“Extraoperative” MRI (eoMRI) for Brain Tumor Surgery: Initial Results at a Single Institution

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BACKGROUND: There is accumulating evidence that extent of resection (EOR) in intrinsic brain tumor surgery prolongs overall survival (OS) and progression-free survival (PFS). One of the strategies to increase EOR is the use of intraoperative MRI (ioMRI); however, considerable infrastructure investment is needed to establish and maintain a sophisticated ioMRI. We report the preliminary results of an extraoperative (eoMRI) protocol, with a focus on safety, feasibility, and EOR in intrinsic brain tumor surgery.

METHODS: Ten patients underwent an eoMRI protocol consisting of surgical resection in a conventional operating room followed by an immediate MRI in a clinical MRI scanner while the patient was still under anesthesia. If findings of the MRI suggested residual safely resectable tumor, the patient was returned to the operating room. A retrospective volumetric analysis was undertaken to investigate the percentage of tumor resected after first resection and if applicable, after further resection.

RESULTS: Six of 10 (60%) patients were thought to require no further resection after eoMRI. The EOR in these patients was 97.8% ± 1.8%. In the 4 patients who underwent further resection, the EOR during the original surgery was 88.5% ± 9.5% (P = 0.04). There was an average of 10.1% more tumor removed between the first and second surgery. In 3 of 4 (75%) of patients who returned for further resection, gross total resection of tumor was achieved.

CONCLUSION: An eoMRI protocol appears to be a safe and practical method to ensure maximum safe resections in patients with brain tumors and can be performed readily in all centers with MRI capabilities.

INTRODUCTION

There is growing evidence that the extent of resection (EOR) in intrinsic brain tumor surgery prolongs overall survival (13, 17) and progression-free survival (PFS); in cases of low-grade gliomas, it may even deter their transformation to high-grade tumors (3, 19). One of the strategies to increase EOR is the use of intraoperative MRI (ioMRI) (11, 12, 18). As one of the first institutions to implement ioMRI, we have had a significant experience in the use of this imaging modality to assist with surgical resections of intrinsic brain tumors (6). The implementation of clinical ioMRI, however, requires considerable investment in infrastructure and personnel (4). This may not be practical for all centers doing brain tumor surgery, especially in the current health care climate. Furthermore, even in centers featuring a functioning ioMRI suite, the demand to use such a suite not uncommonly exceeds the capacity of the ioMRI to accommodate all brain tumor surgeries. In this scenario, a complementary method of using MRI during surgery to assess extent of resection may be additive.

To ensure that all patients receive the benefit of immediate high quality perioperative imaging guidance for maximum EOR, we have recently implemented an “extraoperative” MRI (eoMRI) protocol. This protocol (described herein), consists of transporting patients to a nearby clinical MRI scanner after maximum safe resection was felt to have been accomplished and before extubation, if the case was done under general anesthesia, or full...
awakening if done under monitored anesthesia care (MAC). If during eoMRI it was thought that a greater extent of safe resection could be accomplished, patients are transported back to the operating room (OR). Otherwise, they are awakened in the intensive care unit (ICU). We report below preliminary results of this eoMRI protocol, with a focus on safety, feasibility, and EOR in intrinsic brain tumor surgery.

METHODS

The study was performed under the supervision of the Partners Health Care and Brigham and Women’s Internal Review Board. Adult patients that were seen by the senior author (I.D.) and were consented for possible eoMRI and second resection. Intraoperatively, if the senior author thought that immediate feedback about the EOR was important, patients were included in the study. This was based upon tumor location, imaging characteristics and whether the ioMRI suite was available.

This protocol consists of patients receiving standard of care preoperative imaging and intraoperative neuronavigation, microsurgical, and ultrasonography-guided resection. Patients were induced in the usual fashion with the sedative, propofol 1.5–2.5 mg/kg, and vecuronium, a nondepolarizer muscle relaxant to facilitate endotracheal intubation. The anesthetic was maintained with total intravenous anesthesia consisting of propofol 75–200 µg/kg/min and remifentanil 0.10–0.20 µg/kg/min throughout the procedure depending on the level of surgical stimulation. Neuromonitoring was used commonly to assess motor-evoked and somatosensory-evoked potentials if sensorimotor tract integrity was a concern. Two patients were performed while awake under MAC for intraoperative language assessment.

After the surgeon has completed what is thought to be the maximum resection, the craniotomy is closed in standard manner. At the time of closure, the clinical MRI suite is alerted so as to make sure that there is no wait time between closure and imaging. The patient remains intubated or under MAC, is ventilated with a portable ventilator if necessary, and is transported to a nearby clinical MRI suite, where the he or she undergoes a predefined MRI protocol (discussed later) to assess for tumor residual. We currently maintain sterility in the OR, even after the patient leaves, in anticipation that they might return on the basis of imaging findings, as outlined in the sections to follow.

During transport, all patients are monitored with a 5-lead electrocardiogram, a pulse oximeter, and invasive blood pressure measurement via a radial artery catheter. The transport general anesthetic was maintained with propofol 50–75 µg/kg/min and remifentanil 0.1 µg/kg/min. MRI safety procedures prohibit the introduction of standard MRI-unsafe portable ventilators and intravenous pumps into the scanner room. As such, the patient must be switched to an MR-safe ventilator before he or she enters the MR scanner room. Although it is acceptable to also switch the patient to an MRI safe intravenous pump before bringing the patient into the scanner room, to save time compared with switching the pump, in our institution the patient’s intravenous tubing was rerouted from the portable intravenous pump outside the scanner room through wave-guides in the MR room shielding. This requires that the Henora (Henora Gainesville, Florida, USA) 360 inch coiled MRI extension intravenous set be used, which is of sufficient length and compatible in the MR homogenous field.

With the use of a clinical 1.5-T MRI, a variety of MRI sequences are run, depending on the original imaging characteristics of the tumor. The sequences that are required to decide whether further resection is necessary are run first. These sequences are reviewed on the scanner console without interrupting the MRI acquisition protocol. With the aid of an attending neuroradiologist, a decision is made whether maximum safe resection has been achieved. If it is thought that there may be residual tumor that is safe for resection, the scan is stopped and the patient is returned to the operating suite for further resection (see Figure 1 for a detailed flowchart). If needed, an additional navigation sequence may be acquired before the patient is removed from the scanner and is used for re-registration upon reoperation. If in the surgeon’s judgment a complete resection or maximal safe resection has been achieved, the remainder of a standard postoperative MRI is completed before the patient is transferred to the ICU for extubation or full awakening.

Volumetric Analysis

Semiautomated and manual 3D volumetric analysis was done retrospectively via commercially available software (iPlan Cranial Version 3.0.3, Brainlab AG, Westchester, Illinois, USA). For tumors with a significant contrast-enhancing component, the enhancing tumor volume was measured preoperatively, extraoperatively and postoperatively. For nonenhancing tumors, the volume of tumor on fluid-attenuated inversion recovery T2-weighted images was segmented manually.

RESULTS

Between January 2012 and December 2013, 10 patients underwent eoMRI protocol. Table 1 summarizes the preoperative clinical characteristics of the patients. Technically successful eoMRI was achieved in all 10 patients enrolled (Table 2). Of these patients, 4 (40%) were assessed to have residual tumor that could be safely resected after their first stage resection and were taken back to the operating suite for a completion of their resection (Table 2). In the patients deemed to have a good initial stage resection that did not warrant a second-stage operation, the percentage of tumor removed was 97.8 ± 1.8%, whereas in those returning for a second-stage resection, the percentage of tumor removed was 88.5 ± 9.5% (P = 0.04) (2-tailed Student t test) during their first stage surgery (Figures 2 and 3). All 4 patients who were taken for second surgery had preoperative imaging demonstrating only slight (1 patient) or no (3 patients) contrast enhancement on T1-enhanced imaging and hyperintensity on fluid-attenuated inversion recovery T2-weighted imaging. All 4 of these patients had final pathology of Grade II or III glial tumors.

The average time between second incision and time of out of the room from the first surgery was 1.6 ± 0.2 hours, which includes time for transport, MRI, and re-draping and prepping the patient. The average time for the second surgery was 1.7 ± 0.2 hours. For the patients who underwent further resection, there was an average of 10.1% more tumor removed between the first and second surgery. In 3 of 4 (75%) of cases that returned for further resection, there was a gross total resection (GTR) achieved.
DISCUSSION

Although no class I evidence exists, there is increasing evidence that EOR correlates with survival in patients with glioma (3, 13, 17); this finding has spurred technological advances in the past 10–20 years all in the hopes of increasing the EOR in brain tumor surgery. These technologies include improved microsurgical technique, intraoperative neuronavigation, the use of fluorescent markers and ultrasonography to delineate tumor margins, and advanced imaging techniques for preoperative planning and intraoperative assessment of resection extent (2, 9, 20).

Although the evidence for the use of these technologies varies in terms of strength, a central tenet is that they are used as adjuncts to help the neurosurgeon perform the maximum resection possible, with the important caveat of not leaving the patient with a new neurologic deficit (15). It is because of this caution that for tumors in or close to eloquent cortex, GTR may not always be possible. In a retrospective study of more than 500 patients with histologically confirmed glioblastoma multiforme, subtotal resections were more likely to occur for those tumors residing in presumptive Broca’s and Wernicke’s areas (7).
There is a large body of literature that suggests that early postoperative imaging is the best modality the best way to accurately categorize extent of resection (21). There is a rather poor correlation between the surgeon’s assessment of extent of resection and what is seen on imaging (4). Moreover, there is evidence that waiting longer than 48 hours for postoperative imaging may introduce artifact (5, 10). It is because of this evidence that many institutions, including ours, have adopted early postoperative imaging as a standard method for tracking extent of resection. ioMRI can be thought of as a logical extension of this requirement of postoperative imaging. One advantage of ioMRI protocols is that not only does it give the surgeon an immediate feedback of extent of resection, it allows for an immediate response to this information, as reoperation becomes more feasible.

Although the exact manifestations of ioMRI may be different between institutions, the goal of ioMRI is to provide the neurosurgeon with immediate feedback about the success of maximum safe resection. There is increasing evidence that ioMRI may be helpful in increasing EOR in brain tumor surgery (3, 8, 18). In fact, a recent randomized control trial studying the effects of ioMRI on patients with contrast enhancing lesions worrisome for glioblastoma multiforme suggested that patients undergoing surgical resection within an ioMRI protocol may have had greater rates of GTR and had a longer cumulative PFS, although this was not statistically significant compared to a control group that did not have ioMRI (18). Importantly, there was not a significant difference in the rates of new neurologic deficits between those patients that underwent ioMRI and those who did not (18).

It must be noted that a fully functional ioMRI suite requires considerable capital and human resources to establish and run. It is for this reason that there are only approximately 100 of these suites worldwide. Clearly, an ioMRI investment may not be appropriate for all centers in which intrinsic brain tumor surgery is performed. Moreover, in greater volume centers, only a fraction of tumor cases can be performed in an ioMRI suite because of capacity restrictions.

Besides the costs, another frequent criticism of ioMRI is that it may cause the surgeon not to be as aggressive in the original resection if he or she knows that he or she will receive immediate feedback of the extent of resection. The relatively high EOR (overall 95%) achieved in our eoMRI series suggests that we are being appropriately aggressive in attempting GTR in all cases. In light of recent evidence that there indeed seems to be a stepwise improvement in patient survival with increased resection, even in the 95%–100% EOR range (17, 19), the impetus to achieve these types of resections is high and it appears that adding an eoMRI protocol has allowed us to do this in our small cohort.

It may be that patients with low-grade gliomas or nonenhancing tumors benefit most from use of intra- or extraoperative MRIs because these tumors usually do not have a clear demarcation in terms of tissue consistency during surgery, making the definition of the borders of the tumor very difficult. All the patients taken back to the OR ultimately had tissue pathology consistent with low-grade gliomas, suggesting that this was the case in our limited series. Although our series did not include pediatric patients, it may be that pediatric patients may also benefit from such an eoMRI protocol, because they often require additional general anesthesia and endotracheal intubation for standard postoperative MRI and this protocol would obviate the need for this.

A criticism of these types of protocols is that they may expose the patient to an increased risk of complications of another surgery without obvious beneficial effects. If one closely examines the data on low grade gliomas, however, even the incremental benefit of increased EOR may have true positive effects for the patient. For example, Smith et al. (19) showed that even in those patients with EOR >80%, EOR was a significant predictor of overall survival, hinting that incremental increases in EOR is beneficial to the patient. This observation has been replicated in other subsequent studies (9, 14, 16). Although our study is

### Table 1. Preoperative Clinical Characteristics of the Patients

<table>
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<tr>
<th>Patient</th>
<th>Age at Surgery, years</th>
<th>Tumor Location</th>
<th>Tumor Size, cm³</th>
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<th>Eloquent</th>
<th>Contrast Enhancement</th>
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Mean (±SD) 42 (12) 36.77 (52)

Y, yes; N, no; S, slight.

*These patients had previous debulking surgery elsewhere.
neither designed nor powered to show increased survival benefit or PFS in those patients undergoing eoMRI protocol, the fact that we were able to make a significant change in EOR between the first and second surgeries suggests that this protocol may have an overall benefit to these patients.

Another criticism of ioMRI protocols is the time that these protocols add to the care of patients. For our eoMRI protocol, the time transporting the patients to a nearby clinical high-field MRI, taking the appropriate scans, and returning the patient for another resection if appropriate was 90 minutes, which is slightly longer to the added time that ioMRI protocols have reported (8). This time is also comparable with the time that we have in our institution’s ioMRI. Thus it appears that our protocol does not add significant time to obtaining maximum safe resection compared to an ioMRI protocol. Moreover, while reopening an incision in a second operation in the same day may theoretically confer a greater risk of infection, we have yet to note a postoperative infection in this admittedly small cohort. Importantly, none of our patients had neurologic complications.

By extubating patients done under general anesthesia in the ICU and by completing the postoperative MRI before transferring the patient to the ICU for extubation, our current eoMRI protocol minimizes the economic and safety burden that such an eoMRI protocol could have. Because review and discussion of the critical images takes some time and occurs while the remainder of the postoperative MRI protocol is being acquired, in our experience completion of the full postoperative MRI usually can be completed within 10–15 minutes of the decision not to operate further. This minimal delay to extubation is likely insignificant in the context of time required to transport to the ICU and extubate. This is substantially offset by the improved image quality related to the lack of motion artifacts, and the additional safety, comfort, and convenience that results from not having to return to MRI from the ICU within 48 hours for an additional MRI. Also, from an operational point of view, eliminating the need for a separate postoperative MRI by completion of the postoperative scan at the time of eoMRI reduces the net burden that an eoMRI protocol may have on the MRI department for available MRI scanner time. This may be even more important to smaller institutions with only 1 or 2 MRI scanners available.

Although this particular eoMRI protocol appears to be widely transferrable to institutions with a clinical MRI, there are important requirements to make it successful. First, there must be a multidisciplinary relationship between the neurosurgeons, the neuroanesthesiologists, and the neuroradiologists to make sure this protocol runs smoothly and provides the maximum benefit to the patient while ensuring minimization of risk. There must be open communication between the neurosurgeon and the neuroanesthesiologist so that it is clear, when the primary surgery is over, the patient must remain sedated for the removal of the Mayfield head holder, transport to the clinical MRI suite, and possible return to the OR. There must also be a willingness to extubate the patient in the ICU if needed. The most efficient imaging series must be established so as to ensure complete information for decisions is acquired regarding return to the OR while minimizing the amount of time that patient remains in the MRI suite.

We currently block off one of our clinical MRI suites for a period of time when the surgery is predicted to be finished and we also

<table>
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<th>Table 2. Characteristics of Surgeries</th>
<th>Patient No.</th>
<th>Time for First Surgery, hours:minutes</th>
<th>Time for eoMRI, hours:minutes</th>
<th>Time for Second Surgery, hours:minutes</th>
<th>% of Tumor Resected, I</th>
<th>% of Tumor Resected, II</th>
<th>Volume of Residual I, cm³</th>
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leave the operating theater sterile in case the patient returns of repeat resection. This type of resource management may not be easily transferable to institutions where there is only one clinical MRI suite, or if ORs are restricted.

Although this study was not designed to compare intraoperative MRI and eoMRI in brain tumor surgery, it is clear that each protocol has its own advantage and disadvantages. The ioMRI protocols have the advantage of immediate feedback for the

![Figure 2](image)
Figure 2. eoMRI protocol allows for increased EOR. (A) Preoperative MRI reveals left frontal non-enhancing tumor. (B) Extraoperatively, it was thought that a greater resection could be made in the lateral edge of tumor (black arrow). (C) After the patient returned to the operating room for another resection, it was thought that gross total resection was achieved.

![Figure 3](image)
Figure 3. eoMRI allows for immediate confirmation of gross total resection. (A) Preoperative MRI reveals left frontal tumor that enhances with gadolinium-based contrast agent. (B) Extraoperatively, it was thought that gross total resection had been achieved, and patient was transferred from MRI to the intensive care unit for extubation after completion of the postoperative MRI protocol. eoMRI, extraoperative magnetic resonance imaging; MRI, magnetic resonance imaging.
neurosurgeon about EOR and do not involve reopening an incision. However, as our experience has shown, an ioMRI suite involves a very large capital investment and is not a realistic option for many medical centers. The eoMRI protocol, as we have implemented, does allow for very fast feedback to the neurosurgeon about EOR and allows for increasing this without incurring the risk of putting the patient through anesthesia again, although it admittedly does incur the risk of reopening a fresh surgical incision. Moreover, acquiring more than one MRI during surgical resection is likely more feasible in an ioMRI suite; we have not done multiple MRI sessions in the eoMRI protocol.

An extensive cost analysis is beyond the scope of this article, but this extroperative protocol appears to be more cost efficient than the traditional scheme of intrinsic brain tumor surgery where patients receive a postoperative MRI within 48 hours from their index surgery, followed by a second stage surgery at a later time if necessary. The eoMRI protocol eliminates at least 1 or 2 days in the ICU, reducing total duration of stay, a second anesthetic, and in some cases a second admission. Analysis of our billing data reveals that when all professional and facility charges are included, the total operative case cost of our eoMRI protocol compared with our ioMRI case cost revealed largely equivalent charges. Importantly, these calculations do not include the amortization costs associated with the capital expense of the ioMRI suite.

It must be noted that part of the reason that the sample size is small is that this is a single surgeon trial and that to be included in the study, the primary surgeon needed to believe at the conclusion of surgery that a GTR was in question. This requirement of uncertainty justifying the use of the eoMRI protocol contributed to the small sample size.

Although the number of patients reported in this study is small, it nevertheless provides a roadmap for how MRI can be effectively used to safely increase EOR during brain tumor surgery without need for an intraoperative MRI suite. This approach could be useful in centers with an ioMRI where the demand for imaging during surgery exceeds the capacity of the ioMRI and in centers where installing and maintaining an ioMRI suite isn’t feasible.

CONCLUSIONS
In this small cohort study, we show that the application of an eoMRI protocol is safe and feasible and allows for a greater EOR in surgery for intrinsic brain tumors. As with ioMRI and other new technologies for increasing EOR, it remains to be seen whether increase in EOR will translate to longer PFS and better high-grade transformation of low-grade gliomas. If so, eoMRI could be easily adopted in many centers where an intraoperative MRI (ioMRI) suite is not a practical undertaking.

REFERENCES


William B. Gormley and Ian F. Dunn are co—senior authors.
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