focus on long-term visual follow-up of childhood craniopharyngioma in response to different treatment strategies to provide insight in risks and ways to prevent further loss of vision.

RARE-63. CYST WALL OF ADAMANTINOMATOUS CRANIOPHARYNGIOMA CONTAINS TUMOR CELLS THAT COULD LEAD TO RECURRENCE AFTER SURGERY

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BACKGROUND: Adamantinomatous craniopharyngioma (ACP) is the primary subtype of craniopharyngioma in children, frequently with mutations in exon 3 of the *CTNNB1* gene. Most ACP consists of both a solid tumor and one or more cysts. Despite surgical resection of the solid tumor followed by radiation, recurrence involving the cystic component is common, suggesting that the cyst wall contains tumor cells. We present here conclusive molecular pathology evidence of the presence of tumor cells in the cyst wall similar to those in the solid tumor. METHODS: We used standard H&E staining and immunohistochemistry (IHC) to compare the histopathology characteristics between the matched cyst wall and solid tumor of 11 cases of ACP as well as their *CTNNB1* expression and exon 3 mutation. RESULTS: Samples of the cyst wall and solid tumor were collected separately during the operation of 11 cases of ACP through careful dissection. The cyst wall showed the nested cell clusters and peripheral palisading epithelium which are identical to those in the solid tumor. The cyst wall and solid tumor both showed Ki67 and nuclear β-catenin expression by IHC. There is no difference in the transcription level of *CTNNB1* between the cyst wall and the solid tumor, both being significantly higher than that in normal brain tissue. Exon 3 mutations of the *CTNNB1* gene of the cyst wall and the solid tumor are identical in each case. CONCLUSION: Follow-up of clinical cases suggests that tumor cells in residual cyst wall may be the cause of recurrence after surgery.

RADIATION ONCOLOGY

RONC-01. PROTON BEAM THERAPY IN THE MULTIDISCIPLINARY THERAPY FOR PEDIATRIC BRAIN AND SPINAL TUMOR AT KOBE CHILDREN'S HOSPITAL WITH KOBE PROTON CENTER

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It could be remarked that Radiotherapy (RT) has the important role for the multidisciplinary therapy to Malignant Pediatric Central Nervous System tumor. And recently among RT, Proton Beam Therapy (PBT) is expected to be effective and decrease serious late effects after RT in malignant pediatric tumor. PBT could be controlled precisely the dose and depth and spare the normal structures outside the target. Thus, PBT becomes applicable for pediatric solid tumor to insurance in April, 2016 in Japan. We have worked in closer cooperation with Hyogo Prefectural Ion Beam Medical Center and started PBT from April 2015. And from December 2017, our PBT has transferred to adjacent new medical center (Kobe Proton Center) which has the only institute that equipped the exclusive gantry for children in our country. The treated cases are 28 boys and 35 girls (age average 8.2 years oid). They are 15 Germ cell tumor, 14 Ependymoma, 13 Medulloblastoma, 4 Chordoma, 4 Atypical teratoid/rhabdoid tumor, 2 Craniopharyngioma and others. We have simulated the applications of not only broad beam but also scanned beam to limit the dose distribution and prepare for the cranio-spinal irradiation. All cases underwent magnetic resonance imaging to evaluate the results at out clinic and also the complications are assessed after treatments. The effect of PBT in this series is similar to our experience of traditional RT. There are a few controllable complications such as conventional RT. Farther more follow up is necessary to evaluate the advantage of PBT which could reduce delayed complications of RT.

RONC-02. MEASURING THE EFFECT OF CLINICALLY-RELEVANT RADIOTHERAPY PROTOCOLS ON THE JUVENILE MOUSE BRAIN

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Treatment for medulloblastoma involves craniospinal irradiation which is associated with devastating late effects. Clinical trials that simply reduce radiotherapy dosage have resulted in inferior survival rates, whereas new chemo/radiotherapy combinations that improve survival have been identified using preclinical models. However, the potential late effects of novel treatments are currently understudied and the assessment of radiation-induced late effects in mice remains challenging. Here, we aimed to measure the effect of multifractionated radiotherapy on the juvenile mouse brain as a baseline measure for future studies. NOD/Rag1-/- mice received either 8Gy whole-brain radiotherapy (WBRT) using an X-RAD SmART preclinical platform, 18Gy fractionated WBRT (9x2Gy doses), single, or multiple sham treatments beginning at postnatal day (P)16. Mice were aged to adulthood (>P63), then high resolution anatomical brain scans were obtained on a Bruker 9.4T MRI to measure the effects of WBRT on whole brain and specific regional area volumes. A single 8Gy dose (n=10) markedly reduced brain volume by 8.5% compared to single-sham controls (n=11, $p<0.0001$), whereas fractionated 18Gy treatment (n=7) did not cause significant differences in brain volume compared to multi-sham controls (n=4, $p>0.99$). Current analyses are focused on measuring treatment effects on specific areas of the brain, as well as other anatomical differences using a range of MRI techniques. These results will serve as a valuable tool to measure potential treatment-associated effects caused by novel chemo/radiotherapy combinations on the developing brain. This will enable future studies to assess the potential safety of novel treatment to inform clinical decision making.

RONC-03. NEUROCOGNITIVE CHANGES AFTER RADIATION FOR PEDIATRIC BRAIN TUMOURS: WHICH BRAIN SUBSTRUCTURES ARE MOST IMPORTANT?

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INTRODUCTION: The contribution of different intracranial structures on neurocognitive decline after radiation therapy (RT) in children is unclear. METHODS: This was a retrospective study of children with brain tumours treated from 2005 to 2017. Patients with longitudinal neurocognitive assessments and photon dosimetric data (if RT given) were included. Full scale intelligence quotient (FSIQ) was the primary endpoint; sub-indices of neurocognition were modelled separately (perceptual reasoning [PRI], processing speed [PSI], verbal comprehension [VCI] and working memory [WMI]). Multivariable linear mixed effects models were used to model endpoints, with age at diagnosis & dose to different brain regions as fixed effects and patient-specific random intercepts. RESULTS: Sixty-nine patients were included; ten patients did not receive any RT (i.e. low-grade glioma). Median neurocognitive follow-up was 3.2 years. Right hippocampus mean dose was a strong predictor of declines in FSIQ ($p < .001$), VCI ($p = 0.002$) and PRI ($p = 0.049$). Dose to 50% of the supratentorial brain (D50) was the strongest predictor for WMI ($p < .001$) and PSI ($p < .001$). Each gray increase in mean right hippocampus dose resulted in a decrease of 0.038 FSIQ points/year. After adjusting for dose to brain substructures, younger age & presence of a ventriculoperitoneal shunt were also associated with decreased FSIQ. CONCLUSIONS: Mean dose to the right hippocampus was associated with declines in FSIQ, VCI and PRI, while supratentorial brain D50 was associated with WMI and PSI. Efforts should be made to reduce unnecessary dose to these brain structures.

RONC-04. RE-IRRADIATION AFTER TREATMENT OF MEDULLOBLASTOMA; RELAPSED CASES AND SECOND CANCER CASES

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PURPOSE: Late complications such as brainstem necrosis are great concern of re-irradiation for brain tumor. Proton beam therapy can reduce radiation dose of organs at risk such as brainstem, so is expected to reduce late complications. PATIENTS AND METHODS: Patients with medulloblastoma treated with re-irradiation from January 2015 to February 2019 at the Kobe Children's Hospital and the Kobe Proton Center were reviewed. There were three cases of relapsed medulloblastoma and three cases of second cancer (glioblastomas). RESULTS: In relapsed cases, all three cases treated with 12 Gy in 8 fractions cranio-spinal irradiation followed by gamma knife radiosurgery (one) or 28.8 Gy (RBE) in 16 fractions of proton beam therapy (two). Follow-up periods were 8 to 19 months (median

12 months) and all three cases survived without relapse. In second cancer cases, all three cases were treated with 40.05 Gy per 15 fractions of radiation therapy (2 cases were treated with photon and one case with proton). However, all cases relapsed and two cases died of disease. CONCLUSION: Twelve Gy in 8 fractions cranio-spinal irradiation followed by 28.8 Gy (RBE) in 16 fractions of proton beam therapy is thought to be useful for the relapsed case. Re-irradiation for second cancer was disappointing and further study is warranted.

RONC-05. PRESERVING VISION IN OPTIC PATHWAY GLIOMA AMONG PATIENTS WITHOUT NEUROFIBROMATOSIS TYPE 1

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PURPOSE: Sporadic optic pathway/hypothalamic gliomas (OP/HGs) represent a unique entity within pediatric low-grade glioma. Despite favorable survival, the location makes treatment difficult and local progression debilitating. We conducted longitudinal assessment of visual acuity (VA) among patients treated in the modern era with chemotherapy (CT) or early radiotherapy (RT). METHODS: Clinical characteristics were abstracted for patients treated over a 15-year period (2000–2015) at a single institution. Comprehensive ophthalmologic data taken at three to six-month intervals was examined with age-appropriate VA metrics converted to LogMAR scale. Kaplan-Meir "blindness-free survival" (BFS) curves were calculated as time to bilateral functional blindness (i.e. LogMAR ≥ 0.8 in both eyes), stratified by treatment and compared using log-rank test. RESULTS: Thirty-six patients with median follow-up of 7.6 years (range: 2–17) were identified. Median age at diagnosis was 2.5 years (IQR: <1–5). Early RT was administered as initial therapy (n=6) or first-line salvage (n=5) in a total of eleven patients (31%) at a mean age of 12 years (range: 6–17). Twenty-five patients (69%) were maintained primarily on CT with a mean age at initiation of 2.4 years (range <1–8). Of these, five patients received RT after ≥2 systemic therapy regimens. In terms of visual preservation, five/eight-year BFS rates were 84%/59% and 100%/100%, for CT and early RT, respectively (p=0.046). CONCLUSIONS: In a contemporary cohort, early RT, defined as initial or 1st line salvage therapy for OP/HGs manifested in superior VA. Children undergoing CT are at highest risk of functional blindness following five years of treatment.

RONC-06. VOLUMETRIC-MODULATED ARC WHOLE-BRAIN RADIOTHERAPY FOR THE PREVENTION OF PERMANENT ALOPECIA IN PEDIATRIC PATIENTS

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Permanent alopecia is a grave late complication of multi-drug chemotherapy (CTx) plus cranial irradiation, reducing both patient self-esteem and quality of life in pediatric patients. We started to use craniospinal irradiation (CSI) using the volumetric-modulated arc whole-brain radiotherapy (VMAT-WBRT) in order to prevent permanent alopecia. We treated 5 pediatric patients with CSI using VMAT-WBRT, and report the initial clinical outcome. Five consecutive patients (4–11 years old) who received CSI using VMAT-WBRT from June 2015 to November 2018 were included into this study. One patient with embryonic carcinoma received radiotherapy (RT) with concurrent CTx; four patients with medulloblastoma (two patients with standard risk, and two patients with high risk) received RT followed by CTx. The prescribed doses of CSI were 23.4–35.2 Gy in 13–22 fractions, respectively. Optimization for VMAT-WBRT was performed to reduce doses to the hair follicles with keeping the dose coverage to the planning target volume. Although all patients experienced temporary alopecia, their hair fully recovered over the whole scalp within 8 months after finishing RT. One patient had disease progression after 6 months after completing CTx; this patient who was diagnosed as Group 3 subtype had diffuse meningeal dissemination confirmed with contrast enhanced spinal MRI before RT. The other four patients had no evidence of recurrence. Although CSI with VMAT-WBRT might be one of considerable options, more cases are needed to verify the efficacy to prevent permanent alopecia for pediatric patients who receive multi-drug CTx and cranial irradiation.

RONC-08. SURVIVAL IMPACT OF POSTOPERATIVE RADIOTHERAPY TIMING IN PEDIATRIC AND YOUNG ADULT EPENDYMOMA

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INTRODUCTION: Postoperative radiotherapy is commonly given for WHO Grade 2–3 intracranial ependymoma. Clinicians generally aim to begin radiotherapy ≤5 weeks following surgery, but the optimal timing remains uncertain. METHODS: The National Cancer Database was queried for patients (age ≤39 years) with localized WHO Grade 2–3 intracranial ependymoma treated with surgery and postoperative radiotherapy. Multivariable logistic regression was used to identify factors associated with delayed postoperative radiotherapy, defined as starting >8 weeks after surgery. Overall survival (OS) curves were plotted based on radiotherapy timing (≤5 weeks, 5–8 weeks, and >8 weeks after surgery) and compared by log-rank test. Multivariate analysis (MVA) was used to identify factors associated with OS. RESULTS: In the final analytic set of 1,043 patients, age ≥21 years (OR 2.07, 95% CI 1.56–2.74) and WHO Grade 2 tumors (OR 1.41, 95% CI 1.08–1.85) were significantly associated with delayed time to adjuvant radiotherapy. No difference in 3-year OS was observed in patients who initiated radiotherapy ≤5 weeks, 5–8 weeks, and >8 weeks after surgery (89.8% vs. 89.1% vs. 88.4%; p= 0.796). On MVA, anaplastic histology (HR 2.414, 95% CI 1.784–3.268, p<0.001) and subtotal resection (HR 2.398, 95% CI 1.519–3.788, p<0.001) were significantly associated with reduced OS. Timing of radiotherapy, total radiotherapy dose, age, insurance status, and other factors were not significant. CONCLUSION: Delayed postoperative radiotherapy was not associated with inferior survival in patients with intracranial ependymoma, suggesting delayed radiotherapy initiation may be considered in patients requiring longer postoperative recovery or referral to an appropriate radiotherapy center.

RONC-09. PSEUDOPROGRESSION AFTER PROTON THERAPY OF PEDIATRIC SPINAL PILOCYTIC ASTROCYTOMA AND MYXOPAPILLARY EPENDYMOMA

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BACKGROUND: Pseudoprogression after proton therapy of CNS tumors is a challenging clinical situation. The rate of pseudoprogression after proton therapy of pediatric spinal tumors is unknown. METHODS: Records of pediatric patients with spinal pilocytic astrocytoma (sPA; n = 9) or myxopapillary ependymoma (MPE; n = 6) with gross disease treated with proton therapy with at least 6 months of follow up from completion of proton therapy were retrospectively reviewed for demographics, treatment characteristics, and occurrence of pseudoprogression. Pseudoprogression was defined as a post-radiation increase in tumor size with subsequent decrease in size without additional tumor-directed therapy. RESULTS: The median age at radiation for sPA patients was 10.1y (range, 7.0 – 16.2y) and 12.7y (range, 7.9 – 14.4y) for MPE patients. The median prescribed dose was 45 GyRBE (range, 39.6 – 50.4 GyRBE) for sPA patients and 50.4 GyRBE (range, 45 – 54 GyRBE) for MPE patients. One sPA patient received concurrent vincristine. Median follow up after proton therapy was 44 months (range, 9 – 99 months). Six of nine sPA patients (67%) had pseudoprogression occurring at a median of 81 days (range, 34 – 136 days) after proton therapy; no MPE patients developed pseudoprogression (0%; p < 0.03). Two sPA patients with pseudoprogression were symptomatic and improved with medical therapy. CONCLUSION: Preliminary analysis suggests that pseudoprogression occurs frequently within 6 months after proton therapy for sPA and infrequently after proton therapy for MPE.

RONC-12. TREATMENT AGE AND NEUROCOGNITIVE OUTCOMES FOLLOWING PROTON BEAM RADIOTHERAPY FOR PEDIATRIC LOW GRADE GLIOMA

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INTRODUCTION: Younger age at radiotherapy increases cognitive risk for patients with pediatric low grade glioma (LGG). We examined the impact of age at treatment on cognitive trajectories in LGG patients treated with proton radiotherapy (PRT) compared to patients treated without radiotherapy (surgery only; SO). METHODS: We examined cognitive