Hideaki Yokoo, Yoshiki Mikami, Akitake Mukasa<sup>1</sup>; <sup>1</sup>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. Emergent laminoplasty 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 paidwarced diagnosis, to be found diffuse midline glioma, H3K27M mutant by immunohistopathological 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 clinical 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 Koriyama<sup>1</sup>, Masayuki Nitta<sup>1</sup>, Kenta Masui, Takashi Maruyama<sup>1</sup>, Taiichi Saito<sup>1</sup>, Takashi Komori,

Takashi Maruyama<sup>1</sup>, Taiichi Saito<sup>1</sup>, Takashi Komori, Yoshihiro Muragaki<sup>1</sup>, Takakazu Kawamata<sup>1</sup>; <sup>1</sup>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 specimens 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 Uchida<sup>1</sup>, Toshiaki Akahane, Nayuta Higa<sup>1</sup>, Mari Kirishima, Tsubasa Hiraki, Hajime Yonezawa<sup>1</sup>, Akihide Tanimoto, Koji Yoshimoto<sup>1</sup>; <sup>1</sup>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 astroctoma 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: KBT48 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, KBT48 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 POSITRON EMISSION TOMOGRAPHY FOR DISTINGUISHING THE GRADE OF GLIOMA Hiroaki Takei<sup>1</sup>, Etsuko Ohwashi<sup>1</sup>, Yuka Ikegame<sup>1</sup>, Yoshitaka Asano<sup>1</sup>, Jun Shinoda<sup>1</sup>, Kazuhiro Miwa, Takeshi Ito, Kazutoshi Yokoyama, Noriyuki Nakayama, Hirohito Yano, Sohko Ikuta, Takashi Maruyama, Yoshihiro Muragaki, Toru Iwama; <sup>1</sup>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 contrastenhanced 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 1/30 (3%) in grade 2, 8/43 (19%) in grade 3, and 26/30 (87%) 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 FDG, 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. CON-CLUSION: 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 <sup>11</sup>C-METHIONINE UPTAKE, IDH GENE MUTATION, AND MGMT PROMOTER METHYLATION IN PATIENTS WITH GRADE II AND III GLIOMAS

Yoshiko Okita<sup>1</sup>, Tomoko Shofuda, Daisuek Kanematsu, Ema Yoshioka, Yoshinori Kodama, Masayuki Mano, Manabu Kinoshita<sup>1</sup>, Masahiro Nonaka, Toshiyuki Fujinaka, Yonehiro Kanemura; <sup>1</sup>Department of Neurosurgery, Osaka International Cancer Institute, Osaka, Japan

AIM: We evaluated the association between <sup>11</sup>C-methionine positron emission tomography (<sup>11</sup>C-methionine PET) findings, isocitrate dehydrogenase (IDH) gene mutation, and O<sup>6</sup>-methylguanine-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 <sup>11</sup>C-methionine positron emission tomography (PET) as part of 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  $\geq$ 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  $\geq$ 1.0%) was possible using the T/N ratio under the receiver operator characteristic (ROC) curve with a sensitivity and