nosed oligodendroglioma tumors which are having molecular characteristics of astrocytoma. There is a trend that diagnosed grade II LrGGs are actually grade III based on re-assessment diagnosis.

Key words: Neuropathology | WHO2016 criteria | Molecular diagnosis

MPC-17

2021 WHO CLASSIFICATION OF TUMORS OF THE CNS, 5TH ED.

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The grading of gliomas based on histological features has been a subject of debate for several decades. While the traditional grading system has failed to stratify the risk of IDH-mutant astrocytoma, canonical histological and proliferative markers may be applicable to the risk stratification of IDH-wildtype astrocytoma. Numerous studies have examined molecular markers to obtain more clinically relevant information that will improve the risk stratification of gliomas. The CDKN2A/B homozygous deletion for IDH-mutant astrocytoma and the following three criteria for IDH-wildtype astrocytoma: the concurrent gain of whole chromosome 7 and loss of whole chromosome 10, TERT promoter mutations, and EGFR amplification, were identified as independent molecular markers of the worst clinical outcomes. Therefore, the 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System adopted these molecular markers into the revised grading criteria of IDH-mutant and -wildtype astrocytoma respectively, as a grading system within tumor types. For diffuse gliomas in children, molecular alteration-based classification was adopted, dividing low-grade and high-grade subcategories. New tumor types and subtypes were introduced, some based on DNA methylation profiling. To achieve this novel classification in a resource-limited setting, an integrated diagnosis combining clinical, histological, and molecular information became more important.

Key words: WHO classification | genetics | patholgy

NEUROIMAGING (NI)

NI-2

USE OF NEURITE ORIENTATION DISPERSION AND DENSITY IMAGING(NODDI)FOR EARLY DISTINCTION BETWEEN INFILTRATING TUMOR AND VASOGENIC EDEMA IN NON-ENHANCING LESIONS WITH GLIOBLASTOMA PATIENTS

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Background: Glioblastoma is a highly infiltrative tumor. In the non-enhancing T2-weighted hyperintense area, differentiating between non-enhancing tumors (NETs) and vasogenic edema is challenging. Neurite orientation dispersion and density imaging (NODDI) is a new diffusion MRI technique that reveals the inhomogeneity of the brain microstructure. The aim of this study is to differentiate between NETs and edema in glioblastomas using NODDI. Methods: Data were collected from 20 patients with glioblastoma as well as three patients with metastasis and two with meningioma (control), who underwent MRI as part of pre-surgical examination. The MRI data included T2- and T1-weighted contrast-enhanced images and NODDI images. Three neurosurgeons manually placed the volume of interest (VOI) on the NETs and edema based on the previous reports. ICVF, ODI, ISOVF, FA, and ADC were calculated for each VOI. Results: Fifteen and 13 VOIs were placed on NETs and edema, respectively. Each parameter was measured and the unpaired t-test revealed a significant difference between NETs and edema ($p < 0.0001$). The ROC curve analysis revealed a large difference in the ADC, FA, and ISOVF between NETs and edema compared to ICVF and ODI. Principal component analysis of the five parameters showed that ADC, ISOVF, and FA contributed to the differentiation between NETs and edema. Multiple logistic regression analysis was performed with the three aforementioned parameters. A predictive formula could be created to discriminate between NETs and edema, following the use of which, the ROC curve revealed an AUC value of 0.8891. Furthermore, this formula was applied to the edematous regions of the images of the negative control group, and the prediction degree of the tumor was well below 0.5, thus enabling differentiation as edema.Conclusions: NODDI may prove to be a useful tool to discriminate between NETs and edema in the non-contrast T2 hyperintensity region of glioblastoma.

Key words: glioblastoma | non-enhancing tumor | NODDI

NI-3

MAGNETIC RESONANCE RELAXOMETRY FOR TUMOR CELL DENSITY IMAGING FOR GLIOMA: AN EXPLORATORY STUDY VIA 11C-METHIONINE PET AND ITS VALIDATION VIA STEREOTACTIC TISSUE SAMPLING

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Objective: While visualization of non-enhancing tumors for glioma is crucial for planning the most appropriate surgical or non-surgical treatment of the disease, current MRI cannot achieve this goal. This study aims to test the hypothesis that quantitative and diffusion MRI can estimate tumor burden with the brain. Materials and Methods: Study 1: Ten patients who have undergone Methionine PET (Met-PET), quantitative MRI (qMRI), and diffusion MRI (DWI) were included for analysis. A cut-off of a tumor-to-normal ratio (T/Nr) 1.5 was set on Met-PET, and the values from qMRI and DWI were compared. Study 2: Seventy-nine stereo-tactically sampled tissues from 22 glioma patients were correlated with Met-PET, qMRI, and DWI measurements regarding tumor cell density. qMRI acquisition: Imaging was performed on either a 1.5 or 3 T MR scanner (Prisma or Aera; Siemens Healthcare, Erlangen, Germany). T1-relaxometry was achieved by first acquiring MP2RAGE images, then converting those images into T1-relaxation time maps. At the same time, T2-relaxometry was achieved by first acquiring multi-echo T2-weighted images and then converting those images into T2-relaxation time maps, with both relaxometries performed via Bayesian inference modeling (Olea Nova+; Canon Medical Systems, Tochigi, Japan). **Results:** Study 1 revealed that regions of 1850ms < T1-relaxation time < 3200ms and 115ms < T2-relaxation time < 225ms tended to be Met-PET T/Nr > 1.5. DWI was not useful to separate areas between low and high Met-PET. Study 2 showed that regions of 1850ms < T1-relaxation time < 3200ms showed high tumor cell density than other areas ($p=0.04$). **Conclusions:** Our results supported the hypothesis that qMRI is useful for predicting the tumor load within the brain among glioma patients. T1-relaxation time was notably useful for this means. On the other hand, ADC measured from DWI was limited for tumor load prediction.

Key words: glioma | MRI | tumor cell density

NI-6

PREOPERATIVE DIFFERENTIAL DIAGNOSIS OF GRADE II AND GRADE III IN CASES WITH ASTROCYTOMA, IDH MUTANT

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Purpose: We attempted to differentiate between IDH-mutant astrocytoma Grade II and grade III by using methionine (MET) positron emission tomography (PET) and magnetic resonance spectroscopy (MRS). Subjects and Methods: We retrospectively analyzed 41 adult supratentorial glioma cases with confirmed histological diagnosis and IDH status from June 2015 to June 2020. These included 21 males, with an average age of 38.5 years (19–59 years), including seven astrocytoma grade II (A-II) and 34 grade III (A-III) cases. We determined the accumulation value rate of the maximum tumor to normal cortex accumulation value (T/N ratio) in MET-PET. We obtained the peak ratios of N-acetyl aspartate (NAA)/ creatine (Cr), choline (Cho)/ Cr, and Cho/NAA. We investigated the correlation between the T/N ratios and MRS parameters and examined the contrast effects on MRI. Results: There were no significant differences in the T/N ratio and MRS parameters between A-IIs and A-IIIs. Only Cho/NAA ratios were significantly correlated with the T/N ratios ($r = 0.443$, $P = 0.0037$). We divided the distribution map into four areas with the highest T/N ratio of AII (1.59) and the highest Cho/NAA ratio (3.66). That is, 1) T/N ratio ≤ 1.59 & Cho/NAA ≤ 3.66,

2) >1.59 & ≤ 3.66, 3) ≤1.59 & > 3.66, 4) &gt 1.59 & &gt 3.66. The diagnostic rates for A-III were 1) 61.1% (11/18), 2) 100% (7/7), 3) 100% (9/9), and 4) 100% (7/7). We found the contrast effects in only 7 cases (20.6%) of A-III, which were distributed in areas 2) to 4). Conclusion: A-IIs and A-IIIs distributed in area 1) were difficult to distinguish, and they need careful observation as a step before the transition to areas 2)-4). Meanwhile, A-IIIs reaching widespread distribution to areas 2)-4) because of their wide range of malignancies require clinically aggressive treatment. The method might be beneficial in grade analysis of IDH-mutant astrocytomas.

Key words: glioma | methionine PET | MRS

NI-7

DIFFUSION-WEIGHTED IMAGING FOR MONITORING ACUTE RESPONSE AND RECURRENCE AFTER PHOTODYNAMIC THERAPY IN MALIGNANT GLIOMAS

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Background: Photodynamic therapy (PDT) subsequent to surgical tumor removal is a novel light-activated localized treatment for malignant glioma. Although PDT provides effective local control, even PDT cannot completely suppress local recurrence of malignant glioma. We previously reported that the acute response of malignant glioma to PDT could be detected as linear hyperintense signals on diffusion-weighted imaging (DWI) and a decline in apparent diffusion coefficient (ADC) values that were asymptomatic and transient. However, their long-term clinical significance has not yet been examined. This study aimed to clarify the link between the hyperintense signal on DWI as an acute response and recurrence after PDT in malignant glioma. **Methods:** Thirty consecutive patients (16 men, 14 women; median age 60.5 years) underwent PDT for malignant glioma at our institution between 2017 and 2020. We analyzed signal changes on DWI after PDT and the link between these findings and the recurrence pattern. **Results:** In all patients, linear hyperintense signals of 5–7 mm on DWI were detected at the surface of the resected cavity from day 1 after PDT. These changes matched the PDT-irradiated area and disappeared in about 30 days without any neurological deterioration. Of the 30 patients, 19 (63%) exhibited recurrence: local recurrence in 10 (33%), distant recurrence in 1 (3%), and dissemination in 8 (27%). All local recurrences arose from areas that did not show a hyperintense signal on DWI obtained on day 1 after PDT. Patients with distant recurrence or dissemination tended to have uninterrupted hyperintense signal on DWI obtained on day 1 after PDT. **Conclusion:** The local recurrence in malignant glioma after PDT occurred in the areas without hyperintense signal on DWI as the acute response to PDT. This characteristic finding could aid in the monitoring of not only PDT-irradiated area but also local recurrence site after PDT.

Key words: Glioma | Photodynamic therapy | Diffusion-weighted imaging

NI-8

MOLECULAR DIAGNOSTIC PREDICTION COMBINING T2-FLAIR MISMATCH SIGN, CALCIFICATION, AND METHIONINE PET IN GRADE II AND III GLIOMAS

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Background: The 2016 WHO Classification classified grade II and III gliomas into three molecular subtypes depending on the presence of IDH mutation and 1p/19q codeletion. We combined T2-FLAIR mismatch sign, tumor calcification, and methionine PET uptake to examine whether molecular diagnosis could be predicted. Methods: 53 grade II and III glioma patients with preoperative MRI, CT, and MET-PET who underwent surgical resection or biopsy during 2000–2019 were included in this study. Out of the 53 cases, astrocytic tumors (A group: IDH-mutant, 1p19q non-codeleted) were 17, oligodendroglial tumors (O group: IDH-mutant, 1p19q codeleted) were 15, and IDH wild tumors (W group) were 21. MR and CT scans were evaluated by 3 independent reviewers to assess presence/absence of T2-FLAIR mismatch sign and calcification in the tumor, respectively. 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. Results: Out of the 53 cases, T2-FLAIR mismatch sign was present in 6 cases in group A and 9 cases in group W (p=0.008). Calcification in tumor was present in 2 cases in group A, 7 cases in group O, and 3 cases in group W (p=0.046). In the T2-FLAIR mismatch-positive cases, assuming MET-PET T/N>1.401 was group W and <1.401 was group A, sensitivity was 100% and specificity was 67%. In the T2-FLAIR mismatch-negative and calcification-positive cases, assuming those group O, the diagnostic predictive value was 70%. In the T2-FLAIR mismatch-negative and calcification-negative cases, assuming MET-PET T/N>2.349 was group W and <2.349 was group A or O, sensitivity was 60% and specificity was 94%. Conclusions: Combined diagnostic prediction of T2-FLAIR mismatch, calcification, and MET-PET T/N may be useful for preoperative molecular diagnosis of grade II and III gliomas.

Key words: T2-FLAIR mismatch | methionine PET | glioma

NI-10

RECLASSIFICATION OF DIFFUSE GLIOMAS BASED ON MOLECULAR DIAGNOSIS -EVALUATION OF METHIONINE UPTAKE AND TREATMENT OUTCOME-

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Object: The revised 2016 WHO Classification of Tumours of the Central Nervous System incorporates genetic alterations into the classification system, with the goal of creating more homogenous disease categories with greater prognostic value. In this study, we reclassified diffuse gliomas with molecular diagnosis and examined for 11C-methionine uptake and prognosis. Methods. 182 diffuse glioma patients (Grade II in 42 patients, Grade III in 61 patients, Grade IV in 77 patients) treated at Tokyo Medical and Dental University Hospital from 2000 to 2018 were included in this study. The IDH1/2, ATRX and 1p19q status were analyzed using tumor samples. The tumor-to-normal ratio (T/N) of 11 C-methionine uptake was calculated by dividing the mean standardized uptake value (SUV) for the tumor by the mean SUV of the normal brain. Result. By molecular diagnosis, 11 diffuse astrocytomas and 17 anaplastic astrocytomas were diagnosed as “IDH-mutant”, while 14 diffuse astrocytomas and 29 anaplastic astrocytomas were diagnosed as “IDH-wild”. 5 out of 77 grade IV tumors had IDH mutation. 4 tumors were diagnosed as “Diffuse midline glioma, H3 K27M-mutant”. In the 32 oligodendroglial tumors, 12 oligodendrogliomas and 9 anaplastic oligodendrogliomas were diagnosed as “IDH-mutant and 1p/19q-codeleted”. The median T/N ratios in oligodendroglial tumors with “IDH-mutant and 1p/19q-codeleted” were significantly higher than those in astrocytic tumors with “IDH-mutant”. On the other hand, in tumors with the same genetic background, higher grade tumor has significant higher T/N ratio. Kaplan-Meier survival analysis revealed that oligodendroglial tumors with “IDH-mutant and 1p/19q-codeleted” had significantly better outcomes regardless of WHO grade. Overall survival was 90.9% at 5 years and 77.9% at 10 years in oligodendroglial tumors with “IDH-mutant and 1p/19q-codeleted”. IDH wild tumors had significantly worse outcomes.Conclusions. The results indicated that diffuse glioma categories reclassified with molecular classification correlate with the T/N ratio of methionine and the prognosis.

Key words: glioma | methionine-PET | molecular diagnosis

NI-11

USEFULNESS OF THE MAGNETIC RESONANCE IMAGING ARTERIAL SPIN LABELING METHOD FOR DIAGNOSING POSTERIOR FOSSA HEMANGIOBLASTOMA

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Purpose: It is sometimes challenging to diagnose hemangioblastoma by MRI when the tumor is a solid mass in the posterior fossa. We therefore evaluated perfusion images and diffusion-weighted images to diagnose hemangioblastoma in order to obtain the most useful quantitative features. Methods: Thirty-one posterior fossa tumors whose pathological diagnosis was confirmed by surgery were included in groups A (12 hemangioblastomas) and B (non-hemangioblastoma 19 cases: metastatic tumor 6 cases, pilocytic astrocytoma 3 cases, malignant lymphoma 3 cases, glioblastoma 2 cases, medulloblastoma 2 cases, and other 3 cases). All cases were imaged by 3.0-Tesla MRI, with the apparent diffusion coefficient (ADC) on diffusion-weighted imaging as the parameter, arterial spin labeling (ASL) as the relative value from the CBF map to the region of interest (ROI) in the contralateral hemisphere as perfusion image, dynamic susceptibility contrast (DSC) as rCBF, rCBV, corrected CBV, and K2. The ROI was set to match the contrast-enhanced part, and the two groups were compared and examined. Results: The relative ASL value of group A and the