were retrospectively examined. PATIENTS AND METHODS: Clinical characteristics of seven radiation-induced brain tumors that developed in 6 patients irradiated in their childhood at our hospital were analyzed. The risk factors were evaluated by univariate and multivariate analysis. The outcomes were death due to radiation-induced brain tumor, recurrence, and survival after irradiation to onset, pathological diagnosis, and treatment for radiation-induced brain tumor were examined. RESULTS: Background diseases for irradiation were leukemia in 3 patients, germinoma in 2, medulloblastoma in 1, and stage cranial irradiation dose was 23.2 Gy. The patients tended to be young at irradiation (2-17 years; median:4 years old). The time between irradiation and the onset of radiation-induced brain tumors ranged from 9.5 to 39.1 years (median:28 years). Radiation-induced brain tumors comprised 6 meningioma ( grade I-3, grade II:1 ) and 1 high-grade gliomas. All patients underwent surgical removal of the radiation-induced brain tumors and 2 received additional irradiation. During a median of 5.3 years of follow-up after the diagnosis of radiation-induced brain tumors, 2 underwent second surgery, while the remaining 4 have no recurrence. DISCUSSION: In most cases, radiation-induced brain tumors occur for a long time after irradiation in childhood. Monitoring of radiation-induced brain tumors as well as primary tumor recurrence was considered important.

RCON-19. TWO CASES OF RE-IRRADIATION FOR LATE RECURRENT OR RADIATION-INDUCED TUMOR AFTER RADIATION THERAPY FOR PEDIATRIC BRAIN TUMORS

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BACKGROUND: As the outcome of pediatric brain tumors improves, late recurrence and radiation-induced tumor cases are more likely to occur. However, the number of cases requiring re-irradiation is expected to increase. Here we report two cases performed intracranial re-irradiation after radiotherapy for pediatric brain tumors. CASE 1: 21-year-old male. He was diagnosed with cranioopharyngioma at eight years old and underwent resection. At 10 years old, the local recurrence of suprasellar region was treated with 50.4 Gy/28 fr of stereotactic radiotherapy (SRT). After that, other recurrent lesions appeared in the left cerebellopontine angle, and he received surgery three times. The tumor was gross totally resected and re-irradiation with 40 Gy/20 fr of SRT was performed. We have found no recurrence or late effects during the one year follow-up. CASE 2: 15-year-old female. At three years old, she received 18 Gy/10 fr of craniospinal irradiation and 36 Gy/20 fr of boost to the posterior fossa as postoperative irradiation for anaplastic ependymoma. However, a anaplastic meningioma appeared on the left side of the skull base at the age of 15, and 50 Gy/25 fr of postoperative intensity-modulated radiation therapy was performed. Two years later, another meningioma developed in the right cerebellar tegmentum and 5 years later, the local recurrence of SRT was performed. MRI showed a slight increase of the lesion, but no late toxicities are observed. CONCLUSION: The follow-up periods are short, however intracranial re-irradiation after radiotherapy for pediatric brain tumors were feasible and effective.

RCON-20. RECURRENT HIGH-GRADE ASTROBLASTOMA TREATED WITH STEREOTACTIC RADIOTHERAPY

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INTRODUCTION: Astroblastoma is a rare, mostly supratentorial glial tumor, occurring predominantly in children and young adults. However, treatment strategies have not yet been established for this rare disease. CASE PRESENTATION: A 6-year-old male presented with headache and left temporal swelling. MRI revealed left temporal tumor with slight edema and macrocalcifications. Gross tumor resection was performed. Histological examination found neoplastic cells with astroblastic characteristics, and a striking perivascular array of pseudohastos. The final diagnosis was high-grade astroblastoma. MRI imaging 13 months after surgery suggested local recurrence and enlargement was found 3 months later. Stereotactic radiotherapy (SRT) was performed. MR imaging after SRT showed enhanced cyst formation around the tumor bed, suggesting tumor recurrence. However, PET/CT showed no increased retention of FDG uptake. The last follow-up MR imaging 13 months after SRT showed no further recurrence. CONCLUSION: Astroblastoma is rare, so no optimal management is known. SRT may be effective to treat recurrent astroblastomas. 11C-methionine PET/CT is useful for the differentiation from radiation necrosis.

RCON-21. IDENTIFICATION OF EPIGENETIC DRUGS AS RADIOSENSITIZERS IN PEDIATRIC HIGH-GRADE GLIOMAS

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Pediatric high-grade gliomas (pHGG) are malignant brain tumors with a high mortality rate. Radiotherapy (RT) is one of the cornerstones of current pHGG treatment, while the efficacy of chemotherapeutics remains inferior. The use of chemotherapeutics that specifically sensitize tumor cells to radiation are poorly understood, but may help to increase the effect of RT in pHGG treatment. Since recent studies revealed pHGG to be epigenetically dysregulated, we tested 148 epigenetic drugs on eight primary pHGG tumors both in vitro and in vivo. Radiotherapy was performed in an intracranial rat model. By including high grade glioma cell lines and 2D cultures with clonogenic potential, we identified compounds that resulted in enhanced cytotoxicity in the presence of RT. The effect of these compounds on pHGG was further investigated by tracking spheroid growth microscopically for 30 days, identifying four molecules that stopped spheroid expansion solely in combination with RT (p<0.001, multilevel regression). Parallel cell-viability assays reported identical results. Furthermore, tumor migration in 3D matrigel growth assays, using non-toxic doses of the four identified compounds, revealed that two compounds (the selective HDAC-inhibitors; chidamide and entinostat) stop the infiltrative growth characteristics of pHGG cells, exclusively in combination with RT. RNA-Seq data showed that entinostat and chidamide inhibit DNA-repair pathways like the mismatch repair cascade and DNA double-strand break repair. Furthermore, we anticipate that entinostat- or chidamide-induced radiosensitization can be enhanced by blocking kinase-driven escape mechanisms, we are currently conducting a kinome-wide CRISPRi/Cas9 knockout screen in three primary pHGG models to develop combinatorial therapies. These results highlight entinostat and chidamide as potential radiosensitizers in pHGG treatment.
Abstracts

tire vertebral body (VB) was part of target volume in all patients. The IMPT plan was generated using 3 fields with single field optimisation technique. Last 5 patients were treated using dose gradient (DG) (98-93%) deliberately created in anterior most 3-5 mm of VB. Initial 2 patients were treated with GKS without intention of covering entire VB with 98% isodose. Monte Carlo algorithm was used for dose calculations and optimisation, and robustness assessed for 3 mm setup and 3.5% range uncertainty. RESULTS: The CSI dose ranged from 30 Gy to 35 Gy. In patients without DG, maximum and mean dose to esophagus (36.7 GY vs 25.4 Gy, 31.5 Gy vs 20.4 Gy), midline mucosa (28.9 Gy vs 25.3 Gy, 21.5 Gy vs 14.6 Gy) and bowel bag (32.9 Gy vs 24.7 Gy, 3.5 Gy vs 3.2 Gy) were higher compared to patients with DG. Both patients with DG was not developed, created dose 2 esophageal toxicities requiring supportive care and treatment interruptions (4 and 2 days). All 5 patients with DG did not develop significant esophageal toxicity and had no interruptions. CONCLUSION: Creating a dose gradient over anterior VB using IMPT reduces dose to esophagus and midline mucosa leading to lower acute esophageal toxicity which potentially avoids treatment interruptions during CSI.

RONG-24. PROTON THERAPY FOR PEDIATRIC EPENDYMOMA: MATURE OUTCOMES FROM THE UNIVERSITY OF FLORIDA AND MASSACHUSETTS GENERAL HOSPITAL

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OBJECTIVE: Report long-term efficacy and toxicity of proton therapy for pediatric ependymoma. MATERIALS AND METHODS: Between 2000-2017, 318 children with nonmetastatic grade II/III intracranial ependymoma received proton therapy at Massachusetts General Hospital and the University of Florida. Median age at diagnosis was 3.5 years (range, 0.7-21.3 years); 56% were male. Most (69%) tumors were in the posterior fossa and classified as WHO grade III (64%). Eighty-four percent had a gross total or near total tumor resection before radiotherapy and 30% received chemotherapy. Median radiation dose was 55.8 GyE (range, 50.4-59.4 GyE). RESULTS: Median follow-up was 6 years (range, 0.6-19.2 years). Seven-year local control, progression-free survival, and overall survival rates were 77.1% (95% CI 71.7-81.7%), 64.4% (95% CI 58.6-69.8%), and 88.1% (76.9-90.7%), respectively. Subtotal resection was associated with worse inferior local control (60% vs 80%; p<0.01), progression-free survival (49% vs 67%; p=0.01), and overall survival (69% vs 84%; p=0.05). Male gender was associated with inferior progression-free (59% vs 71%; p=0.01) and overall survival (77% vs 89%; p=0.05). Twenty patients (6.2%) required radiation-hearing aids; of these, 12/20 received cisplatin. Grade 3+ brainstem toxicity rate was 1.6% and more common in patients who received >54 CGE. The rate of second malignancy was 0.9%. CONCLUSION: Proton therapy offers commensurate disease control to modern photon therapy without unacceptable toxicity. The high rate of local control is supported by reductions in these structures with improved cognitive outcomes.

RONG-25. A CASE OF PEDIATRIC PONTINE GLIOMA TREATED WITH GAMMA KNIFE SURGERY

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BACKGROUND: Pediatric brainstem gliomas rarely occur and are a heterogeneous group of diseases, which increases the difficulty of treatment strategy. Here, we present a case of pediatric pontine glioma treated with Gamma Knife surgery (GKS) after open biopsy. CASE DESCRIPTION: An 11-year-old boy presented with diplopia due to the left MLF palsy. MRI showed a well-circumscribed, protruding tumor with partial enhancement in the dorsal pons. An open biopsy was performed via the suprafacial triangle following midline suboccipital approach. Histological examinations revealed high cellularity and mild atypia. Immunohistochemistry demonstrated positive stain for GFAP and Olig2 antibodies, and negative for p53 protein. The K67-labeling index was 6.8%. Pyrosequence analysis indicated ID1/H2 wild type (wt), BRAF V600 wt, H3F3A K27 wt, FGFR1 wt, and TERT wt. The final diagnosis was pediatric diffuse astrocytoma, WHO grade II, pons. GKS was performed one month after biopsy. After transient worsening of the symptom, it disappeared gradually. The tumor is stable for three years with mild shrinkage of the size. DISCUSSION: Gross total resection (GTR) of pediatric low-grade, brainstem gliomas may result in a good prognosis. However, unlike pilocytic astrocytoma, diffuse astrocytoma is not easy to perform GTR without any complications. There are some reports regarding GKS for brainstem gliomas, which prove an increase in progression free survival rate. No marked tumor regression is achieved in our case, but tumor growth is well-controlled so far. CONCLUSION: GKS after biopsy can be a useful treatment option for pediatric low-grade brainstem gliomas.

RONG-26. A CASE OF RADIATION NECROSIS OF THE CEREBELLUM 16 YEARS AFTER CHEMORADIOThERAPY FOR MEDULLOBLASTOMA

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BACKGROUND: If new lesions are observed during follow-up of the malignant tumor after treatment, it is difficult to distinguish whether the tumor is a recurrent lesion, secondary cancer, or radiation necrosis of the brain. We have encountered a patient with symptomatic radiation necrosis of the cerebellum 16 years after treatment of medulloblastoma. CASE PRESENTATION: A 24-year-old man who had received a tumor resection and chemoradiotherapy for cerebellar medulloblastoma at the age of 8 presented with dizziness. For the past 16 years, there was no recurrence of the tumor. He subsequently underwent MRI scan, and T1-Gd image showed enhanced lesion in the right cerebellar peduncle. Cerebrospinal fluid cytology analysis was negative for tumor. We suspected tumor recurrence or secondary cancer, and performed lesion biopsy. The result of the pathological examination was radiation necrosis of the cerebellum. DISCUSSION: Progressive radiation necrosis of the brain and radiotherapy can vary from months to more than 10 years. So, whenever a new lesion is identified, radiation brain necrosis must be evaluated. According to guidelines in Japan, there is no absolute examination for discriminating tumor recurrence from radiation brain necrosis and diagnosis by biopsy may be required. CONCLUSION: We experienced a case of symptomatic radiation necrosis of the cerebellum 16 years after treatment. In patients showing new lesion after long periods of time, the possibility of radiation necrosis to be considered.

RONG-27. PROTON THERAPY REDUCES DOSE TO CRITICAL CENTRAL NERVOUS SYSTEM STRUCTURES IN MEDULLOBLASTOMA: A DOSIMETRIC ANALYSIS OF CHILDREN’S ONCOLOGY GROUP (COG) ACNS0331

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BACKGROUND: Recently published data demonstrated proton therapy (PRT) significantly reduced cognitive decline relative to photons for pediatric medulloblastoma. These findings imply that reductions in dose to critical CNS structures during the boost phase may account for better neurocognitive outcomes over time. Here, we examine differences in dosimetric data for medulloblastoma patients treated on ACNS0331 with photon (Intensity Modulated Radiation Therapy, 3D-Conformal Radiation Therapy) vs PRT to identify potential structures responsible for cognitive benefit. METHODS: COG ACNS0331 was a randomized trial examining the impact of reduced craniospinal irradiation (CSI) dose (standard vs low dose, in patients aged 3–7) and volume (whole posterior fossa vs involved field) in pediatric medulloblastoma patients. We identified 136 patients (IMRT=43, 3DCRT=28, PRT=65) enrolled on ACNS0331. With complete treatment data, we calculated dose to critical CNS structures to calculate dose. RESULTS: Proton therapy significantly reduced the dose to critical structures. For example, temporal lobe mean dose and V30 were 30Gy/58% (IMRT), 40Gy/89% (IMRT), 41Gy/84% (3DCRT), hippocampi mean dose were 51 Gy (IMRT), 52 Gy (3DCRT), and 44Gy (PRT) and cochleae mean dose were 43 Gy (IMRT), 49 Gy (3DCRT), and 31 Gy (PRT). Dose to several other critical structures were also significantly reduced including the whole brain, supratentorium, cerebellum, and pituitary. CONCLUSIONS: PRT therapy greatly reduces dose to critical CNS structures when compared to IMRT or 3DCRT. Further studies are needed to correlate dose reductions in these structures with improved cognitive outcomes.

RONG-31. ADVANCED ECHOCARDIOGRAPHY WITH MYOCARDIAL-STRAIN-ANALYSIS DESCRIBES SUBCLINICAL CARDIAC DYSFUNCTION AFTER CRANIOSPINAL IRRADIATION (CSI) IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH CENTRAL NERVOUS SYSTEM (CNS) TUMORS

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CSI is part of the treatment of CNS tumors and is associated with cardiovascular disease; data in pediatric/young-adult patients are limited. Myocardial-strain-analysis can reveal subclinical dysfunction. Retrospective,