The 70th Annual Meeting Special Topics — Part II: Multidisciplinary Treatment for High Grade Gliomas

Usefulness of Multimodal Examination and Intraoperative Magnetic Resonance Imaging System in Glioma Surgery

Kaori SAKURADA,¹ Kenichiro MATSUDA,¹ Hayato FUNIU,¹ Atsushi KUGE,¹
Sunao TAKEMURA,¹ Shinya SATO,¹ and Takamasa KAYAMA¹

¹Department of Neurosurgery, Yamagata University Faculty of Medicine, Yamagata, Yamagata

Abstract

Extensive surgical removal of tumor tissue can contribute to longer survival for patients with gliomas. Intraoperative magnetic resonance (iMR) imaging is important for safe and maximal resection of brain tumors. A new operating room equipped with a 1.5-T MR imaging system and neuronavigation opened at Yamagata University Hospital in 2008. Using this new suite, we have safely treated over 200 cases. Use of iMR imaging improved glioma resection rates in 25 (34%) of 73 cases, and gross total resection was achieved in 48 patients (66%). Motor evoked potential (MEP) monitoring was performed in combination with iMR imaging for 32 gliomas. MEP monitoring was successful in 30 cases (94%). Transient decreases in MEP amplitude were seen in two patients. One patient showed transient motor weakness and another showed improvement of motor function. The iMR imaging system provides useful information for tumor resection that allows intraoperative modification of surgical strategies. Combining MEP monitoring with iMR imaging appears to offer the most effective method for safe glioma surgery near eloquent areas.

Key words: intraoperative magnetic resonance imaging, glioma, intraoperative monitoring

Introduction

Intraoperative magnetic resonance (iMR) imaging and neuronavigation have substantially changed the principles of surgery for brain tumors. iMR imaging can provide updated information on anatomical structures and unanticipated brain events, thereby allowing safer and more accurate surgery.¹⁻⁴⁾ Our institution installed a fully integrated neurosurgical suite including neuronavigation and an intraoperative 1.5-T high-field MR imaging system (Surgical Suite[®]) in 2008. This system provides high-quality images with short scan times. The Surgical Suite[®] has separate components in the operating room and the MR imaging room, so can be used not only for intraoperative scanning, but also for pre- and postoperative scans and brain checks for inpatients at Yamagata University Hospital. Using this new suite, we have safely treated over 200 cases of brain

tumors, including gliomas, metastatic brain tumors, meningiomas, and pituitary adenomas. This study reviews our initial experiences, to evaluate the advantages and limitations of this suite in glioma surgery.

Material and Methods

Figure 1 shows the appearance of the operating system, Surgical Suite[®] (GE Healthcare, Milwaukee, Wisconsin, USA). The high-field (1.5-T) MR imaging system (Signa HDx; GE Healthcare) is located in a separate room, which allows us to use standard surgical instruments irrespective of their magnetic properties. Intraoperative MR imaging includes T₁-weighted, T₂-weighted, T₂^{*}-weighted, fluid-attenuated inversion recovery, diffusion-weighted, and T₁-weighted with gadolinium imaging. If necessary, diffusion tensor imaging can be performed. About 1 hour is needed for iMR imaging, including patient transfer time.

A total of 202 consecutive patients were treated in the Surgical Suite[®] at Yamagata University Hospital between July 2008 and September 2011. The histological diagnoses were glioma (n = 73, 36.1%), pituitary adenoma (n = 35, 17.3%), meningioma (n = 18, 8.9%), metastatic tumor (n = 19, 9.4%), and others (n = 57, 28.2%).

Surgical planning was based on multiple sequences of MR imaging performed 1 or 2 days before surgery. Using a navigation planning workstation (iPLAN 2.6; Brainlab AG, Feldkirchen, Germany), target lesions and important anatomical structures were coded as colored objects. Diffusion tensor imaging and functional MR imaging were performed to visualize important tract and functional areas (pyramidal tract, motor cortex, and speech area). If the tumor was located in or around the pyramidal tract and/or motor cortex, electrophysiologi-

cal monitoring such as motor evoked potential (MEP) monitoring was performed by transcortical stimulation using reduction to <50% amplitude compared to before tumor resection as the warning level. If the surgeon considered that the goals of surgery had been met or the risk of injury to a functional area or tract was high, iMR imaging was performed. If iMR imaging indicated incomplete resection, the surgical planning was revised according to the newly obtained images, and the surgical procedure was resumed based on the updated navigation information.

The extent of resection (EOR) was determined by comparing the MR images obtained before surgery with those obtained within 72 hours after surgery. EOR was calculated based on manual segmentation of the tumor outline in the planning software. Glioma volume was defined as the volume of increased intensity on T₁-weighted imaging with gadolinium. Tumor volume for non-enhanced tumors was defined as the area of increased intensity on T₂-weighted imaging. Subtotal or greater resection was defined as a postoperative finding of a >95% reduction in tumor volume.

Results

iMR imaging was performed 225 times during the 202 procedures. The period of interruption for each intraoperative MR imaging session was about 1 hour. The results of iMR imaging affected the surgical strategy in 33 of these 202 cases, including strategies for 25 of 73 gliomas (34%), 3 of 35 pituitary adenomas (8.6%), and 5 of 57 others. Additional removal after iMR imaging was performed in over 50% of cases of non-enhanced tumors and recurrent lesions. Gross total resection was achieved in 66% of 73 glioma cases (n = 48).

Volumetric analysis of primary supratentorial gliomas (n = 40) found that mean initial tumor volumes were 54.9 cm³ (range 1.2–160.0 cm³) in

Fig. 1 Layout and photographs of the Surgical Suite[®]. A magnetically shielded sliding door separates the magnetic resonance (MR) imaging room (right) from the operation room (left).

Table 1 Summary of volumetric analysis in primary supratentorial gliomas

	LGG	HGG	All	HGG by Sanai et al. ⁹⁾
Number of patients	7	33	40	500
Gd enhancement (+/-)	2/5	29/4	31/9	—
Tumor volume (cm ³)*	18.3 (1.0–49.0)	54.9 (1.2–160.0)	48.4 (1.0–160.0)	65.8 (0.3–476.1)
Additional removal (+)	2 (33%)	9 (27%)	11 (32%)	—
Additional removal volume (cm ³)*	3.9 (0.4–7.3)	2.4 (0.3–8.0)	2.6 (0.3–8.0)	—
Residual tumor volume (cm ³)*	4.6 (6.5–12.7)	2.3 (0.8–25.5)	2.6 (0.8–25.5)	2.3 (0–80)
Intraoperative resection rate*	80.5% (40.7–100)	93.5% (34.5–100)	91.7% (34.5–100)	—
Resection rate*	83.2% (40.7–100)	95.1% (34.5–100)	93.5% (34.5–100)	96% (10–100)

*Values are mean (range). Gd: gadolinium, HGG: high-grade glioma, LGG: low-grade glioma.

high-grade glioma (HGG) and 18.3 cm³ (range 1.0–49.0 cm³) in low-grade glioma (LGG). The volume of additional removal after iMR imaging was 2.4 cm³ (range 0.3–8.0 cm³) in HGG and 3.9 cm³ (range 0.4–7.3 cm³) in LGG. Residual tumor volume was 2.3 cm³ (range 0.8–25.5 cm³) in HGG and 4.6 cm³ (range 6.5–12.7 cm³) in LGG. The EOR was 95.1% in HGG and 83.2% in LGG (Table 1). In addition, iMR imaging revealed an unexpected brain event in 1 patient (acute subdural hematoma). To evaluate the impact of iMR imaging, we analyzed the relationship between supratentorial glioma surgical staging (Table 2) and the incidence of additional removal after iMR imaging. This surgical staging was proposed by Nomura and Kayama and the Japanese Brain Tumor group in 2004.⁵⁾ We analyzed 44 cases of primary supratentorial glioma (4 cases were added following the volumetric analysis): stage 1, n = 0; stage 2, n = 5; stage 3, n = 21; stage 4, n = 12; stage 5, n = 6. No additional removal was performed for cases in stages 1, 2, or 5. Additional removal after iMR imaging achieved subtotal resection in 3 cases (14%) in stage 3 and 3 cases (25%) in stage 4 (Fig. 2).

MEP monitoring was combined with iMR imaging in 32 gliomas. MEP monitoring was successful

in 30 cases (94%), and was only unsuccessful in 2 patients with preoperative severe motor weakness. Table 3 shows the results of MEP monitoring and postoperative motor function. Preoperative motor deficits were improved in 4 patients and remained unchanged in 19 patients. Permanent motor deficits were identified in 5 patients, 2 patients with decreased amplitude of MEP and 3 patients with no changes in MEP amplitude. Transient decreases in MEP amplitude were seen in 2 patients. One of these two patients had left temporal glioblastoma and showed transient decreases in MEP amplitude caused by middle cerebral artery compression (Fig. 3). iMR imaging showed no ischemic changes, but diffusion-weighted imaging after surgery clearly showed an ischemic lesion around the left internal capsule.

Discussion

The present study suggests that the best use for iMR imaging and integrated navigation seems to be for glioma surgery. In our series, 34% of glioma cases

Table 2 Surgical staging for glioma

Stage	Definition
1	tumor size ≤ 1 cm or within one gyrus
2	Stage 1 (+1) or tumor size > 1 cm to < 3 cm
3	Stage 2 (+1) or tumor size > 3 cm
4	Stage 3 (+1) or stage 2 (+1+1)
5	Stage 3 (+1+1) or stage 2 (+1+1+1) or multiple lesions, disseminated lesions, extra-CNS lesions

+1: Eloquent area (motor, speech, visual); thalamus, basal ganglia, bilateral lesions; sylvian fissure (insular cortex). CNS: central nervous system. Reproduced with permission from Kayama et al.: [A proposed staging system for glioma surgery]. *No Shinkei Geka Journal* 13: 448–453, 2004 (Japanese).⁵⁾ ©2004, The Japanese Congress of Neurological Surgeons.

Fig. 2 Surgical staging and resection rate. Tumors in stages 1, 2, and 5 underwent no additional removal (AR) after intraoperative magnetic resonance imaging. AR was performed for 14% of stage 3 cases and 25% of stage 4 cases.

Table 3 Results of intraoperative motor evoked potential (MEP) monitoring and postoperative motor function

MEP	Postoperative motor function				Total
	Improve	No change	Transient aggravation	Permanent aggravation	
No change	3	19	1	3	26
Transient decrease in amplitude	1	0	1	0	2
Permanent decrease in amplitude (< 50%)	0	0	0	2	2
Total	4	19	2	5	30

Fig. 3 Representative case of left temporal glioblastoma showing transient decrease in motor evoked potential (MEP) amplitude. **A:** Preoperative T₁-weighted magnetic resonance (MR) image with gadolinium. **B:** Intraoperative diffusion-weighted MR image. **C:** Postoperative T₁-weighted MR image with gadolinium. **D:** Postoperative diffusion-weighted MR image. **E:** Temporal changes in response of the thenar muscles. Transient decrease in amplitude occurred during middle cerebral artery compression, but recovered after releasing the compression.

were improved and the EOR was increased following iMR imaging. This modality offers particularly important contributions to modification of surgery in non-enhanced and recurrent tumors. In addition, iMR imaging is a good method to overcome technical problems encountered during surgery, such as unclear margins of microscopic and pathological findings and brain shift. In patients with newly diagnosed glioblastomas, increased EOR parallels improvements in overall survival, even at the highest levels of resection, and subtotal resections as low as 78% confer survival benefits.⁹⁾ Our results are similar to these findings (Table 1). In our series, the resection rate of LGG was lower than that of HGG. Three of 7 LGGs were located in eloquent areas, so we intentionally performed partial resection. The resection rates of these cases ranged from 40.7% to 71.9%. Safer resection could be performed for LGG than for HGG considering the long natural history of LGG. Randomized controlled trials of iMR imaging-guided glioma surgery did not demonstrate survival benefits.¹⁰⁾ However, iMR imaging guidance in glioma surgery did help surgeons achieve the optimum EOR.

This study analyzed surgical staging and additional (modified) removal after iMR imaging. For tumors

classified in stages 1, 2, or 5, no modification was required after iMR imaging. Stage 5 tumors are not resectable to ensure preservation of brain function. In contrast, tumors in stages 3 and 4 underwent the modification after iMR imaging in 15–25% of cases. Moreover, over 50% of recurrent or non-enhanced tumors underwent modification after iMR imaging. iMR imaging is mainly useful for safety management in patients with stage 1, 2, or 5 lesions. Safety management is one of the important purposes of iMR imaging. In our series, we were able to detect left acute subdural hemorrhage during right temporal glioblastoma removal,⁷⁾ and could remove the hematoma immediately after tumor resection. The postoperative course was uneventful and the patient remained alive as of 26 months postoperatively.

Review of iMR imaging-guided resection of glioblastoma pointed out the limitations in the available literature,⁶⁾ and also suggested cost as an important outcome parameter. Our Surgical Suite[®] has separate components in the operating room and MR imaging room. Consequently, the system can be used not only for intraoperative imaging, but also for pre- and postoperative imaging and brain checks for inpatients. We have also tried to use iMR imaging in various neurosurgical operations. T₁-weight-

ed imaging with gadolinium clearly shows residual tumor in the pituitary region, and intraoperative time-resolved contrast-kinetics imaging can reveal complete resection of arteriovenous malformation without the need for conventional catheter angiography.⁸⁾

The present study examined the associations between MEP monitoring and postoperative motor function in 32 patients. MEP monitoring was successful in 30 patients (94%), excluding 2 patients with severe preoperative motor weakness. Preoperative motor deficits recovered in 4 patients, whereas 19 patients showed no changes in motor function. Permanent deficits occurred in 5 patients. We were able to detect decreases in amplitude for 2 patients, but the remaining 3 patients did not show any change in MEP amplitude during surgery. One patient with precentral gyrus glioblastoma suffered motor weakness of the upper limb, and one patient had frontal gliosarcoma. We temporarily clipped the feeding arteries, and checked MEP responses within 20–30 minutes during gliosarcoma removal. We confirmed that MEP responses were unchanged, and then cut the feeder vessels. Postoperative MR imaging revealed an ischemic lesion, including the pyramidal tract. We speculate that the blood supply to the pyramidal tract during surgery was sufficient, but was altered by leptomeningeal anastomosis after surgery. Figure 3 shows the usefulness of MEP monitoring. Compression of the middle cerebral artery caused decrease in MEP amplitude. We were able to prevent permanent deficits based on the warnings provided by MEP monitoring. MEP monitoring is an essential tool for preserving motor function in patients with glioma near the motor cortex or pyramidal tract. We have safely performed 6 awake craniotomies with the use of this iMR imaging system. Combining MEP monitoring with awake craniotomy and iMR imaging appears to offer the most effective method for safe glioma surgery near eloquent areas. Further study of the impact of an iMR imaging system on surgical success and patient survival within the context of a large, prospective, population-based project is needed to confirm the present findings.

The present study shows that iMR imaging provides useful information that allows intraoperative modification of the surgical strategy, and MEP monitoring provides useful information for preserving motor function in patients with gliomas near the primary motor cortex and pyramidal tract. Combined use of iMR imaging, neuronavigation, and MEP monitoring offers the optimal tool for treating brain tumors around the motor cortex or pyramidal

tract. This approach could be very helpful for maximizing resection and minimizing morbidity.

References

- 1) Black PM, Alexander E 3rd, Martin C, Moriarty T, Nabavi A, Wong TZ, Schwartz RB, Jolesz F: Craniotomy for tumor treatment in an intraoperative magnetic resonance imaging unit. *Neurosurgery* 45: 423–430, 1999
- 2) Black PM, Moriarty T, Alexander E 3rd, Stieg P, Woodard EJ, Gleason PL, Martin CH, Kikinis R, Schwarz RB, Jolesz F: Development and implementation of intraoperative magnetic resonance imaging and its neurosurgical applications. *Neurosurgery* 41: 831–845, 1997
- 3) Claus EB, Horlacher A, Hsu L, Schwartz RB, Dello-lacono D, Talos F, Jolesz F, Black PM: Survival rates in patients with low-grade glioma after intraoperative magnetic resonance image guide. *Cancer* 103: 1227–1233, 2005
- 4) Fahlbusch R, Ganslandt O, Buchfelder M, Schott W, Nimsky C: Intraoperative magnetic resonance imaging during transsphenoidal surgery. *J Neurosurg* 95: 381–390, 2001
- 5) Kayama T, Sonoda Y, Sato S, Fujimaki T, Shibui S, Nomura K: [A proposed staging system for glioma surgery]. *No Shinkei Geka Journal* 13: 448–453, 2004 (Japanese)
- 6) Kubben PL, ter Meulen KJ, Schijns OE, ter Laak-Poort MP, Van Overbeek JJ, van Santbrink H: Intraoperative MRI-guided resection of glioblastoma multiforme: a systematic review. *Lancet Oncol* 12: 1062–1070, 2011
- 7) Sakurada K, Kikuchi Z, Kuge A, Takemura S, Kokubo Y, Sato S, Kayama T: [Detection of acute subdural hemorrhage using intraoperative MR imaging during glioma surgery: case report]. *No Shinkei Geka* 38: 1115–1120, 2010 (Japanese)
- 8) Sakurada K, Kuge A, Takemura S, Huniu H, Kokubo Y, Kondo R, Sato S, Kayama T: Intraoperative magnetic resonance imaging in the successful surgical treatment of an arteriovenous malformation: case report. *Neurol Med Chir (Tokyo)* 51: 512–514, 2011
- 9) Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS: An extent of resection threshold for newly diagnosed glioblastoma. *J Neurosurg* 115: 3–8, 2011
- 10) Senft C, Bink A, Vatter H, Gasser T, Seifert V: Intraoperative MRI-guidance and extent of resection in glioma surgery: a randomized, controlled trial. *Lancet Oncol* 12: 997–1003, 2011

Address reprint requests to: Kaori Sakurada, MD, PhD, Department of Neurosurgery, Yamagata University Faculty of Medicine, 2-2-2 Iidanishi, Yamagata, Yamagata 990-9585, Japan.