Abstracts

Key words: LEAT, epilepsy surgery, focal resection

AS2-2
NEUROCOGNITIVE AND PSYCHOSOCIAL DISORDERS IN CHILDREN WITH BRAIN TUMORS
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The survival rate of children with brain tumors has been improving in the recent times. However, treatment outcomes should also include improved functional prognosis, considering motor dysfunction and sensory disorders, such as vision, and neurocognitive and psychosocial disorders, such as impaired intelligence, memory disorders, impaired attention, and impaired social behavior. In children with brain tumors, neurocognitive and psychosocial disorders easily occur due to various factors such as effect of the tumor, complications such as hydrocephalus, and impact of surgical treatment or radiotherapy. In addition, neurocognitive and psychosocial disorders are associated with decreasing quality of life (QoL) of pediatric patients with brain tumors.

When assessing neurocognitive and psychosocial disorders, objective assessments such as a neuropsychological assessment that includes an academic achievement test and an intelligence test, and subjective assessments such as observing behaviors need to be included. However, limited pediatric neuropsychological tests available in Japan.

Little evidence is available on the direct intervention methods that aim to improve neurocognitive and psychosocial disorders. Medical management for epilepsy, hydrocephalus, and endocrine disorders is performed while carefully considering cognitive function even in patients with neurocognitive and psychosocial disorders. Patients’ symptoms and QoL can be improved through cognitive rehabilitation, environmental adjustments such as an intervention in their educational environment, and family support. To integrate these medical and social models, a multidisciplinary team approach is required.

There is limited data on the assessment and intervention methods available for neurocognitive and psychosocial disorders of children with brain tumors. Currently, only a few facilities are equipped to provide expert treatment. The Neuropsychological Assessment Subcommittee (Brain Tumor Committee, the Japanese Children’s Cancer Group (JCCG)) aims to standardize the evaluation of neurocognitive and psychosocial disorders and intervention methods. These will be presented in line with the medical care provided at our hospital.

Key words: neurocognitive and psychosocial disorder, brain tumor, child

MS1
TOWARD ESTABLISHMENT OF ROUTINE MOLECULAR DIAGNOSTICS FOR ADULT GLIOMAS UNDER THE NATIONAL HEALTH INSURANCE
Kosichi Ichimura; Division of Brain Tumor Translational Research, National Cancer Center Japan

Molecular diagnosis is now an official part of the diagnosis of brain tumors. Since WHO 2016 incorporated the status of IDH mutation and 1p/19q codeletion as a part of the definition for oligodendrogliomas, astrocytomas, and glioblastomas, molecular tests have become an essential part of the clinical management of adult gliomas. However, these tests are not covered by the National Health Insurance in Japan, and the cost and the limited availability of tests are prohibitive to perform molecular tests in most hospitals where brain tumor patients are treated. In 2015, the Committee for Molecular Diagnosis of Brain Tumor was established within the Japan Society for Neuro-Oncology in order to develop a standardized molecular tests for adult gliomas under the National Health Insurance. For the detection of 1p/19q codeletion, FISH is the most commonly used method. However, the widely available commercial FISH probe is located within 1p36, the region where partial deletion often occurs in glioblastoma. This could lead to misjudgement of 1p/19q codeletion which may result in miss-diagnosis. We have designed a novel FISH probes located in the region of 1p and 19q where partial deletions are rarely found, and are developing them as an in vitro diagnostic tests. Our ultimate aim is to establish a standardized molecular tests for adult gliomas under the National Health Insurance.

Key words: IDH mutation; 1p/19q codeletion; in vitro diagnostics

MS2
BRAIN TUMORS AND EPILEPSY
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A brain tumor is one of the major causes of epilepsy, and glioma patients frequently exhibit seizures. Epileptic seizure, one of the features of glioma, is also known to be correlated with better outcome of patients. One of the reasons why patients with seizures have a good prognosis is that oligodendrogial tumors tend to cause epilepsy. However, even if limited to glioblastomas, the prognosis with epilepsy is still better than the others.

Recently, the association between IDH mutations and epilepsy has been reported. IDH is an enzyme which converts isocitrate to alpha-ketoglutarate, but when this enzyme is mutated, 2-hydroxyglutarate (2HG) is produced instead of alpha-ketoglutarate. The molecular structure of 2HG is similar to glutamate, and it had been also reported that 2HG binds to the NMDA receptor. Indeed, in our cases, the IDH-mutation rate was higher in cases with epilepsy than the others. From our study of gene expression profiles, it was also clarified that the expressions of neuron-related genes were higher in cases with epileptic seizures, suggesting that many tumors classified as pro-neural type were included in this subset. As described, epilepsy phenotype is important, even in daily practice, because it predict the molecular status of gliomas and estimates the prognosis of the patients.

On the other hand, control of the seizures is important to keep patients’ QoL and to provide effective treatment. In this seminar, the control of epilepsy during and early after surgery, and how to manage status epilepticus will be reviewed.

Key words: LEAT, epilepsy surgery, focal resection

SS1-KL-1
APPLICATION OF AI TECHNOLOGIES FOR MEDICAL CARE
Ryuji Hamamoto; Division of Molecular Modification and Cancer Biology, National Cancer Center Research Institute, Japan

On the basis of progress of the Machine Learning algorithm mainly on the Deep Learning, improvement of the GPU performance, the large-scale public database such as TCGA is available, big attention recently gathers in the AI technology. While large countries such as the United States or China vigorously promote AI research and development by a national policy, Cabinet Office, Government of Japan, also emphasized the importance of AI technologies in the 5th Science and Technology Basic Plan in 2016. As for the AI development, it is wrestled relatively for a long time; the word “Artificial Intelligence” was firstly used in the Dartmouth workshop in 1956. However, the AI development has not been promoted smoothly until now and repeats the active state period and the period of depression. As the current active state period of AI is called as the third AI boom, the most different point of this boom and the other booms is that AI technologies have already been involved in our social life such as the AI-based face authentication device in this period.

Indeed, The US Food and Drug Administration (FDA) has already authorized around 30 AI-based medical instruments, and the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan also authorized the first AI-based medical instrument last year. Therefore, now is the important time that we need to consider deeply for the creation of an affluent society, which enables coexistence of human being and AI. In this lecture, I particularly focus on medical imaging analysis using AI technologies and, would like to lecture on an action to the medical care application of the AI technology based on the experience that promoted medical AI research as the leader of two national projects relevant to medical AI called CREST and PRISM, and RIKEN AIP center.

Key words: AI, deep learning, medical image analysis

LS2
ADVANCES IN MOLECULAR BIOLOGY AND GENETICS IN GLIOMA RESEARCH AND THERAPY
Webster K. Cavenee; Ludwig Institute for Cancer Research, University of California San Diego

The most recent version of the WHO Classification of Tumours of the Central Nervous System includes, for the first time, the joint consideration of tumor pathology with tumor genetics as measured in various ways. This has come decades after the first recognition of genetic lesions in tumor genomes as discerned by cytogenetics and more than 30 years after the first reports of specific and recurrent genetic abnormalities in human tumors, particularly gliomas. This information is vitally important because it is now being used not just for tumor diagnosis but also to indicate specific therapies. In this lecture, I will review the increasingly precise methodologies being employed, the resultant genetic lesions being uncovered and the increasing import of such information for therapeutic selection.

Key words: Glioblastoma Genetics Characterization

LS2
METASTATIC BRAIN TUMORS / MENINGOMAS: CURRENT CONCEPTS AND THERAPEUTIC PERSPECTIVES
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Non-glial brain tumors are the most common neoplasms affecting the central nervous system. Brain metastases are a heterogenous complication of
systemic cancers. Recent research has provided insight into some important aspects of brain metastasis development, interaction of brain-metastatic tumor cells with resident cells of the CNS microenvironment and growth patterns within the brain parenchyma. Treatment choices have to consider clinical presentation, number, size and localisation of brain metastases, status of extracranial tumor burden, prior therapies, co-morbidities and histological and molecular tumor characteristics. Recent advances show that targeted therapies against established brain metastases and some targeted therapies are able to prevent brain metastasis development. Meningiomas are common and can be cured in 70–80% of cases by surgical resection. However, the rest of cases cannot be resected completely due to surgically inaccessibility (e.g. skull base) or show non-benign histopathological features that are associated with tumor recurrence. Meningiomas have been shown to be molecularly variable and carry distinct and recurrent genetic and epigenetic alterations that seem to enable targeted therapy and refined prognostication. Overall, significant advances in the biological understanding of brain metastases and meningiomas drive clinical trial design and improvement of clinical management strategies for these common tumors.

**Key words:** brain metastasis, meningioma, targeted therapy, immunotherapy

**SD52**

CHALLENGES IN TREATMENT OF GliOBLASTOMA: CURRENT CONCEPTS AND THERAPEUTIC PERSPECTIVES

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The natural disease course in glioblastoma is grim, in adults as well as in children. To date, there are no options for primary, secondary or tertiary prevention. However, unlike the fatalistic approach generally taken, there are subgroups of patients or individuals clearly benefitting over a variable time from current treatments, radiation and alkylating chemotherapy, as well as experimental precision or immune interventions. This heterogeneity in treatment response reflects the biological heterogeneity of the disease, which needs to be addressed in current preclinical and clinical investigations as well as this identifies primary and acquired treatment resistance as the key challenge in the field of glioblastoma. Importantly, even for most conventional treatments the basic molecular mechanisms for primary or secondary resistance are unknown or incompletely understood.

The present view is that progress will be made with a more precise classification and grouping of glioblastoma. The methylation subgroups clearly provide a first step, but further tumor bulk but potentially also subclonal or single-cell analyses might provide further insights and will be a prerequisite to meaningfully interpretable trials.

Novel preclinical and translational concepts of glioblastoma in adults reflecting the proposed network architecture of the glioma, but also the glioma-brain interface may for the first time separate options for trial interventions in glioblastoma form the usual mainstream in oncology.

Clinical trials of the past years have revealed the potential for further development of novel therapies. Primary or secondary loss-of-glioma-methylation (O6-methylguanine DNA-methyltransferase (MGMT) promoter hypermethylated glioblastomas and allow leaving out temozolomide for glioblastoma harboring an unmethylated MGMT promoter. The latter is not clinical standard, however we should at some point make sure we still understand, why temozolomide is provided in this clinical situation and how we make a next step.

The field of immunoncology is rapidly growing with preclinical work and trial concepts, but whereas patients with brain metastases seem to benefit from this development, success in glioblastoma is restricted to uncontrolled early-phase developments.

**Key words:** Brain tumor networks, Molecular targeted Therapy, Neoantigens

**MS3-1**

IMPLEMENTATION OF GENE PANEL TESTING USING NEXT-GENERATION SEQUENCING

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The advance of next-generation sequencers (NGS) has dramatically improved the performance of genomic analysis of clinical samples in cancer precision medicine. The practical use of gene panel testing for clinical applications has begun in Japan. At present, “OncomineTM Dx Target Test” is listed as a companion diagnostic system using NGS, and “FoundationOne CDx Cancer Genomic Profile” and “OncoGuide™ NCC Oncopanel System” are listed as gene panel testing under insurance coverage. Formalin-fixed paraffin-embedded specimen have been routinely used for molecular diagnostics testing, therefore quality control such as formalin fixation time and tumor contents is important to ensure validity of diagnostic results. In this presentation, the issue to obtain evaluable results of gene panel testing using formalin-fixed paraffin-embedded specimen will be discussed.

Due to evolution of detection technologies, we can detect gene mutation with high sensitivity. Detection of gene mutation in circulating tumor DNA is feasible approach for diagnostic testing in cancer treatment. Liquid biopsy has been approved as a companion diagnostic testing to detect actionable mutations in NSCLC. Examples of the clinical utility of plasma testing in cancer treatment will be presented.

**MS3-2**

TREATMENT STRATEGY BASED ON THE RESULTS OF GENE PANELS

Masayuki Takeda; Department of Medical Oncology, Kindai University, Faculty of Medicine

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**EL1**

BUILDING A CAREER IN NEURO-ONCOLOGY RESEARCH

Webster K. Cavenee; Ludwig Institute for Cancer Research, University of California San Diego

A young neurosurgeon has several interesting and important possible career paths: clinical care, clinical/translational research and more fundamental research. Each of these has its own requirements for training, talent and commitment. A closer inspection of each of these, however, reveals that they are basically quite similar. From this, several general conclusions can be gleaned and recommendations for optimizing the chances of long-term career success. In this short talk, I will review the aspects of our training program that has allowed each of our Japanese trainees to have remarkable success both while with us in the US and upon their return to Japan. My goal is to explicitly describe and state these as a roadmap for success, particularly in the rapidly developing field involving the application of molecular and genetic technologies to translational and basic neuro-oncology research—but also as more generally applicable principles.

**Key words:** career, research, training

**SKL-1**

UPDATE OF WHO2016 CLASSIFICATION OF ADULT DIFFUSE Gliomas

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The World Health Organization (WHO) central nervous system (CNS) tumor classification has represented the primary source of diagnosis and grading criteria of brain tumors. Nonetheless, recent advances of studies on their molecular alterations require more rapid update of recommendations for classification practice. To accomplish this, (c)IMPACT-NOW (the International Working Group to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy) was established in 2016 and has published four updates. For adult gliomas, update 1 clarified the use of the term NOS (Not Otherwise Specified) and proposed a new term NEC (Not Elsewhere Classified); update 2 revised classifications regarding diffuse astrocytoma/anaplastic astrocytoma, IDH-mutant; update 3 proposed molecular criteria for an IDH-wildtype diffuse or anaplastic astrocytic glioma without histological features of glioblastoma, which would behave similarly to a grade IV glioblastoma. Nonetheless, no consensus on pathologic or molecular markers that could be incorporated into a more clinically relevant grading scheme for IDH-mutant gliomas has been reached. The molecular alterations previously studied using relatively large cohorts include CDKN2A/B homozygous deletion, CDK4 amplification, R1I mutations/homoyzogous deletion, PIK3CA or PIK3R1 mutations, PDGFRA amplification, NMYC amplification, global hypomethylation, genomic instability and chromosome 14 loss. The proliferative activity, based on the mitotic count or Ki67 indices, and other morphologic features typical of a high grade that