IMMUNOLOGIC THERAPY (IMT)

IMT-1

A TRANSLATIONAL RESEARCH FOR PRACTICAL USE OF DENDRITIC CELL-BASED IMMUNOTHERAPY AGAINST MALIGNANT GLIOMA

Yasuharu Akasaki[1], Jun Takei[1,2], Yohei Yamamoto[1], Toshihide Tanaka[1], Yuko Kamata[2], Mutsunori Murahashi[2], Yuichi Murayama[1]; [1]Department of Neurosurgery, Jikei University School of Medicine, Tokyo, Japan [2]Division of oncology, Research Center for Medical Science, Jikei University School of Medicine

Background: Although a therapeutic effect of dendritic cell (DC)-based immunotherapy, a kind of regenerative medicine, has been recognized in various types of cancer including malignant glioma, it is still impractical because of several unsolved problems. This study is aimed to solve the problems in regenerative medicine through a clinical trial of immunotherapy using fusions of DCs and glioma cells (GCs) against malignant glioma, and to put it into practical use. Methods: Primary cultured GCs and glioma stem cells (GSCs) were generated from surgical specimens of patient. DCs were generated from PBMC of same patient, and were fused with GCs and GSCs. The entire process of cell production must be performed by pairs of two cell-culture operators in a dedicated cell processing facility. We developed a remote cell-observation system for reducing hands work of operators. As a project to establish a preservation method, cryopreservation of glioma tissues, GCs/GSCs, DCs and fusion cells followed by their viability examination. Results: The remote cell-observation system worked stable in morphological observation and cell-counting for adhesion cells. A growth curve was also automatically and accurately created. Although a morphological observation of floating cells such as GSCs and DCs was possible, there was some error in counting of those cells. A project to establish a preservation method is currently underway, including the development of storage containers and storage liquids. Conclusions: Although the remote cell-observation system required some modifications at the observation site, depth of focus, etc. for floating cells, there was no problem in accuracy for adhesion cells compared with operator's observation. This system, which can be easily installed at low cost, seemed to be helpful for practical use of regenerative medical products including this therapy. We are working on a project to establish a stable transportation and preservation method for prevalence of this treatment.

Key words: glioma | immunotherapy | dendritic cell

SURGICAL/INTRAOPERATIVE THERAPY/ MONITORING (STMO)

STMO-3

MID- TO LONG-TERM OUTCOME OF SUPRATOTAL RESECTION OF IDH1 WILD-TYPE GLIOBLASTOMA BASED ON 11C-METHIONINE PET: A RETROSPECTIVE, SINGLE-CENTER STUDY

Seiichiro Hirono[1], Ko Ozaki[1], Masayoshi Kobayashi[1], Ayaka Hara[1,2], Tomohiro Yamaki[2], Tomoo Matsutani[1], Yasuo Iwadate[1]; [1]Department of Neurological Surgery, Chiba University Graduate School of Medicine, Chiba, Japan [2]Division of Nuclear Medicine, Chiba Ryogo Center, Chiba, Japan

Purpose: Mid- to long-term outcome in glioblastoma (GBM) patients following supratotal resection (SupTR), involving complete resection both of contrast-enhancing enhanced (CE) tumors and areas of methionine (Met) uptake on ^{11}C-Met positron emission tomography (Met-PET), are not clarified. **Methods.**: A retrospective, single-center review was performed in newly diagnosed, *IDH1* wild-type GBM patients, comparing SupTR with gross total resection (GTR), in which only CE tumor tissue was completely resected. Only patients who were operated on until November 2019 were included for evaluation of mid- to long-term outcome. Following resection, all patients underwent standard radiotherapy and temozolomide treatment, and were followed for progression-free survival (PFS) and overall survival (OS). **Results:** Among the 30 patients included in this study, 7 underwent SupTR and 23 underwent GTR. Awake craniotomy with cortical and subcortical mapping was more frequently performed in the SupTR group than in the GTR group. During the follow-up period, significantly different patterns of disease progression were observed between groups. Although more than 80% of recurrences were local in the GTR group, all recurrences in the SupTR group were distant. Median PFS in the GTR and SupTR groups was 8.8 months (95% confidence interval [CI], 5.2–14.9) and 27.8 months (95% CI, 6.0-not estimable) respectively (p=0.08 by log-rank test). Median OS was 17.7 months (95% CI, 14.2–35.1) in GTR and not reached (95% CI, 30.5-not estimable) in SupTR, respectively; this difference was statistically significant (p=0.03 by log-rank test). No postoperative neurocognitive impairment was observed in SupTR patients. **Conclusion:** Compared to GTR alone, SupTR strategy with aggressive resection of both CE tumors and Met uptake area in GBM patients under awake craniotomy with functional preservation results in a survival benefit associated with better local control.

Key words: supratotal resection | Glioblastoma | positron emission tomography

STMO-5

UTILIZATION OF INTRAOPERATIVE MULTIMODAL TECHNOLOGIES [PET AND 5-ALA] FOR TREATING GLIOBLASTOMA

Keisuke Miyake[1], Daisuke Ogawa[1], Tetsuhiro Hatakeyama[1]; [1]Department of Neurological Surgery, Kagawa University Faculty of Medicine, Kagawa, Japan

Background: We can improve prognosis of glioblastoma by using positron emission tomography (PET) scans to guide them in removing tumors, and intraoperative magnetic resonance imaging (IoMRI) and 5-aminolevulinic acid (5-ALA) for identifying residual tumors. Tau proteins are reported to accumulate in glioblastomas, so we compared the efficacy of their PET tracer, THK5351, against that of ^{11}C-MET, ^{18}F-FLT, and ^{18}F-FMISO. Methods: Patients (n = 11) underwent scans between February 2020 and July 2021 for glioblastoma resection. Tumor-to-normal tissue accumulation ratio (TNR) and accumulation volumes of 4 PET tracers were evaluated. Following excisions, 5-ALA fluorescent evaluation was classified as strong, vague, or none. Residual tumor volumes and removal rates were determined using T1Gd assessments and PET tracers. IoMRI confirmed presence of residual tumors.Results: THK5351 had a TNR of 5.20, and its accumulated volume was greater than that of other tracers: 1.80 for ^{11}C-MET, 1.72 for ^{18}F-FLT, and 2.82 for ^{18}F-FMISO. 5-ALA fluorescent evaluation was vague (n = 7) or none (n = 4); respective residual tumor volumes (mL) were 2.3 and 0.2 (T1Gd), 5.7 and 0.9 (^{11}C-MET), 5.6 and 0.6 (^{18}F-FLT), 1.3 and 0.4 (^{18}F-FMISO), and 7 and 1.4 (THK5351); respective tumor removal rates (%) were 90.4 and 99.6 (T1Gd), 79.2 and 86.4 (^{11}C-MET), 84.4 and 89.2 (^{18}F-FLT), 94.3 and 94.4 (^{18}F-FMISO), and 72.3 and 83.4 (THK5351). The excised tumor tissue was found in the area where only THK5351 was accumulated.Conclusions: THK5351 accumulated in glioblastomas to a greater degree than that of other tracers, making it useful for discriminating between healthy and malignant tissues.

Key words: Glioblastoma | Positron Emission Tomograohy | 5-aminolevulinic acid

STMO-6

IMPACT OF THE EXTENT OF RESECTION ON THE SURVIVAL OF PATIENTS WITH LOWER GRADE GLIOMAS USING AWAKE BRAIN MAPPING

Kazuya Motomura[1], Lushun Chalise[1], Fumiharu Ohka[1], Kosuke Aoki[1], Tomohide Nishikawa[1], Junya Yamaguchi[1], Hiroyuki Shimizu[1], Yuji Kibe[1], Atsushi Natsume[1], Toshihiko Wakabayashi[1], Ryuta Saito[1]; [1]Department of Neurosurgery, Nagoya University Graduate School of Medicine, Nagoya, Japan

Purpose: The aim of this study was to assess the effect of the extent of resection (EOR) of tumors on survival in a series of patients with lower-grade gliomas (LGGs) who underwent awake brain mapping. Methods: We retrospectively analyzed 126 patients with LGGs in the dominant and non-dominant hemisphere who underwent awake brain surgery at the same institution between December 2012 and May 2020. Results: The median progression-free survival (PFS) rate of patients with LGGs in the group with an EOR >100 %, including supratotal resection (n = 47; median survival [MS], not reached), was significantly higher than that in the group with an EOR <100% (n = 79; MS, 43.1 months; 95% CI: 37.8–48.4 months; p = 0.04). In patients with diffuse astrocytomas and anaplastic astrocytomas, the group with EOR >100 %, including supratotal resection (n = 25; MS, not reached), demonstrated a significantly better PFS rate than did the group with an EOR <100% (n = 45; MS, 35.8 months; 95% CI: 19.9–51.6 months; p = 0.03). Supratotal or gross total resection was correlated with better PFS in IDH-mutant type of diffuse astrocytomas and anaplastic astrocytomas (n = 19; MS, not reached vs. n = 35; MS, 40.6 months; 95% CI: 22.3–59.0 months; p = 0.02). By contrast, supratotal or gross total resection was not associated with longer PFS rates in patients with IDH-wild type of diffuse astrocytomas and anaplastic astrocytomas. Conclusions: It is noteworthy that supratotal or gross total resection significantly correlated with better PFS in IDH-mutant type of WHO grade II and III astrocytic tumors. In light of our finding that EOR did not correlate with PFS in patients with aggressive IDH-wild type of diffuse astrocytomas and anaplastic

astrocytomas, we suggest treatments that are more intensive will be needed for the control of these tumors.

Key words: awake brain mapping | lower-grade gliomas | progression-free survival

STMO-7

USEFULNESS OF NU-KNIT IN RETRACTORLESS SURGERY FOR MALIGNANT GLIOMA

Yuji Yamanaka[1], Takeshi Hongo[1], Yuuki Sagehashi[1], Yuta Aragaki[1], Yuko Gobayashi[1]; [1]Department of Neurosurgery, Odawara Municipal Hospital, Kanagawa, Japan

On the removal of the brain tumor, securing of appropriate working corridor and the maintenance of the visibility are one of the most relevant elements regardless of tumor local existence. This is unchangeable extract in these days when a support apparatus such as navigation system and the nerve monitoring was enriched, and, in the malignant glioma that a tumor border is relatively indistinct, the importance does not change either.At our hospital, I protect the access route by two folds of coating of absorbable hemostat(Surgical NU-KNIT) and neurosurgical patties (Delicot) on the removal of the malignant brain tumor in the brain deep part instead without using as possible fixed retractor for the purpose of securing of working corridor under minimum retraction and extract deep part tumor. In this way, normal real protection, wet maintenance, maintenance of the visibility by the control of the bleeding and pressure reduction of the neighborhood organization extracting are provided, and postoperative function recovery gets an early impression. About a method of the securing of working corridor at our hospital, I inspect the usefulness and limit by showing representative cases and want to have an opinion, criticism.

Key words: glioma | retractorless surgery | absorbable hemostat

STMO-9

MAXIMAL SAFE GLIOMA RESECTION USING HIGH RESOLUTION EXOSCOPE

Kuniaki Saito[1], Nobuyoshi Sasaki[1], Yosuke Seiya[1], Ryo Onoda[1], Keiichi Kobayashi[1], Hirofumi Nakatomi[1], Yoshiaki Shiokawa[1], Motoo Nagane[1]; [1]Department of Neurosurgery, Kyorin University Faculty of Medicine, Tokyo, Japan

INTRODUCTION: Maximal safe glioma resection should be achieved using neuronavigation, electrophysiological monitoring, fluorescence visual system, and so on. Heads-up surgery with exoscope is suitable for the multimodal glioma surgery because multi-monitors come in our sights simultaneously. We introduce our glioma surgery using a latest exoscope and neuronavigation system. METHODS: We attempted maximal safe resection for the patients with high grade glioma using 3D/4K exoscope with 5-ALA-induced fluorescence, neuronavigation, and electrophysiological monitoring or awake mapping. An extent of resection, morbidity, and postoperative infarction were retrospectively reviewed. RESULTS: Twenty-one patients (age 26–79, male 11/female 10, glioblastoma 10/lower grade glioma 11, general anesthesia 16/awake craniotomy 5) underwent exoscopic tumor removal. Neuronavigation and electrophysiological monitoring were displayed in sub-monitors close to the main screen. Navigation could be recognized continuously using electromagnetic navigation technology. Intraoperative fluorescence was observed in 100% of the tumor with gadolinium enhancement. Surrounding structures such as white matter, vessels and nerves were clearly visualized under blue light. Supra-total resection or gross total resection was achieved in 8 (80%) of the patients with glioblastoma. Surgical morbidity included hemiparesis in 1 (4.8%) patient, hemianopsia in 1 (4.8%) patient. Postoperative infarction was observed in 2 (9.5%) patients, which was significantly lower compared to 23 of 77 (29.9%) patients with glioblastoma who underwent tumor resection with fluorescence-equipped microscope ($p<0.05$). CONCLUSION: High resolution exoscope surgery is effective for patients undergoing glioma surgery with respect to higher extent of resection and lower ischemic complication. Further studies are needed to assess direct comparisons between exoscope and microscope glioma resection.

Key words: maximal safe resection | exoscope | glioma

STMO-12

EFFORTS FOR SAFE MALIGNANT BRAIN TUMOR SURGERY AT OUR HOSPITAL

Yusuke Kobayashi[1], Yosuke Satou[1], Takashi Kon[1], Daisuke Tanioka[1], Katsuyoshi Shimizu[1], Tohru Mizutani[1]; [1]Department of neurosurgery, Showa University School of Medicine, Tokyo, Japan

Although maximal safe resection is the current standard for glioblastoma surgery, its safety and removal rate conflict with each other. Electrophysiological monitoring, such as motor evoked potential monitoring and awake craniotomy, can be utilized as safety measures; not all facilities can perform them. Herein, we present a representative case report on our efforts for a safe malignant brain tumor surgery.

Case: A 77-year-old woman with glioblastoma in the premotor cortex presented with seizure of the upper left lower limb. Her pyramidal tract ran from the medial bottom to the posterior of the tumor. We performed excision from the site using the lowest gamma entropy. We then removed all parts of the tumor, with the exception of the pyramidal tract infiltration, and no paralysis was observed. She was definitively diagnosed with glioblastoma and is currently on maintenance chemotherapy.

As a preoperative examination, we performed cerebrovascular angiography. We then performed various other tests to ascertain the patient's condition. Considering lesions that affect language, Wada tests were performed regardless of laterality. For all patients with epilepsy onset, preoperative 256-channel electroencephalogram measurement and intraoperative the gamma entropy analysis were performed to confirm epileptogenicity. Considering lesions that affect eloquence, subdural electrodes were placed and brain function mapping was performed the next day. Based on the results, the safest cortical incision site and excision range were determined, and excision was performed on the following day.

Of the 14 operated glioblastoma cases after November 2018, more than 85% of the contrast-enhanced lesions were completely removed in 7 cases, partially removed in 5 cases, and underwent biopsy in 2 cases. Postoperative Karnofsky performance status scores remained unchanged in 11 cases, improved in 1 case, and deteriorated in 2 cases.

Our efforts have resulted in safe and sufficient removal of malignant brain tumors during surgery.

Key words: Glioblastoma | gamma entropy | maximal safe resection

STMO-14

CLINICAL EXPERIENCE OF BRAIN TUMOR SURGERY USING MIDDLEWARE "OPELINK"

Yu Fujii[1], Toshihiro Ogiwara[1], Tetsuya Goto[1,2], Yoshihiro Muragaki[3,4], Kazuhiro Hongo[1], Tetsuyoshi Horiuchi[1]; [1]Department of Neurosurgery, Shinshu University School Of Medicine, Matsumoto, Japan [2]Department of Neurosurgery, St. Marianna University School of Medicine, Kawasaki, Japan [3]Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan [4]Faculty of Advanced Techno-Surgery (FATS), Institute of Advanced Biomedical Engineering and Science, Graduate School of Medicine, Tokyo Women's Medical University, Tokyo, Japan

PURPOSE: The removal of brain tumors requires not only imaging information such as MRI and navigation systems, but also a variety of other information such as neurological function and biological information. To integrate this information, a novel operating room, "Smart Cyber Operating Theater (SCOT)", which connects the medical devices in the operating room via a network has developed. In this SCOT, the intraoperative information is time-synchronized, recorded, and stored by the middleware "OPeLiNK". Clinical experience of brain tumor surgery using OPeLiNK in our institute is reported. **METHODS:** Brain tumor surgeries performed at SCOT, which had been started since July 2018, was enrolled. In all surgeries intraoperative information was integrated by OPeLiNK. Surgical procedure was discussed between main surgeon and supervising surgeon in the Strategy Desk through OPeLiNK intraoperatively, if necessary. Clinical and radiological data from patients who underwent resection at SCOT were analyzed retrospectively. **RESULTS:** Sixty patients were involved. Histopathological diagnosis was glioma in 29 patients, pituitary adenoma in 29 patients, acoustic tumor in 1 patient and intravascular lymphoma in 1 patient. Intraoperative discussion with Strategy Desk through OPeLiNK was useful for not only surgeons but also for medical staff in operation room. Advice for extent of resection and craniotomy from Strategy Desk was conducted by OPeLiNK using conversation and drawing. Intraoperative comment was useful for postoperative review. OPeLiNK, which display multiple intraoperative information, was also used at postoperative conference. **CONCLUSION:** We have reported clinical experience with OPeLiNK for brain tumor surgery in our institute. OPeLiNK was useful for not only sharing intraoperative information with doctors outside the operation room but also postoperative review and education for young doctors.

Key words: brain tumor | middleware | integration

STMO-16

THE USABILITY OF DETAILED PRE-OPERATIVE 3D SIMULATION IMAGE FOR TUMOR RESECTION OF HIGH GRADE GLIOMA

Yoshihiro Tsukamoto[1], Manabu Natsumeda[1], Makoto Oishi[1], Yukihiko Fujii[1]; [1]Department of Neurosurgery, Brain Research Institute, University of Niigata, Niigata, Japan

Introduction: Understanding micro structures is important for the safety and reliable tumor resection for high grade glioma(HGG). The high-resolution 3-demension pre-operative simulation image (3D simulation imege) provides the useful information to the operators. We will report