

emission tomography (Met-PET). Data regarding the pattern of recurrence and overall survival were collected. RESULTS: Among 247 cases with glioblastoma, total resection of CE was achieved in 112. Preoperative Met-PET was performed in 30 out of 112. The median age at operation, a period of follow-up, and the preoperative tumor volume in 30 patients were 56 year-old, 17.9 months, and 18.8 cc respectively. The promoter region of the O6-methylguanine-DNA methyltransferase was methylated in 37%. Radiological comparison revealed that Met uptake was detected beyond the CE area in 13 out of 30, and the Met uptake was also resected with awake mapping technique in 7 patients (supratotal resection group; STR). The median progression-free survival (PFS) in STR was 23 months, and all the patterns of recurrence were distant recurrence. In contrast, the PFS in total resection group (TRG) was 9 months ($p=0.09$, Wilcoxon). Furthermore, 14 out of 17 recurrence were local in TRG subgroup. While the median OS in TRG was 18 months, it has not reached in STR ($p=0.04$, Wilcoxon). CONCLUSIONS: The resection of both of CE and MU was associated with better PFS and OS. This finding must be validated in a larger cohort with a multicenter study.

RADIATION THERAPY (RT)

RT-01

TREATMENT RESULTS OF SALVAGE GAMMA KNIFE AND BEVACIZUMAB (AVAGAMMA THERAPY) FOR RECURRENT GLIOBLASTOMA

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PURPOSE: We report the treatment results of AVAgamma therapy combining gamma knife (GK) and bevacizumab for recurrent glioblastoma. **Subjects:** From August 2013 to April 2020, 44 patients (88 lesions) with recurrent glioblastoma treated with AVAgamma therapy as salvage therapy at the time of relapse after initial treatment. The average age is 61.5 years, with 26 men and 18 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 GK is 15 ml or less, a single irradiation with a boundary dose of 20 to 26 Gy was performed, and when the irradiation volume was 15 ml or more, a single irradiation boundary dose was divided into two divided irradiations of 12 to 15 Gy. 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), 6-month progression-free survival (PFS-6m), 6-month survival (OS-6m), median survival (mOS) from treatment with AVAgamma. Considered mOS from initial treatment. **RESULTS:** The mPFS from AVAgamma therapy was 5 months, PFS-6m was 37%, OS-6m was 79%, and mOS was 9 months. The mOS from initial treatment were 25 months. In relapsing glioma RPA classification, NABTT CNC class 5 mOS is 5.6 months, class 6 mOS is 6.4 months, but mOS from AVAgamma therapy is 9 months in class 5, 9 months in class 6. The survival time has been extended. **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 glioblastoma and play an important role as salvage treatment.

10031-RT-02

RESULTS OF REACTOR-BASED BNCT FOR 44 CASES OF RECURRENT AND REFRACTORY HIGH-GRADE MENINGIOMAS AND ROAD TO ACCELERATOR BASED BNCT

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INTRODUCTION: High-grade meningioma (HGM) is difficult clinical entity to treat. Especially recurrent HGM after some radiotherapy has very miserable prognosis. For example median overall survival (mOS) of recurrent HGM after radiotherapy is reported as 2 years. We applied tumor-selective particle radiation BNCT using nuclear reactor for 44 recurrent HGMs. **METHODS:** From 2005 to 2019, we treated 44 recurrent and refractory HGMs by reactor-based BNCT. The patients' WHO grades are grade 2:20 cases, grade 3:24 cases. Prior to BNCT, totally 114 times operations and 72 times SRS and 14 times external beam radiotherapy were applied for them. OS, tumor shrinkage, causes of treatment failure were analyzed. **RESULTS:** Median follow-up was 26.0 months. MOS after BNCT was 29.6 (95% CI:16.1–40.4) months. Grade 2 and 3 showed mOS as 44.4 (27.4–) and 21.55 (10.6–30.6) months, respectively and there is statistically significance ($p=0.0009$). All treated tumor showed rapid shrinkage on

MRI. Treatment failure patterns are local recurrence, out of field recurrence, systemic metastasis, CSF dissemination, as 35.5%, 20.6%, 17.6%, 8.8 %, respectively. These results showed good local tumor control and prolonged survival for recurrent HGM cases. **CONCLUSIONS:** Our cases were heavily treated with repetitive surgeries and repetitive radiotherapy. In addition the rate of grade 3 patients was extremely high. In a word our cases seemed to have poor prognosis. In spite of these poor condition, reactor-based BNCT exerted good local control and prolonged survival for recurrent and refractory HGMs. Depending on the clinical results, PMDA gave us the permission to apply investigator-lead clinical trial for recurrent and refractory HGMs using accelerator-based BNCT with financial support from AMED (one of the agency of Japanese government). In our talk, let us open some results from this trial.

RT-04

STEREOTACTIC IRRADIATION FOR 2 - 3 CM BRAIN METASTASES: A MULTICENTER RETROSPECTIVE COHORT STUDY

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PURPOSE: We retrospectively analyzed the treatment outcomes of Stereotactic irradiation (STI) for large size (2–3 cm) brain metastasis. **Materials and METHODS:** One hundred and sixty-nine lesions with 156 patients who underwent STI from January 1, 2013 to December 31, 2015 at 21 institutions participating in the Japanese Radiation Oncology Study Group were included in the study. Patients who had a history of whole-brain irradiation in the past and those who received whole-brain irradiation sequentially with STI were excluded. RANO-BM was used to evaluate the effect on each lesion, and the survival time or time to occurrence of local failure was defined as the number of months from the initial day of STI to the day of the events. **RESULTS:** The median age was 66 (33–87) years. The median follow-up time was 14 (1–52) months. Male/female = 95/61 cases. The number of brain metastases was 1/2/3/4 or more = 93/35/14/14 cases. The median doses and fraction size were 30 Gy in 3 fractions. The primary site was lung/breast/colon or rectum/others = 95/14/14/33 cases. The median survival time was 16 months. A 1-year overall survival rate was 62% and a 1-year local control rate was 77%. Comparing the 1-year local control rate by the fraction size, single/3 or 4/5 or more = 66/86/75%, the rate was better in the 3–4 fractions group (Log-rank test, $p = 0.069$). Cerebral necrosis (Grade 1/2/3/unknown = 9/10/8/3 cases) was observed in 39 lesions (18%), and the median time to diagnosis of brain necrosis was 9 (1–41) months. The incidence of necrosis in the single fraction cases was 29%, which was significantly higher than that in the fractionated irradiation cases (15%) ($p = 0.039$). **CONCLUSION:** Fractionated STI seems to be more favorable than single fraction STI for large brain metastases.

MOLECULAR PATHOLOGY/CLASSIFICATION (MPC)

MPC-02

PROGNOSTIC EFFECTS OF MOLECULAR FACTORS IN ELDERLY PATIENTS WITH IDH-WILDTYPE GLIOBLASTOMAS

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BACKGROUND: Geriatric neuro-oncology is an important research field, because the elderly patients is growing at a very rapid rate. This study investigates molecular features and their prognostic effects in the elderly glioblastomas (GBM). **METHODS:** We collected adult cases diagnosed with IDH-wildtype GBM and enrolled in Kansai Molecular Diagnosis Network for CNS Tumors (212 cases). Clinical and molecular features were analyzed retrospectively and independent prognostic factors were identified statistically. Focusing on the elderly (≥ 70 years) cases, the association between molecular factors and overall survivals (OS) was examined. **RESULTS:** Included in the study were 92 elderly cases (43.4%) and median OS was 12.8 months. MGMT promoter was methylated in 50 (54.3%). Triple CNA (EGFR amplification/gain & PTEN deletion & CDKN2A deletion) was detected in 23 (25.0%). NFKBIA was deleted in 23 (25.0%). In the elderly cases, adjuvant radiation and temozolomide (RT+TMZ) was performed in 39 (42.4%) (mOS = 17.1 months). Statistical analyses of the elderly plus non-elderly cases treated with RT+TMZ (148 cases), MGMT promoter, triple CNA and NFKBIA were identified as independent

molecular prognostic factors. In the elderly group, however, there was no significant difference in OS according to MGMT status (methylated = 18.7 vs. unmethylated = 17.1, $p = 0.3885$) or triple CNA status (triple = 13.6 vs. non-triple = 19.6, $p = 0.1734$). On the other hand, statistical difference was observed according to NFKBIA status (del = 12.1 vs. non-del = 18.7, $p = 0.0157^*$) even in the elderly cases. **CONCLUSION:** Prognostic effects of molecular factors might be attenuated in the elderly patients. Further investigation in a larger population is necessary.

MPC-04

UTILITY OF COMPREHENSIVE CANCER GENOME ANALYSIS FOR BRAIN TUMORS

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OBJECTIVE: Our hospital has been designated as a cancer genome medical cooperation hospital, and it is our responsibility to play a central role in cancer medicine. We were one of the first local hospitals to clinically apply cancer genome analysis, and in January 2019, we started PleSsision-Rapid testing as a clinical study without patient burden. This study examines data from patients with brain tumors, subjects it to cancer genome analysis, and reports on its utility and efficacy.

METHOD: Genome analysis was performed by PleSsision-Rapid examination for patients with brain tumors who underwent surgery between January 2019 and July 2020. Tissue DNA extracted from pathological specimens was used to perform next-generation sequencing (NGS) analysis. In the PleSsision-Rapid test, 160 genes are comprehensively analyzed, examined by genomics, and evaluated for the presence or absence of actionable and druggable mutations, and the mutation rate is determined.

RESULTS: There were 15 cases total. Histopathological diagnoses included glioblastoma (n=5), diffuse astrocytoma (n=1), metastatic brain tumor (n=4), meningioma (n=2), central nervous system primary malignant lymphoma (n=1), germinoma (n=1), and Langerhans cell histiocytosis (n=1). Of these 15 brain tumor cases, actionable mutations were detected in 80.0% of cases and druggable mutations were detected in 66.6%. The average mutation rate was 8.59 ± 5.32 (range, 1.3 to 22.8) per patient.

Conclusion: Although future improvements will be needed for cancer genome analysis in brain tumors, this strategy may be useful for the selection of molecularly targeted drugs with high antitumor efficacy. We will continue to accumulate and study such cases in the future.

MPC-06

CUTTING-EDGE OF CANCER GENOMIC MEDICINE FOR BRAIN TUMORS

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Kyushu University Hospital was designated a Cancer Genome Core Hospital in April 2018, and the multi-gene panel test has been introduced since August 2019. The expert panel has been held for 21 cases of the central nervous system (11 adult glioma, 5 pediatric brain tumors, 5 extramedullary tumors). Actionable gene abnormalities were newly detected in two cases. First case is epithelioid glioblastoma with BRAF V600E mutation, and second is embryonal tumor with VCL-ALK fusion. For the first case, BRAF/MEK inhibitor can be used by the prospective trial of patient-proposed healthcare services with multiple targeted agent based on the result of gene profiling by multigene panel test (NCCH1901). For the second case, we are planning to introduce ALK inhibitor by indicator-initiated clinical trial while continuing ICE therapy. The current approved agents for tumor-agnostic treatment are immune checkpoint inhibitors for mismatch repair deficient (dMMR) cases and TRK inhibitors for NTRK fusion gene-positive cases. We selected microsatellite instability (MSI) test and immunostaining of MMR gene for the indication of immune checkpoint inhibitor for recurrent glioma and Lynch syndrome that require dMMR evaluation, but FoundationOne CDx (F1CDx) allows simultaneous evaluation of MSI and MMR gene abnormalities. Regarding the indication of TRK inhibitors, F1CDx assay is selected as a companion diagnosis for ALK, NTRK1/2/3 fusion gene analysis for pediatric cases. At present, the actionable gene abnormalities are detected by multi-gene panel tests in about 10% of brain tumors. Development of tumor-agnostic treatment will expand the molecular target therapy for brain tumor in the future. Based on the experience of different schemes for molecular targeted therapy, it became clear that it is necessary to establish a cancer genome medical system for prompt introduction of precision medicine for highly malignant brain tumors.

MPC-08

MOLECULAR RISK STRATIFICATION USING GENOME-WIDE DNA METHYLATION DATA OF STANDARD-RISK MEDULLOBLASTOMAS TREATED WITH 18-GY CRANIOSPINAL IRRADIATION

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A novel risk stratification of medulloblastoma has been proposed based on retrospective data from patients undergoing standard treatment. However, it remains unclear whether the classification is applicable to patients receiving reduced-dose craniospinal irradiation (CSI). We performed molecular diagnosis and copy number analysis using methylation array on patients with standard-risk medulloblastoma treated with 18 Gy CSI at our institution. Nine tumor samples were available for analysis from seven patients who had a median age of 7.4 years at disease onset and a median observation period of 73 months. Three patients had recurrence, and another patient developed radiation-induced glioblastoma. From the three recurrent cases, one was molecularly diagnosed as SHH subtype with MYCN amplification; another case was a Group 4 tumor without favorable prognostic chromosomal aberrations, and the remaining patient experienced a very late relapse despite low-risk stratification. Of the recurrence-free cases, one was classified as WNT subtype, and another was a Group 4 tumor with chromosome 7 gain, and loss of chromosomes 8 and 11, both of which were associated with good prognosis. Methylation analysis also unveiled the fact that the recurrent tumor diagnosed as relapsing medulloblastoma by conventional diagnostic tools was in fact a radiation-induced glioblastoma. Our data suggested that the new risk stratification may be useful for cases treated with CSI reduced to 18 Gy. However, due to the presence of the late-relapsed case stratified to low risk, further investigations with a larger cohort should be required to confirm the data.

MPC-11

COMPREHENSIVE GENE EXPRESSION ANALYSIS OF IDH-MUTATED ASTROCYTOMAS WITH 19Q-LOSS

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We previously reported that there was a subgroup of IDH-mutated astrocytomas harboring only 19q-loss showing oligodendroglioma-like morphology and significantly longer overall survival (OS) compared with 19q-intact astrocytomas. To further explore the biological characteristics of this possible subgroup and obtain insight into the mechanism of their relatively benign clinical behavior, we compared gene expression pattern between five 19q-loss and five 19q-intact IDH-mutated astrocytomas by microarray analysis. By comparing expression levels of genes of 19q-loss astrocytomas to those of 19q-intact astrocytomas, 136 up-regulated genes and 203 down-regulated genes were extracted. Down-regulated genes in the 19q-loss astrocytomas were heavily clustered to 19q and 4p, and up-regulated genes to 4q. It was noted that fibroblast growth factor 1 associated with stem cell maintenance was down-regulated in 19q-loss astrocytomas and genes associated with glioma progression were differentially expressed, these results were validated with the independent TCGA data set. On t-SNE analysis of the 19q-loss astrocytomas with other IDH-mutant glioma subgroups from the TCGA datasets, 19q-loss astrocytomas did not shift to oligodendrogliomas with 1p/19q codeletion but were a subgroup in astrocytomas. These results indicated that 19q-loss in astrocytomas is more likely to be an acquired event rather than early event in oncogenesis like 1p/19q codeletion in oligodendrogliomas, and the biological and morphological features of 19q-loss astrocytomas were possibly related to differentially expressed genes associated with stem cell maintenance and glioma progression.

NEUROIMAGING (NI)

NI-01

USEFULNESS OF PREOPERATIVE EVALUATION OF GLIOMA ELASTICITY BY THE MAGNETIC RESONANCE ELASTOGRAPHY

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INTRODUCTION: The elasticity of intracranial tumors is difficult to assess non-invasively because the lesion is surrounded by the skull. Therefore, intracranial tumors have not been verified before surgery in terms of elastic