Intraoperative magnetic resonance imaging in pituitary macroadenoma surgery: an assessment of visual outcome

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✓ Pituitary macroadenomas most frequently present with visual loss. Although transsphenoidal surgery remains the treatment of choice for patients with neurological manifestations, there have been several advances in its implementation over the last 5 years. Intraoperative magnetic resonance (MR) imaging has emerged as a novel quality control measure, with the potential to guide the surgeon to tumor remnants concealed from the operating microscope. Investigators have reported enhanced resections when using intraoperative MR imaging, leading to complete tumor removal in a larger proportion of cases. Further debulking of unresectable lesions may also prove beneficial in delaying symptom recurrence and facilitating radiotherapy, where distance between the tumor and optic chiasm is an important predictor of visual outcome. However, confirmation of such advantages is complicated by the fact that most macroadenomas are both indolent and hormonally silent, necessitating years of follow-up. Experienced pituitary surgeons will operate as safely with intraoperative MR imaging as without it, perhaps due to a balance between more elaborate resections and better visualization. Intraoperative MR imaging represents a new technique applied to an old problem in tumor surgery: complete, safe resection. (DOI: 10.3171/FOC-07/11/E12)

KEY WORDS • intraoperative imaging • macroadenoma • transsphenoidal surgery • visual deficit

Pituitary adenomas constitute 10–20% of intracranial neoplasms;1,16 patients with these lesions often present with impaired vision50 due to compression of the optic chiasm or nerve. In rare cases, lesions classified as macroadenomas (≥1 cm) may cause hormonal syndromes due to poor endocrine function. Most react with anti-follicle-stimulating hormone or luteinizing hormone antibodies and cause an insidious peripheral visual field deficit followed by worsening visual acuity. In addition, lateral growth may damage structures within the cavernous sinus including the oculomotor nerve, causing palsy and diplopia.45 Tumor volume correlates with onset of visual field loss and serves as a poor prognostic factor in postoperative visual recovery.18 Once neurological symptoms have developed, surgery alone is capable of providing timely relief.56 At present, the transsphenoidal approach is favored. However, a restricted operating field and limited visualization complicate tumor removal. Between 20 and 50% of adenomas recur, especially those with a suprasellar component.5,14,27,30,34 A smaller yet significant number of these lesions, 7–35%, results in concomitant visual loss.52 In addition, rare yet serious complications such as central nervous system injury, carotid artery laceration, and loss of vision are well-documented risks of transsphenoidal microsurgery.5,25,47 Pituitary insufficiency and delayed cerebrospinal fluid leakage result in meningitis or the need for a repeated operation. Among computed tomography, ultrasonography, gas cisternography, and fluoroscopy, MR imaging has emerged as the most promising intraoperative imaging technique. A summary of the literature is given in Table 1.

Discussion

Serious complications of transsphenoidal pituitary surgery include hemorrhages or hematoma formation, permanent hormonal insufficiency, new visual loss, and cerebrospinal fluid leakage resulting in meningitis or the need for a repeated operation. Authors of large retrospective studies have found that these complications occur in 2.2–3.6% of cases, with mortality rates between 0.5 and 0.9%.56 Larger tumors, such as macroadenomas with suprasellar extension, carry a higher risk. In addition, Ciric et al.5 have shown that surgeons’ level of experience

Abbreviation used in this paper: MR = magnetic resonance.
inversely correlates with the rate of adverse events. This fact bears particular importance in a review, in which many authors' results are compared. Overall, serious complications after transsphenoidal surgery with intraoperative MR imaging occurred in 14 (4.6 ± 3.94%) and death in 2 (0.66%) of 302 patients. Authors who used frameless stereotactic guidance, recommended for repeated operations and adenomas with parasellar extension, reported on 16 patients with complications (8.84 ± 7.99%) and 1 death (0.55% mortality) in 181 patients.

Intraoperative MR neuronavigation allows the surgeon to visualize brain shift and other operative changes, and to reorient to the carotid arteries, optic chiasm, and hypothalamic and pituitary structures. Theoretically, this provides an advantage over image-guided surgery with frameless stereotaxy. Conversely, finding residual tumor on intraoperative MR imaging may result in overzealous exploration and concomitant brain injury. Unfortunately, few studies including discussions of complication rates are available for comparison. In one report of a series of 101 patients who underwent surgery with frameless stereotactic guidance, 3 patients (2.9%) suffered visual deterioration after surgery. It is not clear whether any of these patients were among the 16 who underwent an intracranial technique for resection that carries greater risk to the optic nerve. Five other studies of adenomas treated with frameless stereotactic surgery reported no postoperative visual decline. Despite extended resection with intraoperative MR imaging, including suprasellar folds, damage to the optic nerve is similarly infrequent. The authors of a study of 106 tumors describe the sole case of visual deterioration after surgery in the literature, in a patient with preexisting chiasma syndrome. Six patients (5.6%) developed permanent pituitary insufficiency (5 in the anterior pituitary and 1 case of diabetes insipidus), an acceptable rate for transsphenoidal surgery. Fewer complications have been reported in other studies involving intraoperative MR imaging. The Erlangen group has described another 109 patients, none of whom suffered adverse outcomes.

In performing transsphenoidal surgery with intraoperative MR imaging, Black's group in a 1985 study noted injury to the cavernous portion of a carotid artery, noted one intraoperative tumor bed hematoma, and noted one case of meningitis among 22 patients. The authors point out how intraoperative MR imaging helped in the management of vascular accidents through early detection and monitoring of perfusion to distal areas. Eleven complications reported by researchers at Tiantan Hospital in Beijing involved iatrogenic pituitary insufficiency, representing a high rate (17.4%). The Beijing study used frameless stereotactic surgery to treat adenomas with either suprasellar or lateral sellar extension only, which may explain the discrepancy. Neurosurgeons face distorted anatomy in recurrent tumors and proximity to vital structures in those with parasellar extension. Intraoperative MR imaging has proven safe as—if not safer than—frameless stereotactic guidance in resecting such lesions. Delayed contrast uptake among neoplastic cells and reimaging before deeper exploration help guide an operation, but given the complication rate, intraoperative MR imaging is no substitute for prudence during surgery.

Optic nerve recovery after pituitary surgery is typically rapid, leading to visual field recuperation over the course of hours to 1 week, with continued improvement reported over 3 years of follow-up. Release of a physiological block secondary to optic nerve ischemia or axonal compression is thought to underlie early phase improvement, whereas remyelination may be responsible for delayed recovery, although the precise mechanisms are poorly understood. The authors of numerous studies have evaluated visual outcome after conventional transsphenoidal surgery; however, authors who used frameless stereotaxy alone have not reported adequate data. Analysis is also complicated by differences in visual scoring methods, time to follow-up, and severity and duration of presenting deficits, among other factors. However, some degree of improvement occurred in 73–92% (mean 81 ± 7.12%) of patients in studies reported over the last 30 years.

Ophthalmological results from intraoperative MR imaging assisted procedures are slightly better, with 85–100% (mean 93 ± 5.37%) of patients experiencing improvement. Most—but not all—authors reported data on visual fields. Although the benefits of using MR imaging assistance might be significant, a randomized trial is necessary to control for the interstudy variables described, including patient age, as a younger age correlates with a better outcome.

Even among those who use intraoperative MR imaging, differences in magnetic field strength and ease of use affect image quality, area of visualization, and the number of scans obtained per procedure. Such factors complicate interpretation of the data, as does the use of endoscopy in one study. Nevertheless, both anecdotal evidence and visual outcomes suggest that intraoperative MR imaging enhances suprasellar resection. Black's group describe one tumor adherent to the optic chiasm that could be further manipulated under intra-

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**TABLE 1**

*Summary of the results of pituitary macroadenoma surgery reported in the literature*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>iMRI Used</th>
<th>No. of Patients</th>
<th>Complication Rate (%)</th>
<th>Patients W/ Improved Vision (%)</th>
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<tr>
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<td>—</td>
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* Abbreviation: iMRI = intraoperative MR imaging; — = information not given in study.
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operative MR imaging guidance. Moreover, 2 of 3 adenoma remnants hidden from surgical view in this series were compressing the optic nerve. Data from intraoperative imaging confirms that suprasellar remnants are frequently evasive. As the sellar diaphragm invaginates into the sella, the tumor is enveloped in its folds. Larger studies have shown that intraoperative MR imaging detects residual lesions with 100% sensitivity in the suprasellar region, leading to 19 additional resections in one cohort of 48 patients. Reexploration with only partial removal may still prove useful in clearing the 5-mm space between the optic nerve and residual tumor preferred for adjuvant radiosurgery.2,11,12,37–39

A more complete tumor resection, as accomplished with intraoperative MR imaging, is associated with improved visual recovery, confirming that a tumor’s mass effect on the optic nerve is largely responsible for visual field deficits. Yet even with satisfactory decompression, most deficits do not resolve completely,7,13,17,20 suggesting a more complex pathophysiology. It would be helpful to measure visual fields and acuity over time because the exact degree of improvement after surgery with intraoperative MR imaging is not known.

Achieving total resection when safely permitted and optimizing partial removal as necessary facilitate control of pituitary macroadenomas. As with the patient’s initial presentation, recurrence most often manifests as visual loss. Further treatment may also damage the visual apparatus; therefore, preserving vision is best accomplished by optimizing the initial surgery. Intraoperative MR imaging identified residual tumor in 15–66% of cases thought to be completely resected on microscopic examination. By reexploring suspicious lesions with intraoperative MR imaging, investigators improved their rate of complete resection by 18–56% based on postoperative hormone assays and MR imaging studies. However, surgeons may not have been as aggressive in probing for tumors when they could also rely on noninvasive imaging to reveal them; there is no way to control for inherent interoperator bias in these studies.

Given the slow growth rate of adenomas, continued follow-up imaging for at least 10 years is needed to confirm the absence of tumor recurrence in patients who underwent resection with intraoperative MR imaging guidance. Currently, results from only one study of 17 patients with 3 years of follow-up are available. No radiographic or clinical evidence of recurrence was noted in these patients. Laws and colleagues26 reported a 6.27% tumor recurrence rate based on their study of 2200 patients who were followed up for 10 years after conventional resection. In one study of postoperative MR images, 15 residual adenomas in 50 patients were found, only 2 of which were unrespectable.22 Omission rates of 44–56% have also been reported,43,53 although it is not clear how many such subtotal resections were intentional. Many recurrent and parasellar adenomas cannot be safely resected due to cavernous sinus invasion or attachment to the optic chiasm. Intraoperative MR imaging does not permit resection of such lesions, but has proven useful in enhancing partial removal in an estimated 20–38% of patients.2,11,32,35,39 Certainly, residual tumor may continue to grow. Optimal volume reduction benefits adjuvant radiosurgery in this situation by diminishing radiation exposure to surrounding brain tissue and improving remission rates.

Intraoperative MR imaging has demonstrated sensitivities of 65% compared with hormonal assays, and 100% compared with postoperative MR imaging in detecting adenomas. Despite weaker magnets and the presence of artifact such as blood and packing material, intraoperative MR imaging has proven equal to standard 1.5-tesla scanners in detecting residual lesions. However, concern over comparing an imaging modality to itself is justified by results of bioassays. Data from endocrinologically active tumors demonstrate that both intra- and postoperative MR imaging fail to detect all tumor remnants, resulting in incomplete removal. Unfortunately, many residual macroadenomas are clinically silent, necessitating years of observation before the results of intraoperative MR imaging can be compared with recurrence rates after standard pituitary surgery. In the literature, adenoma regrowth is more often discovered on imaging than clinical examination. It will be interesting to discover how many subtotal resections that were extended because of intraoperative MR imaging findings will have clinically apparent regrowth over patients’ lifetimes. Specificity ranged from 56 to 100% (mean 82%) compared with postoperative MR imaging, and 100% compared with the bioassay. False positive results from intraoperative MR imaging can prolong the operating time as surgeons inspect for nonexistent tumor remnants, but this does not appear to increase the complication rate.

Senior Author’s Experience

Thirteen patients with pituitary adenomas underwent surgery with Polestar intraoperative MR imaging at Lutheran General Hospital between April 2004 and April 2007 (Figs. 1 and 2). A typical procedure is as follows: the patient is brought into the operating room, placed in an MR imaging–compatible head frame, and a 24-second sagittal “Esteady” MR imaging scan is obtained for positional purposes. If this is satisfactory, then a T1-weighted, Gd-enhanced, 7- or 11-minute, 4-mm slice MR image is obtained in a direct sagittal mode. Surgery is then started; after satisfactory resection, another contrast-enhanced direct sagittal T1-weighted MR image is obtained and compared with

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Fig. 1. Sagittal intraoperative Gd-enhanced T1-weighted MR images, 4-mm thick, 7-minute scans. Left: Image obtained at the beginning of the procedure, demonstrating a large pituitary tumor occupying an enlarged sella turcica. The sphenoid sinus is aerated, and the optic nerves appear compressed. Right: Image obtained after resection demonstrating a transsphenoidal retractive system in place, postsurgical change in the sella with a mixture of blood and fluid, and a decompressed optic chiasm. (Figures obtained from a low-quality intraoperative scanner.)
the first study, as well as with any merged preoperative higher definition MR images. A decision is then made whether to return for additional tumor resection or to close the patient’s incision.

In cases in which intraoperative MR imaging impelled further surgery due to findings consistent with the presence of residual tumor, no additional complications occurred. In 8 of 13 patients, the operative technique was adjusted with either additional tumor resection or less probing and manipulation of the remnant pituitary gland. It was believed that information generated by intraoperative MR imaging improved outcomes in these patients. One patient who underwent reoperation with intraoperative MR imaging had additional visual deterioration after surgery. However, a more aggressive approach was not used based on intraoperative MR imaging findings. It is clear that this complication would have occurred regardless of intraoperative MR imaging. As mentioned, intraoperative imaging has allowed us to be more cautious. In some cases, a questionable tumor can be confirmed as nontumor with intraoperative MR imaging; this helps the surgeon in deciding whether or not to proceed with further manipulation. Endocrinological follow-up of our patients with secretory tumors is ongoing, and will serve as a useful control for the sensitivity of intraoperative MR imaging.

Conclusions

Intraoperative MR imaging safely augments resection of pituitary macroadenoma remnants that are poorly visualized under the operating microscope. A higher rate of gross-total resection may lower recurrences, although confirmatory results await further follow-up. At present, intraoperative MR imaging imperfectly detects residual tumor and offers limited assistance in anatomically challenging dissections. Advances such as functional intraoperative MR imaging and scanners that facilitate numerous imaging sessions may help resolve these shortcomings. Meanwhile, as intraoperative MR imaging devices are being acquired primarily for epilepsy and glioma surgery,3,53 their applications are expanding. Pituitary surgeons with access to intraoperative MR imaging still face the problem of incomplete resection, but may find the technology useful.

Disclaimer

The literature review was carried out courtesy of Northwestern University’s Galter Medical Library. Operative perspective and images are based on the author’s personal experience in private practice. No funding has been provided by Polestar, Lutheran General Hospital, or elsewhere, and the authors have no financial ties to Polestar or any other intraoperative MR devices.

References

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