Intraoperative Diffusion-Weighted Imaging for Visualization of the Pyramidal Tracts. Part I: Pre-Clinical Validation of the Scanning Protocol

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Key words
- intraoperative MRI
- diffusion-weighted imaging
- intraoperative neuronavigation
- pyramidal tract

Abstract

Integration of intraoperative diffusion-weighted imaging (iDWI) into neuronavigation can be potentially useful for identification of the pyramidal tract during surgery for parenchymal brain lesions. The technique of iDWI using an intraoperative MR scanner of low magnetic field strength (0.3 Tesla) has been developed. For image acquisition, a specially designed solenoid radiofrequency receiver coil integrated with a modified Sugita head holder (head-holder coil) was used. While the sensitivity characteristics of the head-holder coil were found to be 29% lower compared to a diagnostic quadrature head coil, they were sufficient to obtain iDWI images of good quality. The relationship between the angle of the motion probe gradient (MPG) pulse to the vertical axis and pyramidal tract contrasting were examined in 4 healthy men with a mean age of 30±5.7 years. The contrast ratio reached a maximum when the MPG pulse was applied exactly in the anteroposterior direction. The difference of the contrast ratio between right and left sides was not statistically significant. Pyramidal tract visualization became worse and the contrast ratio was reduced when the MPG pulse was applied at different angles to the vertical axis; the reduction rate varied from 20.1 to 27.9% for each 15 degrees of rotation irrespective of its side. In conclusion, the developed scanning protocol for iDWI using an originally designed head-holder coil allowed effective visualization of the pyramidal tracts using an intraoperative MR scanner of low magnetic field strength.

Bibliography
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Introduction

The introduction of intraoperative magnetic resonance imaging (iMRI) has revolutionized the management of parenchymal brain tumors and created principally new options for their radical and safe resection [1–4]. Currently, not only structural but also functional and metabolic iMRI techniques have found an acceptance during surgery of gliomas. In particular, diffusion tensor imaging (DTI) can be useful for intraoperative identification of the motor white matter tracts and their differentiation from the sensory ones [5]. However, operator-dependent, DTI-based fiber tracking is susceptible for underestimation of the exact size of the pyramidal tract and can erroneously define its position [6,7]. On the contrary, identification of the white matter tracts with diffusion-weighted imaging (DWI) does not require user participation. Integration of the DWI into intraoperative neuronavigation during surgery for parenchymal brain lesions can potentially provide nearly real-time information about spatial interrelationships between pyramidal tract, the lesion, and position of the surgical instrument, including an electrical stimulator for subcortical functional mapping, which can be used to prevent inadvertent tract injury and to avoid postoperative deterioration of the motor function. The technique of intraoperative DWI (iDWI) using an intraoperative MR scanner of low magnetic field strength (0.3 Tesla), has been developed recently in Tokyo Women's Medical University [8,9]. Validation of the scanning protocol constituted the objective of the pre-clinical part of the present study.

Methods and Materials

Intraoperative DWI has been developed using the intraoperative MR scanner (AIRIS II, Hitachi Medical, Tokyo, Japan), which is available in the "intelligent operating theater" of the Tokyo

Women's Medical University and equipped with a disc-shaped permanent magnet with a magnetic field strength of 0.3 Tesla (gradient up to 15 mT/m). For acquisition of iDWI, a specially developed solenoid radiofrequency receiver coil with a copper wire built in the modified Sugita head holder (Head-holder coil; Mizuho Ltd., Tokyo, Japan) was used. The detailed characteristics of the device are provided elsewhere [10]. It is made from glass-fiber-reinforced plastic in order to prevent susceptibility artifacts on iMRI. Titanium fixation pins provide both a stable position of the patient's head during surgery and serve for prevention of image artifacts. Positioning of the coil in the vicinity of the visualized region results in optimal image quality and high sensitivity.

The requirements for iDWI were formulated as follows: (1) possibility to visualize the white matter tracts, particularly the pyramidal tract, during surgery for parenchymal brain lesions; (2) optimal coil sensitivity providing sufficient image resolution for unequivocal interpretation of the obtained data by neurosurgeon; (3) reasonable time required for image acquisition, which can fulfill the needs of the real surgical situation; (4) avoidance of image artifacts, which can lead to mislocalization errors during neuronavigation; (5) positional accuracy within 5 mm during use for intraoperative neuronavigation. To fulfill these requirements the pre-clinical study was separated into two main parts: testing of the sensitivity characteristics of the head-holder coil for their correspondence to the requirements of iDWI, and validation of the scanning protocol on healthy volunteers to confirm the accuracy of iDWI for visualization of the pyramidal tract. The study was approved by the responsible authorities of the Tokyo Women's Medical University and informed consent was obtained from each volunteer.

Testing of sensitivity characteristics of the head-holder coil

To confirm that the head-holder coil can be used for iDWI its sensitivity characteristics were compared with those of a diagnostic quadrature (QD) head coil. Axial multi-slice spin echo images of a cylindrical nickel chloride phantom (18 mmol/L, 160 mm in diameter) positioned at the center of the head-holder coil were obtained using TR 800 msec and TE 20 msec. For each slice the signal-to-noise ratio within the region of interest (120 mm in diameter) was measured for sensitivity characteristics in the direction perpendicular to the coil (craniocaudal direction – z-axis). Signal profiles of the acquired images were also measured in the directions parallel to the coil: horizontal (mediolateral) – x-axis and vertical (anteroposterior) – y-axis. The same measurements were done with a diagnostic QD head coil.

Validation of the scanning protocol

For acquisition of DWI the motion probe gradient (MPG) pulse should be applied in the anteroposterior direction which, in cases of intraoperative imaging, is turned away from the vertical axis due to rotation of the patient's head and its fixation in the head holder. The relationship between the angle of the MPG pulse and pyramidal tract contrasting was examined in 4 healthy men with a mean age of 30±5.7 years (range: 24–37 years). A volunteer was positioned supine on the operating table without any sedation and his head was immobilized with a plastic band. The operating table was moved into the gantry gap of the intraoperative MR scanner and four coronal shots of pulse-triggered diffusion-weighted spin-echo echo-planar imaging with fat suppression were performed after shimming using the diagnostic QD head coil. The scanning parameters were as follows: TE 111 msec; FOV 250 mm; scan matrix size 100×92; reconstruction matrix size 256×256; b-value 700 sec/mm^2; thickness 8 mm; 18 slices to cover the pyramidal tract; 8 excitations. For providing the optimal resolution the slice interval was set at 3 mm. Data acquisition was divided into three parts, which were interleaved for the prevention of interference between slices (1st acquisition: 1, 4, 7, etc.; 2nd acquisition: 2, 5, 8, etc.; 3rd acquisition: 3, 6, 9, etc.). For the suppression of motion artifacts, the time delay from the systole was set at more than 300 msec [11]. Craniocaudal phase encoding was applied in order to prevent mediolateral image distortion corresponding to the usual direction of the surgical manipulations. The scanning time varied from 5 to 10 min.

For simulation of patient head rotation during surgery, sequential DWI were performed with application of the MPG pulses at different angles (θ) to the vertical axis (0, ±15, ±30, ±45, ±90 degrees, where positive values correspond to rotation to the left, and negative – to the right). For evaluation of the visualization quality, the contrast ratios between white matter tracts including the pyramidal tract (signal I_p) and thalamic area including upper brainstem (signal I_t) were calculated as $(I_p - I_t)I_t \times 100$ (%). The angle which provided the optimum contrasting of the pyramidal tract was identified and tract visualization on both sides was compared.

Statistics

The two-tailed t-test was used for statistical analysis. The level of significance was determined at $P < 0.05$.

Results

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Testing of sensitivity characteristics of the head-holder coil

The sensitivity of the head-holder coil at its center was on average 29% lower compared to that of the diagnostic QD head coil (o **Fig. 1**). The sensitivity characteristics in the x-axis and z-axis were symmetrical in relation to the coil center, whereas the sensitivity in the y-axis was asymmetrical and its reduction was marked in the upper side.

Validation of the scanning protocol

The contrast ratio reached a maximum when the MPG pulse was applied exactly in the anteroposterior direction ($\theta = 0$ degrees), and constituted on average 40.7±10.8% with a range from 59.4 to 30.7% (o **Fig. 2**). It permitted optimal differentiating of the pyramidal tracts from surrounding cerebral tissue. The difference of the contrast ratio between the right and left sides was not statistically significant. Pyramidal tract visualization became worse and the contrast ratio was reduced when the MPG pulse was applied at different angles to the vertical axis; the reduction rate varied from 20.1 to 27.9% for each 15 degrees of θ irrespective of its polarity.

Discussion

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Up to date there are only a limited number of reports about intraoperative acquisition of DWI and DTI for visualization of the white matter tracts [12, 13]. This can be particularly caused

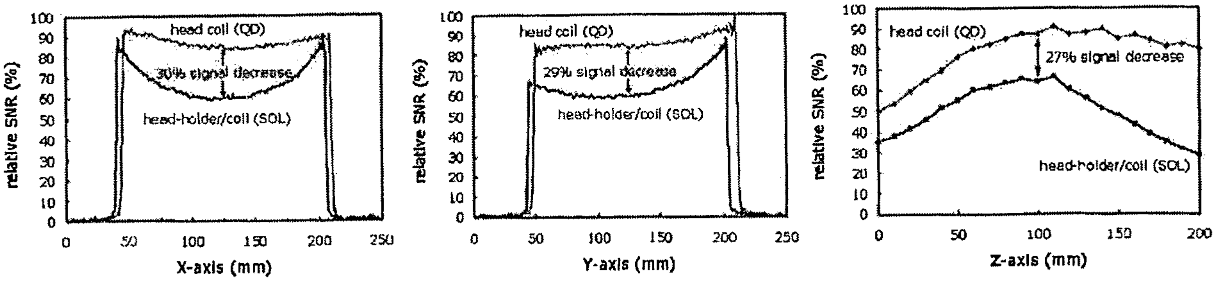

Fig. 1 Comparison of sensitivity characteristics of the solenoid (SOL) radiofrequency receiver coil integrated with a modified Sugita head holder for intraoperative MRI (head-holder coil) and diagnostic quadrature (QD) head coil. *x*-axis: horizontal direction, left side was considered positive; *y*-axis: vertical direction, downside was considered positive; *z*-axis: craniocaudal direction, perpendicular to the coil, cranial side was considered positive. Although the head-holder coil sensitivity was lower than that of the QD head coil, it was sufficient to obtain DWI images of good quality and accuracy. SNR = signal-to-noise ratio.

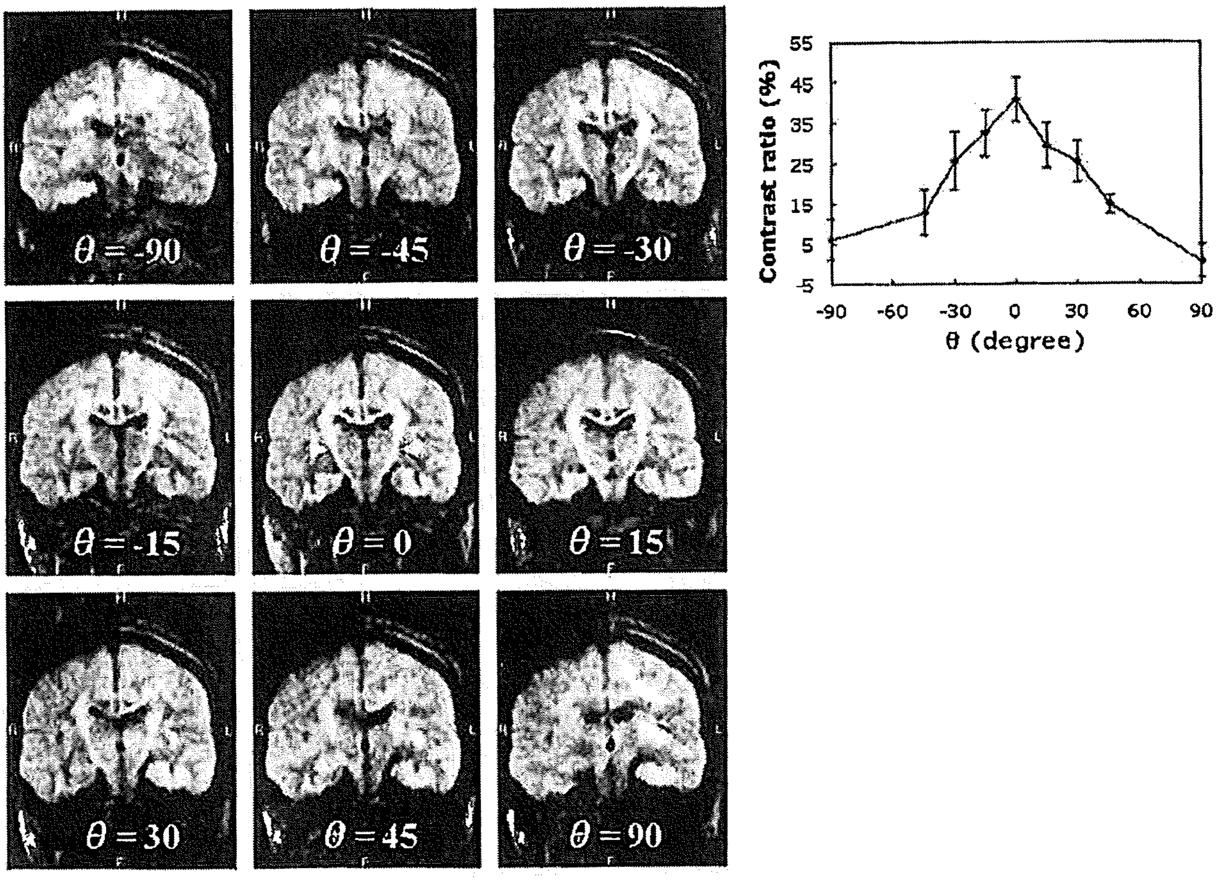

Fig. 2 Influence of the motion probe gradient (MPG) pulse direction on the visualization of pyramidal tracts. Left: coronal DWI obtained in volunteers with the quadrature (QD) head coil using different directions of the MPG pulse [θ – the angle to the vertical axis (anteroposterior direction); positive values correspond to rotation to the left, negative – to the right]. Right: interrelationships between the MPG pulse angle (θ) and contrast ratio between white matter tracts including the pyramidal tract and thalamus region including the upper brainstem. Note that the contrasting of the pyramidal tract was optimum at θ = 0 degree (arrowheads).

by the known technical difficulties of these techniques, which resulted from association of the required echo-planar imaging (EPI) with susceptibility artifacts, image distortion in single-shot imaging, and motion artifacts in multi-shot imaging [14–17]. Moreover, DTI-based tractography may underestimate the exact size and location of the white matter tracts [6]. Kinoshita et al. [7] reported a mismatch between the data of subcortical functional brain mapping with electrical stimulation and information obtained with DTI-based neuronavigation, as used for intraoperative identification of the location of motor tracts. At the same time, integration of DWI and DTI into intraoperative neuronavigation during surgery for parenchymal brain lesions can be done only if image distortion is avoided and underestimation of the tract size and position minimized.

It is known that image distortion caused by susceptibility artifacts is less if MR scanners with a low magnetic field strength are used. However, single-shot EPI performed in such a scanner suffers from image distortion due to the poor magnetic field homogeneity of the permanent magnet and necessitates the use of multi-shot EPI, which is less associated with image distortion. The originally developed head-holder coil provided sufficient sensitivity in its center, where the patient's head and operative field are actually located, which resulted in optimal quality and accuracy of iDWI. The expected lower sensitivity characteristics of the head-holder coil compared to the diagnostic QD head coil in all the directions results from the single solenoid nature of the former. A decrease of the coil sensitivity of about 33% 75 mm cranially from its center along the z-axis, which was found in the present study, corresponds to the data reported by Staubert et al. [18]. The asymmetric sensitivity profile in the y-axis seems attributable to the coil's ellipsoidal shape, but did not result in a reduction of quality of the intraoperative images.

DWI-based identification of the pyramidal tract does not require operator participation, and seems to be promising in the precise identification of the tract's size and position. Pre-clinical testing of the developed scanning protocol for iDWI permitted clear visualization of the pyramidal tract in all cases. In concordance with previously published data [19], application of the MPG pulse along the anteroposterior direction was found to be optimal. Under such settings, the contrasting of the pyramidal tract, which is running craniocaudally, was enhanced due to suppression of the signal of the other white matter tracts, such as the superior longitudinal fasciculus, which are running anteroposteriorly.

In conclusion, the results of the present pre-clinical study show that the developed scanning protocol for iDWI using an original solenoid radiofrequency receiver coil integrated with a modified Sugita head holder allowed effective visualization of the pyramidal tract using an intraoperative MR scanner of low magnetic field strength (0.3 Tesla). Image quality, resolution, and accuracy proved to be sufficient for further clinical testing with integration into the intraoperative neuronavigation system during surgery for parenchymal brain lesions.

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References

1 *Black PM, Moriarty T, Alexander E 3rd, Stieg P, Woodard EJ, Gleason PL, Martin CH, Kikinis R, Schwartz RB, Jolesz FA.* Development and implementation of intraoperative magnetic resonance imaging and its neurosurgical applications. Neurosurgery 1997; 41: 831–845
2 *Sutherland GR, Kaibara T, Louw D, Hoult DI, Tomanek B, Saunders J.* A mobile high-field magnetic resonance system for neurosurgery. J Neurosurg 1999; 91: 804–813
3 *Nimsky C, Ganslandt O, Cerny S, Hastreiter P, Greiner G, Fahlbusch R.* Quantification of, visualization of, and compensation for brain shift using intraoperative magnetic resonance imaging. Neurosurgery 2000; 47: 1070–1080
4 *Muragaki Y, Iseki H, Maruyama T, Kawamata T, Yamane F, Nakamura R, Kubo O, Takakura K, Hori T.* Usefulness of intraoperative magnetic resonance imaging for glioma surgery. Acta Neurochir Suppl 2006; 98: 67–75
5 *Yamada K, Kizu O, Mori S, Ito H, Nakamura H, Yuen S, Kubota T, Tanaka O, Akada W, Sasajima H, Mineura K, Nishimura T.* Brain fiber tracking with clinically feasible diffusion-tensor MR imaging: initial experience. Radiology 2003; 227: 295–301
6 *Clark CA, Barrick TR, Murphy MM, Bell BA.* White matter fiber tracking in patients with space-occupying lesions of the brain: a new technique for neurosurgical planning? Neuroimage 2003; 20: 1601–1608
7 *Kinoshita M, Yamada K, Hashimoto N, Kato A, Izumoto S, Baba T, Maruno M, Nishimura T, Yoshimine T.* Fiber-tracking does not accurately estimate size of fiber bundle in pathological condition: initial neurosurgical experience using neuronavigation and subcortical white matter stimulation. Neuroimage 2005; 25: 424–429
8 *Ozawa N, Muragaki Y, Shirakawa H, Suzukawa K, Nakamura R, Watanabe S, Iseki H, Takakura K.* Development of navigation system employing intraoperative diffusion weighted imaging using open MRI. In: Lemke HU, Vannier MW, Inamura K, Farman AG, Doi K, Reiber JHC (eds). Computer assisted radiology and surgery: Proceedings of the 18th International Congress and Exhibition. Amsterdam: Elsevier, 2004; 697–702
9 *Ozawa N, Muragaki Y, Shirakawa H, Suzukawa H, Nakamura R, Iseki H.* Navigation system based on intraoperative diffusion weighted imaging using open MRI. In: Lemke HU, Inamura K, Doi K, Vannier MW, Farman AG (eds). Computer assisted radiology and surgery: Proceedings of the 19th International Congress and Exhibition. Amsterdam: Elsevier, 2005; 810–814
10 *Taniguchi H, Muragaki Y, Iseki H, Nakamura R, Taira T.* New radiofrequency coil integrated with a stereotactic frame for intraoperative MRI-controlled stereotactically guided brain surgery. Stereotact Func Neurosurg 2006; 84: 136–141
11 *Jiang H, Golay X, Zijl PC van, Mori S.* Origin and minimization of residual motion-related artifacts in navigator-corrected segmented diffusion-weighted EPI of the human brain. Magn Reson Med 2002; 47: 818–822
12 *Mamata Y, Mamata H, Nabavi A, Kacher DF, Pergolizzi RS Jr, Schwartz RB, Kikinis R, Jolesz FA, Maier SE.* Intraoperative diffusion imaging on a 0.5 Tesla interventional scanner. J Magn Reson Imaging 2001; 13: 115–119
13 *Nimsky C, Ganslandt O, Hastreiter P, Wang R, Benner T, Sorensen AG, Fahlbusch R.* Preoperative and intraoperative diffusion tensor imaging-based fiber tracking in glioma surgery. Neurosurgery 2005; 56: 130–138
14 *Mansfield P.* Multi-planar image formation using NMR spin echoes. J Phys Chem 1977; 10: 155–158
15 *Anderson AW, Gore JC.* Analysis and correction of motion artifacts in diffusion weighted imaging. Magn Reson Med 1994; 32: 379–387
16 *Rohde GK, Barnett AS, Basser PJ, Marenco S, Pierpaoli C.* Comprehensive approach for correction of motion and distortion in diffusion-weighted MRI. Magn Reson Med 2004; 51: 103–114
17 *Neufeld A, Assaf Y, Graif M, Hendler T, Navon G.* Susceptibility-matched envelope for the correction of EPI artifacts. Magn Reson Imaging 2005; 23: 947–951
18 *Staubert A, Pastyr O, Echner G, Oppelt A, Vetter T, Schlegel W, Bonsanto MM, Tronnier VM, Kunze S, Wirtz CR.* An integrated head-holder/coil for intraoperative MRI in open neurosurgery. J Magn Reson Imaging 2000; 11: 564–567
19 *Krings T, Reinges MHT, Thiex R, Gilsbach JM, Thron A.* Functional and diffusion-weighted magnetic resonance images of space-occupying lesions affecting the motor system: imaging the motor cortex and pyramidal tracts. J Neurosurg 2001; 95: 816–824

Intraoperative Diffusion-Weighted Imaging for Visualization of the Pyramidal Tracts. Part II: Clinical Study of Usefulness and Efficacy

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Key words
- intraoperative MRI
- diffusion-weighted imaging
- intraoperative neuronavigation
- pyramidal tract

Abstract

Precise identification and preservation of the pyramidal tract during surgery for parenchymal brain tumors is of crucial importance for the avoidance of postoperative deterioration of the motor function. The technique of intraoperative diffusion-weighted imaging (iDWI) using an intraoperative MR scanner of low magnetic field strength (0.3 Tesla) has been developed. Its clinical usefulness and efficacy were evaluated in 10 surgically treated patients with gliomas (5 men and 5 women, mean age: 41.2 ± 13.9 years). iDWI permitted visualization of the pyramidal tract on the non-affected side in all 10 cases, and on the affected side in 8 cases. Motion artifacts were observed in four patients, but were not an obstacle to identification of the pyramidal tract. Good correspondence of the anatomical landmarks localization on iDWI and T_1-weighted imaging was found. All participating neurosurgeons agreed that, in the majority of cases, iDWI was very useful for localization of the pyramidal tract and for clarification of its spatial relationships with the tumor. In conclusion, image quality and accuracy of the iDWI obtained with an MR scanner of low magnetic field strength (0.3 Tesla) are sufficient for possible incorporation into an intraoperative neuronavigation system. The use of iDWI in addition to structural iMRI and subcortical functional mapping with electrical stimulation can potentially result in a reduction of the postoperative morbidity after aggressive surgical removal of lesions located in the vicinity to the motor white matter tracts.

Bibliography
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Introduction

The precise identification and preservation of the pyramidal tract during surgery for parenchymal brain tumors is of crucial importance for the avoidance of postoperative deterioration of motor function. Intraoperative subcortical brain mapping with electrical stimulation [1,2] as well as neuronavigation, based on preoperative diffusion-weighted imaging (DWI) or diffusion tensor imaging (DTI) [3–10] are usually used for this purpose, but both of these techniques has recognizable pitfalls. The first one can provide only functional information and does not permit precise estimation of the exact course of the pyramidal tract, whereas the second is susceptible to mislocalization errors, particularly those caused by brain shift [11,12]. The technique of intraoperative DWI (iDWI) using an intraoperative MR scanner of low magnetic field strength (0.3 Tesla), has been developed recently in Tokyo Women's Medical University [13,14]. After validation of the scanning protocol during a pre-clinical investigation on volunteers [15], the clinical part of the study was initiated with the objective to evaluate the usefulness and efficacy of iDWI during the surgical management of gliomas.

Methods and Materials

The main principles of surgery for gliomas with the use of iMRI and a scanner of low (0.3 Tesla) magnetic field strength (AIRIS II, Hitachi Medical, Tokyo, Japan), as adopted in the Tokyo Women's Medical University have been presented previously [16]. In brief, after induction of general anesthesia, the patient's head was firmly fixed with titanium pins in the modified Sugita head-holder (**Fig. 1**), representing the lower arch of the head-holder coil (Mizuho Ltd., Tokyo, Japan). The head holder was connected to the operating table with a supporting arm incorporating 3 joints and 2 rotational axes, which provided easy

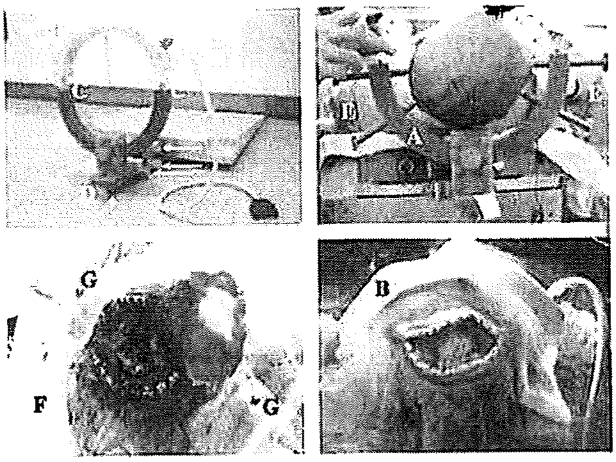

Fig. 1 Radiofrequency receiver coil integrated with a modified Sugita head holder for intraoperative MRI (Head-holder coil; Mizuho Ltd., Tokyo, Japan): general view of the device (upper left), fixation of the patient's head within a modified Sugita head holder before craniotomy (upper right) and during the surgical procedure (lower left), connection of both semicircular arches before intraoperative imaging, which provides a solenoid coil structure (lower right). Marked: modified Sugita head holder with built-in copper wire (A), removable upper semicircular arch (B), electrical connectors (C), supporting arm for fixation to the operating table (D) with its 3 joints (solid arrows) and 2 rotational axes (dashed arrows) for adjustment of the position of the patien's head, titanium fixation pins (E), sterile surgical drapes (F), sterile protective caps, covering the electrical connectors during surgery (G).

adjustment of the head position according to the surgical needs. For preservation of sterile conditions in the surgical field during the procedure, the patient's head was covered with transparent drapes, whereas electrical connectors of the head-holder coil were protected with special caps to prevent contamination with fluids and dust. Before the start of iMRI several fiducial markers were fixed to the skull on the periphery of the surgical field, and an additional one was inserted into the surgical wound and located in the vicinity to the target. The protective caps were removed from the electrical connectors and both semicircular arches of the head holder coil were connected. A wide transparent sterile drape was used to cover the whole body of the patient, his or her head, and the surgical wound, and the operating table was moved into the gap of the intraoperative MR scanner. During routine surgery iMRI was usually performed at least 2 times: after craniotomy and completion of the approach to the tumor and after resection of the neoplasm. If additional resection of glioma was required the iMRI investigation was repeated.

Clinical data

Evaluation of the clinical usefulness of iDWI was performed in 10 surgically treated patients with gliomas located in the vicinity of the pyramidal tract. There were 5 men and 5 women with a mean age of 41.2±13.9 years (range: 26–68 years). Initially diagnosed tumors were present in 8 patients, whereas recurrent tumors were seen in 2. According to histopathological examination, there were two astrocytomas WHO grade II, two anaplastic astrocytomas WHO grade III, two anaplastic oligodendrogliomas WHO grade III, and four glioblastomas WHO grade IV. Nine patients were operated on in the supine, and one in the prone position. The study was approved by the responsible authorities of Tokyo Women's Medical University and informed consent was obtained from each patient and his/her nearest family member.

Evaluation of the pyramidal tract contrasting

According to objectives of the present study in all cases in addition to the usually used axial T_2-weighted and axial T_1-weighted imaging with or without contrast enhancement, which took approximately 10 minutes, additional shimming, DWI, and coronal T_1-weighted imaging were done, which required additional 15–20 minutes. T_1-weighted images and T_2-weighted images were obtained using, respectively, 3D gradient echo (RSSG, RF-spoiled steady state acquisition rewound gradient echo with TR 27 ms and TE 10 ms), and 3D fast spin echo with driven equilibrium pulse (TR 1000 ms, TE 140 ms), with scan matrix size 256×160, 100 slices, 1.5 mm slice interval for both imagings. DWI was acquired according to the protocol described previously [15] with application of the motion probe gradient (MPG) pulse in the anteroposterior direction taking into account the actual position of the patient's head. Intraoperative DWI was performed both before and after tumor resection in 9 cases, and only before tumor removal in one. Two evaluations (one before and one after tumor resection) were excluded from the further analysis due to violation of the unified protocol for iDWI. Seventeen residual investigations, incorporating 306 slices, were evaluated, and pyramidal tract contrast ratios were measured as described previously [15], and compared between affected and non-affected sides. Additionally, the contrast ratio of pyramidal tracts was compared between patients and previously investigated healthy volunteers [15].

Evaluation of iDWI accuracy

For evaluation of distortion artifacts on iDWI, the distances between image centerline (near the midline) to the lateral cerebral ventricle wall, indicating the position of the pyramidal tract, and to the cortical surface were measured, correspondingly in 11 affected and 15 non-affected sides (with the exception of cases in which lateral ventricle wall could not be identified due to mass effects), and 17 affected and 17 non-affected sides. The same distances were measured on T_1-weighted images. The differences of these measurements were calculated and named as distortion indices corresponding to displacement of the lateral ventricle and displacement of the cortical surface, which were compared between each other.

Evaluation of the clinical usefulness of iDWI

For evaluation of the clinical utility of iDWI during surgery for gliomas, 5 neurosurgeons with an average surgical experience of 12.6±4.7 years (range: 8–20 years) were asked to complete a specially designed questionnaire and to answer whether iDWI-based determination of the pyramidal tract was useful and for which purpose, and what problems of this technique seem to interfere with the clinical needs.

Statistics

The two-tailed t-test was used for statistical analysis. The level of significance was determined at $P<0.05$.

Results

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Use of the modified Sugita head holder (lower arch of the head-holder coil) during microneurosurgical procedures provided a

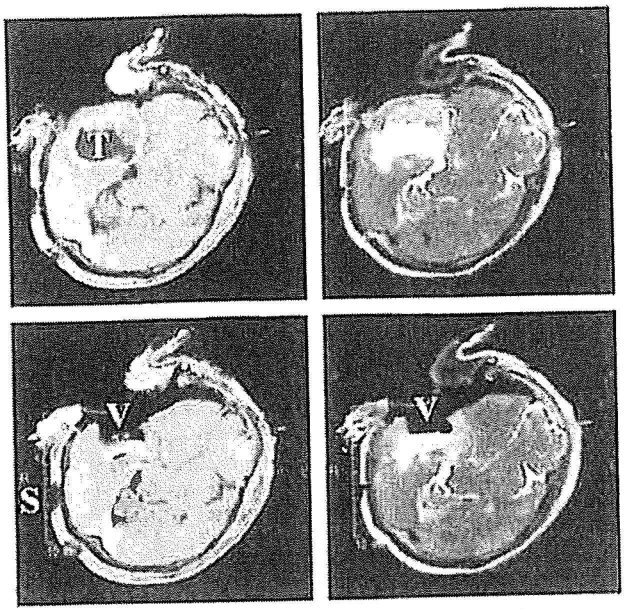

Fig. 2 Axial intraoperative contrast-enhanced T_1-weighted (left column) and T_2-weighted (right column) images before (upper row) and after (lower row) removal of the temporal lobe glioblastoma, which were acquired with an intraoperative MR scanner of low magnetic field strength (0.3 Tesla) using the originally designed radiofrequency receiver coil integrated with a modified Sugita head holder (head-holder coil). Note good image resolution, which permits their use for intraoperative neuronavigation, and minimal area of signal loss (S) at the point of contact of the titanium fixation pin with the scalp and cranium. Marked: tumor (T), resection cavity (V).

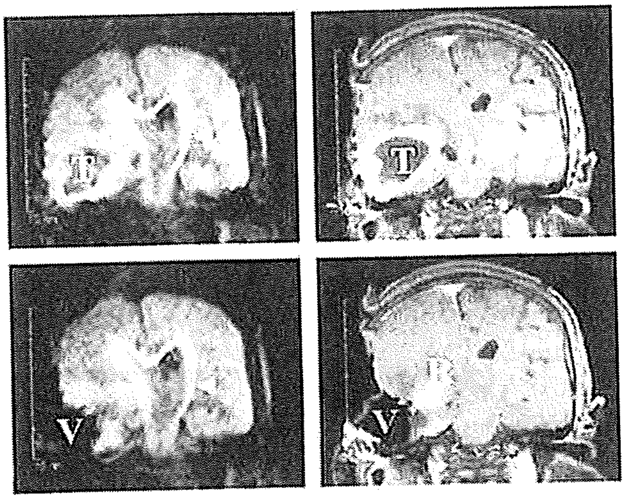

Fig. 3 Coronal intraoperative diffusion-weighted (left column) and contrast-enhanced T_1-weighted (right column) images before (upper row) and after (lower row) removal of the temporal lobe glioblastoma, which were acquired with an intraoperative MR scanner of low magnetic field strength (0.3 Tesla) using the originally designed radiofrequency receiver coil integrated with a modified Sugita head holder (head-holder coil). Note good image resolution, which permits their use for intraoperative neuronavigation, and clear visualization of the pyramidal tract with diffusion-weighted imaging. Marked: tumor (T), resection cavity (V), residual part of the neoplasm after its incomplete resection (R).

firm and stable fixation of the patient's head and was not accompanied by any troubles in any case. In all 10 patients intraoperative T_1-weighted and T_2-weighted images provided sufficient visualization of the brain tumor, as well as its remnants after incomplete resection (**○ Fig. 2**). The total iMRI investigation time in cases which included iDWI, calculated from attachment of the upper semicircular arch of the head holder coil to its removal for continuation of the surgical procedure, constituted approximately 40 minutes.

Evaluation of the pyramidal tract contrasting

Intraoperative DWI permitted visualization of the pyramidal tract on the non-affected side in all 10 cases, and on the affected side in 8 cases (**○ Fig. 3**). In 2 patients with malignant gliomas clear visualization of the pyramidal tract on the affected side was not possible (**○ Fig. 4**). The tract contrast ratios varied from 84.5% to 17.7%, and constituted in average 43.7 ± 16.4%. The differences of the tract contrast ratio between non-affected and affected side, as well as between patients and previously investigated healthy volunteers [15] were not statistically significant. Motion artifacts were observed in four patients with a pulse rate over 70 per minute, but were not an obstacle for identification of the pyramidal tract's position by neurosurgeons.

Evaluation of iDWI accuracy

The average displacement at the lateral ventricle on the affected side constituted 1.0 ± 0.7 mm. The differences of the distortion indices between lateral ventricle wall and cortical surface were not statistically significant on the affected side, but were significant on the non-affected side (**○ Table 1**). Good correspondence for anatomic landmark localization on iDWI and T_1-weighted imaging was found (**○ Fig. 5**).

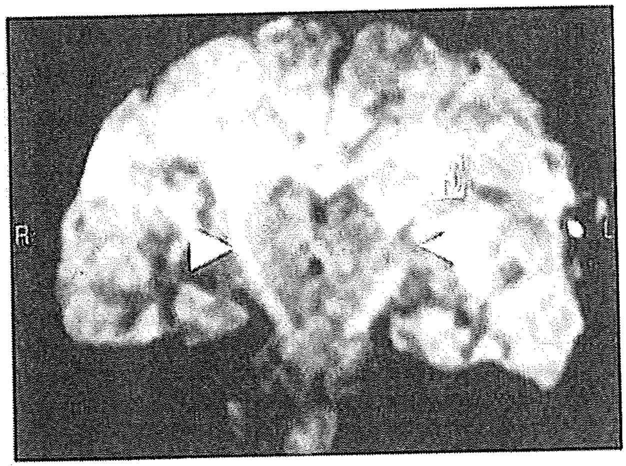

Fig. 4 An intraoperative diffusion-wieghted image with insufficient visualization of the pyramidal tract on the affected side compared to the non-affected side (arrowheads). Marked: peritumoral edema (E).

Evaluation of the clinical usefulness of iDWI

All participating neurosurgeons agreed that iDWI was very useful for localization of the pyramidal tract and for clarification of its spatial relationships with glial tumors and normal cerebral tissue in the majority of patients (**○ Table 2**). Among the problems which can interfere with the clinical needs, the increased time of the required iMRI examination, and poor tract visualization in some cases of malignant gliomas, were noted.

Table 1 Comparison of distortion indices calculated using intraoperative DWI and T_1-weighted images obtained with an MR scanner of low magnetic field strength (0.3 Tesla)

	Affected side	Non-affected side
displacement of the lateral ventricle (mm)	1.0±0.7 (n=11)	0.6±0.5 (n=15)
displacement of the cortical surface (mm)	1.2±1.1 (n=17)	0.9±0.5 (n=17)
P-value	NS	<0.05

Data presented as mean ± standard deviation; NS: non-significant; n: number of cases

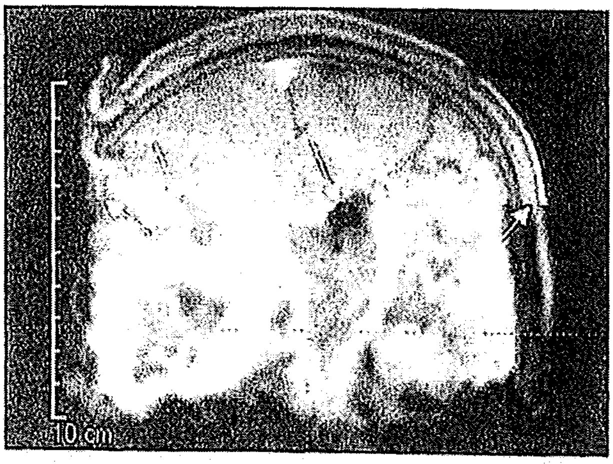

Fig. 5 Evaluation of accuracy of the intraoperative DWI (lower part) superimposed on the corresponding T_1-weighted image (upper part). Note that, with the exception of cortical surface, there was good correspondence of the localization of the anatomic landmarks (arrows).

Table 2 Results of the evaluation of usefulness of intraoperative DWI for visualization of the pyramidal tract

Standard questions to five practicing neurosurgeons	Number of answers
Whether visualization of the pyramidal tract with iDWI was:	
–very useful	5 (100%)
–useful	0
–not useful	0
Whether visualization of the pyramidal tract with iDWI was useful for:	
–determination of its position	5 (100%)
–determination of its shift	2 (40%)
–determination of its spatial interrelationships with the lesion	5 (100%)
–for other purposes	0
What problems with iDWI were encountered:	
–long imaging time	5 (100%)
–poor contrasting of the pyramidal tract	1 (20%)
–poor image resolution	0
–low signal-to-noise ratio	0
–presence of image artifacts	0
–others	3 (60%)

iDWI: intraoperative diffusion-weighted imaging

Discussion

Simultaneous use of iDWI and structural iMRI during surgery for parenchymal brain tumors seems to be extremely useful for determination of both the position of white matter tracts and location of the lesion. However, the additional incorporation of iDWI into an intraoperative neuronavigation system requires a high level of image quality and positional accuracy. We estimated that the latter should be within 5 mm, which corresponds to the conducting depth of the electrical stimulation during subcortical brain mapping. It was previously shown that mean error of the intraoperative neuronavigation system using T_1-weighted images obtained with an MR scanner of low magnetic field strength (0.3 Tesla) in the "intelligent operating theater" of the Tokyo Women's Medical University is as low as 0.90±0.35 mm [17]. In the present study the misalignments between DWI and T_1-weighted images on the affected side were 1.0±0.7 mm for the lateral ventricle wall and 1.2±1.1 mm for the cortical surface, which corresponds to the estimated positional accuracy of approximately 2.1 mm, and, in our opinion, fulfills clinical needs.

Motion artifacts were observed in four patients with pulse rates of over 70 per minute. Jiang et al. [18] reported that effect of pulsation can be minimized by avoiding the period of 100 to 250 msec after systole for data acquisition. In our pre-clinical study [15] motion artifacts in multi-shot DWI-echo-planar imaging were successfully suppressed by setting the time delay from the systole to more than 300 msec. It should be noted that, under general anesthesia, the pulse rate is usually well controlled. Nevertheless, in no one case did motion artifacts interfere with the identification of the pyramidal tract's position by the neurosurgeon.

Diffusion anisotropy of the white matter tracts may be reduced by presence of a lesion or perilesional edema [19] In some cases of the present study, the location of the malignant glioma in the close proximity to the pyramidal tract resulted in its poor visualization on iDWI. While pre-operative DWI can define whether the pyramidal tract can be visualized or not, it may not correspond completely to the results of intraoperative imaging. By using a visual comparison of images obtained with different directions of the pulses, Krings et al. [6] were able to differentiate edema from the large descending fiber tracts in all 10 patients with various brain lesions.

All neurosurgeons participating in the present study found iDWI very useful for determination of the pyramidal tract's position and its spatial relationships with the lesion and surgical instruments. It may become even more convenient in the future, due to development of a special sound alarm, which will be automatically activated when surgical manipulations would come into close proximity to the pyramidal tract [20]. It should be noted, however, that the protocol used for acquisition of iDWI provided a limited image resolution of 2.5×2.7 mm in both mediolateral and craniocaudal directions, whereas the slice thickness of 8 mm resulted in a partial volume effect. These factors can reduce differentiation of the fine structures within the pyramidal tract, and necessitate the use of subcortical brain mapping with electrical stimulation in addition to iDWI [9, 21]. Prolongation of time required for examination, which constituted approximately 40 minutes, was mentioned as a problem which can interfere with the clinical usefulness of the technique. In fact, the investigation time can be shortened if coronal T_1-weighted images were omitted and shimming was minimized to the region of interest. From another side, similar to any other type of iMRI, the potential decrease of postoperative morbidity and improvement of quality of life can be considered as a reasonable price for prolongation of the total length of surgery.

In conclusion, the results of the present clinical study show that iDWI using an MR scanner of low magnetic field strength (0.3 Tesla) in the majority of patients permits clear visualization of the pyramidal tract and identification of its spatial relationships with the lesion and surgical instruments. Image quality and accuracy were sufficient for the possible incorporation of iDWI into an intraoperative neuronavigation system. Use of iDWI in addition to structural iMRI and subcortical functional mapping with electrical stimulation can potentially result in a reduction of the postoperative morbidity after aggressive surgical removal of lesions located in the vicinity of the motor white matter tracts.

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References

1 *Woolsey CN, Erickson TC, Gilson WE.* Localization in somatic sensory and motor areas of human cerebral cortex as determined by direct recording of evoked potentials and electrical stimulation. J Neurosurg 1979; 51: 476–506
2 *Yingling CD, Ojemann S, Dodson B, Harrington MJ, Berger MS.* Identification of motor pathways during tumor surgery facilitated by multichannel electromyographic recording. J Neurosurg 1999; 91: 922–927
3 *Stejskal EO, Tanner JE.* Spin diffusion measurements: spin-echoes in the presence of a time-dependent field gradient. J Chem Phys 1965; 42: 288–292
4 *Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M.* MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. Radiology 1986; 161: 401–407
5 *Pajevic S, Pierpaoli C.* Color schemes to represent the orientation of anisotropic tissues from diffusion tensor data: application to white matter fiber tract mapping in the human brain. Magn Reson Med 1999; 42: 526–540
6 *Krings T, Reinges MHT, Thiex R, Gilsbach JM, Thron A.* Functional and diffusion-weighted magnetic resonance images of space-occupying lesions affecting the motor system: imaging the motor cortex and pyramidal tracts. J Neurosurg 2001; 95: 816–824
7 *Kamada K, Houkin K, Iwasaki Y, Takeuchi F, Kuriki S, Mitsumori K, Sawamura Y.* Rapid identification of the primary motor area by using magnetic resonance axonography. J Neurosurg 2002; 97: 558–567
8 *Coenen VA, Krings T, Axer H, Weidemann J, Kranzlein H, Hans FJ, Thron A, Gilsbach JM, Rohde V.* Intraoperative three-dimensional visualization of the pyramidal tract in a neuronavigation system (PTV) reliably predicts true position of principal motor pathways. Surg Neurol 2003; 60: 381–390
9 *Berman JI, Berger MS, Mukherjee P, Henry RG.* Diffusion-tensor imaging-guided tracking of fibers of the pyramidal tract combined with intraoperative cortical stimulation mapping in patients with gliomas. J Neurosurg 2004; 101: 66–72
10 *Kinoshita M, Yamada K, Hashimoto N, Kato A, Izumoto S, Baba T, Maruno M, Nishimura T, Yoshimine T.* Fiber-tracking does not accurately estimate size of fiber bundle in pathological condition: initial neurosurgical experience using neuronavigation and subcortical white matter stimulation. Neuroimage 2005; 25: 424–429
11 *Dorward NL, Alberti O, Velani B, Gerritsen FA, Harkness WF, Kitchen ND, Thomas DG.* Postimaging brain distortion: Magnitude, correlates, and impact on neuronavigation. J Neurosurg 1998; 88: 656–662
12 *Nabavi A, Black PM, Gering DT, Westin CF, Mehta V, Pergolizzi Jr RS, Ferrant M, Warfield SK, Hata N, Schwartz RB, Wells III WM, Kikinis R, Jolesz FA.* Serial intraoperative magnetic resonance imaging of brain shift. Neurosurgery 2001; 48: 787–798
13 *Ozawa N, Muragaki Y, Shirakawa H, Suzukawa K, Nakamura R, Watanabe S, Iseki H, Takakura K.* Development of navigation system employing intraoperative diffusion weighted imaging using open MRI. In: Lemke HU, Vannier MW, Inamura K, Farman AG, Doi K, Reiber JHC (eds). Computer assisted radiology and surgery: Proceedings of the 18th International Congress and Exhibition. Amsterdam: Elsevier 2004; 697–702
14 *Ozawa N, Muragaki Y, Shirakawa H, Suzukawa H, Nakamura R, Iseki H.* Navigation system based on intraoperative diffusion weighted imaging using open MRI. In: Lemke HU, Inamura K, Doi K, Vannier MW, Farman AG (eds). Computer assisted radiology and surgery: Proceedings of the 19th International Congress and Exhibition. Amsterdam: Elsevier 2005; 810–814
15 *Ozawa N, Muragaki Y, Nakamura R, Iseki H.* Intraoperative diffusion-weighted imaging for visualization of the pyramidal tracts. Part 1: pre-clinical validation of the scanning protocol. Minim Invas Neurosurg 2008; 51: 63–66
16 *Muragaki Y, Iseki H, Maruyama T, Kawamata T, Yamane F, Nakamura R, Kubo O, Takakura K, Hori T.* Usefulness of intraoperative magnetic resonance imaging for glioma surgery. Acta Neurochir Suppl 2006; 98: 67–75
17 *Sugiura M, Muragaki Y, Nakamura R, Hori T, Iseki H.* Accuracy evaluation of an update-navigation system for the resection surgery of brain tumor using intraoperative magnetic resonance imaging. J JSCAS 2005; 7: 43–49 (article in Japanese)
18 *Jiang H, Golay X, Zijl PC van, Mori S.* Origin and minimization of residual motion-related artifacts in navigator-corrected segmented diffusion-weighted EPI of the human brain. Magn Reson Med 2002; 47: 818–822
19 *Field AS, Alexander AL, Wu YC, Hasan KM, Witwer B, Badie B.* Diffusion tensor eigenvector directional color imaging patterns in the evaluation of cerebral white matter tracts altered by tumor. J Magn Reson Imaging 2004; 20: 555–562
20 *Ozawa N, Muragaki Y, Suzukawa H, Nakamura R, Iseki H.* Pyramidal tract navigation based on intraoperative diffusion-weighted imaging: sound navigation using the fiber tract margin (abstract). Int J Comput Assist Radiol Surg 2006; 1 (Suppl 1): 488
21 *Ozawa N, Muragaki Y, Shirakawa H, Suzukawa H, Nakamura R, Iseki H.* Pyramidal tract navigation based on diffusion weighted imaging updated by intraoperative open MRI (abstract). In: Proceedings of the 13th Annual Meeting of ISMRM, Miami 2005, abstract 2155

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Original Article

Long-term Prognostic Assessment of 185 Newly Diagnosed Gliomas—Grade III Glioma Showed Prognosis Comparable to That of Grade II Glioma

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Objective: We evaluated the prognoses of newly diagnosed gliomas through WHO Grades II, III and IV to assess the overall tendency of treatment results for glioma in our institute. Furthermore, statistical analysis was performed to determine factors influencing the prognosis.

Methods: A total of 185 newly diagnosed glioma patients were operated on from 2000 to 2006. The primary endpoint was the overall survival from the date of surgery. The factors assessed as to whether they influenced the prognosis were the WHO grades of sex, age, location of the lesion, pre-operative Karnofsky Performance Status (KPS), extent of resection and whether or not radiation therapy was performed.

Results: The WHO grades influenced the survival significantly ($P < 0.0001$). The Grades II and III showed no statistically significant difference in survival ($P = 0.174$), whereas Grades III and IV showed a significant difference ($P < 0.0001$). The factor influencing survival as well as the grades was the KPS ($P < 0.0001$). The comparison of survival over WHO grades in the same KPS group was performed for 2 KPS groups (KPS = 100, KPS 80–90), and these also showed significant differences ($P = 0.0009$ and 0.0143, respectively).

Conclusions: Despite the different distributions of the KPS, the Grade III glioma patients showed survival comparable to that of the Grade II. On the other hand, the Grade IV glioma patients showed significantly poorer survival compared with Grade II or III.

Key words: glioma – long-term prognosis – WHO grade

INTRODUCTION

Traditionally, researchers have categorized gliomas into two groups, the 'malignant' or 'high-grade' group and the 'low-grade' group, especially when discussing their prognoses. WHO Grade II gliomas, sometimes combined with Grade I gliomas, are considered to be 'low-grade', and WHO Grades III and IV combined are considered to be 'high-grade' or 'malignant'. This categorization is fairly convenient when determining adjuvant therapeutic modalities because the 'malignant' group is almost always treated by concomitant radiation therapy (RT) and chemotherapy.

Though the prognosis of gliomas in general had been considered to be poor, recent developments in diagnostic technologies and treatment modalities seem to have contributed to its improvement. This has resulted in the fact that some 'malignant' glioma patients may be able to expect

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long-term survival under certain conditions. However, there has been little discussion as to whether the old 'low-grade and malignant' categorization is appropriate when evaluating prognostic tendencies of gliomas at present.

In our institute, in striving to achieve extensive but safe resection of tumors, a number of new technological methods have been introduced in recent years, one of which is the intra-operative magnetic resonance imaging (iMRI) (1), which was introduced in 2000. After 6 years of surgical operations using iMRI and the accompanying treatment experiences, we felt the urge to evaluate the prognoses of the glioma patients whom we treated. In addition, we thought that it would be very informative to compare the overall survival of each WHO grade group. We evaluated the prognoses of newly diagnosed glioma through Grades II, III and IV to assess the overall tendency of treatment results for glioma in our institute.

PATIENTS AND METHODS

A total of 304 glioma patients operated on at our hospital from 1 January 2000 to 30 June 2006 were reviewed. The histological diagnoses were available for all cases and were classified according to the grading system defined by the 2000 WHO classification for tumors (2) of the central nervous system. We excluded WHO Grade I cases (11 patients) as they have extremely good prognoses. In order to assess the significance of the first surgery, we also excluded the patients who had undergone initial treatment at other institutes and were referred to our institute for the treatment of recurrent lesions. As a result, the prerequisite for inclusion in this analysis was to be newly diagnosed WHO Grades II, III and IV glioma patients who underwent operations in our institute from 1 January 2000 to 30 June 2006. A total of 185 patients were included in this analysis.

The detailed description of the patients is shown in Table 1, and the histological variation of each WHO grade group is shown in Table 2. Among these patients, 153 (82.7%) were operated on by using iMRI-guided navigation. The extent of resection was assessed by comparing pre- and post-operative iMRI (3). The pre-operative tumor volume was defined as an area of contrast-enhanced T1-weighted images (4), or, if the tumor does not show contrast enhancement, as an area of increased signal intensity on T2-weighted images corresponding to the mass lesion. An area of abnormal signal intensity was computed for each slice and multiplied by the slice width (1.5 mm), and a cumulative value was obtained by adding the values for the individual slices (5).

Table 1. Characteristics of the patients in each WHO grade group

	Total	Grade II	Grade III	Grade IV
Number of cases	185	66	57	62
Sex				
Men	106	34	34	38
Women	79	32	23	24
Age (years old)				
Median	44.0	35.0	39.0	54.5
Range	8–78	11–70	22–78	8–78
Location				
U	168	61	51	56
B	7	1	4	2
I	10	4	2	4
KPS				
Median	100.0	100.0	100.0	80.0
Range	10–100	70–100	50–100	10–100
Extent of resection (%)				
Median	95.0	95.0	95.0	95.0
Range	biopsy–100	biopsy–100	biopsy–100	biopsy–100
RT	131	26	51	54

U, unilateral supra-tentorial lesion; B, bilateral supra-tentorial lesions; I, infra-tentorial lesion; KPS, Karnofsky performance status; RT, Number of patients who received radiation therapy; WHO, World Health Organization.

Table 2. Histological variation in each WHO grade group

WHO grade	Histological diagnosis	Cases
Grade II	Astrocytoma	30
	Oligoastrocytoma	27
	Oligodendroglioma	5
	Ependymoma	3
	Pleomorphic xanthoastrocytoma	1
Grade III	Anaplastic astrocytoma	30
	Anaplastic oligoastrocytoma	21
	Anaplastic oligodendroglioma	3
	Anaplastic ependymoma	3
Grade IV	Glioblastoma	62

All surgical specimens were collected, processed and prepared for histological diagnosis in our neuropathologic laboratory. The specimens were thoroughly prepared with regular hematoxylin–eosin staining and necessary immunohistochemical antibodies were applied including MIB-1 antibody. For the entire study period, every diagnosis was conducted by one sole neuropathologist, Prof. Osami Kubo, who is one of the councillors of the Japanese Society of Neuropathology.

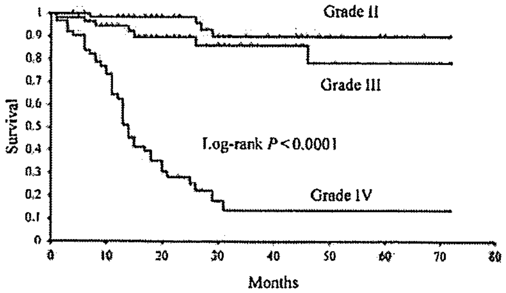
Adjuvant therapy included fractionated external-beam RT (50–60 Gy total, 2 Gy fraction for 5 days per week, unless modulated); and concomitant chemotherapy based on nimustine hydrochloride (ACNU) (6) with or without vincristine and/or procarbazine, temozolomide or autologous vaccine therapy. The clinical administration of temozolomide had not been approved during the study period (except the last few months); thus, it was not used as the first-line chemotherapy for primary glioma patients in this study. Patients to be treated with RT were selected by the following criteria. If the diagnosis was Grade III or IV, radiation was primarily recommended. If the diagnosis was Grade II, radiation was recommended if the patient's post-operative MRI showed any residual tumor and/or the MIB-1 index was 5% or higher. Maintenance therapy followed the initial therapy. In case of recurrence, the salvage therapy included re-operation using other chemotherapeutic agents or RT if the initial therapy did not include it.

The primary endpoint was the overall survival from date of surgery. Comparison of survival among WHO grades was performed using Cox's proportional hazard models.

Next, the patient's background was assessed to investigate whether there was any other factor that influenced the survival more than the WHO grades. The factors assessed were the WHO grades of sex, age, location of the lesion (U, supra-tentorial unilateral lesion; B, supra-tentorial bilateral lesions; I, infra-tentorial lesion), pre-operative Karnofsky Performance Status (KPS), extent of resection and whether or not RT was performed. These seven background factors were used as variables to apply Cox's proportional hazard models.

RESULTS

The median observation time was 13.0 months. Kaplan–Meier survival curves were drawn for WHO Grades II, III and IV (Fig. 1). There was a significant difference in survival among grades ($P < 0.0001$). The number of the patients at risk at 0, 12, 24, 36, 48, 60 and 72 months is also indicated in Fig. 1.



Months	0	12	24	36	48	60	72
Number of patients at risk							
Grade II	66	58	38	20	14	7	3
Grade III	57	40	27	15	9	7	4
Grade IV	62	34	10	3	2	2	1

Figure 1. Overall survival for each grade group. Kaplan–Meier survival curves for Grade II, III and IV are shown. Cox proportional hazard models showed significant difference among grades ($P < 0.0001$). The number of patients at risk at major time points (0, 12, 24, 36, 48, 60 and 72 months) is described at the bottom. The survival of each grade was compared and statistically analyzed by using Cox proportional hazard models. Grades II and III showed no statistically significant difference ($P = 0.1742$), whereas Grades III and IV showed a significant difference ($P < 0.0001$).

Subsequently, the survival of each WHO grade was compared and statistically analyzed by using Cox's proportional hazard models. Grades II and III showed no statistically significant difference ($P = 0.174$), whereas Grades III and IV showed a significant difference ($P < 0.0001$).

As for the influence of background factors on survival, the P values were $P < 0.0001$ for WHO grades, $P = 0.525$ for sex, $P = 0.997$ for age, $P = 0.727$ for location, $P < 0.0001$ for KPS, $P = 0.374$ for the extent of resection and $P = 0.804$ for RT. Only the KPS showed as much influence on survival as the WHO grades.

DISCUSSION

At the outset, it should be clarified that the data presented here were genuinely from a single institute. It may be apparent that the fraction of Grade III was much greater than that of other institutes or other studies, and the Grade III/IV patients were much younger than generally expected. One of the features of our institute is that most of the operative patients were referred from other hospitals or institutes. As is well known, the Grade IV gliomas develop symptoms much more rapidly than Grade II or III, and often need immediate treatment as soon as they are found. Furthermore, there is a tendency for Grade IV gliomas to be found in older age groups when compared with Grade II or III. Sometimes, those patients are not considered for operative therapy because of their age. Thus, those who were referred to our hospital tended to be younger and to contain a smaller fraction of Grade IV. As a result, we had a greater fraction of Grade III patients than Grade IV.

Our data clearly showed that the Grade III group, normally categorized in the malignant glioma entity, showed survival comparable to that of Grade II glioma, which is in the low-grade glioma entity. On the contrary, Grade III and IV glioma, usually combined as malignant glioma, showed significantly different survival.

We have used the same (or at least very similar) treatment strategy for the Grades III and IV gliomas. Once histologically diagnosed as Grade III or IV, the patients were always given RT and concomitant chemotherapy. On the contrary, Grade II glioma patients were not always treated by RT or chemotherapy as is explained in the Patients and Methods section. We have come to an interesting fact: though treated similarly, Grades III and IV showed significantly different prognoses; on the contrary, Grades II and III gliomas were treated based on different therapeutic strategies, and showed comparable prognoses in terms of survival.

As for background factors, the KPS influenced the survival as much as the grades. We examined the distribution of the patients for grades and KPS, shown in Table 3. It indicates that there are a certain number of patients in each WHO grade for the KPS = 100 and the KPS 80–90. Then, comparison of survival over grades was performed for the two KPS groups with KPS = 100 and KPS 80–90; this

Table 3. Distributions of number of patients for KPS and WHO grades

KPS	Grade II	Grade III	Grade IV
100	55	34	12
80–90	9	15	22
60–70	2	7	16
40–50	0	1	8
<30	0	0	4

comparison also showed significant differences ($P = 0.0009$ and 0.0143, respectively). This supported the conclusion that the difference of survival among grades was independent of the deviations among patients' backgrounds.

Subsequently, the survival of each WHO grade in the KPS = 100 group was compared and statistically analyzed using Cox's proportional hazard models. The P values for grade II versus III and Grade III versus IV were 0.532 and 0.0294, respectively. Despite the fact that the patients' backgrounds have some biases throughout the grades, Grade III achieves survival comparable to Grade II, if diagnosed, treated and observed properly. On the contrary, Grade IV still remains in the uncontrollable disease category.

CONCLUSIONS

The results indicated that the Grade III glioma patients have prognoses comparable to that of the Grade II patients and the Grade IV glioma patients showed significantly poorer prognoses compared with Grade II or III. Among the patients' background factors, the KPS influenced the survival of gliomas as much as the WHO grades. However, the comparison of survival among the same KPS groups also showed significant differences over grades, indicating that the differences of survival over grades are independent of patients' background factors.

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Conflict of interest statement

None declared.

References

1. Iseki H, Muragaki Y, Nakamura R, Ozawa N, Taniguchi H, Hori T, et al. Intelligent operating theater using intraoperative open-MRI. *Magn Reson Med Sci* 2005;4:129–36.
2. Kleihues P, Cavenee W. Pathology and Genetics of Tumours of the Nervous System. Vol. 88, Lyon, France: IARC Press 2000.
3. Muragaki Y, Iseki H, Takakura K, Maruyama T, Hori T. Awake craniotomy and functional mapping for surgery of brain tumors. *Nippon Rinsho* 2005;63:330–40.
4. Shi Wildrick DM, Sawaya R. Volumetric measurement of brain tumors from MR imaging. *J Neuooncol* 1998;37:87–93.
5. Muragaki Y, Iseki H, Kawamata T, Yamane F, Nakamura R, Kubo O, et al. Usefulness of intraoperative magnetic resonance imaging for glioma surgery. *Acta Neurochir* 2006;98(Suppl.):67–75.
6. Takakura K, Abe H, Tanaka R, Kitamura K, Miwa T, Takeuchi K, et al. Effects of ACNU and radiotherapy on malignant glioma. *J Neurosurg* 1986;64:53–37.

Advanced Computer-aided Intraoperative Technologies for Information-guided Surgical Management of Gliomas: Tokyo Women's Medical University Experience

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Key words
- intraoperative MRI
- intraoperative neuronavigation
- medical information technology
- information-guided management
- robotic neurosurgery

Abstract

The availability of the intraoperative MRI and real-time neuronavigation has dramatically changed the principles of surgery for gliomas. Current intraoperative computer-aided technologies permit perfect localization of the neoplasm, precise estimation of its volume, and clear definition of its interrelationships with the eloquent brain structures. This allows maximal tumor resection with minimal risk of postoperative disabilities. Under such conditions the medical treatment has become significantly dependent on the quality of the provided information and can be designated as information-guided management. Therefore, appropriate management of the wide spectrum of the intraoperative medical data and its adequate distribution between members of the surgical team for facilitation of the clinical decision-making is very important for attainment of the best possible outcome. Further progress in advanced neurovisualization, robotics, and comprehensive medical information technology has a great potential to increase the safety of the neurosurgical procedures for parenchymal brain tumors in the eloquent brain areas.

Bibliography
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Introduction

Medical treatment in the 20th century was mainly based on feedback-controlled principles. Correspondingly, up to date clinical decision-making is significantly influenced by personal intuition and previous experience of the doctor. Both of those issues are extremely important. The experienced neurosurgeon is able to simulate the whole upcoming surgery in his or her own mind and perform it thereafter precisely and efficiently. This is significantly facilitated with the advances of modern neuroimaging and intraoperative neuronavigation. At present, various diagnostic data obtained with CT, MRI, PET, SPECT, digital angiography etc. may not only be visually inspected and analyzed, but co-registered, fused, and incorporated into computer-based devices for guidance during the surgical procedure. Nevertheless, usually it is not the various images, but the long-life training of the surgeon, that provides perfect orientation in the surgical field, evaluation of the functional importance of the various anatomic structures, and estimation of the optimal resection of the lesion taking into account possible positive and negative consequences of the various intraoperative manipulations and actions. Therefore, up to date the complex neurosurgical procedure, for example removal of glioma in the eloquent brain area, in the best hands represents more an art than science or technique.

It can be expected, however, that in the third millenium the practical medicine will be transformed into a "feed-foward" process with scientifically based prediction of the various risks and their preemptive management. It will necessitate the development of special computer-aided systems for comprehensive analyses of the various diagnostic and management data and precise simulation of the treatment course of the particular patient. Under such conditions the treatment process, which can be designated as information-guided management [1], will become significantly dependent on the quality of the provided information.

Main Problems with the Surgical Management of Gliomas

Requirements of the constantly growing quality standards of medical care enforce neurosurgeons to provide safe and effective management of any intracranial pathology independent on its location. Meanwhile, the decades of clinical experience provide clear evidence that, in the majority of cases, routine surgical technique does not permit aggressive removal of parenchymal brain tumors located in the vicinity of eloquent brain structures without a significant risk of permanent postoperative neurological disability. From another side, incomplete resection of the neoplasm, which is still not uncommon practice, may have a significant negative impact on patient survival. While the effectiveness of aggressive removal of intracranial gliomas is not formally proved to date and the rate of their optimal resection is still questionable [2,3], there is a general agreement that radical resection of the neoplasm is associated with a better prognosis even in cases of malignancies. Lacroix et al. [4] showed that 98% or more resection of glioblastoma multiforme is associated with a significant improvement of the long-term outcome, whereas according to the last edition of the Brain Tumor Registry of Japan [5], the five-year survival rate of patients with such neoplasm is increasing from 11% in cases of 95% resection to 18% in cases of 100% resection.

The main problems with the surgical management of gliomas are well known. First, these tumors arise from the cerebral tissue itself and due to their propensity for infiltrative growth frequently could not be clearly distinguished from the normal brain through the conventional operating microscope, which is especially evident at the periphery of the neoplasm. Second, an intraaxial location of the tumor results in frequent affection of the functionally important cerebral structures, which certainly should be clearly defined and preserved during removal of the neoplasm in order to avoid a postoperative neurological deterioration. Third, while recent progress in MRI technology and intraoperative neuronavigation has significantly facilitated surgery for malignant brain tumors, the effect of brain shift caused by evacuation of the cerebrospinal fluid or lesion removal can result in significant mislocalization errors if guidance is based on the preoperative images [6–8]. It might be expected, however, that introduction of more advanced computer-aided intraoperative devices into clinical practice can diminish or solve the abovementioned problems and facilitate maximal tumor resection with minimal risk of postoperative complications.

Advanced Computer-Aided Intraoperative Technologies for Management of Gliomas

The introduction of technologies for computer-aided diagnosis and treatment has dramatically changed the process of clinical decision-making. At present, preoperative integration of the various diagnostic data and their use for surgical planning and neuronavigation have become routine practice in the majority of neurosurgical centers. Further development of intraoperative imaging devices, such as ultrasonography, CT, and MRI, provided an opportunity to obtain real-time medical information at the time of surgery, and therefore profoundly increased its preciseness. Among the various tools designed for intraoperative imaging, intraoperative MRI (iMRI) seems to be the most promising, because of the absence of radioactivity, high resolution, possibilities to obtain images in different planes, and the opportunity to use various sequences and techniques depending on the goals of the investigation.

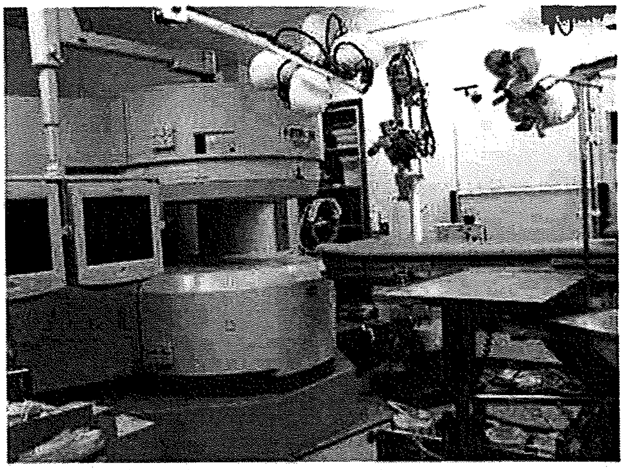

Fig. 1 General view of the intelligent operating theater in the Tokyo Women's Medical University with the hamburger-like open intraoperative MRI scanner (AIRIS II™, Hitachi Medical Co., Chiba, Japan).

Intraoperative MRI

The requirements for an optimal iMRI scanner are determined by the type and quality of images desirable during the neurosurgical procedure. It is clear that use of devices with higher magnetic field strength can provide better quality and resolution, but may be associated with a greater risk of distortion artifacts, which can result in significant mislocalization errors if used for neuronavigation [9]. While some techniques, such as diffusion tensor imaging or proton magnetic resonance spectroscopy [10,11] definitely require an iMRI scanner with a magnetic field strength of, at least, 1.5 Tesla, it should be noted that the majority of neurosurgical procedures are guided by structural, but not by metabolic or functional neuroimaging. Furthemore, integration of the intraoperative neurophysiological and histopathological data with the anatomic information provided by iMRI with low magnetic field strength practically resolves the problem of the slightly lower image quality.

An open iMRI scanner (AIRIS II™, Hitachi Medical Co., Chiba, Japan) installed in Tokyo Women's Medical University (TWMU) has a magnetic field strength of 0.3 Tesla [12,13]. It has a hamburger-like shape with a 43 cm gantry gap and a permanent magnet producing a vertical magnetic field with resonance frequency of 12.7 MHz (○ **Fig. 1**). The low magnetic field strength creates a narrow 5-Gauss line, which extends 2 m from both sides, 2.2 m in front, 1.8 m backwards, and 2.5 m upwards. It permits the surgeon to use some conventional surgical devices and instruments in the working space outside the 5-Gauss line (○ **Fig. 2**). It should be specially noted that this iMRI scanner does not require a cooling system, which significantly reduces its operating costs by approximately 10000 Japanese yen (around 100 US $) per month.

The originally developed radiofrequency receiver coil integrated with the Sugita head-holder (Head-holder coil; Mizuho Ltd., Tokyo, Japan) significantly improves the quality of intraoperative images. It provides an opportunity to perform MRI investigations with minimal distortion artifacts and maximum structure contrasting in any plane irrespectively to the orientation of the object, which allows fixation of the patient's head in the most desirable position for tumor removal. Integration of the head-holder coil with a modified Komai stereotactic frame [14] permits us to perform stereotactically guided surgical

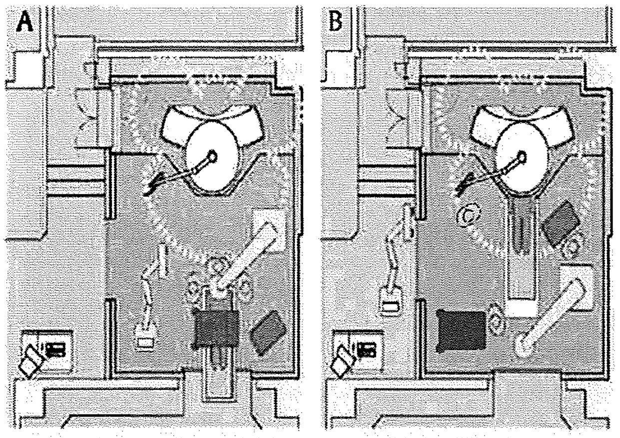

Fig. 2 Scheme of the internal organization of the intelligent operating theater in the Tokyo Women's Medical University during a surgical procedure (A) and MRI scanning (B). The low magnetic field strength of the device (0.3 Tesla) provides narrow distribution of the 5-Gauss line (*dotted line*), which permits the surgeon to use some conventional surgical devices and instruments.

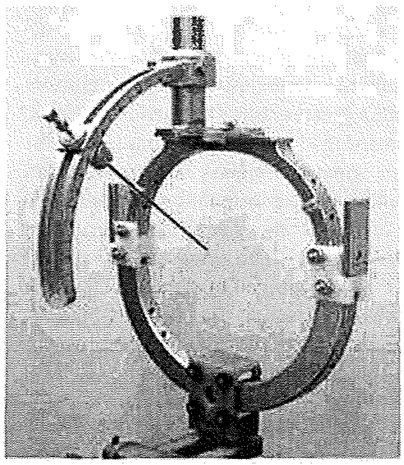

Fig. 3 Radiofrequency receiver coil integrated with a modified Komai stereotactic frame for stereotactically guided surgical procedures under the control of intraoperative MRI.

procedures under the control of iMRI (☞ **Fig. 3**). Use of the device provides an opportunity to perform intraoperatively not only volumetric, but diffusion-weighted imaging (DWI) and functional investigations, with a sufficient quality of images comparable to those obtained on scanners with higher magnetic field strengths (☞ **Fig. 4**). Intraoperative use of DWI seems to be especially promising, because it can permit us to identify motor nerve fibers, such as the pyramidal tract [15–17]. The technique is operator-independent and the images do not require any postprocessing modifications, therefore it can be installed into the neuronavigation system without any delay in time.

Intraoperative MR images are usually taken for verification of the brain shift and deformation, for evaluation of the residual part of the lesion, and for diagnosis of complications. In our practice iMRI investigations are usually performed when approach to the tumor is attained and when the lesion is removed for evaluation of its possible remnants. Nevertheless, it can be done during the procedure as many times as necessary. When the image is obtained it is immediately converted into DICOM format and transferred into the intraoperative neuronavigation system through the local network.

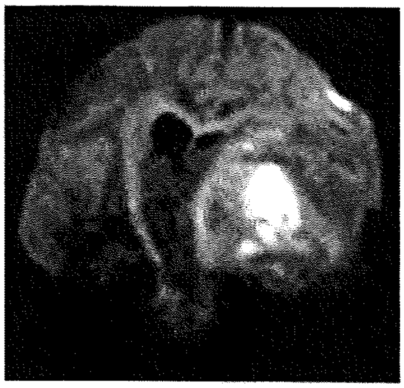

Fig. 4 Intraoperative DWI obtained on MRI scanner with a magnetic field strength of 0.3 Tesla: both pyramidal tracts are clearly seen and the shift on the affected side can be easily evaluated.

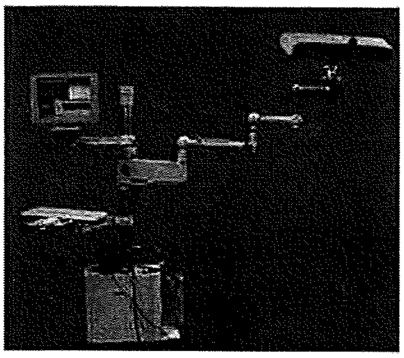

Fig. 5 Intraoperative neuronavigation system (PRS navigator, Toshiba Medical Co. Ltd., Tokyo, Japan).

Intraoperative real-time updated neuronavigation

The main advantage of the real-time updated neuronavigation based on the intraoperative neuroimaging 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. In our practice we use a previously developed navigator for the photon radiosurgery system (☞ **Fig. 5**). It 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. 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 (☞ **Fig. 6**) according to the safety of manipulations and probable risk of complications [18]. The device may be integrated with a special sound alarm that is automatically activated when surgical manipulations would come in close proximity to the high-risk area [19].

It should be noted that anatomic data alone are not sufficient for guidance of tumor resection, even if obtained with iMRI. The location of the eloquent brain strucutres has known individual variability and may be displaced during tumor growth. It necessitates the use of comprehensive neurophysiological monitoring and intraoperative cortical and subcortical brain mapping with or without awake craniotomy, with further integration of the neurophysiological and anatomical data.

Influence on clinical results

The first case with the use of iMRI was done in TWMU on March 13, 2000 and up to now more, than 600 neurosurgical procedures, mainly directed at the removal of parenchymal brain tumors, have been accomplished. The development of a system for advanced neurosurgical management significantly increased

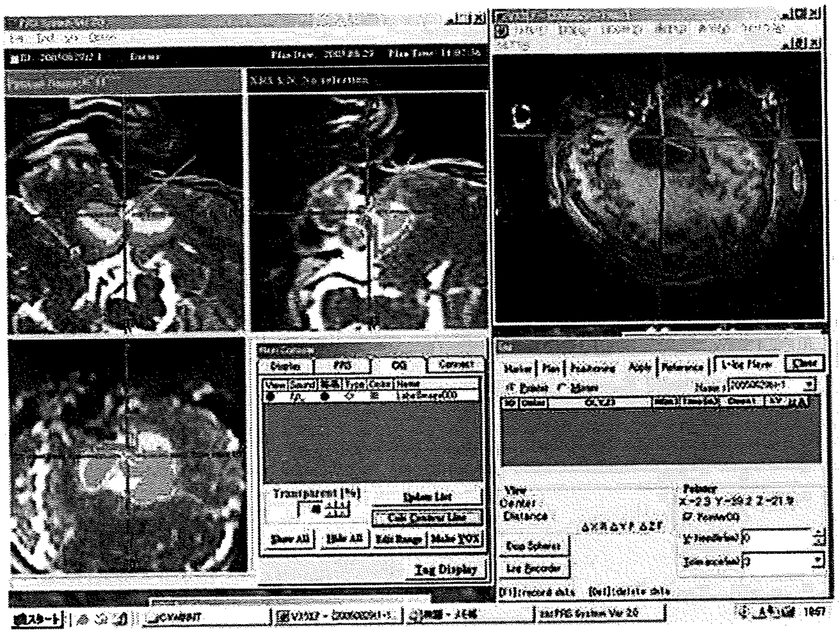

Fig. 6 Intraoperative neuronavigation with color-coded safety areas of tumor resection.

the resection rate of gliomas (up to 93% on average), and reduced residual tumor volume (median: 0.17 mL) [20]. In 46% of cases total tumor removal was attained, which is much greater compared to 12%, recorded in the last edition of the Brain Tumor Registry of Japan [5]. Moreover, a gradual improvement of our surgical results was noted in parallel with the growing experience and technological achievements: in the latest cases the median residual tumor volume was just 0.025 mL [20]. While the rate of temporary postoperative neurological complications was not low (34%), permanent neurological morbidity was noted just in 14% of cases, despite the fact that 83% of gliomas were located in or in the nearest vicinity to eloquent brain structures. Optimal surgical results were reflected in an improved 5-year survival rate of our patients, which constituted 90, 78, and 13% for grade II, III, and IV gliomas, respectively. For comparison, the corresponding rates recored by the Brain Tumor Registry of Japan, are 75%, 40%, and 7% [5].

Intraoperative Presentation and Distribution of the Medical Information

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Appropriate management of the intraoperative medical information may have a significant impact on the clinical decision-making, and, therefore, may influence the outcome. During a 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, these data have to be constantly updated, presented in a real-time regime, and widely distributed between members of the surgical team. As an optimum, the scientific information from evidence-based sources, integrated using probability assessment techniques, should be also available upon request. It is evident that, for the 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. All data should be preferably co-registered and formatted for possible installation into constantly maintained databases, which is extremely important for precise risk evaluation, comprehensive outcome analysis, and effective planning and simulation of the further surgical procedures.

The main information-sharing device we use is the Intraoperative Examination Monitor for Awake Surgery (IEMAS). It provides for the surgeon, anesthesiologist, and other members of the surgical team the wide spectrum of data about the condition of the patient, nuances of the surgical procedure, and details of cortical mapping. The whole set of both anatomic and functional information, such as view of the patient's mimic and face movements during answering of the test questions, type of examination task, position of the surgical instruments on the navigation display, parameters of the bispectral index monitor, and general surgical field of view through the operating microscope and/or endoscope, is presented compactly in one screen with several displays, which allows fast integrated real-time analysis of the multiple data, nearly without interruption of the surgical manipulations (◎ **Fig. 7**). All members of the surgical team can visualize these data on several in-room liquid crystal displays (LCD).

Additionally, a special surgical information strategy desk has been designed to facilitate the search of an optimal solution in a constantly changing surgical situation [21,22]. Seven LCDs of this system provide for the surgeon the whole spectrum of the integrated information about the 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 the transfer of information into the distant areas (at present up to 200 m), therefore, an urgent consulting service with specialists located outside the operating theater, can be provided (◎ **Fig. 8**). All surgical data are progressively incorporated and collected within the system, along with updated relevant technological and scientific information, for possible use during the planning of further surgical procedures. Analysis of this information permits preoperative simulation and significantly improves the

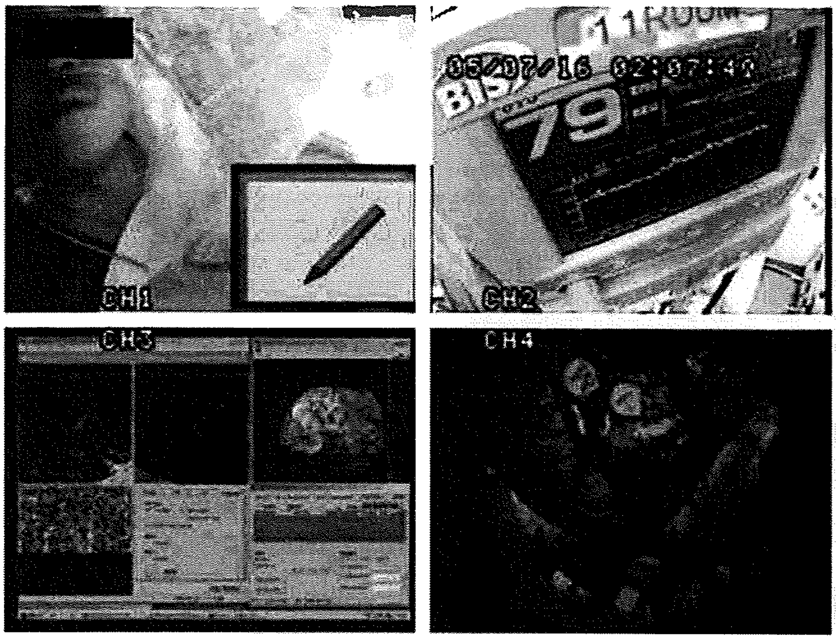

Fig. 7 Intraoperative examination monitor for awake surgery (IEMAS): view of the patient face and verb-generation task (*upper left*), parameters of the bispectral index monitor (*upper right*), position of the surgical instruments on the navigation display (*lower left*), and general surgical field of view with marks used for functional brain mapping (*lower right*) are presented simultaneously in one screen, which allows one fast integrated real-time analysis of the multiple data.

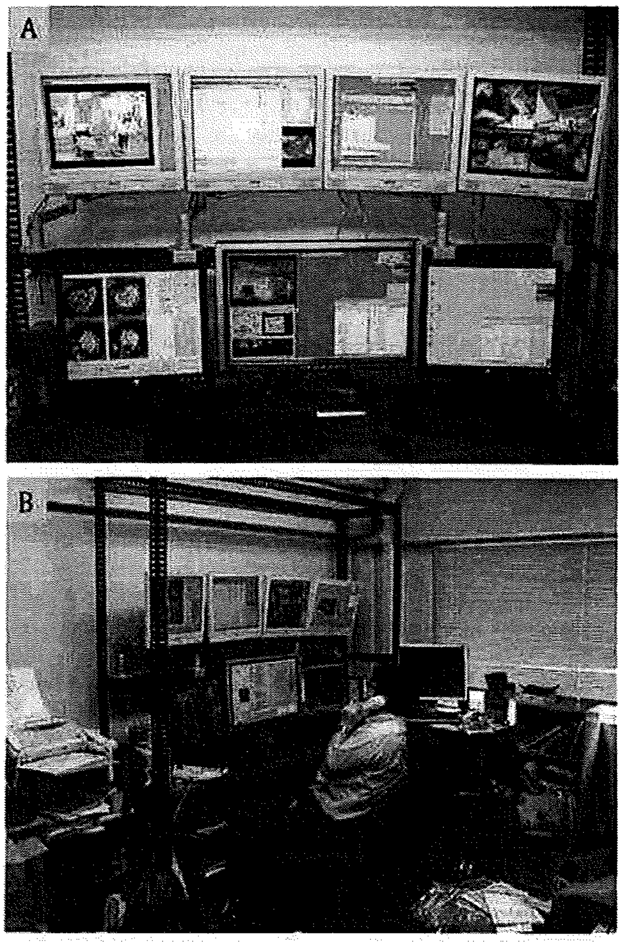

Fig. 8 Surgical information strategy desk: its overview (**A**) and use by the senior neurosurgeon supervising removal of a glioma from eloquent brain area from the neurosurgical office (**B**).

ability of a surgeon to define an optimal treatment strategy. At the time of surgery, the system permits one to get real-time information whether the actual surgical procedure corresponds well to the preliminary developed treatment plan or not.

Future Perspectives

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

Computer-based system for correction of distortion artifacts

Speaking precisely, our intraoperative neuronavigation system, is not "real-time", but nearly "real-time". Therefore, the risk of small mislocalization errors, particularly caused by brain deformation and its movements due to surgical manipulations, could not be excluded. Even if the gap between the estimated and real target positions is small, it may be of critical importance in cases of lesions located within or in the nearest vicinity to eloquent brain areas. Therefore, the development of the special computer-based system for "advanced vision neuronavigation", which would permit constant real-time estimation and correction of the mislocalization errors, will be of great importance for further increase of preciseness and safety of the neurosurgical procedures.

Robotic neurosurgery

The incorporation of robotic systems into neurosurgical practice can potentially increase the preciseness of surgical manipulations, and significantly reduce the risk of neurological deficits if surgery is performed in highly vulnerable brain areas. The robotic systems can perform automatic distinction between the tumor and surrounding tissue, and may provide an opportunity for highly selective management of the neoplasm with extremely

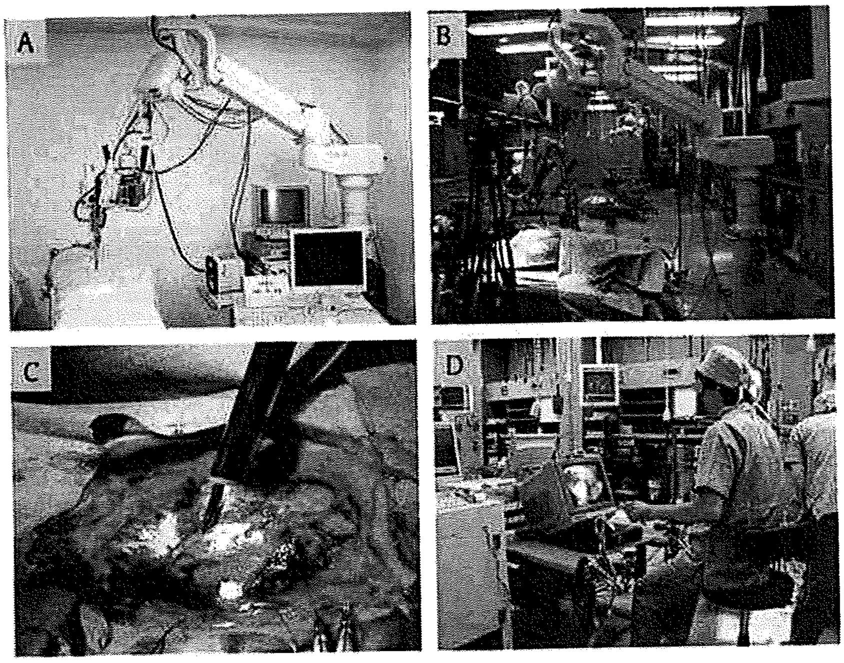

Fig. 9 iMRI-compatible neurosurgical robotic system (A) showed its preciseness in animal experiments (B and C) and allows distant control of all manipulations by the neurosurgeon (D).

high precision (up to 10 μm). Other potential advantages of robotics include the opportunity to perform manipulations in extremely limited space, and the possibility of initial computer-aided modelling and simulation of the planned surgical action.
The introduction of the robotic technologies into clinical medicine started in the 1990s with such systems as da Vinci™ and Zeus™ (Intuitive Surgical Inc., Sunnyvale, CA, U.S.A), and Robodoc™ (CUREXO Technology Co., Sacramento, CA, U.S.A). In the same time we had developed a special neurosurgical robotic system, designated as the Hyper Utility Mechatronic Assiastant for Neurosurgery (HUMAN) or NeuRobot (Hitachi Medical Co., Chiba, Japan). For the first time in the world it was clinically applied in Shinshu University (Matsumoto, Japan) in August 2002 and proved the possible practical utility, particularly for third vetnriculostomy [23]. Currently, an advanced iMRI-compatible model of this device is undergoing experimental testing (○ **Fig. 9**).
The next generation of neurosurgical robots requires integration of the advanced intraoperative neurovisualization and computer technology for comprehensive data assessment. Currently we are developing a manipulator based on the integration of the chemical neuronavigation for identification of the neoplasm in the surgical field and micro-laser for its ablation [24–26]. The management area is determined automatically with a specially designed camera. A mid-infrared continuous wave micro-laser with a wave length of 2.8 μm provides optimal absorption parameters of the brain tissue and extremely limited thermal action. The system has less than 0.5 mm positioning accuracy. All surgical actions are planned and controlled by the neurosurgeon who is located in front of the distant desk, which allows precise planning and simulation of the procedure. It should be noted that this device has been developed not for removal of the whole bulk of the tumor, but for management of its residuals in the highly eloquent brain structures where high levels of preciseness and safety are needed. It is expected that such highly selective pin point neurosurgery will permit us to eliminate the neoplasm while keeping intact functionally important brain structures. The clinical testing of the device is expected in the nearest future.

Information-guided treatment simulation and pre-emptive risk management

In order to improve the safety and effectiveness of 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 merely installation of the surgical records and video into databases is not sufficient, but rather a 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, as optimum 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, evaluating the various risks, and providing scientifically-based choice of the optimal treatment strategy for attainment of the best possible outcome. The development of such a complex computer-aided system based on the construction of the virtual neurosurgical reality is currently under way.

Conclusion

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The incorporation of computer-aided diagnostic and management technologies into everyday clinical practice can significantly improve the quality of the neurosurgical service. It can enable us to optimize the choice of the treatment strategy in each individual case, based not on the individual experience of the particular surgeon, but on the integration of the whole spectrum of the clinical and scientific data. Computer-aided simulation of the treatment course of the particular patient can permit a clear determination of the roadmap to the best possible outcome. Further progress in advanced neurovisualization, robotics, and comprehensive medical information management, has a great potential to increase the safety of the neurosurgical procedures, and hopefully will result in improvements of the long-term outcome of patients with gliomas.

Acknowledgements

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References

1 *Iseki H, Muragaki Y, Taira T et al.* New possibilities for stereotaxis. Information-guided stereotaxis. Stereotact Funct Neurosurg 2001; 76: 159–167

2 *Hess KR.* Extent of resection as a prognostic variable in the treatment of gliomas. J Neurooncol 1999; 42: 227–231

3 *Proescholdt MA, Macher C, Woertgen C et al.* Level of evidence in the literature concerning brain tumor resection. Clin Neurol Neurosurg 2005; 107: 95–98

4 *Lacroix M, Abi-Said D, Fourney DR et al.* A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg 2001; 95: 190–198

5 *The Committee of Brain Tumor Registry of Japan.* Report of brain tumor registry of Japan (1969–1996), 11th edition. Neurol Med Chir (Tokyo) 2003; 43 (Suppl): 1–111

6 *Nimsky C, Ganslandt O, Cerny S et al.* Quantification of, visualization of, and compensation for brain shift using intraoperative magnetic resonance imaging. Neurosurgery 2000; 47: 1070–1080

7 *Hartkens T, Hill DL, Castellano-Smith AD et al.* Measurement and analysis of brain deformation during neurosurgery. IEEE Trans Med Imaging 2003; 22: 82–92

8 *Trantakis C, Tittgemeyer M, Schneider JP et al.* Investigation of time-dependency of intracranial brain shift and its relation to the extent of tumor removal using intra-operative MRI. Neurol Res 2003; 25: 9–12

9 *Novotny J Jr, Vymazal J, Novotny J et al.* Does new magnetic resonance imaging technology provide better geometrical accuracy during stereotactic imaging? J Neurosurg 2005; 102: 8–13

10 *Preul MC, Leblanc R, Caramanos Z et al.* Magnetic resonance spectroscopy guided brain tumor resection: differentiation between recurrent glioma and radiation change in two diagnostically difficult cases. Can J Neurol Sci 1998; 25: 13–22

11 *Stadlbauer A, Moser E, Gruber S et al.* Integration of biochemical images of a tumor into frameless stereotaxy achieved using a magnetic resonance imaging/magnetic resonance spectroscopy hybrid data set. J Neurosurg 2004; 101: 287–294

12 *Iseki H, Muragaki Y, Nakmura R et al* Clinical application of augmented reality in neurosurgical field. In: Proceedings of the Computer Graphics International, July 9–11, 2003. Tokyo, Japan. Los Alamitos: IEEE Computer Society; 2003; 44–49

13 *Iseki H, Muragaki Y, Nakamura R et al.* Intelligent operating theater using intraoperative open-MRI. Magn Reson Med Sci 2005; 4: 129–136

14 *Taniguchi H, Muragaki Y, Iseki H et al.* New radiofrequency coil integrated with a stereotactic frame for intraoperative MRI-controlled stereotactically guided brain surgery. Stereotact Funct Neurosurg 2006; 84: 136–141

15 *Ozawa N, Muragaki Y, Shirakawa H et al.* Navigation system based on intraoperative diffusion weighted imaging using open MRI. In: Lemke HU, Inamura K, Doi K, Vannier MW, Farman AG, eds. Computer assisted radiology and surgery: Proceedings of the 19th International Congress and Exhibition. Amsterdam: Elseiver; 2005; 810–814

16 *Ozawa N, Muragaki Y, Nakamura R et al.* Intraoperative diffusion-weighted imaging for visualization of the pyramidal tracts. Part I: pre-clinical validation of the scanning protocol. Minim Invas Neurosurg 2008; 51: 63–66

17 *Ozawa N, Muragaki Y, Nakamura R et al.* Intraoperative diffusion-weighted imaging for visualization of the pyramidal tracts. Part II: clinical study of usefulness and efficacy. Minim Invas Neurosurg 2008; 51: 67–71

18 *Nakamura R, Suzukawa H, Muragaki Y et al.* Neuro-navigation system with colour-mapped contour generator for quantitative recognition of task progress and importance (abstract). Int J Comput Assist Radiol Surg 2006; 1 (Suppl.1): 489

19 *Ozawa N, Muragaki Y, Suzukawa H et al.* Pyramidal tract navigation based on intraoperative diffusion-weighted imaging: sound navigation using the fiber tract margin (abstract). Int J Comput Assist Radiol Surg 2006; 1 (Suppl.1): 488

20 *Muragaki Y, Iseki H, Maruyama T et al.* Usefulness of intraoperative magnetic resonance imaging for glioma surgery. Acta Neurochir Suppl 2006; 98: 67–75

21 *Iseki H, Muragaki Y, Nakamura R et al.* Surgical information strategy desk. In: Proceedings of the 4th Symposium on "Intelligent Media Integration for Social Information Infrastructure", December 7–8, 2006. Nagoya, Japan. Nagoya: IMI COE Nagoya University; 2006; 181–185

22 *Nakamura R, Sakurai Y, Nambu K et al.* Surgical strategic desk for integration/monitoring/management of intraoperative information. J Jpn Soc Comp Aided Surg 2005; 7: 355–356 [in Japanese]

23 *Hongo K, Kobayashi S, Kakizawa Y et al.* NeuRobot: telecontrolled micromanipulator system for minimally invasive microneurosurgery – preliminary results. Neurosurgery 2002; 51: 985–988

24 *Omori S, Muragaki Y, Sakuma I et al.* Robotic laser surgery with h=28 μm microlaser in neurosurgery. J Robotics Mech 2004; 16: 122–128

25 *Noguchi M, Aoki E, Yoshida D et al.* A novel robotic laser ablation system for precision neurosurgery with intraoperative tumor detection by 5-ALA-induced PpIX fluorescence (abstract). In: Proceedings of the World Congress on Medical Physics and Biomedical Engineering, August 27 – September 1, 2006. Seoul, Korea (CD-ROM)

26 *Nakamura R, Omori S, Muragaki Y et al.* A robotic neurosurgery system with autofocusing motion control for mid-infrared laser ablation. In: Proceedings of the Workshop on Medical Robotics: System and Technology towards Open Architecture, October 5, 2006. Copenhagen, Denmark. Copenhagen: MICCAI; 2006; 108–115