tively, we performed computed tomography imaging and contrast-enhanced magnetic resonance imaging (MRI) for the neuronavigation system. We experienced Curve(TM) Image Guided Surgery (BrainLab, Munich, Germany). The surgical trajectory was planned with functional MRI and diffusion tensor imaging to protect the eloquent area and critical vasculature of the brain. We used a clear plastic tubular retractor system, the ViewSite Brain Access System, for surgery of deep seated gliomas. We gently inserted and placed the ViewSite using the neuronavigation. The tumor was observed and resected through the ViewSite tubular retractor under a microscope and endoscope. If the tumor was large, we switched the ViewSite tubular retractor to brain spatulas to identify the boundary between the normal brain and lesion. We are currently using the combination of the tubular retractor and brain spatulas using navigation system. Here, we present and analyze our preoperative simulation, surgical procedure, and outcomes.

**ES-1**

### CLINICAL RESULTS OF TUMOR TREATING FIELDS IN PATIENTS WITH GLIOBLASTOMA IN JAPAN, COMPARED WITH GLOBAL SURVEILLANCE

Yoshihiro Muragaki[1,2], Masayuki Nitta[1,2], Taiichi Saito[1,2], Shunichi Tutsuki[1,2], Atsushi Fukui[2], Takakazu Kawamata[2]; [1]Faculty of Advanced Techno-Surgery, Institute of Advanced Biomedical Engineering and Science, Tokyo Women's Medical University

INTRODUCTION: The tumor treatment field induces apoptosis of tumor cells by providing a low intensity, intermediate frequency, alternating current electric field via a transducer array. TTFields is based on Phase 3 EF-11 and EF-14 trials for glioblastoma in the US FDA and Japan PMDA. Therefore, I will report the statistics of TTFields use in Japan along with recent papers. METHODS: 410 patients were treated with TTFields in Japan (December 2017-), of which 17 were at Tokyo Women's Medical University. We also referred to papers about global post-marketing surveillance and recent studies. RESULTS: Of the 410 patients, 409 (99.8%) were diagnosed with ndGBM(male: female, 66.8%: 33.2%). As of June 2020, 222 patients (54.1%) were on treatment and 188 (45.9%) were discontinued. In 17 cases at TWMU, the average age was 46.3 years. The average treatment period was 218 days, with 6 patients (35%) continuing treatment, 6 patients (35%) discontinuing due to patient wishes, and 5 patients (30%) discontinuing treatment due to recurrence. Side effects were contact dermatitis under the array in 9 patients (57%) and mild malaise in 7 patients (43%). We experienced long-term progression-free cases with TTF use of 25 months (survival 30 months after surgery) with a glioma partially resected and 21 months (survival 27 months after surgery) with a biopsied glioma. In the biopsy case, bevacizumab was used in combination during the treatment. CONCLUSION: In global surveillance, use for rGBM accounts for 39%, but Japan is limited to use for ndGBM due to insurance coverage. In terms of side effects, it showed a good safety profile comparable to previous trials. Long-term progression-free cases have been observed, and it is necessary to examine the characteristics of patients who respond to treatment and the effect of concomitant use with bevacizumab by prospective studies

**ES-2**

### PHASE 3 TRIDENT TRIAL: RADIATION AND TEMOZOLOMIDE WITH OR WITHOUT TUMOR TREATING FIELDS IN NEWLY DIAGNOSED GLIOBLASTOMA

Mitsutoshi Nakada[1]; [1]Department of Neurosurgery Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Japan

BACKGROUND: Tumor treating fields (TTFields) is a non-invasive, regional antimitotic treatment approved as a standard-of-care for glioblastoma. In the EF-14 Phase 3 trial, TTFields (200 kHz) plus temozolomide (TMZ) significantly increased survival of patients with newly diagnosed GBM(ndGBM) without increasing systemic toxicity. TTFields-related AEs were mainly skin AEs. In preclinical models, TTFields increase the therapeutic effects of radiation therapy (RT). A pilot study showed that TTFields concomitant with RT and TMZ is well tolerated. The benefit of concomitant TTFields with RT and TMZ will be tested in the TRIDENT trial. METHODS: TRIDENT is an international phase III randomized trial comparing standard RT/TMZ vs the triple combination of RT/TMZ with concomitant TTFields. RT is delivered through the TTFields arrays. Patients in both arms will receive maintenance TTFields/TMZ. TTFields (200 kHz) will be delivered over18 hours/day using Optune. Patients will continue TTFields treatment until second recurrence. Patients with pathologically confirmed ndGBM, over 18 years old, KPS over 70, either sex, post-surgery or biopsy, and amenable for RT/TMZ therapy will be stratified by extent of resection and MGMT promoter methylation status. The primary endpoint is overall survival (OS). Secondary end points: progression free survival (PFS; RANO), 1- and 2-year survival rates, overall radiological response (ORR; RANO), progression-free survival (PFS2, PFS6, PFS12); severity and frequency of AEs (CTCAE V5.0); pathological changes in resected GBM tumors post treatment; quality of life (EORTC QLQ-C30); and correlation of OS to TTFields compliance. The hypothesis is that concomitant TTFields/RT/TMZ will significantly improve OS versus RT/TMZ. Sample size (N=950; 475/arm) will detect a HR lower than 0.8 with 5% type I error. Survival will be measured from the time of randomization until date of death. At the time of analysis, patients lost to follow-up or still on protocol follow-up will be censored at the last date known to be alive.

## ANGIOGENESIS/INVASION (ANGI)

**ANGI-03**

### FUNCTIONAL ROLES OF CD166/ACTIVATED LEUKOCYTE CELL ADHESION MOLECULE (CD166/ALCAM) FOR GLIOBLASTOMA INVASION

Noriyuki Kijima[1], Tomoyoshi Nakagawa[1], Takamune Achiha[1], Ryuichi Hirayama[1], Manabu Kinoshita[1], Naoki Kagawa[1], Haruhiko Kishima[1]; [1]Department of Neurosurgery, Osaka University Graduate School of Medicine

CD166/activated leukocyte cell adhesion molecule (CD166/ALCAM) is a transmembrane receptor, widely expressed in various tissues, and is involved in several functions such as cell adhesion, neurogenesis and angiogenesis. We have previously reported that CD166/ALCAM is expressed on glioblastoma progenitor cells and is involved in glioblastoma invasion. However, we only have analyzed the functional roles of ALCAM using glioblastoma cell lines, not using patient derived xenografts. In this study, we investigated the functional roles of CD166/ALCAM using patient derived xenografts. We established CD166/ALCAM knocked-down glioblastoma patient derived cell lines by shRNA. For in vitro analysis, we seeded control and CD166/ALCAM knocked-down glioblastoma cells on culture dishes and performed time lapse analysis to investigate cell motility. For in vivo analysis, we orthotopically injected control and CD166/ALCAM knocked-down glioblastoma cells into the immunodeficient mice. When the mice got sick due to the tumor, we dissected the mice and analyzed the difference in invasion by immunohistochemical analysis. We found that CD166/ALCAM knocked-down glioblastoma cells significantly decreased cell motility by time lapse analysis. In addition, CD166/ALCAM knocked-down glioblastoma cells suppressed cell invasion and leptomeningeal metastasis by immunohistochemical analysis from patient derived xenografts. Our results suggest that CD166/ALCAM is involved in glioblastoma invasion, thus future studies are necessary to investigate whether CD166/ALCAM could be a therapeutic target for glioblastoma.

## CELL BIOLOGY/METABOLISM/STEM CELLS (CBMS)

**CBMS-01**

### MECHANISM OF BRAIN TUMOR MALIGNANCY CAUSED BY AGING AND SOCIAL ISOLATION

Daisuke Yamashita[1,2], Victoria Flanary[2], Shinobu Yamaguchi[2], Yoshihiro Ohtsuka[1], Saya Ozaki[1], Satoshi Suehiro[1], Akihiro Inoue[1], Myriam Gorospe[3], Ichiro Nakano[2], Takeharu Kunieda[1]; [1]Department of Neurosurgery, Ehime University Graduate School of Medicine, Toon, Japan

The rise in population aging worldwide is causing an unparalleled increase in death from many cancers, including glioblastoma (GBM). In advanced countries, the number of elderly people living alone is increasing due to the rapid aging of the population and the socialization of nuclear families. Here, we explored the impact of aging and social isolation on GBM tumorigenesis. In normal brain tissue, aging promoted pathways related to cytokines and inflammation, which were further promoted by social isolation. In tumor tissues, the expression of neuron/synapse-related genes was significantly reduced in aged mice, and their expression was further reduced by social isolation. In addition, the survival period of aged mice was significantly shorter than that of young mice, and the survival period was further shortened by social isolation, which was characteristic of males. This phenomenon was the same in humans, and the survival period in the young group was significantly longer than that in the elderly group, and in the elderly group, the survival period was shortened in the male elderly group living alone. Our data indicate that social isolation contributes to the highly aggressive GBM by the shift to neuro-inflammation in the elderly brain.