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