SURG-10. DEVELOPMENT OF NOVEL TOPICAL FLUORESCENT PROBE FOR INTRAOPERATIVE RAPID DETECTION OF GLIOMA

Shota Tanaka[1], Yosuke Kitagawa[2], Mako Kamiya[1], Yugo Kuriki[1], Kyoko Yamamoto[1], Takenori Shimizu[1], Takahide Nejo[3], Taijun Hana[1], Tsukasa Koike[1], Erika Yamazawa[4], Yoshihiro Kushihara[4], Satoshi Takahashi[5], Masashi Nomura[2], Hirokazu Takami[1], Shunsaku Takayanagi[1], Akitake Mukasa[6], Yasuteru Urano[1], and Nobuhito Saito[1]; [1]The University of Tokyo Hospital, Tokyo, Japan, [2]Massachusetts General Hospital, Harvard Medical School, Boston, USA, [3]University of California, San Francisco, San Francisco, CA, USA, [4]Department of Neurosurgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan, [5]National Cancer Center, Division of Medical AI Research and Development, Hyuou-Ku, Tokyo, Japan, [6]Department of Neurosurgery, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

PURPOSE: Fluorescence imaging is an important surgical adjunct in malignant glioma surgery. 5-aminolevulinic acid (5-ALA) has been proven effective for radical tumor resection and extended progression-free survival in a phase III randomized trial and therefore integrated into surgery for malignant glioma. Importantly, however, some limitations still exist in its use, which include false positivity and false negativity as well as inability of re-administration. In this study, we aimed to develop a novel, spray-type fluorescent probe using hydroxymethyl rhodamine green (HMRG) as a fluorescent scaffold. METHODS: We have previously established a fluorescent probe library comprised of more than 320 kinds of HMRG probes. They have HMRG as a fluorescent scaffold with various types of dipeptides attached to it. Primary probe screening was performed using the homogenized tumor samples from patients with glioblastoma operated at our institution. Secondary screening followed using the selected probes and fresh tumor samples obtained from patients with glioblastoma operated from 2016 until 2018. Diced electrophoresis gel (DEG) assay, two-dimensional gel electrophoresis followed by a multi-well plate-based fluorometric assay, was performed to identify responsible enzymes for the selected probe. Further experiments with inhibitors, real-time PCR, immunohistochemistry, and western blotting were performed for confirmation. RESULTS: Proline-arginine-HMRG (PR-HMRG) was selected as a candidate probe based upon the above two-step screenings. It achieved 79.4% accuracy in receiver operating characteristic curve analysis. Calpain-1 was found to be responsible to cleave PR-HMRG probe by DEG-proteome analysis. Calpain-1 protein was expressed at significantly higher level in tumors that were fluoresced by PR-HMRG than in those that were not. CONCLUSIONS: Our innovative screening method was able to find PR-HMRG as a novel fluorescent probe effective for rapid detection of glioblastoma. A preclinical study is planned to assess the efficacy and safety of the selected probe.

SURG-11. TUMOR RECURRENCE PATTERNS AFTER SURGICAL RESECTION OF INTRACRANIAL LOW-GRADE GLIOMAS

Yoshihiro Muragaki[1], Yasukazu Fukuya[2], Soko Ikuta[1], Masayuki NItta[1], Taiichi Saito[1], Shunsuke Tsuzuki[1], Takashi Maruyama[1], and Takakazu Kawamata[1]; [1]Tokyo Women's Medical University, Tokyo, Japan, [2]Kobe Co-medical College, Kobe, Japan

INTRODUCTION: Tumor recurrence patterns after resection of intracranial low-grade gliomas (LGG) generally remain obscured. The objective of the present retrospective study was their multifaceted analysis, evaluation of associated factors, and assessment of impact on prognosis. METHODS: Study group comprised 81 consecutive adult patients (46 men and 35 women; median age, 37 years) with recurrent diffuse astrocytomas (DA; 51 cases) and oligodendrogliomas (OD; 30 cases). The median length of follow-up after primary surgery was 6.7 years. RESULTS: Early (within 2 years after primary surgery) and non-early (> 2 years after primary surgery) recurrence was noted in 23 (28%) and 58 (72%) cases, respectively. Fast (≤ 6 months) and slow (> 6 months) radiological progression of relapse was noted in 31 (38%) and 48 (59%) cases, respectively. Tumor recurrence was local and non-local in 71 (88%) and 10 (12%) cases, respectively. Recurrence patterns have differed in OD, IDH1-mutant DA, and IDH wild-type DA. Early onset, fast radiological progression, and non-local site of relapse had statistically significant negative impact on overall survival of patients and were often associated with malignant transformation of the tumor (38 cases). However, in subgroup with extent of resection ≥ 90% (56 cases) no differences in recurrence characteristics were found between 3 molecularly defined groups of LGG. Follow-up MRI also showed same results. CONCLUSIONS: Recurrence patterns after resection of LGG show significant variability, differ in distinct molecularly defined types of tumors, and demonstrate definitive impact on prognosis. Aggressive resection at the time of primary surgery may result in more favorable characteristics of recurrence at the time of its development.

SURG-13. THE TENTATIVE APPLICATION OF EN BLOC CONCEPT IN THE PEDIATRIC BRAIN TUMOR: EXPERIENCE FROM A LARGE PEDIATRIC CENTER IN CHINA

Liangliang Cao[1], and Jie Ma[2]; [1]School of Medicine, Shanghai Jiao Tong University, Shanghai, China., Shanghai, Shanghai, China (People's Republic), [2]Xinhua affiliated to Shanghai Jiao Tong University, Shanghai, China (People's Republic)

BACKGROUND: The less allowable blood loss and tolerance of intraoperative blood loss of children lead to the high rate of massive blood transfusion. The surgical concepts of en bloc resection may contribute to the improvement of brain tumor resection. OBJECTIVE: To investigate the effects of en bloc concept on short outcomes of pediatric brain tumors and factors associated with the application of en bloc concept. METHODS: According to the surgical concept involved, the patients were divided into three subgroups-complete en bloc concept, partial en bloc concept and piecemeal concept. The matching-comparison(en bloc group consisting of the first two subgroups and piecemeal group) was conducted to investigate the effect of the en bloc concept on the short-term outcomes. Then the patient data after January 2018, when the en bloc concept was routinely integrated into brain tumor surgery in our medical center, were reviewed and analyzed to find out the predictors associated with the application of en bloc concept. RESULTS: In the en bloc group, the perioperative outcomes, including hospital stay(p=0.001), PICU stay(p=0.003), total blood loss(p=0.015), transfusion rate(p=0.005) and complication rate(p=0.039), were all significantly improved. The multinomial logistic regression analysis showed that tumor volume, bottom vessel, and imaging features, like encasing nerve or pass-by vessel, finger-like attachment, ratio of "limited line" and ratio of "clear line" remained independent predictors for the application of en bloc concept in our medical center.

SURG-14. COMPARABLE SURVIVAL OUTCOMES BETWEEN THE ELDERLY AND THEIR YOUNGER COUNTERPARTS AFTER RESECTION OF BENIGN MENINGIOMAS

Jun Ma[1], Ali Alattar[2], Sanjay Dhawan[1], Asgeir Jakola[3], Jiri Bartek Jr[4], and Clark Chen[1]; [1]University of Minnesota, Minneapolis, MN, USA, [2]University of Pittsburgh, Pittsburgh, PA, USA, [3]St. Olavs Hospital, Trondheim, Norway, [4]Karolinska Institutet, Stockholm, Sweden

OBJECTIVE: Using the Surveillance, Epidemiology and End Results (SEER) database, we characterized the patterns of surgical recommendations and outcomes after benign meningioma resection in the elderly population. METHODS: 27,839 adult meningioma patients were identified in SEER between 1973- 2015 and 6,967 patients were identified between 2016-18. Patients were stratified into four age groups:18-39, 40-59, 60-79, and ≥ 80 years old. The likelihood for recommendation to proceed with resection, extent of resection, and survival outcome were determined using logistic regression models. RESULTS: In a multi-variate model that accounted for gender, race, marital status, tumor size, and tumor location, the likelihood of recommendation to proceed with benign meningiomas resection decreased with advancing age. Relative to patients age 40-59, the likelihood of recommendation for surgery were 1.130 (95%CI=0.925-1.380, P=0.230), 0.593 (95%CI=0.531-0.662, P< 0.001), and 0.173 (95%CI=0.146-0.205, P< 0.001) for patients age 18-39, 60-79, and >= 80, respectively. A similar trend in the likelihood of gross total resection (GTR) was observed. Relative to patients age 40-59, the likelihood of gross total resection were 1.009 (95%CI=0.913-1.114, P=0.867), 0.903 (95%CI=0.849-0.961, P=0.001), and 0.580 (95%CI=0.512-0.657, P< 0.001) for patients age 18-39, 60-79, and >= 80, respectively. However, survival after meningioma resection did not vary significantly as a function of patient age. Relative to patients age 40-59, the hazard of death after GTR of meningioma resection were 1.324 (95%CI=0.795-2/203, P=0.280), 0.813 (95%CI=0.639-1.035, P=0.092), and 0.913 (95%CI=0.618-1.350, P=0.649) for patients age 60-79, and >= 80, respectively. These results were validated using SEER data from 2016-2018. CONCLUSION: This analysis provide evidence that surgeons exert caution in surgical resection of benign meningioma in the elderly, with decreased likelihood for recommending surgery in this population. In patients selected for and underwent gross resection, survival outcome in the elderly was comparable to their younger counterparts, suggesting safety of procedure in appropriately selected elderly.

SURG-15. PITUITARY SPINDLE CELL ONCOCYTOMA: A CASE REPORT AND LITERATURE REVIEW

Taha Taka, Chen Yi Yang, Joshua Limbo, Alvin Chan, Jordan Davies, Edward Kuan, Scott Turner, and Frank P.K. Hsu; UCI, Orange, CA, USA

BACKGROUND: Spindle cell oncocytoma (SCO) of the pituitary gland is an extremely rare non-functional WHO grade 1 tumor. SCO are often misdiagnosed as nonfunctional pituitary adenomas on pre-operative imaging.

They are often hypervascular and locally adherent, which increases hemorrhage risk and limits surgical resection, leading to increased risk of recurrence. We report a case of SCO treated at our institution and provide a review of the current literature. METHODS: A 75-year-old male with a history of hypertension, left thalamic stroke, Parkinson's disease, and normal pressure hypertension presented to neurosurgery clinic with bitemporal hemianopsia, hyponatremia, and abnormal gait and mobility. Imaging showed an enhancing intra- and suprasellar, hyperdense tumor mass measuring 3.0 cm in diameter. We performed a systemic literature search in the PubMed database to identify previous reports of spindle cell oncocytoma. After exclusion of studies that did not meet criteria, 32 publications were selected for critical reading. RESULTS: The patient underwent an endoscopic transsphenoidal resection of the tumor via a multi-disciplinary team. The tumor was fibrous and adherent to the intrasellar dura, with gross invasion of the diaphragm sella, necessitating partial resection of the diaphragm. The defect was repaired, and the patient made an uncomplicated recovery. Post-operatively, the patient experienced improved vision. Upon literature review, SCO present in older adults with an average age of 56.2 ± 14.7 with visual deficits (67.9%), headache (33.3%), hypopituitarism (24.7%), and nausea (11.1%). Full resection was achieved in 38.6% of cases leading to recurrence rate of 23.5% with an average time until recurrence of 32.5 months (range 1-120 months). CONCLUSION: Careful surgical technique is needed due to SCO hypervascularity and strong adherence to minimize risk of injury to surrounding neurovascular structures. Long-term follow up is recommended due risk of recurrence.

TUMOR MICROENVIRONMENT/ANGIOGENESIS/ METABOLISM/INVASION

TAMI-01. BRAIN METASTASES: CURRENT LITERATURE REVIEW

Ruchi Raval[1], Aadi Pandya[1], Jaspreet Behl[1], and Sumul Raval[1]; [1]Garden State Neurology & Neuro-Oncology, PC, West Long Branch, NJ, USA

PURPOSE: As more information is gathered about brain metastases, it still remains that the current prognosis of brain metastases is very poor. Due to this, it is imperative that physicians are aware of the most important components regarding brain metastases. This literature review will encompass the most current literature in order to highlight the most crucial information. METHODS: All mentioned studies and literature reviews cited in the paper were obtained through various sites, and were published between 1996 and 2017. The main components that were required from the papers reviewed included where in the body the brain metastases originated from, where in the brain they tended to spread to, what the signs and symptoms typical of patients with brain metastases are, and what the options are in terms of treatment. RESULTS: Using the results from a variety of studies performed within the past three decades, it is apparent that brain metastases most commonly originate from, in order of increasing frequency, lung cancer, breast cancer, melanoma, and colorectal cancer. In addition, it is reaffirmed that the magnetic resonance imaging (MRI) is the best diagnostic tool to be used when dealing with brain metastases. The most frequent signs and symptoms of a brain metastases include cognitive changes, headaches, weakness, and seizures. Finally, supportive treatment includes use of corticosteroids, antiepileptic drugs (AEDs), and anticoagulation therapy. Definitive treatment for brain metastases varies based on size, location, and prevalence in the brain, but the most effective options include chemotherapy, radiation therapy, and surgery. CONCLUSIONS: The study's results confirm the need for more research to be done regarding brain metastases, and better options to increase the survival of patients.

TAMI-02. DEPLETION OF INTRATUMORAL TUMOR-ASSOCIATED MACROPHAGES AND MICROGLIA (TAM/M) IMPROVES CHECKPOINT-INHIBITION THERAPY FOR BRAIN METASTASIS FROM LUNG CANCER

Philipp Karschnia[1], Tao Xu[1], Esther Fitzinger[1], Julia C. Saliger[1], Jens Blobner[1], Nico Teske[1], Iven-Alex von Muecke-Heim[1], Sigrid Langer[1], Marcel Konhäuser[1], Hellen Ishikawa-Ankerhold[1], Niklas Thon[1], Jörg-Christian Tonn[2], and Louisa von Baumgarten[1]; [1]Ludwig-Maximilians-University School of Medicine, Munich, Germany[2]Department of Neurosurgery, Ludwig-Maximilians-University School of Medicine, Munich, Munich, Germany

BACKGROUND: Brain metastases dramatically limit prognosis of lung cancer patients. Unlike systemic disease, brain metastases from lung cancer poorly respond to checkpoint-inhibition therapy. Targeting the immunosuppressive tumor-associated macrophages and microglia (TAM/M) and their receptor CSF1R may increase efficacy of checkpoint-inhibitors. METHODS: Cranial windows were prepared in fully immunocompetent, transgenic CX3CR1$^{GFP/wt}$-mice with green-fluorescent TAM/M. Intracranial injection of red-fluorescent Lewis Lung Carcinoma-cells was performed, and mice received one of the following three treatments: PD1-inhibition only (n = 8); PD1-inhibition combined with an anti-CSF1R-antibody (exhibiting limited blood-brain-barrier permeability under physiologic conditions, n = 8); or PD1-inhibition combined with a small molecular CSF1R-inhibitor (exhibiting high blood-brain-barrier permeability, n = 7). Tumor growth and TAM/M were followed by repetitive two-photon laser-scanning-microscopy over weeks. RESULTS: Following intracranial injection, metastases were detected in all three treatment groups within eight days. In mice receiving PD1-inhibition only, metastases showed exponential growth which was paralleled by intra- and peritumoral accumulation of TAM/M. Treatment with an anti-CSF1R-antibody resulted in significantly lower numbers of intratumoral TAM/M given increased tumoral blood-brain-barrier permeability, but did not substantially affect peritumoral TAM/M or TAM/M localized in the healthy contralateral hemisphere. In contrast, treatment with a small molecular CSF1R-inhibitor not only reduced the number of intratumoral TAM/M, but also of peritumoral and contralateral TAM/M. Compared to PD1-inhibition only, the addition of either an anti-CSF1R-antibody or a small molecular CSF1R-inhibitor resulted in decreased tumor growth (tumor size on day 12: 8.3 mm^2 (PD1-inhibition only) versus 0.9 mm^2 (PD1-inhibition + anti-CSF1R-antibody) versus 2.5 mm^2 (PD1-inhibition + small molecular CSF1R-inhibitor)) (p = 0.01). The beneficial effects of the small molecular CSF1R-inhibitor in reducing tumor growth were similar to those of the anti-CSF1R-antibody. CONCLUSION: Targeting intratumoral TAM/M using CSF1-inhibition may increase the efficacy of checkpoint-inhibition therapy for cerebral lung cancer metastases. This approach warrants further evaluation in preclinical and clinical studies.

TAMI-03. PROGNOSTIC SIGNIFICANCE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) IN PATIENTS WITH BRAIN METASTASES FROM DIFFERENT TUMOR ORIGINS

Guanhua Deng[1], Lei Wen[1], zhaoming Zhou[1], Changguo Shan[1], Mingyao Lai[1], Cheng Zhou[1], and Linbo Cai[1]; [1]Guangdong Sanjiu Brain Hospital, Guangzhou, China (People's Republic)

PURPOSE: Brain metastases (BMs) represent the most common adult intracranial malignancy. The prognosis of BMs is subject to many factors, *i.e.*, the number, size and locations of the metastatic sites, tumor origins, pathologic types, gene mutation status, metastatic sites, and KPS *etc*. This study aimed to evaluate the prognostic value of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) in brain metastases. METHODS: A total of 480 patients diagnosed with brain metastases from a wide range of tumor origins, *i.e.*, NSCLC, SCLC, breast cancer, melanoma, prostate, kidney, gastrointestinal cancer, cervical carcinoma, ovarian cancer, choriocarcinoma of uterus were retrospectively analyzed. Pre-radiotherapy NLR, PLR, and LMR were calculated as total neutrophil/lymphocyte, platelet/Lymphocyte, lymphocyte/monocyte, respectively. Survival rates were estimated using the Kaplan-Meier survival analysis. Cox regression models were used to identify independent prognostic factors. RESULTS: The median overall survival (OS) was 14.4 months [95%CI: 13.4-15.5]. The median overall survival after radiotherapy was significantly different between patients with NLR< 4 and those with NLR≥4 (OS 16.3 mo. vs. 12.2 mo., P< 0.0001). No significant difference was observed between PLR vs. OS, and LMR vs. OS (PLR< 180: HR=1.221, P=0.240; LMR< 4: HR=0.753, P=0.141). The Cox regression model for the continuous metric values revealed that the NLR increased every 1.0 was associated with additional 5.9% of fatal risk (HR: 1.059; 95%CI = 1.033–1.087, P< 0.0001). NLR was validated as an independent prognostic factor for risk of death after adjusting for sex, age, and KPS. CONCLUSIONS: We revealed pre-treatment NLR is an independent prognostic factor in patients with brain metastases for poor OS, independent of different tumor origins. The NLR warrants further studies using sub-group analysis and validation in external cohorts. Future studies in this parameter have a potential to facilitate more precise risk-stratifications to guide personalized treatment for BM.

TAMI-04. OLFACTORY RECEPTOR 5B21 DRIVES BREAST CANCER BRAIN METASTASIS THROUGH STAT3/NFKB/CEBPB PATHWAY

Mao Li[1], Markus Schweiger[2], Daniel Ryan[1], Ichiro Nakano[3], Litia Carvalho[1], and Bakhos Tannous[4]; [1]Massachusetts General Hospital, Cambridge, MA, USA, [2]MGH/VU Amsterdam, Boston, USA, [3]The University of Alabama at Birmingham, cambridge, USA, [4]Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Olfactory receptors (ORs), responsible for the sense of smell, play an essential role in various physiological processes outside the nasal epithelium, including cancer. In breast cancer, however, the expression and function of ORs remain understudied. We established a breast cancer metastasis model by intracardiac injection of MDA-MB-231 (231P) in immunocompromised mice and produced a series of derivative cell lines from developed metastatic sites, including the brain-seeking clone (231Br). We examined the significance of ORs transcript abundance in primary and metastatic breast cancer to dif-