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found to be a malignant peripheral nerve sheath tumor upon surgical removal.

Conclusions: Repeat SRS for VS is a safe and effective strategy in carefully selected patients.

Abstract 187: GAMMA KNIFE RADIOSURGERY AS PRIMARY TREATMENT FOR SKULL BASE MENINGIOMAS

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Objective: Skull base meningiomas represent challenging tumors as they are often in close proximity to critical structures and surgery can be associated to neurologic morbidity and negative impact on quality of life. In the last decades, Gamma Knife Radiosurgery (GKRS) has shown comparable control rates to surgery with a lower complication rate. The aim of the present study is to assess long-term clinical and radiological outcomes in a large series of skull base meningiomas that underwent GKRS as primary treatment.

Methods: Three-hundred-eleven patients (235 females and 76 males) treated with GKRS as primary therapy at our center for skull base meningiomas, between September 2007 and December 2014, were included in the present series. Patients' age ranged from 26 to 86 years (mean 60.1 years). The total number of treated lesions was 326, with an average tumor volume of 3.96 cm³ (median 2.85 cm³, range 0.03-23.27 cm³). Median tumor margin dose was 15 Gy (range 11-16 Gy). A statistical analysis was performed to correlate clinical and radiological outcomes with dose-planning parameters and patients and tumor characteristics/location.

Results: Mean follow-up (FU) was 68 months. Twenty-seven patients died at last FU, only in one case the death could be attributable to progression of the treated meningioma. At last FU 96% of the lesions were either stable or reduced in size. The actuarial local tumor control rate was 98% at 3-, 5- and 8-year. The 3-, 5- and 8-year progression-free survival rates were 98%, 96% and 96%, respectively. A further treatment after GKRS was needed in 3%. Permanent new onset or worsened focal neurological deficit was registered in 8%.

Conclusions: GKRS demonstrated to be a safe and effective therapeutic option as primary treatment for skull base meningiomas, providing high tumor control rates with low treatment-related morbidity. According to our results, GKRS can be considered a valuable alternative to surgery as the primary treatment of patients harboring small lesions, especially those not eligible because of age, general medical conditions or personal refuse.

Abstract 197: Stereotactic Radiation Therapy, Hypofractionation and Radiosurgery for Craniopharyngiomas in Children

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Objective: Craniopharyngiomas (CPh) are the most common non-glioma tumors in children. According to many trials of Stereotactic Radiation Therapy (SRT) and Radiosurgery (SRS) yield a long recurrence-free survival or help to prevent progression in patients with unresectable and recurrence CPh. We retrospectively reviewed the experience of Burdenko Institute to determine the role of Stereotactic Irradiation in complex treatment of these patients.

Methods: 266 patients with craniopharyngiomas were treated with different types of stereotactic irradiation between 1.2005 and 12.2016 at Burdenko Neurosurgical Institute and Moscow GammaKnife Centre. This is the analysis of the results of treatment of 123 children (under the age of

18) with data of follow up. Were irradiated 88 patients (72%) with residual tumors and 35 patients (28%) with relapses. The study group consisted of 74 boys and 49 girls. The median age was 10,7 years. All the patients had a prior tumor resection. 55 patients underwent SRT / Novalis/ (mean dose 54 Gy), 44 patients underwent hypofractionated irradiation /CyberKnife/ (5fr x 5-5,5Gy, 3 fr x 7Gy) and 24 pts - SRS with GammaKnife (mean dose 16 Gy; average PD=13.5 Gy (8 - 16 Gy), average PI=49.3% (33.3 - 60%). Totally 42 tumors or tumor fragments was treated 44 times. Average tumor volume - 1.7 cm³ (0.07 - 4.89 cm³).

Results: The median follow-up period was 92,9 months (range, 16,9-255) after the patients were diagnosed. All of these patients (123 pts-100%) were available for the follow-up. At the end of the follow-up (6.2017) 118 patients (95,9%) were alive. 5-year OS was 99%. The median follow-up period after irradiation was 38 months (range, 0,13-129). Tumor control or regression was achieved in 112 patients (91%). 9 patients (7%) had a transient enlargement of cysts at early time of irradiation: on average 3,5 month (range 2,7-9,4). There were no statistical differences in the effectiveness of different types of fractionation.

Conclusions: Stereotactic radiosurgery, radiotherapy and hypofractionation are effective methods of treatment for CPh in patients with residual tumors, as well patients with CPh relapses with progressive disease without difference in results. The enlargement of craniopharyngioma cysts in early time (not later than 1 year) after irradiation usually is transient and do not require surgical treatment.

Abstract 199: Behavior of intratumoral and extratumoral cysts after Gamma Knife Radiosurgery in unilateral vestibular schwannomas

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Objective: Behavior of intratumoral and extratumoral cysts in unilateral vestibular schwannoma (VS) after Gamma Knife radiosurgery (GKRS) was investigated based on our experience of long-term follow-up.

Methods: The records and images of 495 patients with unilateral VS with adequate follow up information treated between Jan. 1992 and Dec. 2016 were retrospectively analyzed. Median age was 59 years (17-84 years) and male female ratio was 190: 305. Median and mean tumor volume was 2.9 and 4.0 ccm (0.1- 20.2 ccm). Prior surgical removal was performed in 103 patients. Median and mean prescription dose were 12 and 12.1 Gy (10 - 17 Gy). Mean and median follow up were 89.3 and 82.3 months (0.4-301.7 months). 139 patients were followed for more than 10 years and of which 20 patients were followed for more than 20 years. 19 patients died during the follow up and of which 6 deaths were related to the tumor.

Results: Appearance or noticeable expansion of intratumoral and/or extratumoral (cysts adjoining tumors) was observed in 62 cases. Timing of recognition was between 3 months and 161 months after GKRS. Time to maximum cyst volume from the recognition was 0 to 85 months and in 9 cases slow continuous enlargement lasted more than 3 years. Seven of them well tolerated the situation and cyst finally started regression. In 2 patients, surgical intervention was needed. Salvage surgery was performed in 33 patients of whole patients group and of which cyst expansion was the cause in 12 patients. Six out of 9 salvage surgeries performed within 2 years after GKRS were due to rapid expansion of cyst.

Conclusions: Behavior of intratumoral and/or extratumoral cyst is quite unpredictable. Patients should be informed the possibility of rapid cyst enlargement resulting in surgical removal shortly after GKRS. Cysts may appear or expand even long after the period of transient expansion and good continuous regression of tumor. Many of continuous slow cyst enlargement is self-limiting and eventually turned to regression. So, if the symptom is tolerable for the patients, observation is recommended.

Abstract 200: Gamma Knife Radiosurgery for Craniopharyngioma. Results on 55-treated patients followed-up for at least 12 months

brain metastases ≤ 2.0 cm in diameter, with dose reduction only considered for lesions ≤ 0.5 cm. For patients with favorable and targetable tumor subtypes, local control remains quite favorable with reduced prescription doses. However, dose de-escalation for patients with large lesions from radioresistant subtypes (including renal and wild-type melanoma) should be discouraged given significantly higher rates of local failure.

Abstract 10: GAMMA KNIFE RADIOSURGERY IN PATIENTS WITH FIVE AND MORE BRAIN METASTASES

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Objective: To evaluate overall survival and factors predicting outcome in patients with five and more brain metastases who were treated with Gamma Knife radiosurgery (GKS).

Methods: Medical records from patients with five and more brain metastases treated with GKS between 2005 and 2015 at the Moscow Knife Center were retrospectively reviewed. Patient demographics, tumor characteristics, treatment-related factors, and outcome data were evaluated.

Results: Two hundred fifty three patients were identified, with a median age of 56 years. Gamma Knife radiosurgery was used as an upfront treatment in 181(71%) of patients and as salvage treatment in 72(28%) of patients with multiple brain metastases. The median overall survival after GKS was 7,3 months (95% CI 6,0-8,5).

At the time of GKS, 242 patients (95%) had concurrent extracranial metastases. Seventy two patients (28%) had a history of whole-brain radiation therapy and surgery. One hundred and fifty-five patients (61%) had a Karnofsky Performance Scale (KPS) score ≥ 80 . The median total intracranial disease volume was 7,4 cm³ (95% CI 6,2-8,7 cm³). A total intracranial tumor volume >10 cm³ was observed in 103 patients (41%). Patient age > 60 years ($p = 0,0012$), extracranial metastases ($p = 0,00367$), and KPS ≤ 70 ($p = 0,0075$) were prognostic factors for poor outcome in the univariate and multivariate analyses

Conclusions: These results confirmed that GKS is safe and effective method for upfront and salvage treatment in patients with five and more brain metastases. Gamma Knife surgery should be considered as an additional treatment modality for these patients, especially in the subset of patients with favorable prognostic factors.

Abstract 17: Stereotactic radiosurgery for small brain metastases and implications regarding management with systemic therapy alone

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Objective: While stereotactic radiosurgery (SRS) has been shown effective in the management of brain metastases, small brain metastases (≤ 10 mm) can pose unique challenges. Our aim was to investigate the efficacy of SRS in the treatment of small brain metastases, as well as elucidate clinically relevant factors impacting local failure (LF).

Methods: We utilized a large, single-institution cohort to perform a retrospective analysis of patients with brain metastases up to 1 cm in maximal dimension. Clinical and radiosurgical parameters were investigated for an association with LF and compared using a competing risk model to calculate cumulative incidence functions, with death and whole brain radiotherapy serving as competing risks.

Results: 1596 small brain metastases treated with SRS among 424 patients were included. Among these tumors, 33 developed LF during the follow-up period (2.4% at 12 months following SRS).

this trial. Micro-metastases (defined here as under 0.14cc and maximum diameter under 6mm) were randomised to a single shot with either the 4mm or the 8mm collimator. Brainstem lesions and lesions within 11mm of one another were excluded. A marginal dose of 25Gy was prescribed for 87 lesions. Primary outcome was radiological local control at 12 months post GKR, or at the last imaging follow-up if death occurred during the first year post-GKR.

Results: 87 eligible lesions were identified in 25/44 subjects and underwent randomisation. 44 lesions were randomly assigned to the 4mm collimator and 43 to the 8mm collimator.

A marginal dose of 25Gy was prescribed for all lesions. The mean Prescription Isodose was 71.8% (43-94) for the 4mm group and 95.6% (88-99) for the 8mm.

The outcome has been reached by 60% of the micro-metastases and at least one follow up was available for 88% of the lesions. The mean follow-up time was 6.2 months (1.0-19.5). No lesion has shown definite enlargement (up to 30% TV increase) and no radiological evidence of oedema or radionecrosis has been detected in either arm.

One lesion from each group showed a small asymptomatic haemorrhage that was managed conservatively.

In the 4mm group, 10.8% of the lesions remained unchanged and 89.2% reduced or disappeared. Similarly, in the 8mm group 23.1% were stable and 76.9% reduced/disappeared.

Ten patients developed new metastatic lesions at follow-up. 54% (13) patients have died, three of them from progressive intracranial metastatic disease, at a mean time of 6 months (0.3-11.3) post-GKR.

Conclusions: Initial results suggest that reduction of treatment time for small lesions may be achieved by using the 8mm collimator without compromising clinical efficacy. Further recruitment and follow up is needed.

Abstract 226: GammaKnife Radiosurgery for recurrent anaplastic ependymoma

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Objective: To evaluate the role of gamma knife stereotactic radiosurgery (GKRS) in patients with recurrent or residual intracranial ependymomas after resection and fractionated radiation therapy (RT).

Methods: We retrospectively reviewed patients with anaplastic ependymomas who underwent GKRS between 2006-2016 after progression from initial multimodal treatment.

From April 2005 till September 2017 at "Center "Gamma Knife" Moscow" affiliated with Burdenko Neurosurgery Institute 78 patients with recurrent and metastases of anaplastic ependymoma was treated at 122 single fraction RS procedures using Leksell Gamma Knife Model C (before May 2009) or Perfexion (thereafter).

Group includes 45 male and 33 female with average age on the moment of first GKRS 12 years (from 2 to 59); most patients has age less than 20 (65 patients; 87%). All patients had previous surgical resection of their ependymomas followed by radiotherapy, and underwent chemotherapy. The median time from initial treatment to GKRS was 17.5 months.

23 patients had 2 and more GKRS (maximum 8!). Some of patients additionally treated in hypofractionation regimes using other devices.

In most cases GKRS was done with PD from 18 to 24 Gy, except cases where GKRS was used as boost to craniospinal treatment (12 Gy, 1 case), large local irradiation volume or critical structures like brainstem or optic nerves or chiasm in touch (15 - 16 Gy). Average PD=19 Gy (12 - 24 Gy), average PI=58% (39 - 92%). Average tumor volume - 1.7 cm³ (2 mm³ - 33 cm³).

Results: Progression-free survival after the initial SRS was 68.4%, at 1 year respectively. The distant tumor (metastases) relapse rate despite RT and GKRS was 20.6% at 6 month and 45.0% at 12 month respectively. Overall survival after GKRS was 89.5% at 1 year, respectively. Adverse radiation effects developed in 10 patients (11.3%).

Conclusions: GK Radiosurgery may be effective for local control in the treatment of recurrent and metastases of such resistant tumor as anaplastic ependymomas. The radiosurgical treatment in adult or pediatric patients with local or distant relapses of anaplastic ependymomas is a reasonable option and increases overall survival of these patients.

Abstract 232: Cellular immune responses defined by IFN-gamma production against mesothelin predict survival in patients with CNS metastases

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Objective: Patients with advanced cancer of different histology, including lung cancer, melanoma, colorectal cancer or ovarian cancer often exhibit CNS (central nervous system) metastases. With the advent of improved treatment modalities, including checkpoint inhibitors, the clinical presentation and development of these CNS metastases can critically shape the clinical course of the disease. Disease progression is shaped by the interaction of the immune system with transformed cells; strong anti-cancer directed immune responses, such as cellular and humoral responses directed against mesothelin, have been shown to be associated with improved survival. The tumor-associated antigen (TAA) mesothelin represents a 40kDa cell surface-bound protein that is preferentially expressed in a high number of malignancies, i.e. pancreatic cancer, lung cancer or ovarian cancer. We tested therefore in a prospective study the survival of patients with CNS metastases in association with cellular immune responses directed against tumor-associated targets, as well as control proteins. T-cells in peripheral blood from thirty-six patients with CNS metastases were tested for cytokine production in response to a broad panel of tumor - associated and viral antigens, including the full-length mesothelin.

Methods: Incubation of T-cells with antigens was carried out in i) medium alone, (ii) in a cytokine cocktail of interleukin (IL)-2/IL-15/IL-21, or IL-2/IL-7, specific antigen recognition was tested for interferon gamma (IFN- γ) production, after which univariate and multivariate analyses (Cox stepwise regression model) were performed to identify independent clinical and immunological factors associated with patient survival (followup was at least 500 days after surgery or until death). Univariate analysis identified gender, age, radiotherapy and mutational load as clinical parameters with statistical impact of patient survival.

Results: Cox multivariate analysis showed that radiotherapy ($p=0.004$), age ($p=0.029$) and IFN- γ responses to mature mesothelin, conditioned by IL-2/IL-7 ($p=0.045$) were independent predictors of the survival of patients from surgery up to follow-up or death.

Conclusions: This is the first evidence that immune responses to a tumor - associated antigen, such as mesothelin, represent a marker of survival in patients with CNS metastases, it also suggests that such immunological monitoring can aid to identify patients at increased for tumor progression or in need for more advanced treatment options to contain or to fight off cancer.

Abstract 236: Repeat radiosurgery for locally-recurrent brain metastases

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Objective: Brain metastases are increasingly being treated by stereotactic radiosurgery (SRS). While the safety and efficacy of primary SRS is well established, little data is available regarding the impact of repeat SRS on a previously treated lesion.

Methods: We performed a retrospective metastasis-level analysis of patients who underwent two or

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Objective: Essential tremor (ET) is one of the common movement disorders. Drug-resistant ET can benefit from standard functional neurosurgery procedures. Historically, radiofrequency thermocoagulation has been initially used. Moreover, deep-brain stimulation became a standard of care, after pioneering series of Benabid. Radiosurgery, aiming at same target (ventro-intermediate nucleus, Vim) has been considered a minimally invasive, safe and effective alternative for tremor alleviation. More recently, high focused ultrasound (HIFU), as an alternative to radiofrequency thermocoagulation, has also showed promising results. The mechanisms by which tremor stops after HIFU or stereotactic radiosurgical thalamotomy (SRT) remains largely undiscovered. Resting state functional MRI (rs-fMRI) assesses inter-regional functional connectivity based on physiological connection that changes on a moment-by-moment basis, rather than anatomical connectivity. The present study aims at establishing a correlation between MR-signature volume at 1 year after SRT and rs-fMRI interconnectivity (IC) strength.

Methods: Were enrolled 17 consecutive patients (ongoing protocol). Resting-state fMRI data and standard tremor scores were acquired at baseline, pretherapeutically (n=17) and 1 year after SRT (n=17), considered the maximum delay for tremor alleviation/arrest. We used a data driven approach implying no a priori hypothesis. The mean MR signature volume 1 year after SRT was 0.125 ml (median 0.063 ml, range 0.002-0.600 ml). The former values were used as continuous in a general linear model with rs-fMRI IC data. Furthermore, a group separation was also employed (group 1, <= 0.063 ml, 8 cases; group 2, >0.063 ml, 9 cases).

Results: We report higher MR-signature volumes associated with IC strength within two particular networks. One is represented by brainstem and bilateral thalamus IC with left red nucleus ($p_{FEW-corr}=0.004$, cluster size 94; higher volumes associated with higher IC). The second is exemplified by the brainstem, bilateral thalamus and cerebellum IC with right Brodmann area 6 and parts of the supplementary motor area ($p_{FEW-corr}=0.002$, cluster size 106; higher volumes associated with higher IC).

Conclusions: The MR signature volumes 1 year after SRT are related to a particular functional patient's profile, as depicted by rs-fMRI. Using a data driven approach implying no a priori hypothesis, we suggest that both part of the "tremor ax" (e.g. thalamus, red nucleus) as well as other brain networks (e.g. supplementary motor area) would relate to more prominent thalamic tissue reaction. Both relevant networks involve the thalamus as a central core, suggesting a prominent functional role of the former as linked to higher MR-signature volumes.

OCULAR DISORDERS

Abstract 11: Gamma-knife radiosurgery for intraocular retinoblastoma as an alternative to enucleation. The first world experience

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Objective: In some cases of chemoresistant or recurrent intraocular retinoblastoma (Rb) external beam radiotherapy (RT) is the only way to save the eye. Conventional RT leads to severe complications including bone deformities, secondary malignant tumors, and currently has very limited use. There is no information about Gamma-knife single fraction radiosurgery (GK-RS) in the management of Rb. The purpose of our study is to present the first experience of successful Rb treatment with GK-RS as an alternative to enucleation.

Methods: Five patients (aged 26, 31, 35, 43, and 114 months) with Rb Group B (one) and Group D (4 patients) were treated with GK-RS as the only capacity to save the eye.

Previously all patients received different kinds of chemotherapy including systemic (vincristine, etoposide, and carboplatin), intra-arterial (Melphalan or/and Topotecan) and intravitreal (Melphalan alone or in combination with Topotecan). All patients had chemoresistant Rb with no capability to use any local treatment (brachytherapy, cryo, or laser).

In cases of massive vitreous Rb (three patients) irradiation dose of 20-22 Gy at 50% isodose curve was prescribed along the inner MRI/CT contour of the eye globe and lens.

The juxtapapillar tumors in two patients were treated with 24 Gy at 49% and 35 Gy at 90% isodose curve. Doses for critical structures (the fovea, optic nerve, lens, ciliary body, orbital bones) have been also taken into consideration, collected, and will be presented.

Results: Complete tumor regression was achieved in three patients: one patient with juxtapapillar tumor and two patients with vitreous Rb. In two patients with vitreous and juxtapapillar Rb more than 50% regression was seen.

Vitreous hemorrhage occurred within 7 months after treatment in one patient with vitreous Rb and was successfully managed with pars plana vitrectomy with melphalan irrigation. Optic neuropathy was detected within 6 months in one patient and regressed after subtenon steroid therapy. Mild retinopathy was seen and successfully treated in one eye. One patient developed eccentric opacities of posterior lens capsule. No signs of iridocyclitis, keratopathy, and damage of extraocular muscles, orbital walls, or brain were seen.

Follow-up was from 3 to 25 months. All patients are still under control.

Conclusions: The first to our knowledge world experience of GKRS for retinoblastoma showed that it may be a reasonable and successful treatment as an alternative approach to enucleation in selective cases. Procedure was well tolerated and had no severe complications. GK-RS should be considered in retinoblastoma management.

Abstract 65: Volume-staged Gamma Knife radiosurgery for large orbital venous malformations

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Objective: In view of the orbital venous malformations (OVMs) often involving or wrapping around the optic nerve, the difficulty of treatment significantly increased and easily prone to recurrence. The object of this study report was to evaluate the results obtained using volume-staged Gamma Knife radiosurgery (GKRS) in patients with large OVMs.

Methods: 20 patients with large OVMs were treated with volume-staged GKRS between March 2005 and October 2015. The series included 8 males and 12 females with averagely aged 22.5 years (range 9-45 years). The diagnoses were confirmed by operation and pathology in 14 patients and presumed on the basis of imaging findings in 6 patients. The median OVMs volume was 12.2 ml (range 7.1-34.6 ml). The median interval between stages was 14 months (range 9-20 months). The tumor margin dose for each stage ranged from 11.0 to 13.5 Gy.

Results: At a median follow-up period of 45.5 months (range 18-98 months), periodically scheduled MRI studies demonstrated evidence of a significant reduction (>75%) of the original OVMs volume was achieved in all patients. Visual acuity was preserved in all patients. 10 patients experienced some improvement in vision. Three patients experienced transient conjunctival edema; no other serious acute side effect was observed.

Conclusions: Volume-staged Gamma Knife radiosurgery provides an effective treatment option in