Chapter 52
Extent of Glioma Resection Using Low-field (0.2 T) versus High-field (1.5 T) Intraoperative MRI and Image-guided Frameless Neuronavigation

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INTRODUCTION

Neurosurgeons have long used various image-guided systems, such as fluoroscopy, ultrasound, and three-dimensional (3-D) stereotaxy in an attempt to more accurately localize intracranial targets (34). The development of advanced neuroimaging techniques over the years has provided the neurosurgeon with increasingly more accurate and precise tools to aid in the microsurgical treatment of intracranial lesions, such as intrinsic brain neoplasms. Studies have shown that, without the aid of image guidance, as many as 80% of operations performed to remove brain tumors leave part of the lesion behind (16). Although difficult to prove definitively, many recent papers have reported that the degree of resection of gliomas apparently correlates with both progression-free and overall survival (4, 7, 8, 17, 18, 20, 25, 26, 28, 48, 50). Consequently, real-time intraoperative information regarding the anatomic characteristics of the surgical field remains an important consideration to the neurosurgeon.

The introduction of image-guided frameless stereotactic neuronavigational methods was an important step toward providing an enhanced visualization of the surgical field. However, although helpful in planning the initial approach to resection of intracranial tumors, these methods are often of limited use intraoperatively because of the anatomic alterations (i.e., ¡§brain shift¡¨) caused by surgical retraction, cerebrospinal fluid (CSF) egress, and tumor removal (15, 35, 46). Other studies have documented brain surface deformations of greater than 10 mm after the opening of the dura but before any tumor resection (15). Therefore, the neurosurgeon must eventually revert to direct visual cues as the outdated imaging information becomes increasingly inaccurate during the course of the surgical procedure. This limitation of neuronavigational methods based solely on preoperative images has been documented with residual glial tumor being visualized on postoperative scans in 28 to 64% of operations in which preoperative images are used (6, 23, 30, 32, 37, 50).

Intraoperative magnetic resonance imaging (iMRI) systems were introduced into neurosurgery more than a decade ago and have been increasingly adopted worldwide (2, 5, 9, 12). There are several iMRI configurations available, ranging from very low field strength (0.12 T) compact units (38¡V40) to high field strength (1.5 T) diagnostic units (13, 32, 45). Each has inherent practical advantages and limitations. Weaker magnets are less expensive and can allow near real-time imaging, but suffer from poorer image resolution. The low-field compact magnets also have a very limited area of visualization. Conversely, high-field strength magnets provide high-quality image resolution comparable to the preoperative diagnostic studies, but are more expensive, permit interruptive scanning only, and may introduce additional safety issues because of the stronger magnetic field. Initial descriptions of the usefullness of iMRI purported improved monitoring of surgical progress plus the detection of complications, such as hemorrhage (3, 5, 9, 10, 16, 27, 36, 38, 44). Reports that are more recent have described the technical capability of importing the intraoperative images to the neuronavigation systems (6, 9, 11, 14, 19, 31, 47, 49, 51, 52).

In this retrospective, case-controlled study, our goal was to assess the relative contributions of iMRI field strength and frameless neuronavigation on the ability to achieve an image-complete resection of supratentorial gliomas. Four combinations of intraoperative technologies were compared: 1) standard image-guided frameless stereotactic neuronavigation in the conventional operating room (OR); 2) low field strength iMRI without neuronavigation; 3) high field strength iMRI plus standard neuronavigation; and 4) high field strength iMRI with initial and intraoperatively updated neuronavigation. The percent resection and volume of residual tumor were evaluated for each group. Additional comparisons were made regarding duration of operative time and incidence of intraoperative or postoperative complications.

PATIENTS AND METHODS

Description of Equipment

Approximately 5 years ago, the University of California, Los Angeles (UCLA) Medical Center installed a vertical field, dual-column 0.2-T Magnetom Open iMRI suite (Siemens Medical Systems, Erlangen, Germany) (36). This iron-core resistive system, with two horizontally oriented magnets (Fig. 52.1A), is a design that is common to the open MRI concept (6, 44). Two years later, a second iMRI suite, incorporating a 1.5-T Sonata short-bore donut design MRI (Siemens Medical Solutions, Erlangen, Germany) was installed (Fig. 52.1B). In both the 0.2-T Magnetom Open and 1.5-T Sonata systems, a modified MRI table served as the operating platform, equipped with a MRI-compatible head holder to fix the cranium rigidly to the table. During the operation, the surgical field was situated at or beyond the 5-Gauss fringe field, which allowed for the use of standard operating equipment (including surgical microscopes and ultrasonic aspirators) during surgery (36). When obtaining MRI scans, the surgical field was covered with a sterile towel, and the movable table was rotated into the center of the magnet (for the 0.2-T Magnetom Open suite) or slid into the bore of the scanner (for the 1.5-T Sonata suite) for intraoperative imaging (Fig. 52.1). There was no need to take the patient out of the head holder, re-drape the patient, or transport the patient outside the operating suite.

Patient Population

Informed consent was obtained from all patients in this study according to approved Health Insurance Portability and Accountability Act (HIPAA)-compliant institutional review board (IRB) protocols. Between September 2000 and June 2004, craniotomies for the treatment of supratentorial gliomas performed by the primary brain tumor neurosurgeons at the UCLA Medical Center were reviewed for possible inclusion in this retrospective study. All neurosurgeons were experienced glioma surgeons, each performing more than 50 glioma surgeries per year. Inclusion criteria were: 1) preoperative intent for an imaging-complete ¡§gross total¡¨ resection of all tumor identified on preoperative MRI scan, and 2) enrollment in an ongoing IRB-approved study for which consent had been obtained to analyze imaging studies. For all patients included in this analysis, the surgical goal was defined as removal of all tissues providing an abnormal imaging signal that was thought to be consistent with frank tumor (6). In general, abnormal imaging signal was defined as contrast enhancement for high-grade gliomas and T2-weighted abnormalities for low-grade gliomas. For tumors near eloquent brain areas, preoperative functional MRI (fMRI) scans were performed, and cases were excluded on the basis of fMRI information of anticipated functional tissue within or near tumor tissue, which could limit the amount of tumor removed. The intent to perform a complete resection was standardized by review of each case by at least three neurosurgeons on the UCLA Brain Tumor Board. All three neurosurgeons had to agree that ¡§gross total resection¡¨ was indicated and achievable. On the basis of these considerations, a total of 48 patients met the

criteria for this analysis.

Table 52.1 summarizes the four study cohorts that were evaluated. Twelve operations were performed in the conventional OR with standard frameless stereotactic neuronavigation without intraoperative imaging (Group 1); 13 operations in the 0.2-T open iMRI suite without neuronavigation (Group 2); 10 operations in the 1.5-T iMRI suite with initial frameless stereotactic neuronavigation without intraoperative re-registration (Group 3); and 13 operations in the 1.5-T iMRI suite with initial frameless stereotactic neuronavigation plus updated intraoperative re-registration of the navigational system (Group 4). Although patients were not prospectively assigned to these different groups by precise randomization paradigms, our retrospective analysis revealed that the operating environment in which these patients received their operations (i.e., conventional OR, 0.2-T iMRI suite, or 1.5-T iMRI suite) was assigned randomly on the basis of OR availability. Because our iMRI suites are shared-resource facilities (6), during the duration of this study, our 1.5-T iMRI suite was only available for intraoperative use on Mondays and our 0.2-T iMRI suite was only available on Thursdays. Because of this limited initial availability, we did not actively recruit nor choose which patients would go into the four different groups.

All cases were patients with newly diagnosed or recurrent supratentorial gliomas. Patients ranged in age from 20 to 74 years (mean age, 44 „b 14 yr) and included 21 women and 27 men. The tumor location was predominantly frontal (n = 30; 63%), followed by temporal (n = 14; 29%); and the remaining locations were either parietal or parieto-occipital (n = 4; 8%). The percentages of the different anatomic tumor locations were similar among the four groups analyzed. The histopathological profile of the tumors, according to the World Health Organization (WHO) grading system, consisted of 32 (67%) high-grade gliomas and 16 (33%) low-grade gliomas (Table 52.1). All of the high-grade gliomas were contrast-enhancing, and all of the low-grade tumors were noncontrast-enhancing T2 lesions. All patients underwent craniotomy for tumor resection as an elective procedure, and perioperative antibiotics, corticosteroids, and anticonvulsants were used, as indicated.

Clinical Procedures

Standard Image-Guided Frameless Stereotactic Neuronavigation

Patients had a preoperative MRI scan using a 1.5-T diagnostic magnet within 1 week before surgery to provide a data set for image-guided frameless stereotaxy. Before and after gadolinium contrast-enhanced T1-weighted spoiled gradient-recalled echo (SPGR) studies (TR, 1970 ms; TE, 4.4 ms; plane thickness, 1.2 mm; skip, 0 mm) and turbo spin echo T2-weighted images were obtained (TR, 5400 ms; TE, 108 ms; plane thickness, 3 mm; skip, 0 mm). Other standard diagnostic imaging sequences were obtained but were not imported into the neuronavigational computer.

The BrainLAB VectorVision navigation system (BrainLAB, Heimstetten, Germany) was used. This system consists of a mobile array with two infrared cameras, a computer workstation with a monitor, and handheld pointers. The instruments are equipped with reflective markers that reflect the infrared light to the cameras for position calculation. The software allows for multiple reconstructions, 3-D displays, virtual pointer elongation, and path planning.

During surgery, each patient was positioned and fixed in a head clamp, and the patient-to-image registration was performed using a pointer or a laser-guided (Z-Touch; BrainLAB) registration of the surface contour and anatomic landmarks on the face and scalp. The maximum acceptable mean registration error was 2 mm. Subsequent landmark

checks confirmed intraoperative navigation accuracy. After registration, axial, coronal, sagittal, and other user-defined reconstructions were displayed on the monitor. Each neurosurgeon interpreted the images on the navigational device during the course of surgery, and tumor resections were executed in a standard fashion as judged appropriate by the surgeon involved in the case. Because gross total resection was the preoperatively determined surgical goal of all of the patients included in this study, the procedure was continued until the surgeon thought that the entire macroscopic tumor had been removed.

Intraoperative MRI Craniotomy

Patients who underwent iMRI-guided craniotomy for tumor resection were positioned on the iMRI operating table (in either the 0.2-T Magnetom Open or the 1.5-T Sonata suites), which was connected to a MRI-compatible rigid fixation head holder. Standard microsurgical techniques and equipment, including surgical microscopes and ultrasonic aspirators, were safely used outside the 5-Gauss line. All preoperative MRI studies were performed at least 24 hours before the procedure to allow ample time for elimination of the administered contrast material before intraoperative scanning.

At the point at which an intraoperative image was desired, all ferromagnetic instruments were removed from the patient, and a radiofrequency coil was positioned over the head. The coil was directly attached to the MRI-compatible head holder of the operating table (Fig. 52.1C). The operating table was pivoted and then advanced into the magnet until the patient¡¦s head was located in the center of the magnetic field for intraoperative imaging. Images were obtained with the head fixed in the surgical position (Fig. 52.2), without attempting to realign the imaging in standard axial, coronal, or sagittal views.

In the 0.2-T Magnetom Open suite, multiple T1-weighted intraoperative images were obtained during the course of the operation. In an attempt to determine the optimal intraoperative resolution, slightly different T1 sequences were tried across patients (TR, 200¡V532 ms; TE,7.4¡V15 ms; plane thickness, 5 mm; skip, 2.5 mm; 256 ¡Ñ 256 matrix). If the surgical target was a contrast-enhancing lesion (e.g., high-grade gliomas), then T1-weighted sequences with and without 0.2 ml/kg of gadolinium were obtained, as needed. For nonenhancing lesions (e.g., low-grade gliomas), turbo spin echo T2-weighted images were used (TR, 2845¡V4138 ms; TE, 102¡V117 ms; plane thickness, 5 mm; skip, 2.5 mm).

Because the 1.5-T Sonata iMRI unit was essentially a diagnostic scanner, the intraoperative imaging protocols were identical to those used for standard diagnostic studies. Initial T1-weighted spin echo images in the axial plane (TR, 577¡V677 ms; TE, 14 ms; plane thickness, 5 mm; skip, 2.5 mm) were obtained. If the surgical target was a contrast-enhancing lesion, a T1-weighted sequence with gadolinium (Group 3) or a gadolinium-enhanced SPGR image for intraoperative re-registration of the navigational device (Group 4) was obtained. For non-enhancing lesions, T2-weighted MRI scans were used. Additional sequences (e.g., proton density and fluid-attenuated inversion recovery) and orientations (sagittal and coronal planes) were obtained when appropriate. Total intraoperative scan times varied, depending on the type and number of sequences obtained.

Intraoperative Neuronavigational Re-registration in Combination with iMRI

For patients in Group 4, five bone-fixated MRI-visible fiducials (Stryker Leibinger GmbH & Co, Freiburg, Germany)

were secured at strategic locations around the craniotomy before the intraoperative scan (Fig. 52.1C). The fiducial markers were identified on the intraoperative SPGR image and used for a five-point landmark registration to the patient. This re-registration technique allowed the intraoperative iMRI image data to be used to accurately update the navigation system, thereby compensating for brain shift caused by tumor removal and/or CSF loss during surgery. Further resection of the tumor was then pursued when appropriate, until the surgeon thought a gross total tumor resection had been achieved.

Image Analysis

To evaluate the extent of tumor resection, early postoperative MRI scans (within 48 hours of surgery) were performed. Essentially the same imaging protocols as the preoperative scans were used, except that the contrast study was a T1-weighted sequence (plane thickness, 3 mm) rather than a SPGR sequence. Preoperative and postoperative MRI studies were reviewed by an experienced neuroradiologist (PV) who was blinded to the experimental groups. For contrast-enhancing lesions, residual tumor was defined as enhancing tissue on the postcontrast axial T1-weighted sequences, excluding spontaneously hyperintense T1-weighted material (e.g., blood products) identified on the precontrast T1-weighted MRI scans. For nonenhancing tumor regions, residual tumor was delineated as remaining areas of T2 prolongation surgically targeted as tumor on the preoperative study; taking into account brain shift and other postoperative changes. Quantitative analysis was performed using a commercial software package (Vitrea, Software Versions 3.1-3.4, Vital Images, Minneapolis, MN) that allowed objective 3-D volumetric analysis for each lesion. Window and level settings were maintained constant across imaging studies and sequences to prevent lesion-blooming effects. Liquid-filled interiors of cystic tumors were excluded in the volumetric comparisons.

Statistical Analysis

Analyses of variance (ANOVA) were used for comparison of preoperative tumor volume, postoperative tumor volume, percent resection, and duration of surgery, with computations using the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL). Analysis of the effect of tumor size on each ANOVA calculation was conducted by computing the 95% confidence interval (CI) of the root-mean-square standardized effect (RMSSE) (43). An additional ANOVA of percent resection was conducted, with the preoperative volume treated as a covariate. Analyses of binary outcomes were made with exact statistical methods using Computer Programs for Epidemiologists (PEPI) (1). Statistical significance was set at $P = 0.05$.

RESULTS

Extent of Tumor Resection

The results of the comparisons between the four groups are summarized in Table 52.2. Preoperative volumes were not significantly different by group ($F_{3,41} = 0.242$; $P = 0.87$). Postoperative volumes differed significantly by group ($F = 4.351$; $P = 0.009$). The exact 95% confidence interval (CI) for the RMSSE was 0.178 to 1.056. Post hoc testing showed that Group 4 had significantly smaller postoperative volumes than Group 1, although the preoperative tumor volumes in Group 4 were the largest (Table 52.2). Of the 28/48 cases with preoperative tumor volumes exceeding 40 cm^3, a postoperative residual tumor volume of greater than 10 cm^3 occurred in 6/6 cases in Group 1; 1/7 in Group 2;

1/6 in Group 3; and 0/8 in Group 4 (Fisher exact test = 0.0002). For tumors with preoperative volumes of at most 20 cm3, gross total resection was achieved in all groups.

Percent of resection differed significantly by group (F = 3.848; P = 0.016), with 95% CI for RMSSE of 0.115 to 1.009 (Table 52.2). Post hoc testing found that Group 4 had significantly higher percent resections than Group 1. An analysis of covariance showed that preoperative volume was not a significant factor in determining group differences in percent resection (r = −0.114; P = 0.272). The number of large tumors (≥40 cm3) was equally distributed among the groups (Table 52.1).

High Field Strength (1.5 T) Versus Low Field Strength (0.2 T) iMRI

Figure 52.2 illustrates the differences in image resolution between the Siemens Magnetom Open 0.2-T scanner and the Siemens Sonata 1.5-T iMRI unit. The quality of intraoperative scans obtained in the 1.5-T iMRI suite (Fig. 52.2B) was equal or better (because of head fixation) than that of state-of-the-art preoperative diagnostic studies performed for surgical planning, thereby allowing for optimal intraoperative resolution of tumor. Images obtained in the 0.2-T iMRI were slightly lower in quality (Fig. 52.2A), but generally produced scans adequate for reliable interpretation of tumor margins in the majority of patients. Nevertheless, several of the initial intraoperative scans using the lower field 0.2-T magnet had to be repeated because of image distortion or artifact, and multiple scans were often necessary throughout the surgical procedure to ensure images suitable for accurate interpretation. Repetition of scanning because of inadequate image quality was not the case with the 1.5-T magnet, because high-quality images that adequately delineated the extent of the brain tumors were more consistently generated.

Surprisingly, despite the differences in image quality, there was no statistical difference between glioma surgeries performed using the 0.2-T iMRI (Group 2) and the 1.5-T iMRI without updated neuronavigation (Group 3) with respect to percent of tumor resection (91% versus 92%). The mean postoperative tumor volume was slightly lower in Group 3 (3.7 ± 5.5 cm3) compared with Group 2 (4.2 ± 3.8 cm3); however, this difference was not statistically significant.

Usefulness of iMRI Versus Standard Neuronavigation

Because the iMRI Group 3 included standard neuronavigation and Group 2 did not, the percent resection values of 92% (Group 3) and 91% (Group 2) suggest that intraoperative MRI capability was more important than standard (not updated) neuronavigation, because the efficacy of tumor removal was significantly worse in the conventional OR using standard image-guided frameless stereotaxy alone (79%, Group 1). Although these differences in percent resection were not statistically significant with this sample size, the use of iMRI resulted in less variability and lower mean residual tumor volumes (postoperative tumor, 4.2 ± 3.8 cm3 in Group 2, and 3.7 ± 5.5 cm3 in Group 3) compared with conventional neurosurgery without intraoperative imaging (postoperative tumor, 13 ± 14 cm3 in Group 1). Thus, the reliability and consistency of tumor resection seems to be improved using intraoperative MRI.

Advantages of Combination of iMRI with Updated Neuronavigation

As illustrated in Figure 52.3, the ability to intraoperatively update the neuronavigation system allowed the accurate identification of tumor margins at a time when the brain anatomy was markedly distorted secondary to tissue sag. The inability to compensate for brain shift occurring in the course of removing large intraparenchymal brain tumors

presumably resulted in the relatively lower percent resection (79%) using standard neuronavigational systems alone (Group 1). Adding iMRI capability to standard neuronavigation without updated re-registration of intraoperative imaging data (Group 3) improved the percent resection to 92%. However, the optimal results were obtained with the combination of iMRI with updated re-registration of the neuronavigational system, where a mean 98% percent resection was achieved (Group 4). As illustrated in Figure 52.4, this integration of intraoperative MRI data with the spatial orientation capabilities provided by fully equipped 3-D neuronavigation resulted in the most consistent and favorable results with regards to efficacy of tumor resection (postoperative tumor, 1.2 ± 1.5 cm3 in Group 4).

The difference in extent of resection between Group 3 and Group 4 implies that, despite the information the surgeons were getting with repeated intraoperative MRI scans, the 3-D interpretation of such images and the precise localization of residual tumor was still difficult. Therefore, although there was the capability to update the iMRI images as often as desired, the surgeons were not confident enough with the information provided to significantly modify the surgical resection. The addition of updated neuronavigation provided additional surgical confidence.

Safety and Complications

None of the complications that occurred could be directly attributed to performance of these procedures in the fringe of a magnetic field (neither 0.2-T or 1.5-T). In particular, there were no accidents caused by ferromagnetic instruments or devices used with either of our iMRI suites, despite the higher magnetic field, as long as appropriate safety precautions were observed and the OR zones were respected (36, 44). There were no problems with the maintenance of general anesthesia or with the use of the anesthesia equipment.

Table 52.2 summarizes the incidence of new postoperative neurological deficits and other complications that were documented. Twelve patients (12/36; 33%) who underwent surgery using iMRI experienced neurological worsening in the immediate postoperative period, and two patients who had surgery in the conventional OR (2/12, 17%) had new postoperative deficits. The number of temporary neurological morbidities was highest (6/13, 46%) in Group 2 (0.2-T iMRI suite). With the exception of two patients who developed expected worsening of visual field quadrantanopias, all of the postoperative deficits were temporary and resolved within 1 month after surgery. One patient in Group 2 developed meningitis postoperatively, which resolved with intravenous antibiotic treatment. One patient in Group 4 developed a subgaleal wound empyema, which was successfully treated with re-exploration, drainage, and intravenous antibiotics. The incidence of infections among iMRI patients was 5.5% (2/36). Because of the variety of complications and relatively small sample sizes, statistical analyses comparing complications between the various cohorts was not possible.

Duration of Surgery

Duration of surgery differed significantly by group ($F = 7.881$; $P = 0.001$; with 95% CI for RMSSE of 0.442–1.327), although the surgical durations were highest during our initial experience with each of the new added technologies and the increased OR time in the iMRI suites trended downward over time. Because the duration of surgery time was calculated on the basis of the times at which each patient entered and left the OR, differences among groups may have occurred because of both anesthesia-related management plus varying imaging times. Post hoc testing revealed that Group 4 had significantly longer operative durations than Groups 1 and 2. This can be attributed not only to the additional time required to re-register the patient to the neuronavigational system, but also to the fact that

the preoperative tumor volumes tended to be larger for the cases in Group 4 (Table 52.2).

Because of the relative small sample sizes in each group, other variables, such as tumor histology, tumor location, and neurosurgeon performing the procedure could not be independently assessed.

DISCUSSION

The results of our study suggest that the use of intraoperative MRI improves the reliability and extent of tumor resection as compared with standard image-guided frameless neuronavigation in the conventional OR (approximately 91% resection using iMRI alone versus 79% resection using standard neuronavigation alone). However, if high-quality intraoperative MRI scans can be obtained to allow reliable interpretation and adequate delineation of tumor, further increase of magnet field strength to allow for higher resolution may not necessarily translate into improvement in volumetric resection of intracranial gliomas. Without the aid of modernized frameless neuronavigation in parallel with iMRI, similar percent resection values were obtained using either the 0.2-T Magnetom Open or the 1.5-T Sonata scanner (91% versus 92% average tumor resection, Groups 2 and 3, respectively). With the combination of iMRI and updated neuronavigation, however, the extent of tumor removal was significantly increased, to an average of 98% (Group 4).

These findings demonstrate that there is a hierarchy in usefulness of the intraoperative technologies we tested. Regarding large tumors, the least optimal technology was standard image-guided frameless neuronavigation alone. Although somewhat disappointing, our average glioma resection rate (79% of tumor volume) using standard image-guided frameless neuronavigation in the conventional OR is comparable to rates reported in previous retrospective studies (33). For large non–contrast-enhancing tumors with infiltrative, indiscrete tumor–brain margins (e.g., low-grade gliomas), the brain shift–induced errors inherent to standard neuronavigation may severely limit the usefulness of standard image-guided frameless neuronavigation in the conventional OR. Bohinski et al. previously reported that intraoperative correction for brain shift may be particularly important for tumors with volumes of at least 20 cm3 (6). Our results further emphasize that neuronavigational systems based solely on preoperative image information cannot be trusted to evaluate the extent of tumor resection for large intrinsic brain neoplasms. It is well known that brain shift caused by tumor removal and CSF loss may decrease the accuracy of neuronavigational systems, and only the integration of intraoperative imaging could adequately compensate for this (5, 9, 12, 31).

Of the operations performed in the conventional OR (Group 1), if the preoperative tumor volume was more than 40 cm3, the postoperative residual exceeded 10 cm3 in every case. For all cases with tumor volumes of at most 20 cm3, however, gross total imaging-complete resection was achieved using standard image-guided frameless neuronavigation alone, suggesting that the intraoperative correction for brain shift provided by iMRI may not be as important for small tumors (6). The effect of preoperative tumor volume on percent tumor resection was largely abolished with the use of intraoperative imaging, because there was no difference in the extent of tumor resection of either large (≥40 cm3) or small (≤20 cm3) tumors for the operations performed using iMRI (Groups 2, 3, and 4). A concern in interpreting the results of this study may be that inclusion of smaller tumors in a particular group may lead to biased results. However, our data do not seem to be affected by this potential confounding variable, because an equal number of larger tumors (≥40 cm3) were included in all of the groups (Table 52.1).

Compared with standard neuronavigation, the use of iMRI (without updated neuronavigation) improved the average

percentage of tumor resection from 79% (Group 1) to approximately 91% (Groups 2 and 3). Several studies, however, suggest that increasing the extent of glioma resection to approximately 91% may not have a significant impact on patient outcome. In a study of 416 consecutive patients with histologically proven glioblastoma multiforme, Lacroix et al. recently demonstrated that only resection of 98% or greater of the tumor volume was associated with a significant survival advantage (25). In our current study, at least 98% resection of tumor volume was most consistently achieved with the combination of iMRI with updated neuronavigation (Group 4).

With respect to the quantitation of cytoreductive surgery, it has been argued that the absolute volume of residual tumor may be more important than the percentage of tumor resected. Here again, surgeries performed with only standard frameless neuronavigation in the conventional OR faired worst, with a mean postoperative tumor volume of 13 ± 14 cm3 (6 of 12 patients with more than 10 cm3 of residual tumor). Adding iMRI capabilities reduced the mean residual volume to approximately 4.2 cm3, however, 2 of the 23 patients still had residual tumor volumes greater than 10 cm3. The dramatic benefit of updated neuronavigation integrated with iMRI is evident with a mean residual tumor volume of only 1.2 ± 1.5 cm3. The highest remaining tumor in this cohort (Group 4) was only 3.3 cm3, despite the fact that the preoperative tumor volumes were generally the largest (59 ± 45 cm3). A retrospective study by Berger et al. revealed that residual volumes greater than 10 cm3 in low-grade glial tumors was associated with a higher incidence of recurrence (4). In a study of 119 adult patients with glioblastoma multiforme, Keles et al. reported that patients in whom the residual tumor volume was less than 10 cm3 at the start of chemotherapy had a 6-month progression-free survival rate of 32%, compared with 8% for patients with volumes between 10 and 15 cm3, and 3% for patients with a residual volumes larger than 15 cm3. Patients in whom the residual tumor volume was smaller than 10 cm3 had a 1-year survival rate of 37% compared with 9% for patients with residual tumor volumes between 10 and 15 cm3, and 18% for patients with residual tumor volumes larger than 15 cm3 (20).

Our results demonstrate that the optimal usefulness of intraoperative technology comes with the combination of iMRI with updated neuronavigation, resulting in both increased average percentage of tumor resection (98%) and decreased residual tumor volume ($\leq$3.3 cm3) for resection of supratentorial gliomas. We have found that it is not always straightforward to locate residual tumor simply on the basis of two-dimensional images, particularly given the skewed position of the patient's head during intraoperative scanning in the middle of a procedure. Without computer-assisted neuronavigation, adequate spatial geometric interpretation of the surgical resection cavity often requires several multiplanar intraoperative images, thereby increasing the intraoperative scanning time. Information provided by integrating high-quality iMRI with the frameless navigation system helps in improving the confidence of the surgeon in locating the precise 3-D areas of residual tumor. Currently, this is the latest evolution in the continual increase of neurosurgical precision.

Although our results did not find a statistical difference in the ability to radically resect intracranial gliomas using our low-field 0.2-T versus high-field 1.5-T iMRI units, we are not confident that our findings can be extrapolated to other iMRI units. Our Siemens 0.2-T Magnetom Open iMRI was originally a diagnostic scanner and is comparable to open MRI units used at some centers solely for diagnostic-imaging purposes. As shown in Figure 52.2, this scanner generated full-field, good-resolution intraoperative images. The relationship between magnet field strength and image quality is not linear and depends on multiple other factors, such as shielding, coil design, and software-based image enhancement techniques. Very low-field compact iMRI units ($\leq$0.2 T) that give only a limited view of the surgical field and relatively low-resolution images may not give comparable results (38–40).

There are several potential sources of error in our study. First, this was not a prospective, randomized study. Nevertheless, to the best of our abilities, no conscious effort was made to purposefully select ideal cases nor exclude other cases from any given group. The cases were analyzed from a consecutive series that met the specific inclusion criteria. Secondly, it can be argued that the designation of tumor versus non-tumor on MRI is subjective and not independently verifiable. We chose to rely on an experienced neuroradiologist blinded to the experimental cohorts to minimize this possible source of bias. Thirdly, both high-grade and low-grade glioma histopathological subtypes were included. Despite this, there did not seem to be an obvious dichotomy in surgical results between high-grade versus low-grade tumors in each group. Nevertheless, we appreciate that there are unique surgical and imaging nuances inherent to high-grade versus low-grade glial neoplasms, and a larger series would be needed to address this issue.

Finally, the results reported here do not specifically address the perennial question of the impact of the extent of glioma resection on patient survival. Because of the basic biology of gliomas, with isolated tumor cells that may be located far from the resectable tumor mass visualized on our imaging studies (42), we know that surgery alone cannot achieve histopathologically complete eradication of tumor and does not cure patients with this disease. It is continually debated whether aggressive macroscopically “gross total resection” of gliomas truly improves patient outcome over simple biopsy or subtotal resection (21, 22, 24, 29). In reality, we will probably never know the true impact of surgical resection on the survival of patients with gliomas, because truly randomized prospective studies that would minimize the confounding selection bias of retrospective studies are not likely to be able to be conducted to answer this question.

Although the current results of our study do not allow us to make any conclusive statements about the issue of extent of surgical resection on survival, they do suggest a role for using intraoperative iMRI and neuronavigation as a tool to achieve more reliable and consistent brain tumor resections. As shown in Figure 52.4, the standard deviation of the percent resection and residual tumor volume was lowest in Group 4 (iMRI plus updated neuronavigation). A potential confounding variable of all adjuvant treatment trials for glioma is the variability in tumor burden at the initiation of treatment. The results achieved with iMRI plus updated neuronavigation could potentially eliminate this confounding variable, which, in turn, might allow for more accurate and objective standardization of outcome studies on the role of surgery and other therapeutics (e.g., chemotherapy, biological agents, immunotherapy, etc.) for this disease (41). For this reason, all patients entered in our current study are continuing to be followed prospectively for data on adjuvant treatments, time to tumor progression, and survival. Future outcome data on these and other patients may someday help provide some insight into whether the use of iMRI is worth the increased OR time and monetary investment associated with this technology. As this technology advances, continuous improvements will certainly result in simplification, improved resolution, and, hopefully, beneficial patient outcomes.

CONCLUSION

Intraoperative MRI improves the extent of volumetric resection of intrinsic brain tumors as compared with standard image-guided frameless stereotaxy alone. If adequate image quality is obtainable, magnet field strength (0.2 T versus 1.5 T) does not seem to influence the percent resection of supratentorial gliomas. We favor the combination of intraoperative MRI and updated neuronavigation, which enables the neurosurgeon to pursue more radical tumor resections with no apparent increased risk of complications. Further prospective studies are necessary to demonstrate the actual benefit of this technology on patient outcome.

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FIG. 52.1 Photographs of fully functional intraoperative MRI ORs installed at the UCLA Medical Center. *A*, Siemens 0.2-T Magnetom Open iMRI suite, with a vertical-field open MRI system. Surgery is performed in the fringe field, where the weak magnetic field (<5 Gauss) does not interfere with standard OR instruments and equipment. *B*, Siemens 1.5-T Sonata iMRI suite. Again, surgery is performed in the fringe field (<5 G), safely away from the scanner. For intraoperative scanning, the motorized surgical table must first pivot, then link with the scanner gantry to be slid into the short-bore magnet. *C*, sterile intraoperative radiofrequency head coil (*long black arrows*) attached to MRI-compatible head holder (*short black arrows*). The bone-fixated fiducials (*white arrow*) are visible.

FIG. 52.2 Comparison of low and high field-strength intraoperative images. Upper row: *A*, preoperative contrast-enhanced T1-weighted MRI from a diagnostic 1.5-T MRI scanner; *B*, intraoperative image from the Siemens 0.2-T Magnetom Open iMRI scanner; and *C*, postoperative image from diagnostic 1.5-T MRI scanner. Note the diminished but generally adequate resolution and quality of the intraoperative image, *B*. Despite an aggressive resection, this patient had no new neurological deficits postoperatively. Lower row: *D*, preoperative contrast-enhanced MRI studies from a diagnostic 1.5-T MRI unit; *E*, intraoperative contrast-enhanced image from the Siemens Sonata 1.5-T iMRI scanner; and *F*, postoperative diagnostic MRI. These images are similarly acquired T1-weighted SPGR sequences after the administration of contrast (gadolinium). The resolution of the intraoperative image (*E*) is comparable to that of the preoperative diagnostic study (*D*) and identifies the residual tumor adjacent to the septum pellucidum. As seen in the postoperative MRI scan (*F*), this patient subsequently underwent careful gross total resection with intraoperatively updated frameless neuronavigation. Postoperatively, she had a transient short-term memory deficit that resolved during 1 week.

FIG. 52.3 Screen capture image taken from the BrainLAB VectorVision neuronavigation liquid crystal display (LCD) monitor demonstrating the virtual pointer identifying the contrast-enhancing tumor margin (Group 4, Sonata 1.5-T iMRI with updated neuronavigation). Note the degree of brain shift (right upper image) that would not have been apparent had the preoperative image data set still been used.

FIG. 52.4 *A*, graphical comparison of mean percentage of tumor resection. The 1.5-T iMRI with updated neuronavigational re-registration produced the highest mean and lowest variability in percent tumor removal. *B*, comparison of preoperative (*open circles*) versus postoperative (*closed circles*) tumor volumes (in cm^3) in each group. Again, the 1.5-T iMRI with re-registration allowed the best and most consistent results. Error bars indicate one standard deviation of the mean.