

tients, Grade3:16 patients, Grade 4:47 patients) with recurrent malignant glioma treated with AVAgamma therapy as salvage therapy at the time of relapse after initial treatment. The average age is 55.7 years, with 44 men and 27 women. The tumor volume is 150 ml or less, and KPS is 40% or more as the indication of AVAgamma therapy. When the irradiation volume of the gamma knife was 15 ml or less, the marginal dose was 20 to 26 Gy, and when the irradiation volume was 15 ml or more, the marginal dose was 12 to 15 Gy in two divided doses. The mean therapeutic borderline dose was 24 Gy. Bevacizumab was administered 10 mg / kg or 15 mg / kg 1 to 10 times after GK. Methods: Median progression-free survival (mPFS) from AVAgamma treatment, median survival (mOS), and mOS from initial treatment were examined and compared with mOS in the RPA classification of recurrent glioma. Results: In relapsing glioma RPA classification, NABTT CNC class 2 mOS is 17.2 months, class 3 mOS is 3.8 months, class 5 mOS is 5.6 months, class 6 mOS is 6.4 months, but mOS from AVAgamma therapy is 18 months in class 3, 11 months in class 5, 9 months in class 6. The survival time has been extended in class3, class5, class6. Discussion: By AVAgamma therapy, it was thought that recurrent lesions were locally controlled and life prognosis was prolonged. Conclusion: AVAgamma therapy is thought to prolong the survival of recurrent malignant glioma and play an important role as salvage treatment.

Key words: gamma knife | bevacizumab | recurrent malignant glioma

#### RT-4

##### TREATMENT OUTCOME OF PROTON BEAM THERAPY FOR GLIOBLASTOMA

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**Introduction:** Proton beam therapy enables high dose irradiation for tumors while reducing the dose to surrounding normal tissue due to the sharp energy peak called the Bragg peak. We retrospectively analyzed the efficacy of the high dose radiotherapeutic strategy using proton beam for glioblastoma (GBM) in our institution. **Methods:** Twenty-nine patients with newly diagnosed GBM who underwent high dose proton beam therapy concomitant with temozolomide were investigated. All patients received hyperfractionated concomitant radiotherapy consisting of X-ray radiotherapy (50.4Gy in 28 fractions) and proton beam therapy (46.2Gy [RBE] in 28 fractions). The survival outcome and adverse events were analyzed. **Results:** The median overall survival time and progression free survival time for all 29 patients were 31.0 months (95%CI, 25.9–36.1) and 11.0 months (95%CI, 7.8–14.2), respectively. No significant survival difference according to the MGMT methylation status was shown. Failure patterns after proton beam therapy included 17 cases of local recurrence, 3 cases of distant recurrence, and 5 cases of dissemination. Although there was no significant difference in time to recurrence according to the failure pattern, there was a tendency of longer survival in the local recurrence group. Regarding adverse events, radiation necrosis was observed in 8 cases (including 2 asymptomatic cases). The median time to onset of necrosis after radiation was 18.2 months (95%CI, 10.3–26.2). There were 5 cases of long survivor over 5 years out of 29 cases (17.2%). Of these, 4 cases developed radiation necrosis. **Conclusions:** Our results indicate that high dose proton beam therapy of 96.6Gy (RBE) prolonged survival in selected GBM patients. Particularly in long survivors, special attention and effective treatment to radiation necrosis is a remaining problem.

Key words: glioblastoma | proton beam therapy | high dose radiation

#### RT-5

##### BORON NEUTRON CAPTURE THERAPY HAS EXTENDED PROGRESSION-FREE SURVIVAL ABOUT RECURRENT MALIGNANT PERIPHERAL NERVE SHEATH TUMOR - A CASE REPORT

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**Introduction:** Recurrent malignant peripheral nerve sheath tumor (MPNST) is intractable. Boron neutron capture therapy (BNCT) is a treatment using tumor-selective particle radiation, and is indicated for medical

treatment for head and neck cancer, and also used for malignant glioma and malignant meningioma. <Case>20-year-old woman who has MPNST that extends from the subcutaneous tissue of the right neck to the posterior fossa. <Medical History>Chemotherapy and local irradiation(50.4Gy/28fr) for primary embryonal rhabdomyosarcoma of the right ear canal at the age six. <Current medical history>Right cervical tumor developed at 17-year-old, some chemotherapy regimens and tumor resections were performed as recurrence of rhabdomyosarcoma at the previous hospital. After she was diagnosed with MPNST in the pathology consultation at our hospital, she was irradiated with heavy ion beam 70.8Gy(RBE)/16fr and received additional chemotherapies at our department, but her tumor was refractory. Although BNCT for MPNST is not covered by health insurance in Japan, she wanted to try to be treated for BNCT. After confirming boron accumulation in the tumor (SUVmax 4.28) by FBPA-PET, tumor growth and hydrocephalus occurred while waiting for travel to Taiwan due to the spread of COVID-19 infection. She was performed tumor resection(NTR) and irradiated with SRS 20Gy/fr for the residual lesion, but tumor had a rapid recurrence from the margin of the excision cavity. Finally, she could travel about 3 months after the operation and underwent BNCT, that used neutrons and 10B-boronophenylalanine from the Tsinghua University research reactor in Taiwan. No serious adverse events including cerebral edema were observed, and dramatic tumor shrinkage was maintained after treatment. FBPA-PET of 3 months later showed accumulation in the part of the margin of the cavity, the recurrence was observed on MRI after 3 and a half months. **Discussion:** BNCT for refractory/recurrent MPNST showed acceptable safety and was able to prolong progression-free survival.

Key words: BNCT | MPNST | PFS

## MOLECULAR PATHOLOGY/CLASSIFICATION (MPC)

#### MPC-1

##### DNA METHYLOME ANALYSIS SUGGESTED THE PRESENCE OF “TRUE” IDH-WILDTYPE LOWER-GRADE GLIOMAS

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**Background:** There will be significant changes in the diagnosis of IDH-wildtype adult-type gliomas in the upcoming 5th edition of the WHO Classification of Central Nervous System Tumours. IDH-wildtype lower grade gliomas (IDHwt LGGs) that harbor molecular features of glioblastoma (EGFR amplification, the combination of whole chromosome 7 gain and whole chromosome 10 loss (7+/10-), or TERT promoter mutations) will be diagnosed as glioblastomas (GBMs), while IDH-wildtype astrocytomas will not be included as a separate tumor type. However, IDHwt LGGs are a very heterogeneous group of tumors, and further investigation is warranted particularly in those without molecular features of glioblastoma. To elucidate the biology of IDHwt LGGs, we analyzed DNA methylation profile and survival time. **Materials and Methods:** Of the 724 adult-type diffuse glioma samples from a multi-institutional study, 64 IDHwt LGG, including 54 without any of molecular features of GBM and 10 with PDGFRA amplification or TERT promoter mutation, were examined using Infinium MethylationEPIC BeadChip. The raw data files (IDAT files) were analyzed by the web-based DNA methylation classifier provided by DKFZ (MolecularNeuropathology.org) or by R (Version 4.0.4) using the minfi