Phenytoin reduces 5-ala mediated fluorescence in glioblastoma cells

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Phenytoin reduces S-ala mediated fluorescence in glioblastoma cells
SURGICAL THERAPIES

ST-001. PHASE I TRIAL OF A RETROVIRAL REPLICATING VECTOR (TOCA 511) IN RECURRENT HIGH GRADE GLIOMA PATIENTS DEMONSTRATES THE IMPORTANCE OF REAL-TIME MONITORING DURING DOSE ESCALATION AND ASSESSMENT OF SAFETY AND EFFICACY

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We are conducting investigational dose escalation trials in patients with High Grade Glioma (HGG, NCT011536184 and NCT014707949), using a retroviral replicating vector (Toca 511). Toca 511 (vismagneum amintreprocorex) encodes an optimized yeast cytosine deaminase that converts 5-fluorocytosine (5-FC) to the anti-cancer drug 5-FU in infected tumors. We report here results of a Phase 1/2 trial of direct intratumoral Toca 511 administration to recurrent HGG patients, followed by repeat courses of oral 5-FC. Six Toca 511 dose levels, escalated by half logs, were administered to six patients. 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 tumor uptake and eventual delivery of Toca 511 to tumor. As a result, real-time MRI-guided delivery was introduced using Toca 511 infusion with a stepped-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. ENDOCUTAL PITUITARY TUMOR SURGERY: THE LEARNING CURVE

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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/ ENT surgeon team (PT, LZ). We assessed the extent of resection based on comparison of pre and post-operative imaging for each case. We reviewed complications including post-operative hypopituitarism, diabetes insipidus and CSF leaks. We then compared these outcome parameters in the first half of patients operated on (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 51 years. M:F ratio in both groups was 1.15:1. In Group A 55.8% 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 <.001). 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 Anazii, Eric Gantwerker, Myles Pensak, 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 attempts at maintained facial nerve 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 (PT, MP) for large (Koos 3 & 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 received radiation treatment to their tumors prior to surgery. 18 patients underwent a retrosigmoid 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?

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OBJECT: The role of endoscopy in the resection of malignant lesions remains controversial. Such malignancies are traditionally resected through transfacial approaches and any skull base involvement is addressed through transcranial 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 nasal endoscopy. RESULTS: A total of 9 patients were included in the series. M:F ratio was 5:4. Average age at time of surgery was 52 years. Pathology included Esthesioneuroblastoma, sarcoma, SNUC, melanoma, adenocarcinoma and myofibroblastic tumor. 2 patients (22%) had intra-orbital extension and 1 patient (11%) had pterygopalatine or infra-temporal fossa extension. All patients had skull base involvement, 3 (56%) of which had intradural extension. 6 patients (67%) underwent a purely endoscopic resection and 3 patients (33%) 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 adjunct treatment. Complications included 2 post-op CSF leaks. CONCLUSION: Nasal cavity malignancies involving the skull base can often be difficult to resect. Open transfacial approaches are effective, but can be associated with significant morbidity. We believe that endoscopic and endoscopic-assisted techniques offer a minimally disruptive 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?

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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 servable 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 outcome. 2 patients 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 INTRACRANIAL TUMORS

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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 and paraventricular 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 the 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 twice endoscopic operation. There were 2 total resection, 4 subtotal resections and 8 partial resections. There were no severe complications associated endoscopic resection of the tumors. CONCLUSION: In the dry field, it is possible to surgical procedures, which are difficult in the wet field. The field exchange technique is necessary in the situation during endoscopic management. Compared to tumor removal with microscope, however, there are difficult handlings in endoscopic intraventricular tumor resection, which may be resolved by instruments.
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 upfront resection or 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 NGGCT 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.

ST-011. RESECTION PROBABILISTIC MAPS FOR QUALITY ASSESSMENT OF GLIOMA SURGERY: A COMPARISON OF TWO SURGICAL CENTERS USING INTRAOPERATIVE SIMULATION MAPPING
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BACKGROUND: Intraoperative brain stimulation mapping reduces permanent postoperative deficits when used in patients undergoing removal of glioma. Successful functional mapping is assumed to depend on the expertise of the surgical team. In this study, the extent of glioma resection (EOR) is quantified using a novel approach, so-called resection probability maps (RPM), exemplified by a surgical team comparison, here with long and short experience in mapping. METHODS: Adult patients with glioma were consecutively included by two centers with two and fifteen years of mapping experience. Resective surgery was targeted at non-enhanced MRI tumor volume and was limited by functional boundaries. Neurological outcome was compared. Resective surgery was targeted at non-enhanced MRI extension and was limited by functional boundaries. Neurological outcome was compared. To compare EOR, we applied RPMs to quantify and compare the likelihood of resection throughout the brain. Considerations for spatial dependency of voxels and multiple comparisons were taken into account. RESULTS: The senior surgical team contributed 56, and the junior team 52 consecutive patients. The patient cohorts were comparable in age, preoperative tumor volume, lateralization, and lobe localisation. Neurological outcome was similar between teams. The probability of resection on the RPMs was very similar, with none (0%) of 703,967 voxels in left-sided tumors being differentially resected, and 124 (0.02%) of 644,153 voxels in right-sided tumors. CONCLUSION: RPMs provide a quantitative volumetric method to compare EOR, which we present as standard for quality assessment of resective glioma surgery. Stimulation mapping is a robust surgical technique, because both the EOR and the neurological evaluation are independent of surgical experience, supporting wider implementation.

ST-012. MANAGEMENT AND OUTCOMES IN PATIENTS WITH GLIOMA-ASSOCIATED EPILEPSY
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INTRODUCTION: Seizures are the most frequent presenting symptom in patients with low-grade tumors 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 tumor 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). The 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 tumor group 7 additional resections were performed due to seizure recurrence – all related to residual or recurrent tumor 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 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.

ST-013. SUPRA-MAXIMAL RESECTIONS FOR NEWLY DIAGNOSED GLIOBLASTOMA MULTIFORME
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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 gliomas may allow for the eradication of proximate nonfunctional, tissue with high degree of infiltration by glialoma cells beyond the zone of containment 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 (2005-2011) operated on for primary GBM with either upfront resection (36/79) or biopsy (18/79) procedures. Marker-only diagnosis was done in 26/79 patients, 26 (32%) of whom did not undergo second-look surgery. Maker-only diagnosis was also used as references. After image acquisition patients were transferred to OR and under general anesthesia, as enhanced CT scan or PET study were also used as references. To determine the targets, neuroimages such as T1 post contrast were used for making the decision. Anatomical landmark points identified on images were used to place and secure the frame. Tumor morphology and location was assessed using neuronavigation or freehand frameless techniques. Neuroimaging studies were also used to create and refine targets. Involvement of eloquent brain tissue was determined preoperatively with intraoperative mapping and correlated with postoperative outcomes. RESULTS: The senior surgical team contributed 56, and the junior team 52 consecutive patients. The patient cohorts were comparable in age and sex distribution. Medians follow-up was 15 months. GTR, NTR, and STR were achieved in 21, 11 and 47 patients respectively, and in 21, 9 and 27 patients within the intent-to-treat population. Median survival for the whole group was 15 months, and 34.2, 16.5 and 12 months for 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 independent predictors of survival. CONCLUSION: The sub-pial technique is safe, effective and associated with an overall survival benefit not previously seen in other GBM or GMB series in which a GTR is achieved, in addition to the benefits of the addition of in-cavity carmustine wafer placement may be potentiated with the supra-maximal resections. Neurological deficits and complications were favorable compared to other series and did not prevent adjuvant therapy.

ST-014. STEREOTACTIC BIOPSY FOR DEEP SEATED BRAIN TUMORS USING THE LEKSELL STEREOTACTIC FRAME SYSTEM
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PURPOSE: To evaluate the results of stereotactic biopsy for deep seated intraaxial lesions. PATIENTS AND METHODS: Sixteen patients with intraaxial lesions suspected of brain tumor. The locations of lesions were, deep white matter of cerebrum 4, basal ganglia 1, thalamus 6, midbrain 2, pons 3. Patients age range was 9-81 years (median 61 years), and 9 were men and 7 were women. Under local anesthesia the Leksell stereotactic frame was fixed and the MRI were taken. To determine the targets, neuroimagings such as enhanced CT scan or PET study were also used as references. After image acquisition patients were transferred to OR and under general anesthesia, several samples were taken with 2.1mm diameter needle by aspiration. Most
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 no safe regions, aspiration of the cyst was performed as much as possible. The trajectory should avoid sulci, cortical veins or ventricular system. After the trajectory inside the needle was irrigated repeatedly 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 gliomas (pilocytic 1, grade II 3, grade III 3, grade VI (GBM) 2, high grade 1, gliastumor 1) 3 lymphomas, 1 germinoma and 1 multiple sclerosis. There were no significant 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 lesions. 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

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BACKGROUND: Although High Grade Gliomas (HGG) are significantly more frequent in patients older than 65 years of age, most clinical studies so far have excluded this elderly population. It is well 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 database of 150 patients (90M, 60F) over 65 years with supratentorial gliomas (WHO-IV:137, WHO-III:11, WHO-II:2) 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 subgroup, 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 radiotherapy in MM, 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 overall survival 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 RESECTION OF RECURRENT GlioBLASTOMA PROLONGS SURVIVAL AFTER RELAPSE WITHOUT IMPAIRMENT OF FUNCTIONAL OUTCOME

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OBJECTIVE: Standard of care in newly diagnosed glioblastoma (GBM) is maximal safe tumor resection followed by radio (RT) - and chemotherapy (CTH). At tumor relapse, however, standard of care, particularly the value of re-resection, is still under debate. We addressed the question: does delayed 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 (SRR) 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 second re-resection (10% vs. 13.3%). Adding 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. Importantly, SRR was significantly prolonged in completely resected patient (11 vs. 5 months; p = 0.0348) 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 SRR 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 MENGIAL DERMATOMYXOSIS IN SINGLE INSTITUTION: FOCUSED IN SURVIVAL AND LOCAL CONTROL

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INTRODUCTION: Both hemangiopericytoma (HPC) and malignant meningeal neoplasm (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, recurrences 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 years. 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

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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 improved high precision procedures. METHODS: 33 patients with 9, MM (metastatic brain metastases) and 24, HPC (hemangiopericytoma) patients were included in the study. Conventional post chemotherapy/radiosurgery were scanned by delayed contrast extravasation MRI prior to surgery. High resolution maps were calculated from T1-MRI acquired 2 and 7 min post contrast injection. 44 stereotactic biopsies planned using the maps were acquired from 17 patients. En-block samples were acquired from 3 and gross total samples were acquired from 13. Histological analysis 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...
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 resection of insular tumors can be accomplished 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 = 12). Follow-up ranged from 3-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 (0-4) development of new neurological 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 re-fractory seizures (n = 5) 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 stereotaxic slender border medially, which minimally 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.
complications occurred in this study. Not all of meningiomas fluoresced with 5-ALA, and 5-ALA is available for about 90% of meningiomas. 5-ALA would be easy to use and be useful to find residual tumor and also useful to prevent recurrences by total removal in meningiomas.

ST-023. UPDATED THERAPEUTIC STRATEGY FOR ADULT LOW-GRADE GLIOMA STRATIFIED BY RESECTION, HISTOLOGY, AND MOLECULAR MARKERS
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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 of 133 patients (mean age: 39 y, 56 male, 44 female) with LGG who underwent surgery between 2005 and 2013. Patients were divided into two groups: 90% EOR were obtained and others were treated with radiation and/or chemotherapy. RESULTS: Median preoperative tumor volume was 29.0 cm³ and median EOR was 93%. 10-year OS and 5-year PFS for all the patients were 95.1% and 60.2%, respectively. Eight-year OS for DA, OA and O were 70.9%, 91.2%, and 98.3%, respectively. Both OS and PFS were significantly longer in patients with ≥95% EOR than those with <95% EOR (P = 0.01). Increased EOR resulted in better PFS for diffuse astrocytoma (P < 0.01) but not for oligodendroglia. Multivariate analysis identified age (HR = 4.08; 95% CI, 1.08-16.96; P = 0.038) and EOR (HR = 4.75; 95% CI, 0.76-26.48; P = 0.013) as parameters significantly associated with OS. The only parameter associated with PFS was EOR (HR = 2.69, 95% CI, 1.43-5.04; P = 0.002) and Chemotherapy prolonged PFS in patients with oligodendroglial subtypes (P = 0.006). However, there was no survival benefit of radiation and chemotherapy in diffuse astrocytoma. CONCLUSIONS: Our updated therapeutic strategy for LGG is followings; 1. Patients with ≥95% 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 impossible, radiotherapy and nimustine hydrochloride (ACNU) based chemotherapy are conducted. 3. OA and O patients with <90% EOR and could prevent 1P9q loci of treatment with ACNU and the others are treated with both radiotherapy and ACNU.

ST-024. SURGERY USING A TRAJECTOGRAPHY-INTEGRATED NAVIGATION SYSTEM AND MOTOR EVOKED POTENTIALS FOR PRESENTATION OF MOTOR FUNCTION IN PATIENTS WITH MALIGNANT GLIOMA
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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 resection. The line of resection closely approached the PT, subcortical MEPs were observed without any adjuvant therapy regardless of tumor subtype. 2. DA patients with <90% EOR are considered second look resection and if impossible, radiotherapy and nimustine hydrochloride (ACNU) based chemotherapy are conducted. 3. OA and O patients with <90% EOR and could prevent 1P9q loci of treatment with ACNU and the others are treated with both radiotherapy and ACNU.

ST-025. 5-ALA GUIDED RESECTION OF MALIGNANT GLIOMA: A SINGLE INSTITUTION EXPERIENCE
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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-aminolevulinic 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, using 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, when MRI documented heterogenous tumor 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
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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 benefit to glioblastoma patients through both brain decompensation (assessed by extent of resection) and a reduction in the volume of viable tumor (assessed by residual tumor volume).

METHODS: A consecutive population of patients who underwent craniotomy, tumor resection were included in the analysis. Resection 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.
with non-resectable tumors (p = 0.399 and p = 0.356, respectively). CONCLUSION: Maximal safe resection likely provides a greater benefit to glioblastoma patients with resectable tumors than to those with non-resectable tumors. Surgical resection may confer a survival benefit by decreasing the degree of compression on the brain and by reducing the volume of viable tumor.

ST-027. FLUORESCENCE GUIDE SURGERY IN HIGH GRADE GLIOMAS USING A HIGH-DEFINITION EXOSCOPE SYSTEM: AN ALTERNATIVE MICROSCOPE
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INTRODUCTION: Fluorescence-guided microsurgical resections of high-grade gliomas using 5-aminolevulinic acid (5-ALA) have proved to be superior to conventional microsurgery. An optical device, usually a modified microscope, is needed for these procedures. However, an exoscope may 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 neuronavigation guided biopsy. METHODS: Twenty-five three were operated using ALA fluorescence in an exoscope system. Tumor fluorescence signal were 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). Histological analysis indicated that 14 had glioblastoma multiforme, 2 grade-III oligodendroglioma and 1 anaplastic astrocytoma, 5 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 cost 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
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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, 18/78% 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
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The neurological cost of access to subcortical tumors often precludes surgical removal, thus denying these 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 13.5 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, nine 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
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OBJECTIVE: Prognosis of recurrent malignant gliomas (WHO III and IV) is dismal and despite numerous efforts post-recurrent survival (PRS) remains short. This pivotal study evaluates the effectiveness and treatment-associated risks 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 18F-FET-PET, and a KPS of ≥70%. Biomarker status included MGMT-methylation, IDH1/2 mutations, LOH 1p/19q. SBT was performed via temporary 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 patients (35 males, 36 females) were included. Median age at seed implantation was 52 years, the median KPS was 90%. All patients had received prior treatment. Histological diagnoses included 41 glioblastomas WHO IV, 20 astrocytomas 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 430 hours. The median FU was 34 months. Median PRS after SBT was 9.3 months (C95% 7.6-18.4) and 25.7 months (C95% 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 significant 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
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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 recur 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 recurring 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 = 0.036). 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.

ST-032. PHENOTYIN REDUCES 5-ALA MEDIATED FLUORESCENCE IN GLOBLASTOMA CELLS
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Glioblastoma multiforme (GBM) is a devastating form of cancer, and essentially all GBM tumors recur causing fatigue. 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 prodrug 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 using a YFP-U87 cell line constitutively expressing yellow fluorescent protein (YFP-U87). 5-ala mediated fluorescence within the cells was standardized to cell number via the fluorescence emission spectra ratio of porphyrin (403 nm) to YFP (525 nm). 5-ala induced accumulation of porphyrins was measured after treating YFP-U87 cells with phenytoin, dexamethasone, or desipramine for 3 days. After a 6 hour incubation with 5-ala, no significant difference in porphyrin accumulation was observed in cells treated with dexamethasone or desipramine. Porphyrin therapy, however, significantly reduced the fluorescence of porphyrin within the YFP-U87 cell line by nearly 50% compared to the control, which diminishes fluorescence during surgery and improve patient survival results this 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
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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. METHODS: Ten patients with chordomas were included. Histology was centrally reviewed, as well as N- and E-cadherin expression by immunohistochemistry. 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, and median OS was not reached. Eighteen of 50 patients received less than subtotal resection recurring 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 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.

ST-034. PHOTODYNAMIC THERAPY OF BRAIN TUMORS
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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 neurotoxicity, one after laser treatment using an intrasulcal 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-1. 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 neurologica 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 supra or infratentorial 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 mg/kg, and 3.0 mg/kg. Photoactivation 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.

ST-035. RE-OPERATION FOR RECURRENT GLOBLASTOMA MULTIFORME
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BACKGROUND: The standard of care for patients with newly diagnosed glioblastoma multiforme (GBM) is surgical resection followed by radiation and temozolomide chemotherapy. Treatment regimens 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 with recurrent GBM. Multivariate analyses were carried out to identify pre- and post-operative clinical and radiographic variables independently associated with overall survival after re-operation. RESULTS: Median progression free survival after re-operation 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 neurological 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 supra or infratentorial 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 mg/kg, and 3.0 mg/kg. Photoactivation 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.

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 recurrence 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.
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.