Abstracts

INVITED LECTURES

II-1 SRS WITHOUT THE BUNKER: INTRODUCTION AND CLINICAL EXPERIENCE OF ZAP-X GYROSCOPIC RADIOSURGERY
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Each year more than two million patients worldwide are potential candidates for SRS, yet due to the significant costs and complexities of historical delivery systems, only 150,000 patients currently receive such treatment. Japan Shionogi cleared in 2020, ZAP Surgical’s ZAP-X Gyroscopic Radiosurgery platform was designed to solve this challenge, and ultimately bring world-class SRS to more patients in more places. ZAP-X is recognized for being the first and only vault-free SRS delivery system to reduce unnecessary radiotherapy shielding and treatment times. Modern electronic linear acelerator with robotic gatways and built-in motion tracking systems allows ZAP-X to produce radiation, which is also the first and only dedicated radiosurgery system to no longer require Cobalt-60 radioactive sources, thereby eliminating the significant costs to license, secure, and regularly replace large radioactive isotopes.

Built on a distinctive dual-gimbaled gantry design, the ZAP-X system uses gyroscopic mobility to direct radiosurgical beams from hundreds of unique angles to precisely concentrate radiation on the tumor target. This pioneering approach supports the clinical objective of protecting healthy brain tissue and patient neuro-cognitive function, as well as enable future potential SRS re-treatments without the unnecessary risks associated with multi-purpose radiation delivery technologies.

II.2 NEURAL STEM CELL REGULATION AND BRAIN DEVELOPMENT
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Quiescent neural stem cells (NSCs) in the adult mouse brain are the source of neurogenesis that regulates innate and adaptive behaviors. Adult NSCs in the subventricular zone (SVZ) are derived from a subpopulation of embryonic neural stem-progenitor cells (NPCs) that is characterized by a slower cell cycle relative to the more abundant rapidly cycling NPCs that build the brain. We have previously shown that slow cell cycle can cause the establishment of adult NSCs at the SVz, although the underlying mechanism remains unknown. We found that Notch and an effector Hey1 display a non-oscillatory stationary expression pattern of neurogenesis that regulates innate and adaptive behaviors. Adult NSCs in the SVZ exhibited a non-oscillatory expression pattern of neurogenesis that regulates innate and adaptive behaviors. Adult NSCs in the SVZ are the source of neurogenesis that regulates innate and adaptive behaviors.

IL-1 ANGIogenesis/INVASION (ANGI)

ANGI-1 IMPACT OF NEOADJUVANT BEVACIZUMAB ON TRANSCRIPTIONAL FACTOR FOR STEMMENESS, MACROPHAGE POLARIZATION, AND OXYGENATION OF TUMOR MICROENVIRONMENT IN GLOBLASTOMA
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Background: Previously we reported that bevacizumab (Bev) produces tumor oxygenation with immunosuppressive tumor microenvironment (TME) and inhibition of stemness. To confirm whether these effects might contribute prolongation of clinical outcome, in the present study paired samples from same patients with newly diagnosed GBM who received Bev during its effectiveness and refractoriness were investigated by immunohistochemistry. Methods: Eighteen samples from 9 patients with newly diagnosed GBM who received preoperative neoadjuvant Bev (neobev) followed by surgical operation and chemoradiotherapy in addition to salvage surgery after recurrence were investigated. Expressions of FOXM1, HIF-1, and CD163 were evaluated by immunohistochemistry. Overall survival (OS) were analyzed with the present cohort divided into two groups between good and poor responder (GR and PR, respectively) of Bev defined as tumor regression rate judged by T1 gadolinium enhancement (T1Gd) and fluid attenuated inversion recovery (FLAIR) images. Results: In the group of good responder of T1Gd (T1Gd-GR; defined as $>38\%$ of regression rate after neoBev), OS was prolonged compared with T1Gd-PR along with inhibition of FOXM1 expression and HIF-1a. In contrast, in the group of good responder of T1Gd (T1Gd-GR; defined as $>38\%$ of regression rate after neoBev), there were no significant differences of OS and FOXM1 expression in comparison with T1Gd-PR. Conclusion: T1Gd-GR after neoBev might contribute proliferation of clinical outcome, leading to inhibition of stemness and TAM infiltration during its effectiveness. These results suggested that Bev combined with immunotherapy for newly diagnosed GBM might provide clinical benefits including inhibition of stemness and induction of immunosupportive TME, when tumor volume assessed by T1Gd was significantly decreased following neoBev.

Key words: neoadjuvant bevacizumab | glioblastoma | tumor microenvironment,

IL-3 CHANGING CANCER GENOMICS AND CANCER GENOMIC MEDICINE BY ARTIFICIAL INTELLIGENCE AND LARGE-SCALE DATA ANALYSIS
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In MEXT Program for Scientific Research on Innovative Areas “Systems Cancer” and “Systems Cancer in Neo-Dimension” (2010-2019), we developed a large-scale genome data analysis pipeline called Genomon in collaboration with Professor Seiji Ogawa (Kyoto University). Our efforts successfully produced innovative results on cancer genomics. This system is implemented on the supercomputers SHIROKANE and FUGAKU. One of the contributions unraveled the overall picture of genetic abnormalities in malignant brain tumors (Mutational landscape and clonal architecture in grade II and III gliomas. Nat Genet 2015) that exploited Genomon on SHIROKANE. However, with the spread of new measurement technology and new computing environments, no one thinks that the future can be figured out this simple extension. On the other hand, for cancer genomic medicine, Institute of Medical Science University of Tokyo made a research team analyzing whole genome sequences. The challenge we faced was to transform thousands to millions of genomic aberrations per case into precision medicine. It is what we now call “digital transformation.” IBM’s Watson for Genomics was introduced for our research purpose. In the process, we identified the effectiveness of AI, the indispensability of specialist intervention, and bottlenecks. We recognized that natural language processing technology such as BERT and Google Knowledge Graph AI technology will open up the future. Automatic document creation is also a realistic issue. Cancer research is getting more difficult and larger in scale. For example, analysis of genomic data from 60, 954 cases revealed a new underlying mechanism in which multiple mutations within the same oncogene synergistically work (Nature 2021). AI with an accuracy of X% does not seem to be the goal. What is needed is a black box, but explainable AI that explains “why” in a human understandable way. We are currently conducting research with Fujitsu Laboratories for this direction.

Key words: cancer genomics | artificial intelligence | large-scale data analysis.