Image Guidance in Pituitary Surgery


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Abstract

Image guidance in pituitary surgery has evolved since diagnostic imaging of the sellar region was first introduced at the turn of the 20th century. These advances have played a key role in the decrease in morbidity and mortality once associated with pituitary surgery. This chapter details the history of sellar imaging as a preoperative diagnostic aide, and then examines the subsequent development of image guidance systems and intraoperative imaging. The utility and limitations of common intraoperative aides including video fluoroscopy, frameless stereotaxy, ultrasound, and magnetic resonance imaging are reviewed.

Introduction

Surgery for pituitary tumors has significantly evolved since 1893 when Caton and Paul [1] of Liverpool first approached the sella turcica. Improvements have been made possible by significant progress in the fields of radiology, endocrinology, neurosurgery, and pathology. This chapter discusses the utility and limits of radiology in the evolution of diagnosis and surgical management of pituitary disorders.

History of Sellar Imaging

The introduction of X-rays was reported by Roentgen [2] in 1895. Cushing [3] recognized its clinical utility and in 1897 described the use of X-ray technology for the diagnosis of a bullet fragment within the spinal cord. In 1899 at a meeting of the Berlin Society of Psychiatry and Nervous Diseases, the neurologist, Hermann Oppenheim, demonstrated that the sella turcica was enlarged

Plain radiographs allowed surgeons to preoperatively confirm what they previously could only speculate about. For the first time, surgeons could see the site of pathology prior to the first incision. This increased surgical confidence and encouraged the pursuit of operative solutions for pituitary tumors. It should be noted, however, that the early equipment was expensive and cumbersome, limiting its applicability to intraoperative image guidance.

Continued advances occurred in the field of radiology during the 20th century. After the plain X-ray, the next major advance in neuroradiology came when Dandy [7, 8] of Baltimore introduced ventriculography (1918) and subsequently pneumoencephalography (1919). Preoperative encephalography more accurately indicated the size and extent of sellar lesions than plain radiographs and was regularly employed [9–11]. Lesions which did not induce radiographic changes to the sella turcica, but rather extended primarily in the suprasellar direction, could now also be diagnosed due to disruption of the suprasellar cisternal anatomy. The principles of air-contrast enhanced imaging brought the ability to conceptualize soft tissue structures indirectly through an understanding of anatomic planes and potential spaces.

More progress in the diagnosis of intracranial pathology came in the late 1920s with the introduction of cerebral angiography by Moniz [12]. The technique of percutaneous carotid angiography, introduced in 1936, allowed the procedure to gain wider acceptance [13]. Although not universally used preoperatively, angiography allowed surgeons to understand the position of the carotid arteries as well as the working distance between them. This represented the first time that information regarding neurovascular structures and their relation to the bony anatomy could be appreciated in a direct manner.

After the introduction of linear tomography in 1931, polytomography was developed in the 1950s and came into increasing use in the early 1960s [14]. Biplanar polytomograms of the sella and sphenoid sinus allowed improved comprehension of bone thickness and asymmetries within the sphenoid sinus that would be encountered intraoperatively [15].

Imaging studies began to be used intraoperatively as well. In 1962 Hardy [10, 11] described his use of intraoperative radiofluoroscopy for image guidance and by 1965 had reported the utility of intraoperative air encephalography to gauge the extent of tumor removal. Intraoperative imaging allowed surgeons to correlate their anatomical findings with imaging in real time, thereby increasing the safety of surgery. This, in addition to significant advances in
perioperative care, led to a significant decline in the morbidity and mortality associated with transsphenoidal surgery.

Thus, in the late 1960s and early 1970s, at the time of the renaissance of the transsphenoidal technique for pituitary surgery, the radiologic techniques available to most surgeons included plain radiographs, video fluoroscopy, encephalography, angiography, and polytomography. This armamentarium of imaging modalities represented a significant advance over the plain radiographs available to pioneers of pituitary surgery at the beginning of the 20th century.

Nevertheless, there were limitations. These images did not provide a direct view of the pituitary gland nor of the adjacent brain parenchyma and cranial nerves. Surgeons were still unable to visualize the precise anatomy and intracranial extensions of a neoplasm. The diagnosis of hypersecretory syndromes due to microadenomas relied heavily on the expertise of the endocrinologist. No imaging study could direct the surgeon regarding the laterality of these tumors. Also, none of these imaging modalities was suited for routine postoperative assessment of the extent of tumor removal or surveillance for recurrence.

The introduction of computerized tomography (CT) and magnetic resonance imaging (MRI) into clinical practice in the 1970s and 1980s revolutionized the perioperative management of patients presenting with pituitary-based disease. By this time, Hardy had popularized the use of the operative microscope in transsphenoidal surgery and its utility in selective adenomectomy [16–22]. As these imaging techniques improved in resolution, increasing numbers of hypersecreting microadenomas without mass effect could be identified and lateralized. At the other end of the spectrum, these imaging modalities also allowed a greater understanding of the intimate relationship between large, invasive pituitary tumors and critical neurovascular structures, thereby improving preoperative planning. These imaging modalities in conjunction with biochemical assays also improved the postoperative surveillance of patients with residual and recurrent disease.

**Image Guidance**

The improvements in diagnostic radiology initially played a significant role in the perioperative management of the patient with pituitary pathology. Although information regarding the working distance between the carotid arteries, position of the optic chiasm and nerves, and exact morphology and extent of disease could be well documented with these diagnostic imaging modalities, the morbidity associated with transsphenoidal surgery remained more or less unchanged [23]. Continuous attempts to reduce the risk of surgery through the improvement in surgical techniques led to the innovative use of existing imaging
techniques to guide the surgeon intraoperatively. Image guidance in pituitary surgery began with the use of intraoperative air encephalography and c-arm video fluoroscopy [10, 11], and continues to expand with the addition of newer techniques such as intraoperative ultrasound, computer-based neuronavigation, intraoperative MRI, and endoscopic assisted surgery.

**Video Fluoroscopy**

Although it is possible to rely solely on anatomic landmarks to reach the sphenoid sinus and sella, intraoperative imaging is used by most surgeons as an integral part of the transsphenoidal approach. The most widely used intraoperative imaging device is the c-arm video fluoroscope. Standard positioning for transsphenoidal surgery is employed, with the head placed onto a horseshoe headrest (fig. 1). Most often, the c-arm is positioned such that a lateral image is obtained and confirms the appropriate trajectory to the sella turcica, defining its superior and inferior confines [11] (fig. 2). Knowing the superior and inferior limits of the sella turcica allows the surgeon to confirm adequate exposure and prevents unnecessary opening of the planum sphenoidale and the risk of a cerebrospinal fluid leak and anosmia [24, 25].
The advantage of using a standard fluoroscope is its simplicity and accuracy. Its disadvantages are the radiation exposure and its inability to depict soft tissue anatomy, including the tumor and neurovascular structures. Any intraoperative rotational adjustment of the head for an improved surgical viewpoint requires a concurrent adjustment in the c-arm angle to maintain a true lateral image. It is ineffective in demonstrating the midline in the anteroposterior view, and its use for this intraoperatively is limited due to microscope positioning conflicts and disruption of surgical access to the operative corridor. The ubiquitous presence of c-arm video fluoroscopy has enabled this quick, cost-effective, real-time image guidance technique to find a niche within pituitary surgery. The c-arm video fluoroscope is sufficient for most routine, first-time transsphenoidal operations where tumors confined to the sella can be removed under direct microscopic visualization.

**Frameless Stereotaxy**

A more recent advance in intraoperative imaging has been frameless stereotaxy. Frameless stereotactic systems were introduced in the 1990s and are
widely available at most neurosurgical centers. These systems allow the surgeon to refer intraoperatively to preoperative images (CT, MRI, or radiographs) in several planes of view simultaneously. In the setting of radiographs, the c-arm video fluoroscope is utilized to obtain the images after fixation of the reference array but is removed prior to starting surgery (fig. 3). Preoperative CT and MRI scans are obtained with fiducial markers, and these are calibrated with the affixed reference array at the time of surgery. We have previously published our preliminary experience with the systems as they pertain to transsphenoidal surgery [26, 27]. The sagittal plane view, much like the traditional fluoroscopic image, provides information regarding the trajectory to the sphenoid sinus and sella. The coronal and axial views are most useful in maintaining the midline and thereby preventing errant exposure of the carotid arteries and cavernous sinus (fig. 4). Nevertheless, each system has a small but inescapable degree of inaccuracy, and anatomic markers seen within the surgical field should be used to confirm the data provided by the navigational system [28].

After initially using the system for all transsphenoidal procedures, we have now limited the use of frameless stereotaxy. In our practice we use radiograph-based neuronavigation only in selected settings, such as repeat surgery in which the normal anatomic structures may be disrupted, and we believe that an accurate

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Fig. 3. Intraoperative set-up with frameless neuronavigation techniques requires reference array fixation (inset), but allows removal of the c-arm video fluoroscope (when plain radiograph reference images are utilized) and decreased intraoperative radiation exposure.
assessment of the anatomic midline may be difficult to discern. We also use neuronavigation in first-time transsphenoidal surgery when the carotid arteries are closely approximated. Again, in this situation the information regarding the midline helps to safeguard against vascular injury. These indications for the use of neuronavigation have been reported by others [29, 30]. Although we believe that these systems do improve accuracy and safety in second-time surgery, we do not believe that they should be considered the standard of care.

MRI-based neuronavigation is used in the removal of either suprasellar tumors that have not expanded the sella or tumors that extend along the anterior skull base [31]. In these extended transsphenoidal approaches, the planum sphenoidale and the tuberculum sellae are removed to provide increased access to the either the suprasellar region or the anterior cranial fossa. Under guidance by the neuronavigational system, bone is removed to the lateral limits of the carotid arteries and the anterior limit of the cribriform plate, and a direct trajectory to the extrasellar components of lesions can be identified.

At one time, the cost of the neuronavigational systems represented a significant deterrent to their widespread utilization. Currently, most neurosurgical centers have access to frameless stereotaxy, and this is not a major issue. Another small inconvenience is the need to rigidly fixate the reference array to a head holder (fig. 3, inset). Although the skull pins rarely cause major morbidity, they do cause some minor discomfort. Fixation of the reference array with pins does not require skull fixation to the operative table, and thus the head can still be adjusted to improve the surgical vantage point. Evaluation of headset-based fixation of the reference array not requiring skull pins has shown similar accuracy,
thereby providing a less invasive option for optical and electromagnetic-based neuronavigation systems [32, 33]. The primary limitation in the systems now is that the setup and registration of the system adds to surgical times.

In routine first-time transsphenoidal surgery, we believe that the benefit of the information regarding soft tissue structures and the anatomic midline is offset by the time added to the procedure to set up the system. Therefore, standard c-arm video fluoroscopy is used for our first-time uncomplicated transsphenoidal operations. In pituitary surgery, frameless stereotaxy cannot be used to gauge the extent of tumor removal. During tumor debulking, the morphology of the tumor necessarily shifts, as do the intracranial neurovascular structures. The surgeon must be aware that the images provided are preoperative.

Intraoperative Imaging

Intraoperatively gauging the extent of tumor removal is a major issue in transsphenoidal surgery. The inherently narrow and deep surgical corridor renders the suprasellar and lateral sellar compartments difficult to visualize. The relation of the tumor to the anterior cerebral circulation often cannot be determined, and an accurate estimation of the extent of tumor resection may not be possible. Because of this limited view, the surgeon must rely on surgical clues that the suprasellar tumor has been removed. The primary visual clue is seeing the diaphragma descend into the sellar compartment and surgical field. This does not, however, ensure that the suprasellar component has actually been completely removed. A lateral fluoroscopic image after air is instilled via a lumbar drain has traditionally allowed the surgeon to indirectly assess the extent and adequacy of surgical resection.

Ultrasonography

To circumvent these difficulties, surgeons have recently described the use of transcranial ultrasonography during resection of these large tumors [34]. By using right frontal trephination, ultrasonography can accurately differentiate tumor from brain and provide a color Doppler depiction of the anterior circulation (fig. 5). Unlike other modalities, ultrasonography provides true real-time feedback to the surgeon as the resection is being performed (fig. 6). The surgeon is able to visualize the dynamic changes in tumor geometry during the excision, in a cost- and time-efficient manner. Importantly, standard surgical instruments can be monitored within the tumor cavity in real time. Although the data published are preliminary, ultrasonography may improve the extent of
**Fig. 5.** A Doppler color flow image of the tumor (surrounded by the dotted white line). Major arteries surrounding the lesion are identified. ACA = Anterior cerebral artery; IC = internal carotid artery; MCA = middle cerebral artery. With permission from Suzuki et al. [34].

**Fig. 6.** Serial sagittal B-mode echo images obtained during tumor removal. *a* The bulk of the tumor is clearly seen at the start of the operation (1 and dotted white line). *b* The visibility of the preptine cistern (2) has increased due to debulking of the tumor. *c* A clearer identification of the cistern (3) is possible. *d* The visibility of the suprasellar cistern (4) has increased because of the gross total removal of the suprasellar tumor and the cistern is seen folding into the sella turcica. With permission from Suzuki et al. [34].
surgical resection for massive macroadenomas [34, 35]. The drawback of intraoperative ultrasonography remains, however, the clarity and resolution of the images. Ultrasonography can guide the surgeon during macroscopic tumor removal but its resolution does not allow the surgeon to monitor for small tumor remnants. Additionally, a separate cranial incision and burr hole must be performed, adding minimally to the surgical risk [36] (fig. 7).

**Intraoperative Magnetic Resonance Imaging**

MRI has become the preferred modality for the preoperative evaluation of brain tumors and epilepsy [37, 38]. With the advent of open MR systems, the applicability of MRI as an intraoperative tool was realized. The first interventional unit was installed in Boston in 1994. Since then, selected centers have used MRI in the interventional and operative forum and reported that the extent of tumor resection can be monitored with significantly improved accuracy [39, 40]. There are several types of intraoperative MRI (iMRI), and they differ based on field strength (low and high), the surgeon’s access to the patient, ease of utility, and time efficiency in image acquisition [41].

Among the low-field systems are the GE 0.5 Tesla double doughnut, the Siemens 0.2 Tesla open magnet, the Hitachi 0.3 Tesla shared resource magnet, and the Odin 0.12 Tesla magnet [42–48]. With the exception of the GE double...
doughnut, surgery is not performed within the magnet. In the other low-field systems, surgery is performed outside the 5-Gauss line where standard operative equipment and microscope can be utilized, except for a specially designed nasal speculum and drill bit [42]. This also allows free access to the patient. The disadvantage is the relative difficulty in obtaining images compared with the double doughnut system. To obtain images using the Siemens and Hitachi systems, surgery is halted and the patient is brought within the magnet for image acquisition. This process tends to lengthen the operative time and disrupts the flow of the operation. The ultra-low-field Odin system resides beneath the operative table and is brought into the surgical field much like a c-arm fluoroscope. The image quality is poor relative to the other systems, but the ease in obtaining images is superior to that of the Siemens and Hitachi magnets.

When the double doughnut is used, surgery is performed within the magnet itself without the need to move either the patient or the magnet and allows the surgeon to acquire images easily (each plane within 60–120 s). Indeed, surgeons who use the double doughnut take images throughout the procedure; those using systems where the patient must be brought into the scanner tend to take images at the end of the resection. The GE double doughnut system, however, creates a somewhat restricted surgical field and requires specific MR-compatible instruments, microscope, and anesthesia equipment. The constrained surgical field limits the application in transsphenoidal surgery.

Also in use are high-field systems made by Phillips (at the University of Minnesota), the 1.5-T Magnex system in use in Calgary, and the Siemens 1.5 Tesla unit. These systems provide superior quality images and allow the surgeons to use MRI-incompatible equipment outside the 5-Gauss line. High-field systems improve the signal-to-noise ratio and provide standard diagnostic MR capabilities including MR spectroscopy, MR angiography, MR venography, diffusion weighted imaging, and functional imaging [49, 50]. The high-field imager allows shorter examination times but its primary drawback is the significant financial and structural investment in comparison to their low-field system counterparts. Each of these systems requires transportation of either patient or magnet to obtain images. Whereas in the Phillips and Siemens systems patients are transported into the scanner, in the Calgary system it is the scanner that is brought around the patient [51].

Transsphenoidal surgery series have been published using the Siemens 0.2 Tesla open magnet [42], the Hitachi 0.3 Tesla shared resource magnet [46, 47], and the Siemens 1.5 Tesla imager [52]. Using the open Siemens magnet, Fahlbusch et al. [42] reported that iMRI led to further tumor resection in 34% (15/44) of patients with large intrasellar and suprasellar macroadenomas (fig. 8). Of course, iMRI does not improve resection of tumors that cannot be removed (i.e., those with cavernous sinus invasion). Indeed, even with iMRI, 30% (13/44)
of tumors with difficult suprasellar and parasellar extension could not be resected. The interpretation of iMRI can be difficult: 27% (12/44) of the iMRI results could not be definitively interpreted. In 20% (9/44) of cases, iMRI was interpreted as revealing residual tumor, but this interpretation was subsequently found to be incorrect upon second look and 3-month postoperative MRI. Nevertheless, false-negative results were not encountered. When the iMRI could be interpreted and was determined to have shown no residual tumor, follow-up study confirmed complete resection.

The application of the Hitachi shared-resource magnet to transsphenoidal surgery has also been assessed [46, 47]. This magnet is also used as diagnostic MRI as well, thus helping to offset the costs of the scanner. iMRIs were obtained at the perceived completion of the operation. In 66% (19/30) of cases, further surgery was performed after complete or optimal resection was thought to have been accomplished. A second MRI was performed in 8 of 19 patients, revealing persistent residual tumor in 3. A third image acquisition was not pursued in any patient. Operative time for a single imaging session was reported to be

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**Fig. 8.** Coronal (a–d) and sagittal (e–h) MRIs obtained in a 59-year-old man with a large intra-, para-, and suprasellar, endocrinologically asymptomatic pituitary adenoma. a, e Preoperative images. b, f Intraoperative images revealing some remaining tumor (arrows), which led the surgeon to take a second look and remove the remaining portions of tumor. c, g Additional images obtained at the end of surgery demonstrating that the remaining adenoma has been removed. d, h Follow-up MRIs confirming that the tumor is no longer present. With permission from Fahlbusch et al. [42].
extended by approximately 20 min. Although the authors noted some difficulty interpreting the intraoperative images secondary to blood products or leakage of contrast material into the operative bed, they reported that adequate images were obtained in 100% of cases. Early postoperative endocrinological results were comparable to those in large surgical series. One patient sustained a vascular injury to the right A1 vessel and required conversion to a craniotomy. Although it is a risk in any surgery, it is conceivable that iMRI might encourage surgeons to remove tumor from locations where it might have been prudent to leave residual tumor. Because of the added time, the surgeons reported that they tended to use the iMRI judiciously and concluded that iMRI will likely have limited use for purely sellar tumors and microadenomas.

In 2004, Nimsky et al. [52] reported on the use of the intraoperative high-field strength MRI in transsphenoidal surgery. Although operating within the high-magnetic field with MRI-compatible instruments is possible, the principal surgical position was at the 5-Gauss line, approximately 4 m from the center of the imager, where the microscope is positioned and standard microinstruments could be used. Intraoperative MRI was performed in 77 transsphenoidal operations, and resulted in a modification of surgical strategy through an extension of resection in 27 cases (35%). Among 48 patients with pituitary adenomas with distinct suprasellar extension that appeared to be respectable, findings at iMR led to repeated inspection in 29 cases (60%). Ten of these cases represented false-positive findings including fibrin glue, blood, and a suprasellar diaphragmatic fold. Of the remaining 19 patients, 15 were found to have residual tumor that was resected in its entirety, thereby increasing the rate of complete tumor removal in this subset of patients with pituitary adenomas from 56.2 (27/48) to 87.5% (42/48). No adverse events were reported because of the high-magnetic field strength. Additionally, early visualization of tumor remnants that are not removed via the transsphenoidal route make them amenable to immediate planning for postoperative treatment.

At this time, each available iMRI system is a prototype. The balancing of expense, signal-to-noise ratio and resolution, ease of access during surgery, and time efficiency have made the development of the ideal system difficult. Of course, it would be one that provides rapid high-quality multiplanar images with maximal access to the patient in a variety of surgical positions without requiring new surgical equipment or instruments. We are confident that the shortcomings are temporary and that iMRI will find its place in the resection of certain pituitary tumors. Unresectable tumors will remain so, and purely sellar lesions will likely not benefit from iMRI. To substantiate and solidify its presence as a necessary imaging technique in transsphenoidal surgery, long-term results will be needed to assess whether iMRI decreases recurrence in nonfunctioning adenomas or improves the biochemical remission rate in secreting...
adenomas. Although it may be that direct endoscopic inspection of possible tumor remnants will be adequate for most tumors, there is an obvious advantage of iMRI in assessing the adequacy of resection of the suprasellar portion of the tumor.

**Conclusions**

Major advances in radiology have played a key role in the decrease in morbidity and mortality once associated with pituitary surgery [23, 24, 53, 54]. As intraoperative image guidance techniques such as frameless stereotaxy and iMRI advance the concept of immediate feedback to the operating neurosurgeon, it is imperative that we maintain an understanding of economic restraints and global availability of such expensive neuronavigational modalities. The judicious use of appropriate resources based on the level of intraoperative guidance that will be required and an understanding of the relative utility and limitations of each modality will limit the superfluous use of advanced neuroimaging techniques (table 1). The use of intraoperative neuroimaging is not a replacement for surgical experience and a thorough knowledge of regional anatomy, but provides another tool by which the neurosurgeon can reduce the risk associated with surgical access and treatment of pituitary pathology.

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Indications</th>
<th>Utility</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative video fluoroscopy</td>
<td>Exposure of intrasellar pathology in patients</td>
<td>Establishes target trajectory in the vertical axis</td>
<td>No information on the midline approach to the sella in the horizontal axis</td>
</tr>
<tr>
<td></td>
<td>whose midline structures remain intact</td>
<td>Identifies superior and inferior borders of the sella turcica</td>
<td>No image based feedback regarding extent of tumor resection</td>
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<tr>
<td></td>
<td></td>
<td>Real-time feedback regarding depth but not laterality within the operative field</td>
<td>Intraoperative radiation exposure</td>
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<td></td>
<td></td>
<td>Simple and accurate</td>
<td>Cumbersome and bulky equipment</td>
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<td></td>
<td>In conjunction with air encephalography</td>
<td>Indirect information regarding extent of tumor resection</td>
<td>Lumbar intrathecal drain placement required</td>
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**Table 1.** Utility and limitations of selected image-guidance technologies
<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Indications</th>
<th>Utility</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>Frameless stereotaxy</td>
<td>Decrease intraoperative radiation exposure Multiplanar information aids in the midline approach to the sella</td>
<td>Requires fixation of array to skull Increases setup time (preoperative films required) Inescapable degree of inaccuracy</td>
<td></td>
</tr>
<tr>
<td>Fluoroscopy-based</td>
<td>Images acquired preoperatively, at the time of surgery</td>
<td>Poor soft tissue imaging</td>
<td>Expense (additional cost of CT scan) Preoperative imaging required</td>
</tr>
<tr>
<td>CT-based</td>
<td>Bone thickness variation and sphenoid sinus asymmetry better appreciated</td>
<td>Expense (additional cost of CT scan)</td>
<td>Preoperative imaging required</td>
</tr>
<tr>
<td>MRI-based</td>
<td>Direct trajectory to anterior skull base lesions and suprasellar lesions can be ascertained</td>
<td>Intraoperative shift of soft tissues structures</td>
<td>Expense (additional cost of MRI scan) Preoperative imaging required</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>Large invasive tumors with significant suprasellar components</td>
<td>Direct, real-time imaging of tumor No radiation exposure Identification of major vascular structures with duplex color Doppler imaging Cost-effective</td>
<td>Poor image resolution Concurrent surgical procedure needed</td>
</tr>
<tr>
<td>iMRI</td>
<td>Large invasive tumors with significant suprasellar components</td>
<td>Improved resolution and differentiation of soft tissue structures Improve suprasellar and extratumoral imaging Early visualization of tumor remnants that are not removable allows immediate planning for postoperative treatment</td>
<td>Image acquisition lengthens surgical time Although intraoperative images are relatively up-to-date, not true real-time imaging Significant capital investment required</td>
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Table 1. (continued)
References


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