re-consideration of treatments for tumors diagnosed as so-called PNET. In this study, we propose the optimization of treatments for tumors diagnosed by the new classification to clarify which treatments were effective for the tumors, those were diagnosed as PNET, MATERIALS AND METHODS: The tumor samples diagnosed as so-called PNETs were analyzed. The molecular information was extracted from tumor specimens. We used high throughput analysis with microarray, FISH, and immunohistochemistry. They all had treated in our institution in last 6 years and their clinical courses were followed by medical records. Informed parental consent was obtained from their guardians and this study was approved by the institutional review board of Juntendo university. RESULTS: Nine tumor samples were able to be analyzed and they are re-classified into high-grade gliomas, low-grade gliomas, sarcoma, embryonal tumors with multilayered rosettes, C19MC altered (ETMR). They resembled each other closely in morphology, and therefore, it was not able to be classified by histopathological findings. There was a case of pineoblastoma, whose molecular background suggested that the tumor was re-classified into neuroblastoma. In terms of treatments, we have succeeded in neuroblastoma cases so far, ETMRs were required multiple surgeries and radiations to maintain remissions. CONCLUSIONS: Re-classification of diagnosis based on the molecular background is necessary to clarify the optimization of treatments for pediatric brain tumors, and the comprehensive methods is required. We present our methods for molecular diagnosis in clinical field and future plans.

MPC-11
IDHI/2 MUTATIONS ARE ASSOCIATED WITH SEIZURE ONSET AND VETEY IMAGING IN PATIENTS WITH DIFFUSE GLIOMA VISUALIZING 2-HYDROXYGLUTARATE BY MASS SPECTRUM
Makoto Ohno1, Hiroaki Aikawa1, Yoko Matsuhashi1, Yasuji Miyakita1, Masamichi Takashahi1, Koichi Ichimura1, Akinobu Hamada1, Yoshitaka Narita2,1; Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital

BACKGROUND: Mutations in isocitrate dehydrogenase 1 or 2 genes (IDHI/2) frequently occur in lower-grade gliomas. Mutant IDHI/2 proteins gain a new ability to produce 2-hydroxyglutarate (2HG). IDHI/2 mutations have been shown to be related with seizure through the structural similarity of 2HG to glutamate. We, therefore, sought to investigate the relationship between seizure and IDHI/2 mutations and to visualize tissue 2HG distribution in patients with diffuse gliomas. METHODS: We assessed 149 patients with diffuse glioma, and measured tissue 2HG concentrations in 104 patients by using liquid chromatography-tandem mass spectrometry. The matrix-assisted laser desorption/ionization high resolution mass spectrometry imaging (MALDI-HR-MSI) was used to visualize tissue 2HG distribution for 12 tissue samples. RESULTS: Seizure onset was observed in 34 among 56 (60.7%) patients with IDHI/2 mutant tumor, whereas in 18 among 93 (19.4%) patients with IDHI/2 wild-type tumor (p<0.0001). The tissue 2HG concentration was significantly higher in IDHI/2 mutant tumor than in IDHI/2 wild-type tumor (median: 4862 ng/mg vs 75 ng/mg (p<0.0001), Multivariate analysis, including tissue 2HG concentration, IDHI/2 status, histology, grade, and location, showed that IDHI/2 mutations was significantly correlated with seizure onset. The MALDI-HR-MSI showed that 2HG spread in various concentration independent of cellularity and also in extracellular space in IDHI/2 mutant tumor tissues. CONCLUSIONS: We demonstrated the association between IDHI/2 mutations and seizure, and the heterogeneous 2HG distribution not only in cellular area but also in extracellular space. These findings suggest the potential role of 2HG as an intercellular mediator to tumor environment, resulting in epileptogenesis formation.

MPC-12
ACCURACY OF INTRAOPERATIVE SIMPLE FLOW CYTOMETER FOR HIGH GRADE GLIOMA OPERATION COMPARED WITH INTRAOPERATIVE FROZEN DIAGNOSIS
Kenichiro Asano1, Toshio Fumoto1, Akio Kamataki2, Kenji Takeda1, Akira Kurose2,1; Department of Neurosurgery, Hirosaki University Graduate School of Medicine Zaifu-cho, 2Hirosaki-shi, Aomori, Japan

INTRODUCTION: Intraoperative simple flow cytometer (iFC) was developed in recently, we examined the correlation intraoperative frozen diagnosis (IOFD) and intraoperative frozen section of resection margin (IOMF) to iFC. METHOD AND MATERIAL: Total 33 cases of high grade glioma patients underwent operation in April 2017 ~ May 2019, and IOMF and IOFD were compared to iFC. Sample of iFC were retrieved just same parts of IOMF and IOFD. We compared to microscopical findings, MIB-1, malignant index (MI), and MI Level (G0-4). RESULTS: Accuracy rate of iFC and IOFD in high grade glioma was 82.4%, and the concordance rate of grading was 71.2%. Correlation coefficients between MIB-1 and iFC of IOMF was r=0.5019 P=0.0065. Accuracy rate of IOFD was 46.8%, and concordance rate of grading was 35.5%. Correlation coefficients between MB-1 and iFC of IOFD was r=0.5899 P=0.0001. CONCLUSIONS: Although iFC accuracy rates of IOMF and IOFD was high, iFC concordance rates and grade were low. Correlation between MB-1 and iFC of IOFD was better than that of IOFD. Probably, iFC of IOFD was a little difficult because of sample heterogosity.

MPC-14
BRAF V600E MUTANT OLIGODENDROGLIOMA-LIKE TUMORS WITH CHROMOSOMAL INSTABILITY IN ADOLESCENTS AND YOUNG ADULTS
Keihei Kuromura1, Uri Tabori, Cynthia Hawkins, 1Department of Hematology/Oncology, Sattama Children’s Medical Center, Sattama, Japan

We performed genome-wide methylation analysis on 136 pediatric low grade gliomas, identifying a unifying molecular subclass consisting of oligodendroglioma-like BRAF V600E mutant tumors with Recurrent gain of Chromosome 7 and loss of Chromosome 10 (OLIVER). Hierarchical clustering and stochastic neighbor embedding analyses cluster them with previously described pediatric-type low grade gliomas, separate from adult gliomas. OLIVERs exhibit distinct clinical behavior as temporal lobe lesions in adolescents and young adults, prolonged history of seizures and all are alive with no recurrence (follow-up 3.2 to 13.2 years). Morphologically, all showed oligodendroglioma-like features, including round or oval nuclei with pink perinuclear halos, a chicken-wire pattern of branching capillaries and microcalcification. None showed astrocytic features or characteristics suggestive of high-grade tumors including necrosis or mitotic figures. All tumors harbored multiple chromosomal copy number abnormalities (more than 10 chromosomes per OLIVER), but none showed 1p/19q co-deletion or IDH1 mutation. Interestingly, one tumor showed a TERT promoter mutation. Although the series is small, OLIVER may represent a new category of IDH wild-type low grade glioma which may be confused with molecular GBM. Further, they highlight the heterogeneity of IDH wild-type gliomas and the relatively indolent behavior of pediatric-type gliomas.
Hideaki Yokoo, Yoshiki Mikami, Akitake Mukasa; Department of Neurosurgery, Kumamoto University

A 17-year-old boy presented with a 2-week history of lower back pain, progressive gait difficulty and sensory deficit of bilateral lower limbs. Magnetic resonance imaging of neuroaxis showed intramedullary tumor with spinal cord expansion from Th12 to L2 and irregular areas of enhancement. Histopathological and biopsy was performed. Histopathological examination showed small atypical cells, but most cells had too much degeneration and necrosis to confirm the diagnosis definitively. Leptomeningeal dissemination caused conscious disturbance, nuchal rigidity and epilepsy. 2 weeks after decompression, we performed cordotomy again for abdominal pain, to be found diffuse midline glioma, H3K27M mutant by immunohisto pathological examination and DAN sequence. He was treated with combination of whole brain and spine radiation therapy and chemotherapy with temozolomide and bevacizumab. He is still alive over 6 months. The pathological significance of H3K27M mutant in spinal gliomas is unclear. Further examinations are needed.

MPC-17
USEFULNESS OF INTRAOPERATIVE MOLECULAR DIAGNOSIS OF GLIOMA USING REAL-TIME PCR
Shunichi Koriyama1, Masayuki Nitta1, Kenta Masui, Takashi Maruyama1, Taichi Saito1, Takashi Komori, Yoshitomo Muragaki, Takakazu Kawamata1; Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan

BACKGROUNDs: Based on the comprehensive gene association studies in recent years, the revision was issued in 2016 WHO classification, integrating genetic information in glioma diagnosis. Many studies have been reported the correlation between each molecular subtype and prognosis in the new classification. Gliomas surgery is required to maximum tumor resection with functional preservation. Currently, our institute decides a surgical strategy based on the morphological diagnosis and genetic information from the obtained tissue during the operation. We evaluated the IDH 1/2 gene mutations and 1p/19q codeletion by using real-time PCR intraoperatively. We report the usefulness of this method in this presentation. OBJECTIVE: 58 patients were obtained during surgery from March to November 2017, IDH 1/2 gene mutations and 1p/19q codeletion were evaluated intraoperatively by real-time PCR. IDH 1/2 gene mutations were detected using HRM, and SNP genotyping was used for TERT promoter mutations expected as a surrogate marker for 1p/19q codeletion. RESULT: Each gene mutation was detected in approximately 90 minutes from DNA extraction of obtained surgical tissue to analysis. The accuracy of HRM of IDH 1/2 mutations was 97.3% (72/74 cases) evaluated by the result of IDH1-R132H IHC or Sanger sequencing, and SNP genotyping of TERT promoter mutations was 94.3% (50/53 cases). There was almost no difference from final genetic information. CONCLUSION: Real-time PCR is feasible as an intraoperative molecular diagnosis. The accuracy of diagnosis is very high, and it can be evaluated in a short time, so it’s useful for decision making during operation.

MPC-18
CATEGORIZATION OF LOWER GRADE GLIOMA USING OncoPanel
Hiroyuki Uchida1, Toshikai Akahane, Nayuta Higa1, Mari Kirishima, Tsubasa Hiraki, Hajime Yonezawa1, Akitake Tamimoto, Koji Yoshimoto1; The Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

PURPOSE: We are developing a 48-gene OncoPanel (Kagoshima Brain Tumor 48 OncoPanel) specializing in glioma diagnosis. Clinical application of genetic diagnosis derived from genetic alterations detected by OncoPanel, including IDH mutation, 1p/19q-codeletion, and other gene mutations in lower-grade glioma was verified. METHODS: The 48 genes consist of 24 genes related to glioma and 24 genes on chromosomes 1 and 19. DNA was extracted from tumor FFPE samples and blood samples, and then single nucleotide variants and copy number variants were detected using next-generation sequencer. RESULTS: Among the 99 diffuse glioma cases that had undergone OncoPanel analysis by July 2019, 40 cases diagnosed histologically as WHO grade 2 or 3 diffuse glioma were included. The integrated diagnosis by conventional gene analysis were Diffuse astrocytoma 10 cases, anaplastic astrocytoma 11 cases, oligodendroglioma 10 cases, anaplastic oligodendroglioma 9 cases. IDH1 mutation was detected in 30 cases, of which in 19 cases 1p/19q-codeletion was detected, all with TERT mutation. Among 11 cases with 1p/19q-non-codeletion, ATRX mutation was detected in 10 cases and was almost mutually exclusive with TERT mutation. In 10 cases without IDH mutation, EGFR amplification or mutation was detected in 6 cases, of which 4 cases were accompanied by TERT mutation. DISCUSSION: KBTG4 can detect TERT and ATRX mutations in a mutually exclusive manner and can improve the classification accuracy of oligodendroglioma and astrocytoma. Groups with gene profiles similar to glioblastoma with EGFR amplification/mutation and TERT mutation can also be classified. CONCLUSIONS: In the diagnostic classification of lower-grade glioma, KBTG4 can well classify into oligodendroglioma group, astrocytoma group and glioblastoma-like group, and is considered to be applicable in clinical practice.

NEUROIMAGING (NI)

NI-01
CONTRAST-ENHANCED MRI AND POSTION EMISSION TOMOGRAPHY FOR DISTINGUISHING THE GRADE OF GLIOMA Hiroaki Takei1, Ensko Ohwash1, Yuka Ikegami1, Yoshitaka Asano1, Jun Shinoda1, Kazuhiro Miwa, Takeshi Ito, Kazutoshi Yokoyama, Noriyuki Nakayama, Hirohito Yano, Sobko Ikuta, Takashi Maruyama, Yoshitomo Muragaki, Toru Iwama1; Department of Neurosurgery, Chubu medical center for prolonged traumatic brain dysfunction, Kizawa memorial hospital.

OBJECTIVE: Grading of glioma according to the WHO classification plays an important role in the treatment of patients with glioma. It is widely recognized that malignant gliomas exhibit contrast enhancement on MRI, whereas low-grade gliomas do not exhibit contrast enhancement. However, we sometimes encounter malignant gliomas without contrast enhancement on MRI. In this study, we evaluated the diagnostic accuracy of contrast-enhanced MRI and PET for distinguishing the WHO grade of glioma. METHODS: A total of 105 patients with newly diagnosed cerebral glioma were included in the study. All patients underwent 11C-Methionine (MET), 11C-Choline (CHO), 18F-Fluorodeoxyglucose (FDG) PET and MRI. The specificity and sensitivity of MRI contrast enhancement and mean T/N ratios of these three tracers for each WHO grade were analyzed. RESULTS: Contrast-enhancement was observed in 35 patients (33%) of the total. Contrast enhancement was observed in 13/30 (43%) in grade 2, 11/24 (46%) in grade 3, and 6/51 (12%) in grade 4. The sensitivity and specificity of MRI for differentiating grade 2 from grade 3 was 11.1% and 54.7%, respectively. In contrast, the cutoff value, sensitivity, and specificity of each tracer for differentiating grade 2 from grade 3 were: 1.70, 66.7%, and 58.1% for MET; 2.15, 76.7%, and 51.2% for CHO; and 0.64, 80.0%, and 32.6% for FDGs, respectively. DISCUSSION: A correlation between contrast enhancement of MRI and WHO grade was observed to some extent; however, only 19% grade 3 gliomas showed contrast enhancement. The sensitivity and specificity of PET for differentiating between grade 2 and 3 was relatively higher than that of MRI; however, it was not suitable for clinical use. CONCLUSION: Contrast-enhanced MRI may not be reliable for determining the WHO grade for glioma, in particular differentiating between grade 2 and 3. Comprehensive evaluation with MRI and PET can provide more accurate diagnosis.

NI-02
THE ASSOCIATION BETWEEN 11C-METHIONINE UPTAKE, IDH GENE MUTATION, AND MGMT PROMOTER METHYLATION IN PATIENTS WITH GRADE II AND III GLIOMAS Yoshiko Okita1, Tomoko Shofuda, Daisuke Kanematsu, Ema Yoshioka, Yoshinori Kodama, Masayuki Mano, Manabu Kinoshita1, Masahiro Nonaka, Toshiyuki Fujinaka, Yonehiro Kanemura; Department of Neurosurgery, Osaka International Cancer Institute, Osaka, Japan

AIM: We evaluated the association between 11C-methionine positron emission tomography (11C-methionine PET) findings, isocitrate dehydrogenase (IDH) gene mutation, and 5-methylcytosine DNA methyltransferase (MGMT) promoter methylation in patients with grade II and III gliomas. MATERIALS AND METHODS: Data were collected from 40 patients with grade II and III gliomas who underwent both magnetic resonance imaging (MRI) and 11C-methionine positron emission tomography (PET). Examiners were blinded to their pre-surgical examination. We examined IDH mutation through DNA sequencing, and MGMT promoter methylation through quantitative methylation-specific polymerase chain reaction (PCR). RESULTS: A threshold of MGMT promoter methylation of 1.0% was significantly associated with tumor/normal tissue (T/N) ratio. The T/N ratio in samples with MGMT promoter methylation ≥1.0% was higher than that in samples with MGMT promoter methylation <1.0%, and the difference was statistically significant (p = 0.011). Reliable prediction of MGMT promoter methylation (<1.0% vs ≥1.0%) was possible using the T/N ratio under the receiver operator characteristic (ROC) curve with a sensitivity and