RT-06

PLANNING OF BORON NEUTRON CAPTURE THERAPY (BNCT) USING POSITRON EMISSION TOMOGRAPHY (PET)

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Boron neutron capture therapy (BNCT) is the particle irradiation therapy that the selective radiation for tumor cells is available for theoretically. The role that the amino acid (phenylalanine) PET (18F-BPA-PET) that we used boronophenylalanine (BPA) which is a boron compound for neutron capture reaction as a tracer carries out is major in our BNCT especially for the recent non-craniotomy BNCT, and it covers by treatment, observation from indication. In this report, we introduce this PET as a principal axis about BNCT and a relation of the PET.In our BNCT, we calculated the drug accumulation to the tumor from BPA-PET before neutron irradiation and reflected it for individual treatment. We become able to decide indication of BNCT by using this PET study, and the indication expansion to other systemic cancers including head and neck cancer and lung, liver is now worked on actively. Also, in other irradiation modalities, they make a radiation plan based on PET study, and several reports to try the improvement of results had been present, however, high radiation doses will be " exposed " to the lesion showing high accumulation in BPA-PET in BNCT. We determine the neutron exposure time from the dosage for the normal tissue in the actual treatment, but the Lesion / Normal tissue ratio obtained from BPA-PET is reflected by the evaluation of the tumor dose and the following treatment plan. Also, after the treatment, diagnoses of the pathologic condition such as an increase in tumor volume, a recurrence or the radiation necrosis might be difficult, and we found that the PET study was useful in the follow-up stage for the patients with already treated malignant brain tumor.

MOLECULAR PATHOLOGY/CLASSIFICATION (MPC)

MPC-01

PROGNOSTIC ROLE OF TERT PROMOTER IMPROVES THE STRATIFICATION OF IDH-MUTATED LOWER GRADE GLIOMA.

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TERT promoter mutation is associated with favorable prognosis and 1p/19q codeletion in IDH-mutated gliomas. The current diagnostic system, however, did not incorporate this change as a diagnostic marker in this entity. We investigated the value of prognostication incorporating TERT using the Japanese original cohort of 560 IDH-mutated adult gliomas. We collected the information of molecular status of IDH, TERT and 1p/19q and patient clinical data including Karnofsky performance status (KPS). TERT mutation and 1p/19q codeletion were found in 303 and 285 cases, respectively. For the purpose of this study, the patient cohort was divided into four groups by a combination of 1p/19q and TERT status, and the characteristics of 1p/19q intact-TERT mutated group (Astro-TERT group) (n=24) were dissected in light of the differences comparing with 1p/19q intact-TERT wild (Astro-group, n=251) or 1p/19q codeleted-TERT mutated (Oligo-group, n=279) cases. Astro-TERT group with any grade showed intermediate overall survival between the Oligo-group and Astro-group although the survival differences were not statistically significant (median OS: not reached (NR) versus NR, and 106 months, respectively. p>0.05). In grade II-III gliomas, the survival curve of the Astro-TERT group overlapped with that of the Oligo-group while the Astro-TERT group showed short survival as well as the Astro-group. We further conducted subgroup analysis by adjusting KPS in grade II-III tumors. In the subgroup with favorable KPS (90–100) and gradeII-III (n=438), The OS of Astro-TERT group (median NR) was significantly longer survival than that of Astro-group (median NR p=0.032), and was comparable with that of the Oligo-group (median NR, p>0.05). Thus, TERT promoter status provides the additional information for prognostication at least in grade II-III gliomas in the current diagnostic system.

MPC-02

REVIEW OF MEDULLOBLASTOMA FOR THE ASSESSMENT OF CONSENSUS IN PATHOLOGICAL DIAGNOSIS USING JPMNG CASES

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Medulloblastoma (MB) is now classified by WHO 2016 classification as "genetically defined" and "histologically defined" variants. The aim of this

study is to search for consensus on pathological diagnosis and assess the correlation between the central pathological diagnosis and the molecular subgrouping. We performed the pathological and molecular analyses in a total of 176 JPMNG (The Japan Pediatric Molecular Neuro-Oncology Group) cases. The diagnosis of MB was made by three expert neuropathologists (AS, JH, and TH) without knowledge of the molecular data. Subgroup affiliation was determined by expression profiling of 22 medulloblastoma subgroup-specific genes using the nanoString nCounter system. Histologically, classic MBL accounted for approximately 80% of all MB cases. Genetic analyses of 176 cases revealed four distinct molecular subgroups: WNT (14%), SHH (27%), group 3 (16%), and group 4 (43%). The central review reached a diagnosis of AT/RT for 3 cases that had been diagnosed as MB by the local pathologists. Immunohistochemically, WNT MBs showed nuclear accumulation of β-catenin protein, but the immunoreactivity was patchy in approximately one-quarter of WNT cases. GAB1 often exhibited little or no reactivity in the SHH subgroup. No reliable staining was observed for YAP1. All D/N MBL (16 cases) or MBEN (6 cases) were defined as SHH tumors. All MBEN cases were in infants (<3 years of age), and genetically subdivided into SHH-TP53 wild-type tumors. Variable degrees of anaplasia, including LC/A MB, occur across the genetic subgroups, and the LC/A MB WNT type was rare (2/24=8.3%) among WNT subgroups. This study demonstrated that the combination of morphological and molecular analyses can precisely diagnose MB. More robust, surrogate markers should be developed as ancillary diagnostic testing for subgroup classification. Further exploration of the clinical significance of the variable degree of LC/A histology and some subtypes (i.e. LC/A, WNT) will be necessary for risk stratification.

MPC-03

IMMUNOHISTOCHEMICAL ANALYSIS OF TUMOR ASSOCIATED MACROPHAGE INDUCED AFTER BIODEGRADABLE CARMUSTINE WAFER IMPLANTATION IN HUMAN GLIOBLASTOMA

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The carmustine (BCNU) wafer, a biodegradable polymer, currently is the only drug that is able to be placed at the surgical site to treat malignant tumors. Biomaterials to treat cancers hold therapeutic potential; however, how they behave inside the tumor microenvironment requires further study. We previously investigated the tumor microenvironment after BCNU wafer implantation, and found that CD68-positive macrophage was significantly introduced around the wafer (Shibahara et al. J Neurooncol 2018). Recent studies demonstrated the importance of tumor-associated macrophage (TAM). However, we could not clarify whether the increased macrophage around the wafer was pro-tumor or anti-tumor phenotype. In the present study, we immunohistochemically examined expressions of CD68, IBA1, CD163, TMEM119, BIN1, CD31, and VEGF to investigate TAM after the wafer implantation. Quantitative evaluation revealed that CD68-positive cells were significantly increased (P = 0.0009), whereas TMEM119-positive cells were significantly decreased (P = 0.0081) after wafer implantation compared to tissue from cases without wafer implantation. CD163, a known marker of poor prognosis in glioblastoma, did not differ with and without wafer implantation. Among factor analyzed, BCNU wafer did not induce protumor TAM, but reduced microglial marker, TMEM119. In addition to the aspect of chemotherapy, BCNU wafer may have potential to modify the tumor microenvironment such as TAM.

MPC-04

MOLECULAR FEATURES AND CLINICAL OUTCOMES OF ELDERLY GLIOBLASTOMA PATIENTS: ANALYSES OF KANSAI NETWORK AND TCGA COHORTS

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INTRODUCTION: Aging is a negative prognostic factor in glioblastoma (GB) and the genetic background in clinical outcome of elderly GB could exist. This study investigates the difference of elderly patients from younger ones regarding molecular characteristics as well as clinical outcomes in IDH-wildtype GB. METHODS: We collected adult cases diagnosed with IDH-wildtype GB and enrolled in Kansai Molecular Diagnosis Network for CNS Tumors (Kansai Network) (212 cases) and The Cancer Genome Atlas (TCGA) project (359 cases). Clinical and pathological characteristics were analyzed retrospectively and compared between elderly cases (≥70 years) and younger ones (≤50 years). Molecular analysis included copy number alterations (CNAs) of eight genes (EGFR, PDGFRA, PTEN, CDKN2A, CDK4, MDM2, TP53, NFKBIA). RESULTS: Included in the study were 92