We included patients with oligodendroglioma by 1p/19q-codeletion or traditional histopathology. Fisher's exact test was used to associate factors with chemotherapy group. The log-rank test was used to compare OS and PFS by chemotherapy group and clinical characteristics. RESULTS: 52 patients were included with a median follow-up of 44 months (range, 3–259). Median age was 44 (range, 22–73), 49 (94%) underwent STR, and 28 (54%) were male. Presenting symptoms were seizure in 35 (67%) patients, sensory in 14 (27%), and motor in 8 (15%). Oligodendroglioma classification was by 1p/19q-codeletion in 27 (52%) and traditional histopathology in 25 (48%) patients. Median radiation dose was 54 Gy (range, 45–60). Chemotherapy was TMZ in 34 (65%) patients and PCV in 18 (35%). Patients who were older (P=0.003), lacked seizures (P=0.03), or had motor symptoms (P=0.04) were more likely to receive TMZ. Median OS was 223 months (95% CI, 181-not estimable) and median PFS was 118 months (95% CI, 69–223). Treatment with TMZ versus PCV was not associated with OS (median 186 vs. 223 months, respectively; P=0.71) or PFS (median 110 vs. 131 months, respectively; P=0.19). Age >40 (P=0.009) and motor symptoms (P=0.027) were associated with adverse OS. Presence of motor symptoms was associated with worse PFS (P=0.008). CONCLUSION: There was no statistically significant difference in OS or PFS between adjunctive TMZ versus PCV for adult high-risk grade II oligodendroglioma. A larger cohort with longer follow-up will provide additional insight.

RTHP-21. TREATMENTS FOR RECURRENT MALIGNANT GLIOMAS AND THEIR PROGNOSIS

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For improvement of glioma therapy, advances in treatment after recurrence are essential, but no standard second line therapy has been estimated. Lately, bevacizumab (Bev) and BCNU wafer became available in Japan, we have more therapeutic choices. Since we took part in Kansai molecular diagnosis network for CNS tumors in 2013, we have referred molecular information. We retrospectively examined and report our experiment about recurrent malignant gliomas in Kansai Rossi Hospital. Twenty-two histopathologically proved grade 3 and grade 4 patients who were diagnosed as recurrence between January 2013 and December 2018 were included. We examined treatment and analyzed factors that influenced overall survival (OS) after recurrence. Glioblastoma were 14 cases (IDH wild 12 cases, IDH mutant one case, unknown one case) Median age and KPS at recurrence were 70 years old and 60%, respectively. Ten patients received any anti-cancer treatment and 2 received best supportive care (BSC). Radiation therapy (RT) with Bev were used in 9 patients (5 with gamma knife). Their median OS after first recurrence was 324 days and significantly longer than that of BSC patients (p=0.00174). Grade 3 gliomas were 8 cases (IDH-mutant 3 cases, IDHwild 5 cases, H2F3A mutant 1 case). Median age and KPS at recurrence were 45 years old and 70%, respectively. Five patients were treated with temozolomide (TMZ) and others were observed. In addition to TMZ, Bev were used for 4 patients and RT for 3. Median OS of these patients was significantly longer (p=0.0198). In both grade, patients with better KPS (>60%) statistically lived longer than poor KPS, but methylation status of MGMT promoter and IDH mutation did not influent their OS. Radiation with Bev for good KPS patients might improve prognosis. Further multicenter prospective study must be needed.

RTHP-22. EDEMA PROGRESSION DURING MRI-GUIDED GLIOBLASTOMA RADIOTHERAPY

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PURPOSE: Despite the common finding of pseudoprogression or true progression one month after primary chemoradiotherapy for glioblastoma, there are few studies evaluating brain MRI changes that occur during concurrent chemotherapy and radiotherapy (RT). With the first generation combination MRI-RT device, daily predominantly T2-weighted MRIs are obtained of glioblastoma during RT. We quantified how many patients had significant MRI detectable volumetric changes through the six week course of primary chemoradiotherapy. This is of particular importance since glioblastoma RT is only planned at the beginning of therapy and not commonly re-planned for changes during therapy. METHODS: We retrospectively reviewed the daily set-up imaging of 8 patients at our institution who received RT for glioblastoma using the Cobalt-60 MRI-RT system. Patients received standard chemoradiation at 60 Gy in 30 fractions with temozolomide per EORTC22981/26981. We contoured the abnormality on the initial ViewRay setup scan and the set-up scan for fraction 30. After rigid fusion of the contours of the initial setup MRI and fraction 30 MRI, the volumes were compared. RESULTS: Of the 8 patients, 3 patients (37.5%) demonstrated edema expansion greater than 5 mm. The maximum distances of T2-weighted abnormality volume growth for these patients were 1.0 cm, 1.5 cm, and 4.1 cm. These findings were correlated with the post-treatment diagnostic MRIs at 3–4 weeks which demonstrated similar FLAIR abnormalities and expansion in T1 with gadolinium contrast volumes within these areas of the radiotherapy fields (pseudoprogression vs. true progression). CONCLUSION: Review of MRIs obtained by daily MRI-RT for glioblastoma indicates that 3 of 8 patients had over 5 mm of change in T2-weighted dimensions from beginning to end of radiotherapy. Groups using limited CTV margins for treatment planning should be aware that MRI volumes could significantly increase during radiotherapy.

RTHP-23. PROSPECTIVE TRIAL OF CONVENTIONALLY FRACTIONATED DOSE CONSTRAINTS FOR RE-IRRADIATION OF PRIMARY BRAIN TUMORS

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PURPOSE/OBJECTIVE: Dose constraints for re-irradiation of recurrent primary brain tumors are not well-established, especially for treatment volumes too large for stereotactic radiotherapy. This prospective trial was performed to test dose constraints for conventionally-fractionated re-irradiation of recurrent primary brain tumors MATERIALS/METHODS: A single-institution, prospective trial of 21 adults with recurrent brain tumors was performed. Electronic dosimetry records from the first course of radiation (RT1) were obtained and deformed onto the simulation CT for the second course of radiation (RT2). Treatment plans for RT2 were developed that met protocol-assigned dose constraints for RT2 alone and the composite dose of RT1+RT2. Dose constraints were also based on histology and interval since RT1. The primary endpoint was the rate of symptomatic brain necrosis after RT2. RESULTS: Twenty one adults enrolled from March 2017 to May 2018. Twelve had glioblastoma, four had oligodendroglioma, two had anaplastic astrocytoma, and one each had choroid plexus papilloma, hemangiopericytoma, and pleomorphic xanthroastrocytoma (PXA). Twenty patients were treated with VMAT and one was treated with proton CSI. Median RT1-RT2 interval was 45 months (range, 9–141 months). Median RT2 dose was 42.8 Gy (range, 17.5–60 Gy). Median PTV volume was 208 cc (range, 7–1537 cc). Median imaging followup was 9 months (range, 1–20 months). Two months after RT2, the patient with PXA developed a trapped temporal horn adjacent to the RT2 treatment volume; pathology from emergent resection revealed necrotic brain tissue. The patient recovered fully and lived another 18 months until dying of disease progression. No other patient developed symptomatic radionecrosis. Median overall survival from RT2 for all patients was 11 months (range, 3–20 months). CONCLUSION: Re-irradiation can be performed with conventionally fractionated schemes. Given the low rate of symptomatic radionecrosis, the dose constraints described here are a starting point for future studies of conventionally fractionated re-irradiation.

RTHP-24. TRENDS IN THE UP FRONT USE OF STEREOTACTIC RADIOSURGERY FOR GLIOBLASTOMA

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BACKGROUND: GBM is typically managed with a combined modality approach including resection followed by adjuvant chemoradiation. Despite aggressive up front treatment local failure occurs in the vast majority of patients. The concept of dose escalation through use of stereotactic radiosurgery (SRS) was tested in RTOG 9305 in the pre-temozolomide era with the hopes of improving control, ultimately showing no benefit. We used the National Cancer Database (NCDB) to examine trends in the use of up-front SRS, to see if it had truly fallen out of favor, and if it had any impact on outcome. METHODS: We queried the NCDB from 2004–14 for GBM patients that had radiation and 2 months of follow up. Odds ratios were used to determine predictors of SRS. Univariable and multivariable Cox regressions were used to determine potential predictors of overall survival (OS). Propensity adjusted multivariable analysis was used to account for any indication bias. RESULTS: We identified 62,681 patients meeting eligibility criteria, of which 1,046 had SRS. SRS decreased over time from 3% to less than 1%. Predictors of SRS were increased age, government insurance, lower comorbid score, treatment at an academic facility, metropolitan location, increased distance to facility, smaller tumor, lack of surgery, no chemotherapy, and more remote year of treatment. Median overall survival was 13.1 months in the non-SRS group and 12.9 months in the SRS group, p=0.28. On multivariable analysis increased age, lack of chemo-

therapy, higher comorbidity score, extent of surgery, non-academic facility, decreased education, government insurance, urban location, Caucasian race, male gender, larger tumor, and more remote year of treatment predicted for worse overall survival. CONCLUSIONS: Use of up-front SRS in the management of GBM has decreased over time, in concordance with past randomized trials examining its use. Our analysis did not show any benefit in survival with its use.

RTHP-25. TTFIELDS DOSE DISTRIBUTION ALTERS TUMOR GROWTH PATTERNS: AN IMAGING-BASED ANALYSIS OF THE RANDOMIZED PHASE 3 EF-14 TRIAL

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INTRODUCTION: A recent post-hoc analysis of the EF-14 phase 3 trial showed a connection between TTFields dose at the tumor and Overall Survival in new diagnosed Glioblastoma (ndGBM) patients [1]. Here we expand the results of that study and show a connection between TTFields dose distribution in the brain and progression patterns in ndGBM patients. METHODS: Participants of the EF-14 trial who exhibited radiological progression were included in this study (treatment: N=306/466, control: N=122/229). Enhancing tumor was segmented on T1c MRIs at baseline and progression. Regions of progression disconnected from the original lesion were defined as distal. The rates of occurrence and distances of distal progressions from primary lesions were compared between the arms. Computational head models were created and delivery of TTFields numerically simulated for n=229 patients in treatment for over 2. Dose in regions of progression was compared to dose in regions where no progression occurred. RESULTS: The median distance between primary and distal lesions was larger in the treatment arm (control: 14.2±14.4 mm, TTFields 23.2±29.8 mm, p=0.03 Wilcoxon rank-sum). A higher rate of distal progression outside of a 20mm boundary zone around the primary lesion was observed in the treatment arm. (Control: 10/122, TTFields: 53/306 p< 0.02 chi-squared). In proximity to the primary lesion (a 3 mm ring around the tumor), TTFields dose was lower in regions of progression than in regions where no progression occurred (0.73 mW/cm^3 vs. 0.79 mW/cm^3 p< 0.0001 t-test) DISCUSSION AND CONCLUSIONS: This study suggests that TTFields alters progression patterns and that progression is more likely to occur in regions exposed to low TTFields dose. The study emphasizes the rationale for adaptive TTFields treatment planning targeting regions of progression. [1] Ballo et. al., IJROBP (2019)

RTHP-26. DOSIMETRIC FEASIBILITY STUDY USING HIPPOCAMPAL AVOIDANCE WITH SIMULTANEOUS INTEGRATED BOOST WHOLE BRAIN RADIOTHERAPY (HA-SIB-WBRT)

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BACKGROUND: Recently Hippocampal Avoidance (HA-) WBRT has become a recommended treatment option in patients with multiple (≥ 5) brain metastases and good prognosis. We wanted to investigate the dosimetric feasibility of dose painting technique combining HA-WBRT with a simultaneous integrated boost (SIB) to tumours. METHOD: 5 patients who had a CT simulation fused with brain MRI with fine cuts, were selected for this study. Volumes were contoured on T1w contrast images. Whole brain prescription dose was 30Gy in 12 fractions. A PTV margin of 2mm was applied to lesions, except when these were ≤5mm from organs at risks (OARs). A simultaneous integrated boost (SIB) of 48Gy and 40.2Gy was prescribed to these volumes respectively. Hippocampal constraints followed RTOG 0933 protocol. For lesions ≤5mm from OARs, the acceptable $D_{0.03cc}$≤42Gy was allowed. All plans were planned on Eclipse™ v.13.6 TPS using 6MV photons, VMAT technique with 3 coplanar and 1 non-coplanar arcs for Varian TrueBeam machine. RESULTS: Plans had between 6–24 lesions with GTV and PTV of 3.02–11.32cc and 7.05–31.74cc respectively. 3 of the plans had lesions within/adjacent to brainstem or hippocampus. The achieved PTV_40.2Gy $D_{95\%}$ 37.42–39.05Gy with Conformity Index (CI)(95%) 0.63–1.06, PTV_48Gy $D_{95\%}$ 44.64–47.04Gy with CI(95%) 0.75–0.97 and GTV_48Gy $D_{95\%}$ 47.44–50.16Gy. Whole brain D_{mean} 31.87–33.15Gy with a Homogeneity Index ($D_{2\%}$-$D_{98\%}$/D_{mean}) 0.18–0.58. Hippocampal $D_{100\%}$ 8.69–10.1Gy, $D_{0.03cc}$ 16.5–40.43Gy and D_{mean} 12.66–24.68Gy. SUMMARY: There was a steep learning curve when adopting this technique and multiple plan iterations were made to achieve target constraints. To meet acceptable OAR constraints, SIB coverage was compromised. Lesions ≤5mm from hippocampus resulted in higher Hippocampal average D_{mean} 22.8Gy *vs.* 12.8Gy. The significance of this value should be tested in clinical trials. Overall, HA-SIB-WBRT seems feasible even with ≥ 5 brain metastases and could result in better brain metastases control then HA-WBRT alone.

RTHP-27. RARE INTRACRANIAL PRIMARY YOLK SAC TUMORS IN ADOLESCENT PATIENTS: A REPORT OF 10 CASES DEPARTMENT OF ONCOLOGY

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OBJECTIVE: To retrospective analyze 10 patients with intracranial primary yolk sac tumors(YST) for exploring an optimal treatment strategy. METHODS: Ten patients with YST were confirmed by pathological diagnosis (9 male and 1 female), with a median age of 13 years. Except for 1 case was lost to follow-up, 9 patients were treated with partial resection, followed by WBRT and local boosts, and then adjuvant chemotherapy. The time it took for serum AFP to decrease to the lowest level (including abnormal situation) or to return to the normal level was recorded. The brain tumor apoplexies before and after treatment were studied. Finally, OS and PFS of the patients were analyzed. RESULTS: The patients were followed-up to 02-2019, with a mean follow-up time of 25.44 months. The analysis showed that the mOS and mPFS were 18 months and 7 months, respectively, and that 1y-OS and 2y-OS were 77.8% and 22.2%, while 1y-PFS and 2y-PFS were 22.2% and 11.1%. The time it took for serum AFP to decrease to the lowest level or to return to the normal level was 0–382 days, with a median time of 144 days (165.22±131.71 days). After being followed-up to 02-2019, 4 patients still survived; 4 patients died of tumor recurrence; 1 patient died of severe pneumonia. Although one of the 4 patients (tumor recurrence) was treated with 3 times of surgeries, died of tumor progression, with a survival time of 17 months. The other one patient had a 1y-PFS of 3 months, and he received surgery and chemotherapy for recurrent tumors, achieving a 2y-PFS up to 71+ months. CONCLUSION: YST has a low incidence rate and is easy to recurrence, with a poor prognosis. Resection combined with chemoradiotherapy can prolong the survival time of patients, but the optimal treatment strategy remains unclear and needs further research.

RTHP-28. TTFIELDS TREATMENT AFFECTS TUMOR GROWTH RATES: A POST-HOC ANALYSIS OF THE PIVOTAL PHASE 3 EF-14 TRIAL

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INTRODUCTION: The pivotal EF-14 trial showed that Tumor Treating Fields (TTFields) extend Progression Free Survival (PFS) in newly Diagnosed Glioblastoma (ndGBM) patients. This leads to the hypothesis that TTFields therapy leads to local control of tumors, yielding a significant decrease in tumor growth rates. Here we present an analysis testing this hypothesis in biopsy-only patients who participated in the EF-14 trial. METHODS: Biopsy patients of the EF-14 trial who exhibited radiological progression were included in this study (treatment: N=37/60, control: N=12/29). Volumes of enhancing tumor were segmented on T1c MRIs at baseline and at progression. Tumor growth rate was calculated as: growth_rate=(ln(v0)-ln(v1))/dt. (v0- tumor volume at baseline), v1- Tumor volume at progression, dt- days to progression), which models tumor volume as increasing exponentially over time. Median growth rates in the treatment and control arms were compared. RESULTS: The median growth rate was lower in the treatment arm than in the control. (control: 0.14±0.12 mL/month, TTFields -0.011±0.11 mL/month, p< 0.008 Wilcoxon rank-sum) DISCUSSION AND CONCLUSIONS: This study shows that tumor growth rates are slower in patients treated with TTFileds+Temozolomide (TMZ) than in patients treated with TMZ alone. This analysis was restricted to biopsy-only patients since the definition of tumor volume is ambiguous in patients that underwent resection since a large portion of the tumor has been removed. The negative median growth rate for patients in the treatment arm may indicate that a significant number of TTFields-treated patients a decrease in tumor volume was observed, suggesting that TTFields enhances local tumor control. References: [1] Stupp, Roger, et al. Jama 318.23 (2017): 2306–2316. [[2 Stensjøen, Anne Line, et al. Neuro-oncology 17.10 (2015): 1402–1411.

RTHP-29. HYPOFRACTIONNATED RADIOTHERAPY FOR REFRACTORY SKULL BASE CHORDOMA

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OBJECTIVE: Skull base chordoma is difficult to be totally excised by surgery because of the complex anatomical structures of skull base.