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

Kazuhiro Miwa[1], Hiroaki Takei[1], Takeshi Ito[1], Kazutoshi Yokoyama[1], Hirohito Yano[2], Jun Shinoda[2], Satoshi Ishihara[3], Noriyuki Nakayama[4], Toru Iwama[4], Yasutka Kato[5]; [1]Department of Neurosurgery, Kizawa Memorial Hospital, Minokamo, Japan

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

Masahiro Mizoguchi[1], Nobuhiro Hata[1], Daisuke Kuga[1], Ryusuke Hatae[1], Yuhei Sangatsuda[1], Yutaka Fujioka[1], Kosuke Takigawa[1], Yusuke Funakoshi[1], Yuhki Koga[2]; [1]Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University, Japan

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

Tomoya Irikura[1], Kohei Fukuoka[1], Makiko Mori[1], Koichi Oshima[1], Yuki Arakawa[1], Yutaka Tanami[2], Koichi Ichimura[3], Atsuko Nakazawa[4], Jun Kurihara[5], Katsuyoshi Koh[1]; [1]Department of Pediatric Hematology/Oncology, Saitama Children's Medical Center, Saitama, Japan

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

Ryohei Otani[1], Akitake Mukasa[4], Takeo Uzuka[2], Fumi Higuchi[2], Hadzki Matsuda[2], Shota Tanaka[3], Phyo Kim[2], Keisuke Ueki[2]; [1]Department of Neurosurgery, Tokyo Metropolitan Komagome Hospital

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

Shinichiro Koizumi[1], Kazuhiko Kurozumi[1]; [1]The Department of Neurosurgery, Hamamatsu University School of Medicine, Hamamatsu, Japan

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

modulus. Magnetic resonance elastography (MRE) is an epoch-making method capable of non-invasively imaging the elasticity of internal organs. We have examined the elasticity of meningiomas and pituitary adenomas and reported their usefulness. This time, we measured the glioma elasticity and verified usefulness of MRE.

METHOD: Twenty-four gliomas (mean age 51.8±15.7 years, male: female = 17: 7) who underwent tumor resection after MRE imaging from July 2017 to May 2020 were targeted. The average elasticity was measured as an evaluation of tumor elastic modulus by MRE. Gliomas were divided into a low-grade glioma group (LGG: Grade 1, 2) and a high-grade glioma group (HGG: Grade 3, 4). Then, a comparative statistical study was conducted.

RESULTS: The average values of the average elasticity of LGG group (9 cases) and HGG group (15 cases) were 1.8±0.8 kPa and 2.5±0.8 kPa, respectively. The average elasticity was significantly higher in the HGG group (p=0.023). In the ROC analysis, the cutoff value was 2.1 kPa (sensitivity 70%, specificity 70%). Therefore, it was suggested that the tumor is likely to be HGG when the average elasticity is 2.1 kPa or more.

DISCUSSION: The glioma elasticity by preoperative MRE was significantly higher in the HGG group. Based on actual surgical experience, the tumor seems to be hard in the HGG group, and it was judged to be consistent with this our MRE research. The preoperative evaluation of glioma elasticity by MRE was considered useful, and it might help in planning a surgical strategy considering malignant grade.

NI-04

EVALUATION OF POST BORON NEUTRON CAPTURE THERAPY FOR RECURRENT MENINGIOMA USING FLUORIDE-LABELED BORONOPHENYLALANINE PET

Satoshi Takai[1], Yoko Matsushita[3], Shinji Kawabata[1], Koji Ono[2], Kayako Isohashi[2], Masahiko Wanibuchi[1], Shinichi Miyatake[2]; [1]Osaka medical college hospital, Osaka prefecture, Japan

We have applied boron neutron capture therapy (BNCT) for 46 recurrent high grade meningiomas (HGM). Twelve cases among them, fluoride-labeled boronophenylalanine positron emission tomography (18F-BPA-PET) were utilized before and after BNCT to evaluate the tumor activity. The lesion to normal brain (L/N) ratios of 14 lesions of these 11 cases were investigated. In all cases L/N ratio decreased after BNCT. The L/N ratio of recurrent (HGM) was 3.2±1.5 (mean±SD) before BNCT and 2.1±0.6 after that. In contrast enhanced MRI, 13 out of 14 lesions shrank or unchanged at least 3 months after BNCT, while one lesion transiently increased and then decreased within 3 months, showing pseudoprogression. In addition, 6 of 12 lesions which could be followed on MRI for more than 3 months progressed after 8 months. 4 of them were performed PET at the time of progressing. The L/N ratio of 2 progressing lesion which were diagnosed as recurrence due to continuously increasing were showed increasing. The L/N ratio of the other 2 lesions which were diagnosed radiation necrosis due to unchanged or shrinkage showed decreasing. Moreover, some systemic metastasis detected in PET image. F-BPA-PET seems to be useful for the evaluation of tumor activity.

NI-08

UTILITY OF MULTIPLE POSITRON EMISSION TOMOGRAPHY TRACERS IN THE DIAGNOSIS OF BRAIN TUMORS ACCORDING TO THE 2016 WORLD HEALTH ORGANIZATION CLASSIFICATION

Keisuke Miyake[1], Takeshi Fujimori[1], Yasunori Toyota[1], Daisuke Ogawa[1], Tetsuhiro Hatakeyama[1], Masanobu Okauchi[1], Masahiko Kawanishi[1], Takashi Tamiya[1]; [1]Department of Neurological Surgery, Kagawa University Faculty of Medicine, Kagawa, Japan

OBJECTIVE: Magnetic resonance imaging alone is not sufficient for the diagnosis and therapy outcomes in brain tumors. We herein examined the utility of positron emission tomography (PET) studies for diagnosis in brain tumors. METHODS: Between April 2009 and June 2020, 320 patients with central nervous diseases, including 140, 65, 52, 52, and 11 patients with glioma, metastatic brain tumor, malignant lymphoma, meningioma, and demyelinating disease, respectively, underwent PET studies (FDG, MET, FLT, and FMISO) in our department. Lesion/normal (L/N) ratios for FDG, MET, and FLT and lesion/blood ratio (L/B ratio) for FMISO were compared. The glioma subtypes were compared based on the 2016 World Health Organization classification (IDH-mut, Codel, IDH-wt, GBM), and metastatic brain tumors, malignant lymphomas, meningiomas, and demyelinating diseases were compared with GBM. RESULTS: In glioma, the cutoff MET L/N ratios to distinguish between IDH-mut and Codel, IDH-mut and GBM, Codel and GBM, and IDH-wt and GBM were 3.61, 4.42, 4.92, and 4.33, respectively, and the cutoff FLT L/N ratios to distinguish between IDH-mut and IDH-wt, IDH-mut and GBM, Codel and GBM, and IDH-wt and GBM were 3.43, 6.46, 3.39, and 7.56, respectively. The cutoff FDG and MET L/N ratios between metastatic brain tumors and GBM were 2.27 and 4.89; the cutoff FDG L/N and FMISO L/B ratios between malignant lymphoma and GBM were 4.68 and 2.13; and the cutoff FDG and MET L/N ratios between meningioma and GBM were 1.58 and 4.36. Demyelinating disease and GBM were distinguishable by FDG, MET, and FLT L/N ratios of 2.29, 3.32, and 5.85, and FMISO L/B ratio of 1.68. CONCLUSION: Four PET tracers were required to differentiate glioma subtypes. FDG and MET are useful for distinguishing GBM from metastatic brain tumor, malignant lymphoma, and meningioma, whereas accumulation was lower for all four PET tracers in demyelinating diseases than in GBM.

NI-09

AMIDE PROTON TRANSFER (APT) IMAGE IS USEFUL FOR DIAGNOSTIC IMAGING OF GLIOMA

Masami Shirota[1], Masayuki Nitta[2], Taiichi Saitou[2], Syunsuke Tuduki[2], Atsushi Fukui[2], Souko Ikuta[3], Ayako Yoshida[4], Kayoko Abe[5], Yoshihiro Muragaki[2,3], Takakazu Kawamata[2]; [1]Tokyo Women's Medical University Yachiyo Medical Center

INTRODUCTION: APT image(APT),which images the concentration of amide groups that increases in tumors, is expected to be applied clinically in diagnostic imaging of glioma. PURPOSE: APT was compared with MET-PET based on the pathological diagnosis results, and it was retrospectively verified that APT was useful for diagnostic imaging of glioma. METHODS: A total of 46cases with glioma (WHO 2016 Grade: GII/III/IV) and Pseudoprogression were included. APT measured the APT measurement value by placing the region of interest in the tumor part. MET-PET was administered with 370MBq and the accumulation ratio(TNR) between the tumor part and the normal part was measured. RESULTS: The APT measurement value in all cases was 2.22±1.01 and the TNR was 2.58±1.50,and a correlation was observed between the APT measurement value and the TNR($r=0.6$, $p<0.001$).When the accuracy of discrimination between GII/III/IV (32cases) and Pseudoprogression(14cases) by APT measurement was verified, the sensitivity was 91% and the specificity was 100% at the threshold of 1.81. In the verification of malignancy diagnosis, the measured APT value of GII (6cases) was 2.18±0.43,the measured APT value of GIII (11cases) was 2.67±0.69,and the measured APT value of GIV (15cases) was 2.99±0.61.The measured value showed a significant difference. The measured APT value in the oligodendroglioma group (GII/III:10cases) was 2.37±0.66,the TNR was 3.52±1.41,and the measured APT value in the astrocytoma group (GII/III: 7cases)Was 2.67±0.45 and TNR was 2.41±0.87.In the oligodendroglioma group, the measured APT value was lower and the TNR was higher than in the astrocytoma group. CONCLUSION: It was suggested that APT may have the same diagnostic ability as MET-PET in diagnosing malignant tumors and distinguishing between recurrence and Pseudoprogression. Patients with an actual APT of 1.81 or higher should consider treatment strategies, and follow-up may be an option for patients with an APT of <1.81.APT,which is not affected by the blood-brain barrier, has little variation in measured values and is considered to be useful for diagnostic imaging of glioma.

NI-10

T2/FLAIR MISMATCH SIGN AND METHIONINE PET UPTAKE IN GRADE II AND III GLIOMAS

Yusuke Ebiko[1,3], Kaoru Tamura[1], Shoko Hara[1], Motoki Inaji[1,2], Yoji Tanaka[1], Tadashi Nariai[1,2], Kenji Ishii[2], Taketoshi Maehara[1]; [1]Department of Neurosurgery, University of Tokyo Medical and Dental University, Tokyo, Japan

BACKGROUND: Recent study suggests that "T2/FLAIR mismatch" sign is specific MRI finding for isocitrate dehydrogenase mutated (*IDH*-mut) 1p19q non-codeleted gliomas (Grade II and III astrocytic tumors). T2/FLAIR mismatch sign may be useful for predicting the histological type of glioma before surgery. However, it is not known what this finding reflects. Therefore, we examined the correlation between T2/FLAIR mismatch sign and uptake of methionine with positron emission tomography (MET-PET), and molecular classification of glioma.

METHODS: 74 glioma patients (grade II: 30 cases, grade III: 44 cases) with preoperative MRI and MET-PET who underwent surgical resection during 2000–2019 were included in this study. MR scans were evaluated by 3 independent reviewers to assess presence/absence of T2/FLAIR mismatch sign. The tumor-to-normal (T/N) ratio of methionine uptake was calculated by dividing the maximum standardized uptake value (SUV) for the tumor by the mean SUV of the normal brain. We examined the relationship between *IDH* mutation, 1p/19q codeletion, mismatch, and T/N ratio of MET-PET.

RESULTS: Out of the 74 cases, astrocytic tumors (A group: *IDH*-mutant, 1p19q non-codeleted) were 21 (28%), oligodendroglial tumors (O group: *IDH*-mutant, 1p19q codeleted) were 19 (26%), and *IDH* wild tumors (W group) were 34 (46%). The T2/FLAIR mismatch sign was present in 16 cases (22%). The T/N ratio of MET-PET in the tumor with T2/FLAIR mismatch sign was 1.56, which was significantly lower than that in the tumor without mismatch sign (2.01, p=0.016). T2/FLAIR mismatch sign was found in 7 (33%)