometimes palliative in nature, intending to slow the progression of the disease instead of providing a cure.

**ST-009. miR-21 IN THE EXTRACELLULAR VESICLES (EVs) OF CEREBROSPINAL FLUID (CSF): A PLATFORM FOR GliobLASTOMA BIOMARKER DEVELOPMENT**

Johnny Aker1, Valya Ramakrishnan1, Ryan Kim1, Johan Skog1, Ichiro Nakano2, Sandeep Pingle1, Juliyan Klimentova3,1, Xandra Breakfield1, Fred Hochberg3, Erwin Van Meer4, Bob Carter1,a n d Claire Alapetite5, Maria-Luisa Garre6, Umberto Ricardi7, Frank Saran8, and Thomas Czech1; 1Department of Neurosurgery, San Francisco Hospital, Nuoro, Sardinia, Italy; 21Department of Neurosurgery, Ohno Memorial Hospital, Osaka, Japan; 3Department of Neurosurgery, San Francisco Hospital, Nuoro, Sardinia, Italy; 4Medical University, Leipzig, Germany; 5Institut Curie, Paris, France; 6Gaslini Children’s Hospital, Genova, Italy; 7Medical University, Torino, France; 8Royal Marsden Hospital, London, UK; 9Medical University, Münster, Germany

Glioblastoma cells secrete extra-cellular vesicles (EVs) containing microRNAs (miRNAs). Analysis of these EV miRNAs in the biofluids of afflicted patients represents a potential platform for biomarker development. However, the analytic algorithm for quantitative assessment of EV miRNA remains under-developed. Here, we demonstrate that the reference transcripts cytokeratin 12 and ribosomal protein L32 (RPL32) are both used for quantitative PCR (qPCR) for EV miRNA quantification. Using this method, we examined the abundance of EV miR-21 in 103 samples from patients with glioblastoma, in EVs. In a panel of glioblastoma cell lines, the cellular levels of miR-21 correlated with EV miR-21 levels (p<0.05), suggesting the glioblastoma cells actively secrete EVs containing miR-21. Consistent with this hypothesis, the CSF EV miR-21 levels of glioblastoma patients (n=13) were, on average, ten-fold higher than levels in EVs isolated from the CSF of non-oncologic patients (n=13, p<0.001). Notably, none of the glioblastoma CSF harbored EV miR-21 level below 0.25 copies per EV in this cohort. Using this cut-off value, we were able to prospectively distinguish CSF derived from glioblastoma patients from non-glioblastoma patients (Sensitivity = 87%; Specificity = 93%; AUC = 0.91, p<0.01). Our results suggest that qCSF EV miRNA analysis of miR-21 may serve as a platform for glioblastoma biomarker development.

**ST-010. ROLE OF SURGERY IN PATIENTS WITH INTRACRANIAL NON GERMINOMATOUS GERM CELL TUMORS (NGGCT) TREATED ACCORDING TO SIOP CNS GCT 96 PROTOCOL WITH RESPECT TO THE SITE AND TIME OF RESSECTION**

Thomas Czech1, James Nicholson2, Didier Frappaz3, Rolf-Dieter Kortmann4, Claire Alapetite5, Maria-Luisa Garre6, Umberto Ricardi7, Frank Saran8, and Thomas Czech1; 1Department of Neurosurgery, San Francisco Hospital, Nuoro, Sardinia, Italy; 21Department of Neurosurgery, Ohno Memorial Hospital, Osaka, Japan; 3Department of Neurosurgery, San Francisco Hospital, Nuoro, Sardinia, Italy; 4Medical University, Leipzig, Germany; 5Institut Curie, Paris, France; 6Gaslini Children’s Hospital, Genova, Italy; 7Medical University, Torino, Italy; 8Royal Marsden Hospital, London, UK; 9Medical University, Münster, Germany

BACKGROUND: Data from SIOP CNS GCT 96 and other trials suggest improved outcome with delayed resection of residual tumour in patients with intracranial NGGCTs. The relevance of tumour site on the overall treatment algorithm has not been evaluated. METHODS: Until 31.05.2012, 206 patients with NGGCT were treated according to SIOP CNS GCT 96. Median
age was 12 years (range 0-30yrs), 150 were boys. Primary tumour site was pineal in 107 and suprasellar in 51 patients. A bifocal tumour was present in 20 patients, and in 22 patients there was another primary tumour site. We analysed the impact of resective surgery in relationship to the tumour site, pineal vs sellar-suprasellar. RESULTS: In pineal tumours 54/107 had histology at diagnosis with either upfront resection (36/54) or biopsy (18/54). 53/107 had diagnosis by markers only. Of 20 patients with an upfront gross-total resection 7 had an event. Second-look surgery was performed in 29 patients, 4 of these 29 patients had an event. An event occurred in 28/46 patients with residual tumour after chemotherapy who did not undergo second-look surgery prior to radiotherapy. In suprasellar tumours 26/51 had histology at diagnosis with either 21/26 operative and 5/26 biopsy procedures. Marker-only diagnosis was done in 25/51 patients. Of 4 patients with primary gross-total resection 1 had an event. Second-look surgery was done in 7 patients, 2/7 had an event. An event occurred in 6/31 patients with residual tumour who did not undergo second-look surgery. CONCLUSION: While second-look surgery seems to improve outcome in NCGCT primarily located in the pineal region, the impact of this strategy is less clear in hypothypo-hypothalamic tumours and an attempt at second -look gross total resection needs to be weighted against potentially harmful side-effects.

INTRODUCTION: Seizures are the most frequent presenting symptom in patients with low-grade tumours and are more prevalent when the lesion is located in or around the temporal lobe. Resection strategies in these patients vary between lesionectomy and epilepsy operations with no clear consensus on optimal approaches. METHODS: A prospectively compiled database of epilepsy and tumour patients was used to identify patients who underwent surgical resection of a glial neoplasm but then developed epilepsy, or who presented with epilepsy and were found to harbor a low grade neoplasm. Seizure frequency, histology, type of surgical resection and outcomes were compiled. RESULTS: Of 235 patients that underwent cranial procedures for epilepsy and 79 patients with low/intermediate grade gliomas, 14 (6%) and 20 (25%) respectively had tumoral epilepsy. Etiology was WHO grade 1 gliomas (DNET, Gangliogliomas, JPA) in 33%, grade 2 gliomas in 36% and grade 3 in 30%. One epilepsy patient had a PNET. Median age was 37 years (22 male). Most common locations were temporal - 44% (7 lateral, 5 mesial and 3 extending to insular cortex) and peri-rolandic - 27% (SMA in 5; lateral in 4). In the epilepsy group, following lesionectomy in 3 and tailored resections in the majority, seizure outcomes were Engel class one in all (1A-10, 1B-2) except for one (class 3). In the tumour group 7 additional resections were performed due to seizure recurrence – all related to residual or recurrent tumour after initial surgery. Outcomes were 1A in 18, 1B, 1C and 2A in 1 each. CONCLUSION: We used an aggressive surgical intervention targeting the lesion except where medial temporal structures were involved, where a surgical temporal lobectomy was performed. The excellent outcomes (Engel 1 in 94%) relate to aggressive initial surgical intervention and re-resection in the context of recurrence.

INTRODUCTION: Despite recent advances, the median overall survival for patients with GBM remains < 2 years. A substantial body of evidence suggests that cytoreductive surgery is essential for prolonging survival in these patients. A “supra-maximal” resection, using sub-pial techniques for low-grade glomas may allow for the eradication of proximate nonfunctional, tissue with high degree of infiltration by glioma cells beyond the zone of contrast enhancement and may result in improved outcomes. The purpose of this study is to evaluate the safety, feasibility and any addition survival benefit of this technique in patients with GBM. METHODS: We retrospectively evaluated 79 consecutive patients (2005-2009) who underwent surgery for GBM and analyzed the impact of resective surgery in relationship to the tumour site, pineal and temporal. RESULTS: The senior surgical team contributed 30% (22/74) of the resections. GTR, NTR and STR respectively. Two transient and two permanent neurological complications related to surgery occurred. Multivariate regression revealed that intraoperative mapping and % residual tumor were the only predictors of survival. CONCLUSION: The “supra-maximal” technique is safe, effective and associated with an overall survival benefit not previously seen in other GBM series in which a GTR is achieved in > 50% of patients. Other similar GBM series in which a GTR is achieved. The benefits of the addition of intra-cavitary carmustine wafer placement may be potentiated with the supra-maximal resection. Neurological deficits and complications were favorable compared to other series and did not prevent adjuvant therapy.
of the cases the biopsy was done through frontal lobe, but in some cases through temporal lobe or through cerebellum. The samples were taken deeper and nearer regions of the designed targets with same trajectory, also. If there were cysts, aspiration of the cyst was performed as much as possible. The trajectory should avoid sulci, cortical veins or ventricular system. After system. Fast outside the needle were irrigated repeated with 0.1 - 0.2 ml saline using thin plastic tube to ensure hemostasis. RESULTS: In all patients appropriate samples for pathological diagnosis were obtained. The diagnoses were 11 gliomas (pilocytic grade I, grade II, grade III, grade IV (GBM) 2, high grade 1, glioblastoma 3, lymphomas, 1 germinoma and 1 multiple sclerosis. There were no symptomatic bleeding nor neurological complications.

CONCLUSION: With detailed planning, stereotactic biopsy was safely performed even from brainstem. Trajectories other than from frontal can be also considered for lessons. Repeated irrigation with saline might effective to prevent symptomatic bleeding.

ST-015. SPECIFIC TREATMENT CONSIDERATIONS AND OUTCOME DATA IN ELDERLY GLIOMA PATIENTS - A SINGLE CENTER EXPERIENCE

Markus Hoffermann, Lukas Bruckmann, Kariem Mahdy Ali, Martin Asslabe, Franz Payer, and Gord von Campme; Medical University of Graz, Graz, Austria

BACKGROUND: Although High Grade Gliomas (HGG) are significantly more frequent in patients older than 65 years of age, most clinical studies so far do not exclude the elderly population. It is known that age itself is an independent risk factor in glioma patients and individualized treatment is mandatory, given the prevalence of comorbidities in the elderly. Recent multicenter clinical trials have defined the role of different adjuvant therapies, but the role of surgery, especially regarding extent of resection, remains a matter of lively discussion. MATERIALS AND METHODS: A retrospective clinical data analysis of 150 patients with HGG over 65 years with supratentorial gliomas (WHO grade III-IV) was performed, with emphasis on survival data, adjuvant therapies and neurosurgical intervention. RESULTS: Mean progression free survival was 6.8 months and mean overall survival (OS) was 8.6 months. In 156 surgical procedures (GTR=43, STR=32, PR=37, biopsies=30, reoperations=14) we experienced a mortality rate of 3.3% and morbidity of 18.3%, highest in STR. In the High Grade Glioma sub-group, GTR and STR led to significantly improved median OS compared to PR, biopsy or no surgical procedure (15 and 12 months vs. 4, 4 and 2 months; p=0.000). Reoperations were performed in selected cases of HGG (n=10) and these patients showed significantly higher OS (21 vs. 7 months median OS; p=0.035). Regarding mean OS, adjuvant therapy according to the STUPP-protocol proved to be more efficient (21.4 months, p=0.000) than radio- or chemotherapy alone (3.3 and 8.6), concomitant chemoradiotherapy (6.3) or best supportive care (3.4) but not significantly different from radiation followed by chemotherapy (18.6 months, p=0.94).

CONCLUSION: Our single center experience provides helpful information on the value of neurosurgical treatment and its impact on outcome in elderly glioma patients, despite limitations regarding treatment heterogeneity. It supports the need for further prospective studies in this age group.

ST-016. COMPLETE, BUT NOT PARTIAL RESSECTION OF RECURRENT GliOBLASTOMA PROLONGS SURVIVAL AFTER RELAPSE WITHOUT IMPAIRMENT OF FUNCTIONAL OUTCOME

Christine Jungk, Bernhard Beigel, Vitali Abb, Franz Payer, and Gord von Campme; Medical University of Graz, Graz, Austria

OBJECTIVE: Standard of care in newly diagnosed glioblastoma (GBM) is maximal safe tumor resection followed by radio (RT)- and chemotherapy (CHT). At tumor relapse, however, standard of care, particularly the value of re-resection, is still under debate. We addressed the significance of recurrent GBM surgery with regards to functional outcome and survival and special attention paid to the extent of resection (EOR). METHODS: 30 patients were identified from our tumor database, diagnosed with GBM between 2005 and 2010, having been re-resected at least once for tumor relapse and deceased at the time of analysis. Patient demographics, functional status, adjuvant therapies and survival times were extracted from medical charts. EOR was determined on postoperative MRI scans where available. Survival after re-resection (SRK) was calculated by log-rank test. RESULTS: At initial diagnosis, patients were treated by complete (CR) or partial resection (PR) followed by radio-/chemotherapy. 93% of patients received one, 7% two re-resections. Only 10% were treated with second-line RT or CHT prior to re-resection. At 1st re-resection, CR was achieved in 53%, PR in 40%, EOR could not be determined in 7%. Incidence of permanent neurologic deterioration did not increase from first to re-resection (10% vs. 13,3%). Among patients with CR (n=16) and PR (n=12) at re-resection only, both groups were comparable with respect to demographic data, tumor eloquence, KPS, number of re-resections and adjuvant therapies for tumor relapse. Interestingly, survival was prolonged in completely resected patients (11 vs. 5 months; p=0.034) while the rate of permanent deficits was comparable. CONCLUSION: In this analysis, complete resection of recurrent GBM, compared to PR, was associated with a significantly prolonged SR without additional neurologic impairment. These findings stress the significance of maximal tumor resection even at the time of relapse. Certainly, larger studies are warranted to confirm these findings.

ST-017. COMPARATIVE STUDY OF LONG-TERM RESULTS FOR INTRACRANIAL MENINGEAL HEMANGIOPERICYTOMA AND MALIGNANT MENINGIOMA IN SINGLE INSTITUTION: FOCUSED ON SURVIVAL AND LOCAL CONTROL

Jeong Hoon Kim, Young Hyeon Cho, and Chang Jin Kim; Asan Medical Center, Seoul, Republic of Korea

INTRODUCTION: Both hemangiopericytoma (HPC) and malignant meningioma (MM) are a rare tumor of meningeal origin that behaves aggressively with a high rate of local recurrence and distant metastases. Two diseases are clinically very similar but there are no comparative study for long term outcome between HPC and MM. Therefore, we present our experiences. MATERIAL AND METHODS: We retrospectively reviewed pathologically proven 30 patients of HPC and 39 patients of MM treated from 1991 to 2006 with at least 5 years follow-up period. Data including clinical characteristics, treatment modalities, recurrence and survival were reviewed. Statistical analysis was done with regards to overall survival (OS) and recurrence free survival (RFS) using Kaplan-Meier survival analysis. RESULTS: The median age at presentation of HPC and MM was 43.0 and 52.0 (p=0.047). Twenty seven of 30 (90%) in HPC and 28 of 39 (72%) in MM underwent complete resection (Simpson Grade 1 and 2). The 3-, 5-, and 10-year overall survival rates of HPC were 100%, 100%, and 43%, and those of MM were 87%, 64%, and 32%, respectively. The 3-, 5-, and 10-year recurrent rates of HPC were 23%, 40%, and 56% and those of MM were 47%, 49% and 75%. Adjuvant radiotherapy (RT) after surgical resection was an important significant prognostic factor for OS and RFS (p=0.026, p=0.024), but complete resection was not in HPC (p=0.565, p=0.226). In contrast, complete resection was important prognostic factor for OS and RFS (p=0.004, 0.047) although adjuvant RT was not significant factor in MM (p=0.432, p=0.742). CONCLUSION: We conclude that both HPC and MM are very aggressive tumor with high recurrent and low survival rate. While complete resection is the best treatment modality in MM, surgical resection with adjuvant RT is best treatment modality in HPC. Long-term and meticulous follow-up is mandatory for local recurrences and distant metastases.

ST-019. MRI-BASED HIGH RESOLUTION MAPS FOR PLANNING/GUIDING HIGH PRECISION PROCEDURES IN BRAIN TUMOR PATIENTS

Yael Mardor1,2, Ozzi Nissim1, Yuval Grober1, David Guez1, David Last1, Dinae Danieli1,2, Chen Hoffmann1,2, Dvora Nass1, Alisa Talianski1, Roberto Spiegelmann1,2, Zvi Cohen1,2, and Leor Zach1,2; Sheba Medical Center, Ramat Gan, Israel; 1Tel Aviv University, Tel Aviv, Israel

BACKGROUND: Conventional MRI is currently unable to differentiate tumor from non-tumoral tissues (such as radionecrosis). We have applied delayed contrast extravasation MRI for calculating high resolution maps clearly differentiating tumor from non-tumoral tissues. Here we demonstrate the application for targeting improvement of high precision procedures. METHODS: 30 patients with glioma of 33 patients with metastasis were scanned by delayed contrast extravasation MRI prior to surgery. High resolution maps were calculated from T1-MRI acquired 2 and 75 min post contrast injection. 44 stereotactic biopsies planned using the maps were acquired from 17 patients. Twenty six cases were acquired from 3 and gross total samples were acquired from 13. Histological assessment was then compared with the pre-surgical maps for all patients. RESULTS: The maps showed two primary populations: the delayed contrast accumulation population (red in the maps) and the delayed contrast clearance population (blue). In all cases, samples obtained from blue regions in the maps consisted of morphologically active tumor while samples obtained from red regions...
ST-019. LONG-TERM OUTCOMES OF PATIENTS UNDERGOING AGGRESSIVE SURGICAL MANAGEMENT OF INSULAR TUMORS

INTRODUCTION: Aggressive surgical resection of insular tumors is neurosurgically challenging due to anatomically and functionally complex cortical structure of the insula. The effects of insular neoplasms on surrounding architecture further complicate resection. Some advocate stereotactic biopsy followed by radiotherapy. However, we demonstrate that aggressive surgical management of insular tumors can be achieved with minimal morbidity using specialized microsurgical techniques. METHODS: We performed a retrospective review of all patients undergoing surgical resection for insular tumors at our institution since 2006 (n=21). Follow-up ranged from 2-months to 6-years (median = 5-years). Each patient underwent circumferential microsurgical dissection and en bloc insular tumor removal. All procedures were performed by a single neurosurgeon. The surgical procedure included skeletonization of insular branches of the middle cerebral artery and preservation of perforators (lenticulostriate arteries). Patients presenting with intractable seizures underwent Wada test and PET imaging prior to surgery. Postoperatively, surgical outcomes were characterized by the following: 1) histological diagnosis, 2) control of seizures, 3) extent of tumor removal (4) development of new neurologic deficits, and 5) long-term outcomes. RESULTS: Nine patients had insular tumors histologically classified as gliomas; remaining lesions included metastases and primary CNS lymphoma. All patients underwent gross total resection. No patient had persistent motor or speech deficit on long-term postoperative follow-up. All patients with refractory seizures (n=3) had good seizure control from the comprehensive resection. Low-grade gliomas involving the insular lobe remain confined. Due to the expansive growth of insular gliomas, the lenticulostriate vessels are extensively shifted and displaced medially. Insular gliomas demonstrate a stereotyped sharp border medially, which initially aids in creating the plane of resection. CONCLUSION: Our neurosurgical technique optimizes volumetric resection of insular tumors with preservation of surrounding neurovascular structures, preventing long-term neurologic morbidity. With new technical refinements in imaging and neuronavigation, radical removal of insular tumors is feasible with minimal morbidity.

ST-021. LASER INTERSTITIAL THERMAL THERAPY (LITT) AS A TREATMENT MODALITY FOR DIFFICULT-TO-ACCESS HIGH GRADE GLIOMAS: A MULTI-CENTER STUDY

Alireza Mohammadi1, Ammar Hawasli2, Analiz Rodriguez3, Jason Schroeder4, Adrian Laxton1, Paul Elson1, Stephen Tatter3, Gene Barnett5, and Eric Leuthardt2. 1Cleveland Clinic, Cleveland, OH, USA; 2Wake Forest University, Winston-Salem, NC, USA

INTRODUCTION: Surgical extent-of-resection has been shown to have an impact in high grade glioma (HGG) outcomes, but it is rarely achievable in difficult-to-access (DTA) tumors. Controlled thermal damage to the tumor may have the same impact in DTA-HGGs. We report our multi-center results of Laser Interstitial Thermal Therapy (LITT) in DTA-HGGs. METHODS: We retrospectively reviewed 35 consecutive DTA-HGG patients (24 GBM, 11 anaplastic gliomas) who underwent LITT in the Cleveland Clinic, Washington University, and Wake Forest University during 3/13-12/12. LITT was performed under MR-thermography guidance using the NeuroBlate device (Monteris, Winnipeg). Extent of thermal damage was determined as thermal-damage-threshold (TDT) lines including: yellow TDT-line = 43°C for 2 minutes and blue TDT-line = 43°C for 10 minutes. Pre- and post-operative MRI scans as well as TDT-lines were imported into the iPlan software (BrainLAB, Germany) for volumetric analysis. Extent of coverage (EOC) by TDT-lines and residual tumor volume (RTV) uncovered by TDT-lines were measured. Patient outcomes were evaluated statistically. RESULTS: Median age was 56 years and 40% were female. Treatment was upfront in 19 and salvage in 16 patients. Median tumor volume was 10.1cc (0.7-49cc). One patient died because of meningitis and 7 patients had neurologic worsening after procedure (temporary in 3 patients). After a median of 7.2 months follow-up, 80% of patients have progressed and 34% died. Median overall-survival was not reached, median survival was 11.5 months; p = 0.02 which was still prognostic in the subgroup of 24 GBM patients (p = 0.04). CONCLUSIONS: LITT can be used safely and effectively for treatment of DTA-HGGs. More complete coverage of tumor by TDT-lines improves PFS which can be translated as the extent of resection concept for surgery.

ST-022. USE OF 5-AMINOLEVULINIC ACID FOR DETECTION OF RESIDUAL Meningioma FOR TOTAL REMOVAL AND AVOIDANCE OF NEUROLOGICAL DEFICITS

Shunuke Moriyachi1, Makoto Deharai2, Takamori Fukuoka3, Yasushi Hagiwara1, Hakao Soda2, and Masami Imakita3. 1Department of Neurosurgery, Rinku General Medical Center, Izumisano, Osaka, Japan; 2Department of Neurosurgery, Rinku General Medical Center, Izumisano, Osaka, Japan; 3Department of Pathology, Rinku General Medical Center, Izumisano, Osaka, Japan

5-Aminolevulinic acid (5-ALA) has been used successfully to resect meningiomas without residual mass. However, authors report that in the resections of 15 patients with meningioma using 5-ALA. Except one case, all meningiomas fluoresced intraoperatively under microscope. Invasions to the dura matter, the brain parenchyma or skull fluoresced, allowing for confirmation of residual tumor and total removal of the meningioma could perform more easily and prevent unexpected neurological deficit by precise removal of the tumor under microscope. In a case with invasions to dura matter or skull, the extent of dural removal was decided by 5-ALA fluorescence with 1-2 cm safety margins. In another case with parenchymal invasions, close removal of the tumor without residual tumor could be performed with 5-ALA fluorescence. With the above methods, no serious side effects or
ST-023. UPDATED THERAPEUTIC STRATEGY FOR ADULT LOW-GRADE GLIOMA STRATIFIED BY RESSECTION, HISTOLOGY, AND MOLECULAR MARKERS
Masayuki Nitta1, Takashi Maruyama2, Hiroshi Iseki1, Soko Ikuta2, Kazuaki Furukawa, Seiji Nakamura, Yuki Okamoto, Yoshihisa Okada1, and Yoshihiro Muragaki1,2; 1Department of Neurosurgery, Neurological Institute, Tokyo Women's Medical University, Tokyo, Japan; 2Institute of Advanced Biomedical Engineering & Science, Tokyo Women's Medical University, Tokyo, Japan

BACKGROUND: There is no established standard therapy for adult low-grade glioma (LGG), and there is a large difference in therapeutic strategy between institutes. Based on the outcome of ten years in our institute, we have recently established our updated therapeutic strategies for LGG.

METHODS: We retrospectively analyzed 133 patients (mean age: 39 yr, 56 male, 44 female) with LGG who underwent surgical treatment between 2002 and 2012. Histological subtypes were 92 diffuse astrocytoma (DA), 45 oligoastrocytoma (OA), 59 oligodendroglioma (O). Patients with ≥95% EOR were observed and others were treated with radiation and/or chemotherapy. RESULTS: Median preoperative tumor volume was 29.6 cm^3 and median EOR was 95.1% in DA, 91.2% and 98.3%, respectively. Eighty-four of 133 patients showed significant decrease in the volume of viable tumor (assessed by residual tumor volume). Multivariate analysis identified age (HR = 4.08, 95% CI, 1.08-16.96; P = 0.038), and DOR (HR = 4.75, 95% CI, 0.77-26.48; P = 0.039) as parameters significantly associated with OS. The only parameter associated with DFS was EOR (HR = 2.69, 95% CI, 1.43-5.04, P = 0.045).

Chemotherapy prolonged PFS in patients with oligodendrogliol subtype (P = 0.006). However, there was no survival benefit of radiation and chemotherapy in diffuse astrocytoma. CONCLUSIONS: Our updated therapeutic strategy for LGG is follows: 1. Patients with ≥90% EOR are carefully observed without any adjuvant therapy regardless of tumor subtype. 2. DA patients with <90% EOR are considered second look resection and if possible, radiotherapy and nimustine hydrochloride (ACNU) based chemotherapy are conducted. 3. OA and O patients with <90% EOR and close proximity of 1p/19 loci to treatment with ACNU and the others are treated with both radiotherapy and ACNU.

ST-024. SURGERY USING A TRACTOGRAPHY-INTEGRATED NAVIGATION SYSTEM AND MOTOR EVOKED POTENTIALS FOR PRESERVATION OF MOTOR FUNCTION IN PATIENTS WITH MALIGNANT GLIOMA
Shiro Ohue, Shohei Kohno, Akihito Inoue, Daisuke Yamashita, Yoshikatsu Kumon, and Takanoori Ohnishi; Department of Neurosurgery, Ehime University Graduate School of Medicine, Toon, Ehime, Japan

INTRODUCTION: The optimal surgery for malignant gliomas, at present, is maximal tumor resection without deterioration of neurological function. We evaluated the contribution of using tractography-integrated navigation system and motor evoked potentials (MEPs) to surgical and functional outcomes.

METHODS: Subjects comprised 50 patients who underwent resection for malignant glioma near the pyramidal tract (PT) in our hospital. Diffusion tensor imaging (DTI) was performed using a 3-T magnetic resonance scanner, and DTI-based tractography of the PT was loaded into the navigation system for intraoperative guidance. If possible, silicone catheters as fence posts were inserted along the tumor boundaries, avoiding the course of the PT before surgery is represented by fluorescence-guided resection, taking advantage of metabolic and structural changes induced by 5-amino-levulinic acid (ALA), a natural precursor of heme biosynthetic pathway. METHODS: The present experience is related to 48 patients affected by malignant glioma (28 newly diagnosed and 20 recurrent tumors): 42 glioblastoma (GBM), 4 anaplastic oligodendroglioma, 1 oligodendroglioma 1 WHO and 1 pleomorphic xanthoastrocytoma. All patients underwent preoperative and early postoperative MRI including contrast-enhancing lesions. All patients were selected for fluorescence-guided resection. An oral dose of 20 mg 5-ALA /kg bw was administered to each patient. Microsurgical resection was performed by an operating microscope enabled to visualize the fluorescence. All the patients, as first line treatment, have been submitted to radiotherapy and chemotherapy; second and in some cases third line treatments were utilized in recurrent cases. RESULTS: In more than 90% of patients tumor tissue showed intraoperative red fluorescence; mainly in recurrent GBM, where MRI documented heterogeneous tumors with enhancing areas mixed with gliotic scars; fluorescence-guided surgery allowed a better definition of active tissue, with net margins from perilesional “healthy” brain. Early postoperative MRI confirmed gross total resection in 80% of the patients. In the present experience the procedure did not determine any relevant additional neurological deficit. Considering overall survival of recurrent patients we obtained a median extension of at least 9.0 months (4 – 16+ months). CONCLUSIONS: Fluorescence-guided surgery improves tumor detection and allows extended resection of malignant glioma, without any relevant impact on neurological status, resulting helpful mainly in the recurrent setting with a consistent effect on overall survival.

ST-025. 5-ALA GUIDED RESECTION OF MALIGNANT GLIOMA: A SINGLE INSTITUTION EXPERIENCE
Pierandrea Oppido, Veronica Villani, Antonello Vidri, Andrea Pace, Alfredo Pompili, and Carmine Carapella; Regina Elena National Cancer Institute, Roma, Italy

INTRODUCTION: Malignant glioma represent a relevant therapeutic issue and the value of extensive surgical resection remains debated; recent evidence suggests that radical removal is associated with better survival. An interesting tool for identifying tumor tissue and increasing the extent of surgery is represented by fluorescence-guided resection, taking advantage of metabolic and structural changes induced by 5-amino-levulinic acid (ALA), a natural precursor of heme biosynthetic pathway. METHODS: The present experience is related to 48 patients affected by malignant glioma (28 newly diagnosed and 20 recurrent tumors): 42 glioblastoma (GBM), 4 anaplastic oligodendroglioma, 1 oligodendroglioma 1 WHO and 1 pleomorphic xanthoastrocytoma. All patients underwent preoperative and early postoperative MRI including contrast-enhancing lesions. All patients were selected for fluorescence-guided resection. An oral dose of 20 mg 5-ALA /kg bw was administered to each patient. Microsurgical resection was performed by an operating microscope enabled to visualize the fluorescence. All the patients, as first line treatment, have been submitted to radiotherapy and chemotherapy; second and in some cases third line treatments were utilized in recurrent cases. RESULTS: In more than 90% of patients tumor tissue showed intraoperative red fluorescence; mainly in recurrent GBM, where MRI documented heterogeneous tumors with enhancing areas mixed with gliotic scars; fluorescence-guided surgery allowed a better definition of active tissue, with net margins from perilesional “healthy” brain. Early postoperative MRI confirmed gross total resection in 80% of the patients. In the present experience the procedure did not determine any relevant additional neurological deficit. Considering overall survival of recurrent patients we obtained a median extension of at least 9.0 months (4 – 16+ months). CONCLUSIONS: Fluorescence-guided surgery improves tumor detection and allows extended resection of malignant glioma, without any relevant impact on neurological status, resulting helpful mainly in the recurrent setting with a consistent effect on overall survival.

ST-026. THE PROGNOSTIC SIGNIFICANCE OF EXTENT OF RESECTION AND RESIDUAL VOLUME IN Glioblastoma Patients
Daniel Orringer, Darryl Lau, and Yashar Niknafs; University of Michigan, Ann Arbor, MI, USA

INTRODUCTION: Conflicting evidence exists on the importance of maximal resection in glioblastoma patients. Furthermore, the mechanism by which resection prolongs survival remains unclear. We hypothesize that maximal resection is most beneficial in patients where gross total resection is feasible and that surgical resection confers benefits to glioblastoma patients through both brain decompression (assessed by extent of resection) and a reduction in the volume of viable tumor (assessed by residual volume).

METHODS: A consecutive population of patients who underwent craniotomy for GBM resection from 2005-2011 were identified. FIJI image analysis software was used to perform volumetric analysis of pre- and post-operative MRIs to determine tumor volume, EOR and RV. Resectability was determined with a published grading scheme that is based on tumor location relative to brain function. Statistical comparison of survival by EOR, and RV was performed via log-rank test and Kaplan-Meier curves. RESULTS: Sixty-five patients had sufficient images for analysis. Overall 1-year survival was 61.5%. Greater EOR (p < 0.001) was associated with higher 1-year survival rates: in patients where EOR was greater than 90%, 1-year survival was 85.3%. Higher RV was significantly associated with poorer survival (p = 0.012): when RV was greater than 8,000 mm^3, the 1-year survival rate was 35.0%. When RV was less than 8,000 mm^3, 1-year survival rates were in excess of 80%. EOR and RV were found to be significant predictors of survival in patients with resectable tumors (p < 0.001 and p = 0.045, respectively). However, EOR and RV were not predictive of survival in patients throughout tumor resection, the other 42 patients showed obvious responses of subcortical MEPs at ≥20 mA. The degree of resection was total in 22 patients, subtotal in 13, and partial in 13. At one month postoperatively, only one patient showed worsened motor function because of tumor progression.

CONCLUSION: A tractography-integrated navigation system and MEPs are useful for preserving motor function during tumor resection in patients with malignant gliomas near the PT.

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ST-027. FLUORESCENCE GUIDE SURGERY IN HIGH GRADE GLIOMA USING A HIGH-DEFINITION EXOSCOPE SYSTEM: AN ALTERNATIVE MICROSURGICAL APPROACH TO SUBCORTICAL TUMORS
Jose Piquer, Jose Luis Llacar, Vicente Rovira, Pedro Riesgo, and Antonio Cremades; Hospital Universitario de la Ribera, Alzira, Valencia, Spain

INTRODUCTION: Fluorescence-guided microsurgical resections of high-grade gliomas using 5-aminolevulinic acid (5-ALA) have proven to be superior to conventional microsurgery. An optical device, usually a modified microscope, is needed for these procedures. However, an exoscope can be implemented for fluorescence techniques. OBJECTIVE: We present the use of an exoscope to perform tumor resection guided by 5-ALA fluorescence in 21 consecutive patients with high-grade glioma and 2 neuroanatomical guided biopsies. METHODS: Twenty-five three were operated using ALA fluorescence guided system. Tumor fluorescence signal was quantified with pre- and postoperative volumetric magnetic resonance imaging in non biopsy cases. RESULTS: In non biopsy cases the age range in our series was 20 to 79 years, with a median of 56 (interquartile range = 45-66). Histopathological analysis indicated that 14 had glioblastoma multiforme, 2 grade III oligodendroglioma and 1 anaplastic astrocytoma, 3 metastases and 1 low grade astrocytoma. Total resection was achieved in 15 cases, subtotal resection was performed in 5 patients, and in one case, the result was a partial resection. There was no perioperative mortality. The median fluorescence intensity, on a scale of 1-5, was 4.5 in the GBM group (IQR = 4-5), 3 (IQR = 2.5-3.5) in the cases of anaplastic glioma and 2.5 (IQR = 2.25-2.75) for the oligodendrogliomas. Of the three metastases, one showed a level 4 degree of fluorescence. In the two biopsy cases, 1 was an anaplastic astrocytoma and 1 a glioblastoma multiforme. In both cases the samples obtained from tumor were fluorescence. CONCLUSIONS: An exoscope can be also used to for fluorescence-guided surgery and with 5-aminolevulinic acid (5-ALA) and neuronavigation guided biopsy. With an important advantage of low costs allows the surgeon to perform collaborative surgeries and adds agility to the procedure.

ST-028. PREOPERATIVE nTMS GENERATED MOTOR AND LANGUAGE MAPS: FEASIBILITY AND OUTCOME
Roderick Kotta, Nicholas Lescure, Ajit Prabhu, Raymond Sawaya, Jeffrey Weinberg, Ganesh Rao, Sudhakar Tummala, and Catherine Tilley; University of Texas MD Anderson Cancer Center, Houston, TX, USA

INTRODUCTION: The management of brain tumors adjacent to speech and motor areas presents a surgical challenge. The goals are maximal safe resection and preservation of neurological function. Pre-surgical functional information about the cortical and subcortical areas at risk is crucial for the avoidance of neurological deficits during tumor surgery. Intraoperatively direct electrical stimulation (DES) is the “gold standard” to identify and preserve essential function. Recently nTMS has been shown to be useful in generating both motor and speech maps prior to surgery. METHODS: We describe our 23 consecutive patients with brain tumors located adjacent to eloquent areas (motor and language). All cases were performed with nTMS, intraoperative DES and awake craniotomy during language mapping. RESULTS: Of the 23 patients 84% were HGG (grade III and IV), 4% LGG (grade II), 4% Grade I and 20% Metastases. Parietal lobe was the most frequent location of tumors seen in 13 (56%) cases. In 95% of patients a positive response in upper extremity (UE) nTMS, correlated well with those generated by DES (94%), In 4(23%) cases nTMS was superior to DES in isolating the lower extremity (LE) response. Of the 6 (25%) cases performed for speech mapping, 1(17%) case had a true positive response and 1(17%) a false positive while true negative was seen in 4(66%). A gross total resection (GTR) was achieved in 14 (61%) patients, and at 1 month follow-up, 187/8% had no deficit, 4 (18%) stable and 1(4%) worsening. There were no adverse events during the stimulation. CONCLUSION: Navigated transcranial magnetic stimulation can be safely used in pre-surgical mapping of the motor cortex involving both the UE and LE and the results correlate well with DES. A 66% rate of true negative response in speech mapping, nTMS helped understand the functional cortical organization preoperatively and facilitated successful resection.

ST-029. MINIMALLY INVASIVE SURGICAL RESECTION OF SUBCORTICAL TUMORS USING THE SIX PILLARS SYSTEM
Richard Rowin1 and Amin Kassam2; 1Marquette General Hospital, Marquette, MI, USA; 2The Ottawa Hospital, Ottawa, ON, Canada

The neurological cost of access to subcortical tumors often precludes surgical removal, thus denying patients a biologically meaningful intervention available to their counterparts with more superficially located lesions. By integrating the latest technologies from mapping, image guidance, access, optics, resection and therapeutic platforms, the Six Pillars System optimizes the minimally invasive approach to deep tumors. At the heart of the system is the FDA approved BrainPath device—a 1.3.5 mm tubular retractor that is directed to the tumor via a trans-sulcal trajectory designed to minimize shear force to the intervening white matter fiber tracts. The first surgeries in the United States using the Six Pillars System were performed at Marquette General Hospital. To date, 17 patients with tumor have been treated. There were six men and eleven women. Five patients harbored primary tumors (two glioblastomas and three grade III astrocytoma). Twelve patients had metastatic tumors. Following surgery, five patients improved neurologically, none were unchanged, and one patient had a persisting deficit. Two patients had postoperative seizure. No patient developed a postoperative infection. One patient expired, one month after surgery. The average length of stay for patients treated with the Six Pillars System was 2.25 days, compared to 4.82 days for patients undergoing open craniotomy. The authors conclude that the minimally invasive approach to subcortical tumors using the Six Pillars System is safe and effective for appropriately selected patients.

ST-030. LOW-DOSE RATE IODINE-125 BRACHYTHERAPY IN RECURRENT MALIGNANT GLIOMAS
Christoph Schwat Z1, Alexander Romagna1, Niklas Thon1, Jörg-Christian Tonn1, Silke Birgit Schwarz2, and Friedrich-Wilhelm Kreth1; 1Department of Neurosurgery, Munich, Bavaria, Germany; 2Department of Radio-Oncology, Munich, Bavaria, Germany

OBJECTIVE: Prognosis of recurrent malignant gliomas (WHO III and IV) is dismal and despite numerous efforts postrecurrent survival (PRS) remains short. This pivotal study evaluates the effectiveness and treatment-associated morbidity of low-dose—rate iodine-125 stereotactic brachytherapy (SBT) in highly selected patients with circumscribed tumor recurrence. METHODS: Data of patients with treatment between 2003 and 2011 were prospectively collected and retrospectively analyzed. Indications for SBT were histologically verified recurrent gliomas WHO III or IV with a diameter of <4 cm based on MRI and 18FET-PET, and a KPS of ≥70. Biomarker status included MGMT-methylation, IDH1/2 mutations, LOH 1p/19q. SBT was performed via tem- porary iodine-125 seed implantation. Reference dose was 50 GY, dose rates were low (<5 cGy/h). Date of last follow-up (FU) was 02/2012. Survival analysis was performed with the Kaplan-Meier method. RESULTS: 71 pa- tients (35 males, 36 females) were included. Median age at seed implantation was 52 years, the median KPS was 90%. All patients had received prior treat- ment. Histological diagnoses included 41 glioblastomas WHO IV, 20 astrocyto- mas WHO III, 9 oligoastrocytomas WHO III, and 1 oligodendroglioma WHO III. The median tumor volume was 2.5 cm3 and the median treatment time was 450 minutes. The median FU was 34 months. Median PRS after SBT was 9.3 months (CI95% 7.6-18.4) and 25.7 months (CI95% 11.5-42.3) for WHO IV and III tumors. Favorable prognostic factors for PRS after SBT were patient age at SBT (p = 0.002) and LOH 1p/19q (p = 0.04). Neither tumor grade, nor MGMT-methylation, nor IDH1/2 mutations had any signif- icant impact. Transient morbidity was seen in 17% of patients, no permanent morbidity was found. CONCLUSIONS: Low-dose rate Iodine-125 SBT is an attractive additive local treatment option for highly-selected patients with recurrent malignant gliomas who had previously undergone multimodal therapy. SBT efficacy is seemingly independent from MGMT-methylation and IDH 1/2 mutation status.

ST-031. THE ROLE OF SURGERY FOR ANAPLASTIC GLIOMAS WITH IDH GENE MUTATION
Yukihiko Sonoda1, Ichiyo Shibahara1, Ryuta Saito1, Masayuki Kanamori1, Tomohide Kuroki1, Takamichi Uetani2, and Satoru Nishio1; 1Department of Neurosurgery, Kuma Medical University, Japan; 2Department of Neurosurgery, Jichi Medical University, Japan

INTRODUCTION: IDH gene mutation was frequently found in anaplastic gliomas. Although IDH gene mutation has been reported to be a favorable prognostic factor, anaplastic gliomas with IDH gene mutations sometimes re- curr as secondary glioblastoma. In this study, we investigated the role of
surgery for anaplastic gliomas with IDH gene mutation. METHODS: We analyzed clinical (extent of resection), genetic (1p19q codeletion, TP53 gene mutation) factors for correlation with progression free survival (PFS) and overall survival (OS). RESULTS: Eighty-one patients with IDH mutant anaplastic gliomas were investigated. Thirty patients received total resection on MRI. Median PFS was 187 months and median OS was not reached. Eighteen of 50 patients received less than subtotal resection during follow-up period (median PFS 74 months). 12 of 18 tumors had TP53 gene mutations and other 6 tumors had 1p19q co-deletion. On the other hand, tumor recurrence was observed in only four patients which underwent total resection. Three of those had TP53 gene mutation. Overall survival of total resection group and non-total resection group were not reached and 3.6 months respectively (p = 0.0036). 10 years survival rate of total resection group and non-total resection group were 93.4% and 50.4% respectively. CONCLUSION: Patients of anaplastic gliomas with IDH mutation had favorable prognosis. Particularly, total resection was significantly associated with survival. Even in patients with IDH mutant gliomas, TP53 gene mutation still had risk for recurrence.

Adjuvant radiotherapy (including proton beam irradiation) was applied in 63.8% of the patients. Median progression free survival was 7.3 years. Multivariate analysis identified male gender as an independent risk factor for tumor progression (p = 0.04) and death (p = 0.03), despite the fact that radical resection was achieved more often in males (p = 0.036). Neither expression rates of E-cadherin and N-cadherin nor their ratio did gain prognostic influence. None of the other patient-, tumor- or treatment related prognostic factors (age, duration of symptoms, Karnofsky score, extent of resection, adjuvant radiotherapy) proved to be of prognostic relevance in the multivariate model. CONCLUSION: In skull base chordomas, male patients bear a significantly higher risk of recurrency and death. Expression of E- and N-cadherin has no prognostic significance. These data might help to identify high risk patients in whom more aggressive adjuvant therapy or at least a closer follow-up schedule is warranted. Moreover, further studies are needed to elucidate the potential mechanism of gender disparity with regard to tumor progression and prognosis.

COURSE OF SKULL-BASE CHORDOMAS

Natalia Kremenevskaya5, Niklas Thon1, and Robert Winn1,2; 1Department of Neurosurgery, Munich, Germany; 2Department of Neurosurgery, Marquette, MI, USA

We conducted a human brain tumor PDT study that evaluated the toxicity of PDT based on both light-emitting diode (LED) and laser technology in selected patients with recurrent/ progressive brain tumors. Two patients displayed neuroradiology, one after laser treatment using an interstitial fiber directly inserted into the tumor, one with the laser-balloon adapter combination. Escalating doses of Photofrin® were tolerated to the maximum dose of 2.0 mg/kg. Light dose was 100 J/cm2. PDT in the posterior fossa or near eloquent brain was tolerated using the LED or laser-balloon adapter. All patients had tumor responses as documented by MRI scan and the mean time to tumor progression after PDT was 67 weeks. Eight were pediatric patients, all of whom received Photofrin®, who exhibited relapse-free survival times ranging from 8 weeks to 13 years. None showed neurotoxicity. Of the 20 patients, four had tumors in the posterior fossa area, with one developing a significant neurologically deficit. This patient was one of the two using interstitial fiber illumination. 111In-Photofrin® was determined using external imaging and quantitation with a gamma camera. 99mTc-DTPA was used as a control for nonspecific uptake. Specific tumor uptake of the 111In-Photofrin® occurred well beyond that resulting from blood-brain barrier breakdown. A phase 1 study is being performed on pediatric patients with supratentorial primary brain tumors who undergo neurosurgery at the Children’s Hospital of Wisconsin in Milwaukee. A minimum of 12 study subjects will be used with four different photofrin dose levels: 0.5 mg/kg, 1.3 mg/kg, 2.0 kg/m2, and 3.0 mg/kg. Photocytotoxicity of Photofrin® is controlled by the total light dose delivered over the treatment time. PDT lasers are equipped with a calibration unit to calibrate the fibers and yield the required power density output (mW) necessary to deliver a light dose of 240 J/cm2.

ST-032. PHENYTOIN REDUCES 5-ALA MEDIATED FLUORESCENCE IN Glioblastoma cells

M. Anthony Brown1, Kareem A. Zaghloul1, Grace E. Park2, and John K. Park1; 1Department of Neurosurgery, Munich, Germany; 2Department of Neurosurgery, Erlangen, Germany

Abstract

Glioblastoma multiforme (GBM) is a devastating form of cancer, and essentially all GBM tumors recur causing fatality. A new surgical technique, fluorescence-guided resection of GBM using 5-aminolevulinic acid (5-ala), improves the extent of resection and positively impacts the length and quality of patient survival. The fluorescence achieved in neoplastic tissue depends directly on the accumulation of porphyrins derived from the metabolism of the 5-ala produrg within the cancer cell. However, 5-ala induced fluorescence has been reported to be inconsistent. In an effort to determine the cause of the inconsistent fluorescence, the authors investigated the effect of medications commonly prescribed to brain tumor patients on 5-ala induced fluorescence. A model was developed to quantify intracellular porphyrin accumulation via a U87/MG GBM cell line constitutively expressing yellow fluorescent protein (YPF-U87). 5-ala mediated fluorescence within the cells was standardized to cell number via the fluorescence emission spectra ratio of porphyrin (405 nm) to YFP (525 nm). 5-ala induced accumulation of porphyrins was measured after treating U87 cells with phenytoin, dexamethasone, or desipramine for 3 days. After a 6 hour incubation with 5-ala, no significant differences were observed in cells treated with desamethasone or desipramine. Phenytoin, however, significantly reduced the accumulation of fluorescent porphyrins within the YPF-U87 cell line by nearly 30% compared to the control. In an effort to minimize fluorescence during surgery and improve patient survival these results suggest that further investigations are warranted to determine the effects of commonly administered medications on 5-ala fluorescence-guided resection of GBM.

ST-033. MALE GENDER IS A RISK FACTOR FOR THE CLINICAL COURSE OF SKULL-BASE CHORDOMAS

Walter Rachinger1, Matthias Simon1, Stephan Dutzmann1, Gunther Feith2, Natalia Kremenevskaya1, Niklas Thon1, and Jörg-Christian Tonn1; 1Department of Neurosurgery, Munich, Germany; 2Department of Neurosurgery, Erlangen, Germany

OBJECTIVE: Chordomas of the skull base are rare, locally invasive and have a poor prognosis. Recently, the expression ratio of the transmembrane cell adhesion proteins N-cadherin and E-cadherin has been suggested to provide additional prognostic information for patients who were deemed of this retrospective multicentric confirmatory study was to evaluate prognostic factors including expression of N- and E-cadherins in patients initially treated with microsurgical tumor resection. METHODS: 47 patients (21 women, 26 men, mean age 49 years) treated in five academic centers were included. Histology was centrally reviewed, as well as N- and E-cadherin-expression by immuno-histochemistry. Prognostic factors were obtained from multivariate regression models. For survival analysis the Kaplan-Meier method was used. RESULTS: The median follow-up period was 5.2 years. Gross total resection, subtotal resection and extended biopsy were done in 14.9%, 80.9%, and 4.2%, respectively.

Of 47 patients, 28 received further surgical treatment, including re-operation. Volumetric area under the curve (AUC) analysis of 619 serial post-operative magnetic resonance imaging (MRI) studies (median 4 per patient) was performed to determine the regrowth rate of tumors following re-operation. RESULTS: The median post-operative survival of all patients following re-operation was 12.4 months (95% CI, 9.0–15.6). In a multivariate regression model, patients with recurrent tumor at the time of tumor recurrence, which occurs in virtually all patients, have not been standardized and repeat surgical resection (re-operation) is considered in only one in four patients. METHODS: This retrospective study comprised 97 consecutive patients who underwent neurosurgery at the Children’s Hospital of Wisconsin in Milwaukee. A minimum of 12 study subjects will be used with four different photofrin dose levels: 0.5 mg/kg, 1.3 mg/kg, 2.0 mg/kg, and 3.0 mg/kg. Photocytotoxicity of Photofrin® is controlled by the total light dose delivered over the treatment time. PDT lasers are equipped with a calibration unit to calibrate the fibers and yield the required power density output (mW) necessary to deliver a light dose of 240 J/cm2. 2...
independently associated with decreased survival \((p < 0.001)\), along with greater age \((p = 0.003)\) and lower pre-operative Karnofsky performance status (KPS) \((p < 0.001)\). Larger volume residual tumors had higher rates of subsequent regrowth \((p = 0.003)\), and a higher regrowth rate in turn independently associated with decreased survival \((p < 0.001)\).

CONCLUSIONS: The median survival of patients re-operated for recurrent GBM compares favorably to historical controls. Re-operation should be considered in all patients who meet favorable pre-operative clinical and radiographic criteria. For patients undergoing re-operation, the surgical goal should be to leave a minimal amount of residual tumor tissue in order to slow tumor regrowth and maximize survival benefit.