

Advanced Surgical Management of Gliomas: Technological Requirements, Concept of Information-Guided Resection, and Clinical Results

Yoshihiro Muragaki et al.*

*Department of Neurosurgery and
Faculty of Advanced Techno-Surgery
Tokyo Women's Medical University, Tokyo
Japan*

1. Introduction

Contemporary technological developments revolutionized surgical management of intracranial gliomas. In fact, decades of the previous clinical experience clearly demonstrated that in such cases routine surgical technique usually does not permit to perform aggressive resection of the lesion without significant risk of the permanent postoperative neurological morbidity. The main associated surgical problem is evident. Arising from the cerebral tissue itself the majority of these tumors has a propensity for invasive growth, therefore their borders could not be clearly distinguished and precisely differentiated from the adjacent functionally important brain structures, which may preserve their function even in presence of tumor infiltration. It typically led to incomplete resection of the neoplasm, which, however, may have significant negative impact on prognosis.

Nowadays, the availability of the intraoperative MRI (iMRI) and related updated neuronavigation permits for neurosurgeons to perform resection of glioma under precise anatomical guidance. Moreover, the efficacy and safety of surgery is further enhanced by use of comprehensive neurophysiological monitoring, cortical and subcortical brain mapping, particularly performed during awake craniotomy, neurochemical navigation with 5-aminolevulinic acid (5-ALA), and regular histopathological characterization of the resected tissue. Combined application of these techniques provides an opportunity for aggressive removal of the intraaxial brain lesions with minimal risk of neurological complications. Surgery performed under such conditions can be designated as "information-guided procedure" (Iseki et al., 2008; Muragaki et al., 2011).

*Hiroshi Iseki, Takashi Maruyama, Mikhail Chernov, Takashi Suzuki, Kitaro Yoshimitsu, Manabu Tamura, Soko Ikuta, Masayuki Nitta Taiichi Saito, Jun Okamoto and Kintomo Takakura
*Department of Neurosurgery and Faculty of Advanced Techno-Surgery
Tokyo Women's Medical University, Tokyo, Japan*

The present chapter summarizes the experience with resection of the intracranial gliomas gained in the Tokyo Women's Medical University (TWMU) from 2000 till 2011 with an emphasis on applied intraoperative technology, treatment concept, and clinical results.

2. Rationale for aggressive resection of intracranial gliomas

The well-known benefits of resective surgery in cases of glioma include relief of compression of the tumor bulk on the surrounding brain (important for neurological improvement), reduction of the volume of the neoplasm (can render postoperative radiochemotherapy more effective), and establishment of the precise histopathological diagnosis, which is important for choice of the adjuvant therapy, optimal follow-up, and prediction of prognosis. Additionally, extensive removal of the tumor may positively influence patients' survival. While the latter does not formally proved up to date (Proescholdt et al., 2005) there is a growing agreement, that total resection of glioma is associated with better long-term outcome, even in cases of malignancies.

Stummer et al. (2008) adjusted biases of age and eloquent area location in the dataset of randomized study on use of neurochemical navigation with 5-ALA during resection of glioblastoma multiforme (GBM), and found that median overall survival after complete removal of the contrast-enhanced lesion was significantly longer compared to cases with its incomplete resection (17 months vs. 12 months). In concordance, in the report on EORTC 26951 randomized trial of combined chemotherapy for anaplastic gliomas, the overall survival was better after complete tumor removal compared to partial ones or to biopsy (van den Bent et al., 2006). It was demonstrated that 98% or more resection of GBM is associated with significant improvement of the long-term outcome (Lacroix et al., 2001), whereas recently the same trend was revealed even at 78% resection rate (Sanai et al., 2011). The similar results were marked by The Committee of Brain Tumor Registry of Japan (2003): analysis of 6400 cases of WHO grade III and IV gliomas showed that more than 90% tumor removal is associated with survival advantage, while such resection rate was attained in 6%-to-10% of cases only.

It is still questionable what should be defined as total removal of glioma. In our practice such resection rate is considered if postoperative MRI performed within first week after surgery confirms elimination of more than 95% of the mass lesion with regard to signal hyperintensity on T₂-weighted images in cases of low-grade neoplasms, or contrast-enhanced area on postgadolinium T₁-weighted images in cases of high-grade ones.

It should be specifically emphasized that complete surgical resection is highly desirable, but not ultimate goal of surgery for glioma, therefore it should not be performed if can cause major permanent postoperative neurological morbidity or lead to significant decline of the quality of life.

3. Surgical strategy for intracranial gliomas

Selection of the optimal surgical strategy for intracranial gliomas is based on the detailed preoperative clinical and radiological evaluation of the patient. The main details of the typical clinical protocol, which is used in our clinic, are following.

Before surgery the history of the disease, general condition and neurological status of the patient are carefully assessed. The Karnofsky Performance Scale (KPS) score and Medical Research Council (MRC) Neurological Scale grade are defined. Of note, in our practice age

of the patient has limited influence on the choice of the treatment strategy, but presence of co-morbidities definitely plays an important role. Risk of surgery is estimated by anesthesiologist according to American Society of Anesthesiologists (ASA) grading system. Preoperative neuroimaging protocol includes volumetric MRI (T_1 -weighted images in axial, coronal, and sagittal projections without and with single-dose gadoteridol, and T_2 -weighted images), Fluid Attenuation Inversion Recovery (FLAIR) images, diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), perfusion-weighted imaging (PWI), single- and multivoxel proton magnetic resonance spectroscopy (^1H -MRS). For this purpose at present we use 3 Tesla MR scanner due to its advantages in image acquirement and resolution. Additionally, positron emission tomography (PET) with ^{11}C -methionine, [^{18}F] Fluorodeoxyglucose, and ^{11}C -Choline is performed (Kato et al, 2008). At present cerebral angiography in patients with gliomas is usually omitted, whereas interrelationships between the tumor and vascular structures are evaluated on MR angiography and SWI. Based on results of these investigations tumor size, location, and mass-effect are evaluated, and histopathological type and grade of the neoplasm are predicted.

The functional grade of the tumor is assigned according to its location (Sawaya et al., 1998). If the neoplasm is located in close vicinity to the pyramidal tract diffusion-tensor imaging (DTI) is attained for evaluation of its interrelationships with the lesion and estimation of the possible shift in location. In cases of cortical gliomas functional MRI is performed for identification of the motor and language areas and their correspondence to the tumor location. If according to functional MRI glioma occupies the language area Wada test is performed.

Preoperative invasive cortical or subcortical brain mapping with implanted subdural grid or stereotactic electrodes is used occasionally, particularly in cases with symptomatic epilepsy.

3.1 Indications for stereotactic biopsy

Image-guided stereotactic biopsy represents a standard neurosurgical technique, routinely used in cases of parenchymal brain lesions. Tissue sampling from the area, which looks the most abnormal on MRI, results in high rate of positive histopathological findings. Nevertheless, heterogeneity of the lesion, frequently observed in gliomas, limits the diagnostic accuracy of the procedure, and not infrequently leads to erroneous tumor typing and/or grading. Moreover, the stereotactic tissue sampling does not seem justified if further resection of the lesion is planned.

Since we advocate aggressive surgical management of gliomas, not more than 10% of patients with parenchymal brain lesions undergoing stereotactic biopsy in our clinic (Muragaki et al, 2008; Chernov et al., 2009). The indications for this procedure are limited to following:

- clarification of the histopathological diagnosis, which can not be established based on clinical and radiological investigations, particularly for differentiation of neoplastic and non-neoplastic lesions;
- histopathological confirmation of the diagnosis of the tumor, for which treatment with chemotherapy and/or irradiation is planned (for example, malignant lymphoma);
- stereotactic implantation of electrodes for preoperative brain mapping in cases of gliomas (simultaneous tissue sampling is usually performed);
- extremely extensive or diffuse lesions, which are not amenable even for subtotal resection (such as gliomatosis cerebri).

For guidance of stereotactic brain biopsy combined use of structural MRI and metabolic imaging (^1H -MRS and/or PET) is reasonable, especially in recurrent cases or highly vascular lesions (Chernov et al., 2009).

3.2 Strategy for glioma resection

Optimal strategy of glioma resection is mainly determined by 3 interrelated factors: tumor size, histopathological grade, and functional grade. The goal of surgery should be attainment of the maximal possible removal of the neoplasm, defined as radiologically total, or as subtotal leaving the residual lesion within the functioning eloquent brain structures identified with neurophysiological monitoring and/or brain mapping.

In general, the best result of surgery is maximal possible removal of the whole area of the hyperintense signal detected on preoperative T_2 -weighted or FLAIR images. It can be frequently achieved in cases of low-grade neoplasms, but rarely attained in high-grade lesions surrounded by prominent peritumoral edema. In latter cases surgery is usually directed on the maximal possible resection of the contrast-enhanced area.

In rare occasions resection of extensive tumors affecting functioning eloquent brain structures can be directed on the most metabolically active part of the neoplasm detected according to ^{11}C -methionine uptake on PET.

4. Intelligent operating theater of the Tokyo Women's Medical University

Intelligent operating theater was established in TWMU in 2000. Its internal organization is presented below.

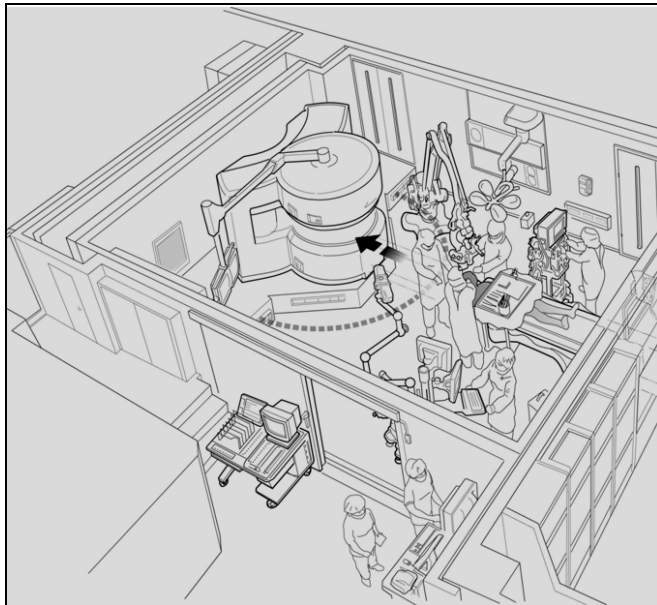


Fig. 1. Internal organization of the intelligent operating theater in TWMU. Arrow indicates direction of the operating table movement during iMRI investigation. Dots correspond to 5-gauss line.

4.1 Intraoperative MRI

First iMRI systems were introduced in neurosurgery at the end of 1990's. Since then, such devices have been used for real-time observation of surgical manipulations, for assessment of the extent of tumor resection, and evaluation of the intraoperative complications. While real-time guidance of the surgical manipulations with iMRI is theoretically presumed to be the most effective, such systems usually provide relatively narrow working space and necessitate all surgical devices to be composed of non-ferromagnetic materials (Iseki et al., 2005). By contrast, if iMRI investigations are performed at some temporary break points during surgical procedure, it can provide a higher degree of freedom for the surgeon and permit to use standard (not MRI-compatible) neurosurgical instrumentarium. It should be noted that any type of iMRI system increases the operation time, because MR imaging by itself is a time-consuming process.

During the last decade there is a trend for introduction of iMRI scanners with high magnetic field strength of 1.5 and 3 Tesla. Their advantages include high image quality, possibility to attain diffusion tensor and spectroscopic images, as well as short scanning time. Increase of magnetic field strength, however, is associated with greater possibility of image distortion artifacts. The risk of the latter is 5 times greater in 1.5 Tesla MR scanner compared to 0.2 Tesla one (Fransson et al., 2001). Additionally, the maintenance costs of high-field-strength iMRI scanners is significant.

Intelligent operating theater of the TWU is equipped with a low-field-strength (0.3 Tesla) open iMRI scanner (AIRIS II™; Hitachi Medical Co., Chiba, Japan). It has a hamburger-like shape with a 43 cm gantry gap and a disc-shaped permanent magnet producing vertical magnetic field with resonance frequency of 12.7 MHz. This scanner does not require a cooling system, which significantly reduce its operating cost by approximately 10.000 Japanese yen (around 100 US \$) per month. Low magnetic field strength creates narrow 5-gauss line, extending 2 meters from both sides, 2.2 meters in front, 1.8 meters backwards, and 2.5 meters upwards, which permits for the surgeon to use some conventional surgical instruments in the working space outside of it (for example, high-speed drill). Nevertheless, all surgical devices that are used within the 5-gauss line, such as operating table (MOT2000-MRI; Mizuho Ltd., Tokyo, Japan) and operating microscope (MRI-30; Mitaka Co., Tokyo, Japan) are constructed from non-ferromagnetic material to prevent accidents and avoid image artifacts.

Originally developed radiofrequency receiver coil integrated with Sugita head-holder (Head-holder coil; Mizuho Ltd., Tokyo, Japan) significantly improved the quality of the intraoperative images (Ozawa et al., 2008a, 2008b). Positioning of the coil in close vicinity to the visualized region provides one an opportunity to perform MRI investigations with minimal distortion artifacts and maximum structure contrasting in any plane irrespectively to orientation of the object. It means, that fixation of the patient head can be done in the most desirable position for tumor removal, therefore use of any required surgical approach, including retrosigmoid and transtentorial, is possible. In fact, the quality of the intraoperative images in our practice is comparable to those ones obtained on scanners with higher magnetic field strength.

After induction of the general anesthesia the patient's head is firmly fixed with titanium pins in the modified Sugita head-holder, representing the lower arch of the Head-holder coil. It is connected to the operating table with a special supporting arm, which provides easy adjustment of the head position according to the surgical needs. Before iMRI

investigation several fiducial markers are fixed to the skull on the periphery of the surgical field, and an additional one is inserted into the surgical wound and located in the vicinity to the target. Both semicircular arches of the Head-holder coil are connected. A wide transparent sterile drape is used to cover the whole body of the patient including the head, and the operating table is moved into the gap of the iMR scanner.

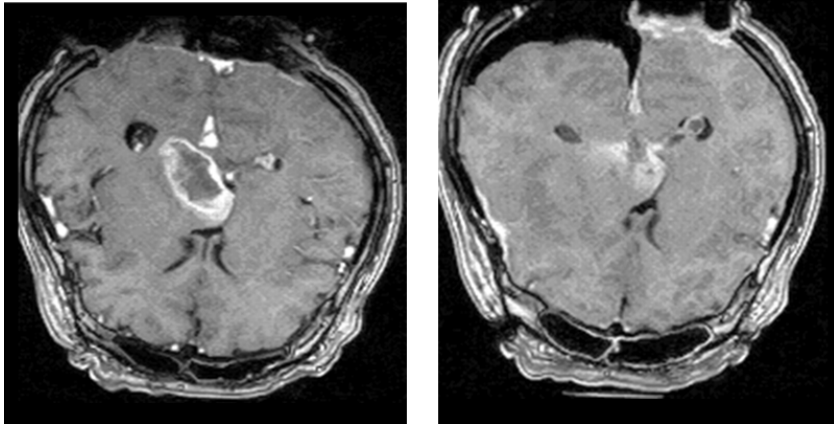


Fig. 2. Intraoperative images obtained using 0.3 Tesla MR scanner before (*left*) and after (*right*) 85% resection of the of GBM of the left thalamus via occipital-transtentorial approach in prone position of the patient.

Integration of the Head-holder coil with modified Komai stereotactic frame permits to perform stereotactically guided surgical procedures under the control of iMRI (Taniguchi et al., 2006).



Fig. 3. Head-holder coil integrated with modified Komai stereotactic frame for stereotactically guided surgical procedures under the control of intraoperative MRI.

4.1.1 Intraoperative diffusion-weighted imaging

Use of Head-holder coil permits for us to acquire intraoperatively not only volumetric MR images, but to perform MR angiography, functional investigations (Gasser et al., 2011), and DWI. The latter is of particular importance, because it provides nearly real-time information on spatial interrelationships between the pyramidal tract, the lesion, and position of the surgical instruments, including the electrical stimulator for subcortical functional mapping, which can be effectively used for prevention of the inadvertent injury of the pyramidal tract and corresponding avoidance of the postoperative deterioration of the motor function.

The estimated positional accuracy of iDWI in our practice is within 5 mm, which corresponds to the conducting depth of the electrical stimulation during subcortical brain mapping (Ozawa et al., 2009a). It should be marked, however, that diffusion anisotropy of the white matter tracts may be reduced by presence of the tumor or peritumoral edema, which may occasionally lead to poor visualization of the pyramidal tract on the affected side (Ozawa et al., 2008b).

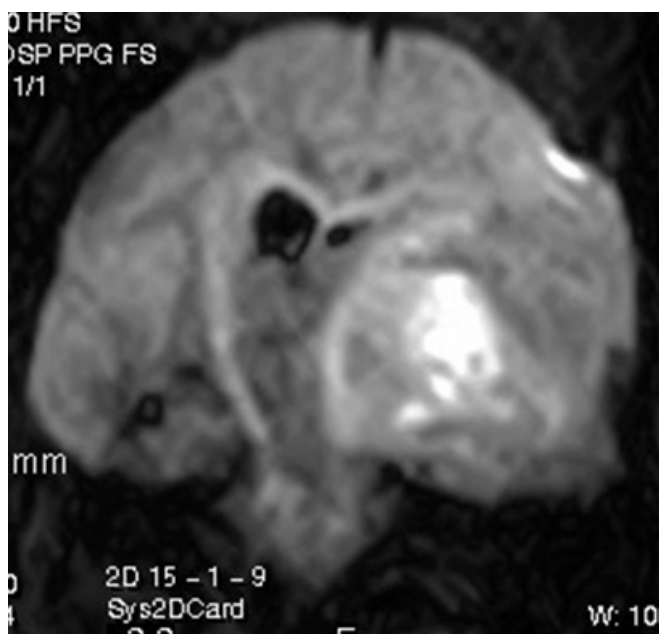


Fig. 4. Intraoperative DWI obtained on MRI scanner with magnetic field strength of 0.3 Tesla: both pyramidal tracts are clearly seen and its shift on the affected side can be easily evaluated.

4.2 Updated intraoperative neuronavigation

Simultaneous to installation of iMRI in the intelligent operating theater of TWUM, the special system for updated neuronavigation based on the intraoperative neuroimaging has been developed in 2000. Its main advantage is avoidance of the adverse effects caused by brain shift and deformation, which allows precise identification of the tumor position and its interrelationships with surrounding brain structures.

For facilitation of the tumor removal and detection of the neoplastic remnants we use previously developed navigator for photon radiosurgery system (PRS navigator; Toshiba Medical Co. Ltd., Tokyo, Japan), which allows fast and easy updating of the information obtained with iMRI. The mislocalization errors of the device constitute 0.8 mm in average, 1.5 mm at maximum, and 0.5 mm at minimum, and typically do not exceed 1 mm (Iseki et al., 2008). The system permits co-registration, fusion and three-dimensional reconstruction of the various images, and provides easy-to-understand information. The different areas of the perilesional brain can be color-coded according to the safety of manipulations and probable risk of complications. Additionally, the device may be integrated with special sound alarm, which is automatically activated if surgical instruments are coming in close proximity to the high-risk area.



Fig. 5. Intraoperative neuronavigation system (PRS navigator; Toshiba Medical Co. Ltd., Tokyo, Japan) used in intelligent operating theater of TWUM (*left*) and its screen with color-coded safety areas of the tumor resection (*right*), showing areas located less than 5 mm, between 5 and 10 mm, and more than 10 mm to the pyramidal tract, which are demarcated, respectively, as red, yellow, and green.

4.3 Intraoperative neurophysiological monitoring, brain mapping, and awake craniotomy

During surgical procedures in the intelligent operating theater of TWUM comprehensive intraoperative neurophysiological monitoring is used routinely. The depth of anesthesia, which may interfere with results of such examinations is constantly monitored with bispectral index (BIS) monitor.

Somatosensory evoked potentials (SEP) are recorded with stimulation of the median nerve. The values of the latencies and amplitudes obtained after craniotomy just before the dural incision are considered as an individual baseline. The central sulcus is localized based on the polarity inversion of the N20 component of SEP.

Motor evoked potentials (MEP) are monitored using transcranial electrodes and measurement of the electromyograms at the thenar, quadriceps femoris, anterior tibial, and gastrocnemius muscles on both sides. Direct cortical mapping of the primary motor area is also performed. The parameters of stimulation depend on the various surgical conditions,

but as a rule low-frequency current is used initially for prevention of seizures (Otani et al., 2005; Mikuni & Miyamoto, 2010).

The main indication for awake craniotomy in our practice is location of glioma in the vicinity to the language centers. During examination speech production, repetition, object naming, verb generation, and reading tasks are used with simultaneous stimulation of the different language areas. Meanwhile, several problems may arise with identification of the cortical speech centers using brain mapping. Particularly, elimination of anarthria produced by positive motor response of the tongue and face or from the negative motor response of the tongue during cortical stimulation is of paramount importance for precise evaluation of the language function (Mikuni & Miyamoto, 2010).

4.3.1 Intraoperative examination monitor for awake surgery (IEMAS)

To facilitate the process of brain mapping our group had developed dedicated Intraoperative Examination Monitor for Awake Surgery (IEMAS). It is an information-sharing device, which provides ones an opportunity for simultaneous real-time visualization of the wide spectrum of co-registered intraoperative data (Iseki & Nambu, 2005; Iseki et al., 2008; Sakurai et al., 2011). For example, the patient's mimic and face movements during answering on the specific test questions, type of the examination test, position of the surgical instruments and cortical stimulator in the surgical field, parameters of BIS monitor, and general view of the surgical field through the operating microscope, can be presented compactly in one screen with several displays. From 2010 wireless modification of the device became available (Yoshimitsu et al., 2010).

4.4 Neurochemical navigation with 5-ALA and intraoperative histopathological diagnosis

Neurochemical navigation with 5-ALA during resection of gliomas is based on the effect of its accumulation in the tumor cells and areas with impaired blood-brain barrier (BBB) and further conversion into protoporphyrin IX, which fluorescence is visible under ultraviolet light (Ando et al., 2011). This method can be effectively used for identification of the neoplastic tissue and its differentiation from the brain itself, which may be particularly important at the periphery of the neoplasm.

It should be noted, however, that erroneous results of neurochemical navigation with 5-ALA are possible. False negative cases may be met in low-grade gliomas due to relative preservation of the BBB, or be caused by presence of the adherent blood on the tissue surface since erythrocytes can absorb ultraviolet light, which in such case does not reach protoporphyrin IX in the pathological tissue (Ando et al., 2011). Contrary, false positive fluorescence may be observed in the areas with high vascularisation, reactive astrocytosis, or BBB impairment in the absence of the neoplastic elements.

Regular intraoperative histopathological investigation of the resected tissue on the frozen sections effectively complement neurochemical navigation and may be efficiently used for guidance of the tumor resection, identification of the neoplastic remnants, and confirmation of completeness of the lesion removal.

4.5 Management of the intraoperative information and surgical information strategy desk

Appropriate management of the intraoperative medical information may have a significant impact on the clinical decision-making, and, therefore, may influence the outcome. During

neurosurgical procedure a wide spectrum of data, such as various pre- and intraoperative images, details of the intraoperative neuronavigation, parameters of the neurophysiological monitoring, nuances of the cortical mapping, and main characteristics of the current patient condition, should be provided. Moreover, those data have to be constantly updated, presented in a real-time regime, and widely distributed between members of the surgical team. At optimal, the scientific information from evidence-based sources, integrated using probability assessment technique, should be also available upon request. It is evident, that for a purpose of high quality surgery all information should be not only precise and proved, but presented in a most compact, comfortable and friendly way for optimal visualization, easy understanding, and effective use.

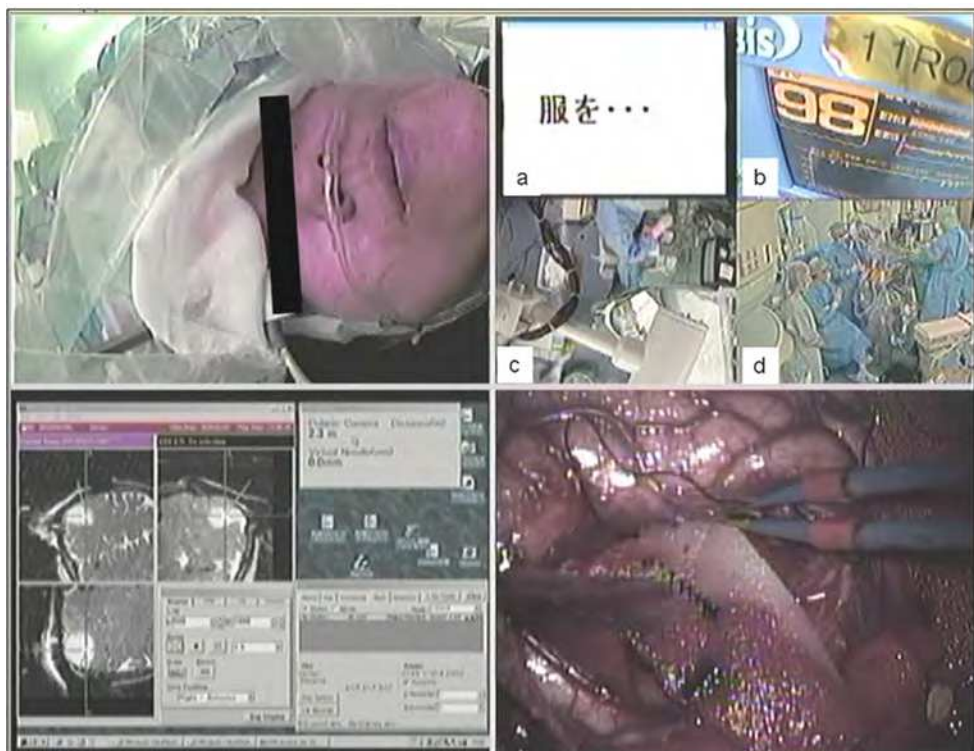


Fig. 6. Integration of the multiple intraoperative data on the screen of IEMAS. On the upper left display, the patient's face can be seen to facilitate checking of the consciousness status and mimics during response to test questions. On the lower left display, the anatomical data from the real-time updated neuronavigation system is shown, which allows localization of the exact position of the cortical stimulator. On the lower right display the view of the surgical field through the operative microscope is seen, which can be helpful for precise identification of the timing of stimulation. On the upper right display, 4 different types of information are presented: the test question provided for a patient (a), parameters of the BIS monitor reflecting the patient's awakening state (b), and general view of the operating theater (c and d).

Intelligent operating theater of TWMU has several in-room liquid crystal display (LCD) monitors, therefore integrated real-time information can be easily distributed and quickly analyzed by all members of the surgical team, practically without interruption of the surgical manipulations. Additionally, a special surgical information strategy desk has been designed to facilitate search of an optimal solution in a constantly changing surgical situation. It provides for a surgeon the whole spectrum of the integrated information about situation in the surgical field, chemical neuronavigation, neurophysiological monitoring, intraoperative images, histopathological investigation etc. All data are presented in a real time regime and their visualization can be easily changed or combined in a different way just by a click of the network switch. The system makes possible transfer of the information into the distant areas, therefore, urgent consulting service with the specialists, located outside the operating theater, can be provided.



Fig. 7. Senior neurosurgeon supervising removal of glioma from the neurosurgical office using surgical information strategy desk.

5. Concept of the information-guided tumor resection

The concept of the information-guided surgical management of gliomas is based on the integration of the various intraoperative anatomical, functional, and histopathological data with a purpose to attain maximal surgical resection of the tumor with minimal risk of postoperative neurological morbidity.

In our usual practice the initial iMRI investigation is performed after craniotomy and completion of the approach to the tumor. After removal of the neoplasm, the investigation is repeated for assessment of the completeness of resection, identification of the residual lesion or possible adverse effects such as hemorrhage. If residual glioma is identified and considered suitable for additional resection, the newly obtained iMRI data are installed into neuronavigation device and further removal of the neoplasm is performed using this updated information (Muragaki et al., 2006, 2011). After completion of such additional resection iMRI is repeated once again.

It should be clear, however, that anatomical data alone, even if obtained with iMRI, are not sufficient enough for guidance of the tumor resection. Location of the eloquent brain

structures has known individual variability and may be displaced during growth of the neoplasm, which necessitates use of comprehensive neurophysiological monitoring and intraoperative cortical and subcortical brain mapping with or without awake craniotomy, and further integration of the neurophysiological and anatomical data within the updated neuronavigation system. In any occasion the first priority in surgical decision-making should be given to such functional information (Senft et al., 2010).

Additionally, resection of the residual part of the neoplasm after removal of its main bulk should be guided by neurochemical navigation with 5-ALA and regular intraoperative histopathological investigations of the walls of the surgical cavity (Muragaki et al., 2011). Certainly, effectiveness of the information-guided tumor resection is strongly depended on the quality of the related information (Iseki et al., 2008).

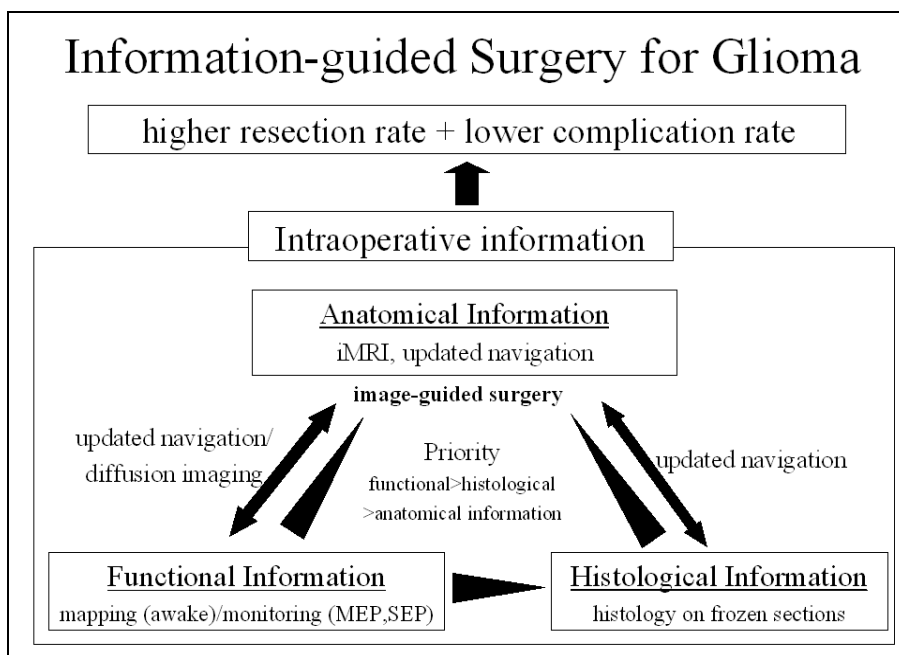


Fig. 8. Main principles of the information-guided surgery for glioma (iMRI, intraoperative MRI; MEP, motor evoked potentials; SEP, somatosensory evoked potentials).

6. Surgical experience and outcome

From March 2000 till January 2011, 939 neurosurgical interventions directed on resection of the intracranial gliomas, including 220 awake craniotomies, were performed in the intelligent operating theatre of the TWMU.

6.1 Resection rate

Maximal possible resection of glioma was attained in 99% of cases. Mean resection rate was 92%. It did not depend on histopathological grade and constituted, in median, 91%, 93%, and 92% for WHO grade II, III, and IV tumors, respectively.

Median residual tumor volume was 0.17 cc. In general, it was greater in neoplasms of higher histopathological and functional grade, but such trends did not reach statistical significance. Radiologically total tumor removal was achieved in 46% of cases.

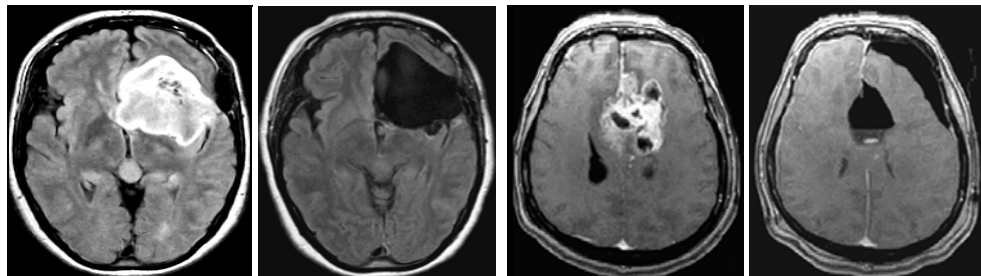


Fig. 9. Examples of the total surgical resection of the low-grade (*left*) and high-grade (*right*) gliomas.

6.1.1 Effectiveness of iMRI

Low-field-strength iMRI showed high sensitivity for detection of the residual glioma, which was confirmed by postoperative high-field-strength MRI investigations. In no one case of our series unexpected residual tumor was disclosed.

6.2 Technical failures and complications

In 0.3% of cases technical troubles with iMRI did not permit to perform aggressive surgery. In 2% of awake craniotomies tumor resection was not completed as planned due to lost of cooperation with the operated patient.

Immediately after surgery more or less prominent neurological deterioration was marked in 34% of patients. It should be noted, however, that in more than half of these cases, the symptoms regressed at least up to preoperative level within 3 subsequent months. The risk of such temporary postoperative neurological deterioration was found to be higher in cases with greater resection rate.

Wound infection after tumor removal was met in 2% of cases. Hemorrhage complicated stereotactic brain biopsy in 1% of cases.

6.2.1 Learning curve

Gradual gaining of experience of surgical management of gliomas in the intelligent operating theater resulted in statistically significant increase of tumor resection rate, and decrease of the volume of residual neoplasm, especially in cases of histopathological WHO grade IV and Sawaya functional grade III tumors.

Nevertheless, in our latest series of patients with WHO grade II and III gliomas the resection rate was intentionally decreased (in median up to 84-88%) for avoidance of postoperative neurological deterioration and providing optimal quality of life.

6.2.2 Diagnostic accuracy of stereotactic biopsy

In overall the diagnostic yield of stereotactic biopsy in our practice constituted 94%, while attained 100% in $^1\text{H-MRS}$ -supported procedures (Chernov et al., 2009). However,

comparison of the histopathological diagnoses after stereotactic biopsy and subsequent surgical resection of the lesion revealed complete diagnostic agreement in 35% of cases only, whereas minor disagreement was noted in 38%, and major one in 27%. Among the latter undergrading of non-enhancing WHO grade III gliomas was the most common (Muragaki et al., 2008; Chernov et al., 2009).

6.3 Neurological outcome after glioma resection

In 13% of patients pre-existing signs and symptoms improved after surgery, whereas in 12% of patients permanent neurological deterioration was marked. After intentional decrease of resection rate in our latest series of patients with WHO grade II and III gliomas, the risk of permanent postoperative neurological deterioration reduced to 9%.

6.4 Long-term survival

In patients with available long-term follow-up the prognosis was significantly worse for WHO grade IV gliomas, but did not reach statistically significant differences between WHO grade II and III tumors (Shinohara et al., 2008). Among patients who were followed more than 2 years after surgery (46% of the total number of cases) with WHO grade II, III, and IV gliomas the corresponding actuarial 5-year survival rates were 87%, 69%, and 19%, respectively. For comparison, according to The Committee of Brain Tumor Registry of Japan (2003) the same rates in general neurosurgical practice, constitute 75%, 40%, and 7%, respectively (Muragaki et al., 2011).

In patients with low-grade glioma the extent of tumor resection was significantly associated with prolonged overall survival, progression-free survival, and malignant-progression-free survival.

7. Further perspectives

Use of iMRI and real-time updated neuronavigation has proved their great efficacy in the neurosurgical management of parenchymal brain tumors. Anyway, several problems still require solution, and necessity of further technological improvements is evident.

7.1 Computer-based system for correction of distortion artifacts

In fact, the intraoperative neuronavigation system, which is used in our practice, is not "real-time", but nearly "real-time". It means that the risk of some mislocalization errors, particularly caused by brain deformation and its movements due to surgical manipulations, is still preserved. It may be of critical importance if the lesion is located in the nearest vicinity to the eloquent brain structures. For example, the magnitude of pyramidal tract displacement due to removal of the neoplasm varies on the affected side from 0.5 to 8.7 mm (Ozawa et al., 2009b). Therefore, development of the special computer-based system for constant real-time estimation and correction of the mislocalization errors is required.

7.2 Overcoming the shortages of the low-magnetic-field iMRI

While use of low-field-strength iMRI has definite practical advantages, it also has some shortages compared to the high-field-strength devices. It is evident, that despite any technological achievements the spatial resolution of 3 Tesla MR scanner is much better. Additionally, some specific investigations, such as ^1H -MRS, can not be effectively attained

with 0.3 Tesla iMRI. To overcome these limitations the special computer-based program for fusion of the preoperative images obtained at high-field-strength MRI or PET, with intraoperative images of low-field-strength iMRI is highly desirable, since it can potentially provide highly informative anatomic and metabolic data adjusted to intraoperative brain shift and deformation.

7.3 Robotic neurosurgery

Incorporation of the robotic systems into neurosurgical practice may provide extremely high preciseness (up to 10 μm), and may potentially reduce the risk of neurological deficit if surgery is performed in highly vulnerable brain areas. Other potential advantages of the robotics include opportunity to perform manipulations in extremely limited working space, as well as possibility of initial computer-aided modeling and simulation of the planned surgical actions.

7.4 Information-guided treatment simulation and pre-emptive risk management

In order to improve safety and effectiveness of the neurosurgical procedures their precise planning is absolutely necessary. Therefore, it is important to develop special computer-aided modalities and tools for neurosurgical simulation based both on the previous clinical experience and available scientific data. To attain such a purpose just installation of the surgical records and video into databases is not sufficient, but special system for their automatic analysis with possible immediate extraction of the very particular information important for intraoperative decision-making should be created. Such a system should permit prediction of the possible risks and inform the surgeon about their probability. The possible consequences of the various surgical manipulations have to be analyzed and the optimal solution "what to do" in constantly changing surgical situation should be offered. Moreover, at optimal such a system should simulate not only the surgical procedure, but the whole clinical course of the particular patient with comparison of the different treatment options, evaluation of the various risks, and scientifically-based choice of the optimal treatment strategy for attainment of the best possible outcome (Iseki et al, 2008, 2010).

7.5 Development of effective adjunctive treatment options

It is evident, that despite further development of the intraoperative technology, significant proportion of the intracranial gliomas will not undergo total resection due to safety concerns. It necessitates continuous search for effective adjuvant treatment modalities. Seemingly, radiosurgery may be successful in some low-grade gliomas. In cases of high-grade neoplasms addition of tumor vaccine therapy to the standard treatment protocol may provide some benefits for the patients. Individually-based choice of the chemotherapeutic drugs based on the genetic profile of the tumor also requires further investigation.

8. Conclusion

Information-guided surgical management of intracranial gliomas based on the intraoperative integration of the various anatomical, neurophysiological, and histopathological data permits to perform aggressive tumor resection with minimal risk of permanent postoperative neurological morbidity, and may result in meaningful prolongation of the patients' survival. Particularly, survival advantage in patients with WHO grade III neoplasms seems to be of special clinical significance, since may render their long-term prognosis similar to cases of low-

grade tumors. It can be expected, that further development of the intraoperative technologies will permit to increase the rate of glioma resection. Nevertheless, due to safety reasons total removal seemingly will not be possible in significant proportion of these tumors, which necessitates continuous search for effective adjuvant treatment modalities.

9. Acknowledgements

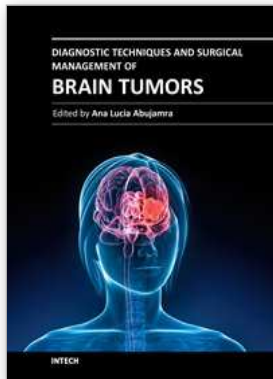
The authors wish to express their gratitude to the members and technical staff of the Departments of Neurosurgery and Anesthesiology, Surgical Facility Unit, and Faculty of Advanced Techno-Surgery of the Tokyo Women's Medical University, as well as to maintenance team of the Hitachi Medical Corporation, for long-term friendly and fruitful collaboration during clinical work both inside and outside of the Intelligent Operating Theater, which allows for us to provide the best possible care for the patients with brain tumors. Special thanks are devoted to prof. Yoshikazu Okada, prof. Tomokatsu Hori, and Dr. Masahiko Tanaka for their constant support of our clinical and research activities.

10. References

- Ando, T.; Kobayashi, E.; Liao, H.; Maruyama, T.; Muragaki, Y.; Iseki, H.; Kubo, O. & Sakuma, I. (2011). Precise comparison of protoporphyrin IX fluorescence spectra with pathological results for brain tumor tissue identification. *Brain Tumor Pathology*, Vol. 28, No. 1, (February 2011), pp. 43-51, ISSN 1433-7398
- Chernov, M.F.; Muragaki, Y.; Ochiai, T.; Taira, T.; Ono, Y.; Usukura, M.; Maruyama, T.; Nakaya, K.; Nakamura, R.; Iseki, H.; Kubo, O.; Hori, T. & Takakura, K. (2009). Spectroscopy-supported frame-based image-guided stereotactic biopsy of parenchymal brain lesions: comparative evaluation of diagnostic yield and diagnostic accuracy. *Clinical Neurology and Neurosurgery*, Vol. 111, No. 6, (July 2009), pp. 527-535, ISSN 0303-8467
- Fransson, A.; Andreo, P. & Potter, R. (2001). Aspects of MR image distortions in radiotherapy treatment planning. *Strahlentherapie und Onkologie*, Vol. 177, No. 2, (February 2001), pp. 59-73, ISSN 0179-7158
- Gasser, T.; Szelenyi, A.; Senft, C.; Muragaki, Y.; Sandalcioglu, I.E.; Sure, U.; Nimsky, C. & Seifert, V. (2011). Intraoperative MRI and functional mapping. *Acta Neurochirurgica Supplementum*, Vol. 109, pp. 61-65, ISSN 0065-1419
- Iseki, H.; Muragaki, Y.; Nakamura, R.; Ozawa, N.; Taniguchi, H.; Hori, T. & Takakura, K. (2005). Intelligent operating theater using intraoperative open-MRI. *Magnetic Resonance in Medical Sciences*, Vol. 4, No. 3, (February 2006), pp. 129-136, ISSN 1347-3182
- Iseki, H. & Nambu, K. (2005). Intraoperative Examination Monitoring for Awake Surgery (IEMAS). *No Shinkei Geka*, Vol. 33, No. 10, (October 2005), pp. 1028-1031, ISSN 0301-2603
- Iseki, H.; Nakamura, R.; Muragaki, Y.; Suzuki, T.; Chernov, M.; Hori, T. & Takakura K. (2008). Advanced computer-aided intraoperative technologies for information-guided surgical management of gliomas: Tokyo Women's Medical University experience. *Minimally Invasive Neurosurgery*, Vol. 51, No. 5, (October 2008), pp. 285-291, ISSN 0946-7211
- Iseki, H.; Muragaki, Y.; Maruyama, T.; Chernov, M.; Suzuki, T.; Yoshimitsu, K.; Ikuta, S. & Tamura, M. (2010). Neurosurgical workflow in TWIns. Proceedings of the 6th Asian

- Conference on Computer Aided Surgery (ACCAS 2010), pp. 31-32, Busan, Korea, November 26-27, 2010
- Kato, T.; Shinoda, J.; Nakayama, N.; Miwa, K.; Okumura, A.; Yano, H.; Yoshimura, S.; Maruyama, T.; Muragaki, Y. & Iwama T. (2008). Metabolic assessment of gliomas using ^{11}C -methionine, ^{18}F fluorodeoxyglucose, and ^{11}C -choline positron-emission tomography. *AJNR Am J Neuroradiol*, Vol. 29, No. 6, (June 2008), pp. 1176-1182, ISSN 0195-6108
- Lacroix, M.; Abi-Said, D.; Fourney, D.R.; Gokaslan, Z.L.; Shi, W.; DeMonte, F.; Lang, F.F.; McCutcheon, I.E.; Hassenbusch, S.J.; Holland, E.; Hess, K.; Michael, C.; Miller, D. & Sawaya R. (2001). A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. *Journal of Neurosurgery*, Vol. 95, No. 2, (August 2001), pp. 190-198, ISSN 0022-3085
- Mikuni, N. & Miyamoto, S. (2010). Surgical treatment of glioma: extent of resection applying functional neurosurgery. *Neurologia Medico-Chirurgica*, Vol. 50, No. 9, (September 2010), pp. 720-726, ISSN 0470-8105
- Muragaki, Y.; Iseki, H.; Maruyama, T.; Kawamata, T.; Yamane, F.; Nakamura, R.; Kubo, O.; Takakura, K. & Hori, T. (2006). Usefulness of intraoperative magnetic resonance imaging for glioma surgery. *Acta Neurochirurgica Supplementum*, Vol. 98, pp. 67-75, ISSN 0065-1419
- Muragaki, Y.; Chernov, M.; Maruyama, T.; Ochiai, T.; Taira, T.; Kubo, O.; Nakamura, R.; Iseki, H.; Hori, T. & Takakura K. (2008). Low-grade glioma on stereotactic biopsy: how often is the diagnosis accurate? *Minimally Invasive Neurosurgery*, Vol. 51, No. 5, (October 2008), pp. 275-279, ISSN 0946-7211
- Muragaki, Y.; Iseki, H.; Maruyama, T.; Tanaka, M.; Shinohara, C.; Suzuki, T.; Yoshimitsu, K.; Ikuta, S.; Hayashi, M.; Chernov, M.; Hori, T.; Okada, Y. & Takakura, K. (2011). Information-guided surgical management of gliomas using low-field-strength intraoperative MRI. *Acta Neurochirurgica Supplementum*, Vol. 109, pp. 67-72, ISSN 0065-1419
- Otani, N.; Bjeljac, M.; Muroi, C.; Weniger, D.; Khan, N.; Wieser H.G.; Curcic, M. & Yonekawa, Y. (2005). Awake surgery for glioma resection in eloquent areas: Zurich's experience and review. *Neurologia Medico-Chirurgica*, Vol. 45, No. 10, (October 2005), pp. 501-511, ISSN 0470-8105
- Ozawa, N.; Muragaki, Y.; Nakamura, R. & Iseki, H. (2008a). Intraoperative diffusion-weighted imaging for visualization of the pyramidal tracts. Part I: Pre-clinical validation of the scanning protocol. *Minimally Invasive Neurosurgery*, Vol. 51, No. 2, (April 2008), pp. 63-66, ISSN 0946-7211
- Ozawa, N.; Muragaki, Y.; Nakamura, R. & Iseki, H. (2008b). Intraoperative diffusion-weighted imaging for visualization of the pyramidal tracts. Part II: Clinical study of usefulness and efficacy. *Minimally Invasive Neurosurgery*, Vol. 51, No. 2, (April 2008), pp. 67-71, ISSN 0946-7211
- Ozawa, N.; Muragaki, Y.; Nakamura, R. & Iseki, H. (2009a). Identification of the pyramidal tract by neuronavigation based on intraoperative diffusion-weighted imaging combined with subcortical stimulation. *Stereotactic and Functional Neurosurgery*, Vol. 87, No. 1, (February 2009), pp. 18-24, ISSN 1423-0372
- Ozawa, N.; Muragaki, Y.; Nakamura R.; Hori, T. & Iseki, H. (2009b). Shift of the pyramidal tract during resection of the intraaxial brain tumors estimated by intraoperative diffusion-weighted imaging. *Neurologia Medico-Chirurgica*, Vol. 49, No. 2, (February 2009), pp. 51-56, ISSN 0470-8105

- Proescholdt, M.A.; Macher, C.; Woertgen, C. & Brawanski A. (2005). Level of evidence in the literature concerning brain tumor resection. *Clinical Neurology and Neurosurgery*, Vol. 107, No. 2, (February 2005), pp. 95-98, ISSN 0303-8467
- Sakurai, Y.; Muragaki, Y.; Okada, Y.; Nambu, K. & Iseki, H. (2011). The development and application of the device for intraoperative examination monitor for awake surgery. *Journal of Tokyo Women's Medical University*, Vol. 81, No. 1, (February 2011), pp. 32-40, ISSN 0040-9022
- Sanai, N.; Polley, M.Y.; McDermott, M.W.; Parsa, A.T & Berger M.S. (2011). An extent of resection threshold for newly diagnosed glioblastomas. *Journal of Neurosurgery*, (in press), ISSN 0022-3085
- Sawaya, R.; Hammoud, M.; Schoppa, D.; Hess, K.R.; Wu, S.Z.; Shi, W.M. & Wildrick, D.M. (1998). Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. *Neurosurgery*, Vol. 42, No. 5, (May 1998), pp. 1044-1056, ISSN 0148-396X
- Senft, C.; Franz, K.; Ulrich, C.T.; Bink, A.; Szelenyi, A.; Gasser, T. & Seifert, V. (2010). Low field intraoperative MRI-guided surgery of gliomas: a single center experience. *Clinical Neurology and Neurosurgery*, Vol. 112, No. 3, (April 2010), pp. 237-243, ISSN 0303-8467
- Shinohara, C.; Muragaki, Y.; Maruyama, T.; Shimizu, S.; Tanaka, M.; Kubota, Y.; Oikawa, M.; Nakamura, R.; Iseki, H.; Kubo, O.; Takakura, K. & Hori, T. (2008). Long-term prognostic assessment of 185 newly diagnosed gliomas: Grade III glioma showed prognosis comparable to that of Grade II glioma. *Japanese Journal of Clinical Oncology*, Vol. 38, No. 11, (November 2008), pp. 730-733, ISSN 0368-2811
- Stummer, W.; Reulen, H.J.; Meinel, T.; Pichlmeier, U.; Schumacher, W.; Tonn, J.C.; Rohde, V.; Oettel, F.; Turowski, B.; Woiciechowsky, C.; Franz, K.; Pietsch, T. & ALA-Glioma study group. (2008). Extent of resection and survival in glioblastoma multiforme: identification of and adjustment for bias. *Neurosurgery*, Vol. 62, No. 3, (March 2008), pp. 564-576, ISSN 0148-396X
- Taniguchi, H.; Muragaki, Y.; Iseki, H.; Nakamura, R. & Taira, T. (2006). New radiofrequency coil integrated with a stereotactic frame for intraoperative MRI-controlled stereotactically guided brain surgery. *Stereotactic and Functional Neurosurgery*, Vol. 84, No. 4, (September 2006), pp. 136-141, ISSN 1423-0372
- The Committee of Brain Tumor Registry of Japan. (2003). Report of brain tumor registry of Japan (1969-1996), 11th edition. *Neurologia Medico-Chirurgica*, Vol. 43, Supplement, (September 2003), pp. 1-111, ISSN 0470-8105
- van den Bent, M.J.; Carpentier, A.F.; Brandes, A.A.; Sanson, M.; Taphoorn, M.J.; Bernsen, H.J.; Frenay, M.; Tijssen, C.C.; Grisold, W.; Sipos, L.; Haaxma-Reiche, H.; Kros, J.M.; van Kouwenhoven, M.C.; Vecht, C.J.; Allgeier, A.; Lacombe, D. & Gorlia, T. (2006). Adjuvant procarbazine, lomustine, and vincristine improves progression-free survival but not overall survival in newly diagnosed anaplastic oligodendrogliomas and oligoastrocytomas: a randomized European Organisation for Research and Treatment of Cancer phase III trial. *Journal of Clinical Oncology*, Vol. 24, No. 18, (June 2006), pp. 2715-2722, ISSN 0732-183X
- Yoshimitsu, K.; Suzuki, T.; Muragaki, Y.; Chernov, M. & Iseki H. (2010). Development of modified Intraoperative Examination Monitor for Awake Surgery (IEMAS) system for awake craniotomy during brain tumor resection, *Proceedings of the 32nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 6050-6053, ISBN 978-1-4244-4123-5, Buenos Aires, Argentina, August 31- September 4, 2010



Diagnostic Techniques and Surgical Management of Brain Tumors

Edited by Dr. Ana Lucia Abujamra

ISBN 978-953-307-589-1

Hard cover, 544 pages

Publisher InTech

Published online 22, September, 2011

Published in print edition September, 2011

The focus of the book *Diagnostic Techniques and Surgical Management of Brain Tumors* is on describing the established and newly-arising techniques to diagnose central nervous system tumors, with a special focus on neuroimaging, followed by a discussion on the neurosurgical guidelines and techniques to manage and treat this disease. Each chapter in the *Diagnostic Techniques and Surgical Management of Brain Tumors* is authored by international experts with extensive experience in the areas covered.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Yoshihiro Muragaki, Hiroshi Iseki, Takashi Maruyama, Mikhail Chernov, Takashi Suzuki, Kitaro Yoshimitsu, Manabu Tamura, Soko Ikuta, Masayuki Nitta Taiichi Saito, Jun Okamoto and Kintomo Takakura (2011). *Advanced Surgical Management of Gliomas: Technological Requirements, Concept of Information-Guided Resection, and Clinical Results*, *Diagnostic Techniques and Surgical Management of Brain Tumors*, Dr. Ana Lucia Abujamra (Ed.), ISBN: 978-953-307-589-1, InTech, Available from:
<http://www.intechopen.com/books/diagnostic-techniques-and-surgical-management-of-brain-tumors/advanced-surgical-management-of-gliomas-technological-requirements-concept-of-information-guided-res>

INTECH

open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike-3.0 License](#), which permits use, distribution and reproduction for non-commercial purposes, provided the original is properly cited and derivative works building on this content are distributed under the same license.