

Epilepsy surgery with intraoperative MRI at 1.5 T

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Epilepsy and its treatment

Epilepsy is a term that represents a heterogeneous group of syndromes with different etiologies, severities, clinical impact, and treatment options. The cardinal feature of epilepsy is a predisposition to recurrent unprovoked seizures that are classified as partial or generalized [1]. Epileptic seizures occur when a population of hyperexcitable neurons discharge excessively [2]. Current understanding of epileptogenesis, the cellular and molecular mechanisms by which epilepsy develops, remains incomplete [1].

As knowledge of the natural history and pathophysiology of epilepsy syndromes increases, the approach to treatment changes. An important conceptual advance has resulted—the view that surgical therapy should not be considered a last resort but rather the treatment of choice for defined surgically remediable syndromes [3]. Contemporary surgical procedures for the treatment of epilepsy include resection, disconnection, and neural modulation. Advances in diagnosis, neuroimaging, and microsurgery are contributing to improvements in the safety and efficacy of epilepsy surgery.

Surgical management of epilepsy is based on a number of variables, including the type of epilepsy, localization of the epileptogenic focus, patient's wishes, and surgeon's expertise. Before

proceeding with surgery, it is imperative that reasonable evidence indicates a structural abnormality of the brain or that clinical and electrographic analysis localizes the epileptogenic focus. The immediate goal of surgery is maximal safe resection of epileptogenic tissue or anatomic and functional disconnection to eliminate or reduce the number of clinically significant seizures without causing significant deficit. Other goals include decreasing medication dependence and improving quality of life together with global brain function.

Efficacy of epilepsy surgery

Surgical treatment of focal epilepsy has a reported success rate, with respect to seizure control, ranging from 33% to 90% [4–13]. Surgical outcome has improved in recent trials and case series [5,6,9,10,13]. Factors predicting this include patient selection based on the presence of a single unilateral MRI abnormality, unilateral hippocampal sclerosis, and localized ipsilateral ictal and interictal epileptiform activity [5,14]. Factors associated with poor outcome include nonlocalizing electroencephalographic (EEG) results, absence of an MRI abnormality, bilateral atrophy, suspected cortical dysplasia, and multiple cortical MRI abnormalities [5].

When the preoperative electrophysiologic workup, clinical history, and adjunctive test results are considered and a single abnormality is identified on MRI, the surgical success rate (Engel class I or II) ranges from 80% to 90% [15]. Surgical cure of epilepsy is more likely with complete resection of the MRI abnormality or, in nonlesional cases with EEG localization only, complete resection of the appropriate anatomic structures [16]. As imaging techniques improve

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and the results of studies evaluating failed surgical procedures become available, it is evident that persisting epileptogenic foci often correlate with residual imaging and pathologic abnormalities [5].

Epilepsy surgery: a brief history

Two main factors have contributed to the advancement of epilepsy surgery: scientific knowledge and technology. Understanding the natural history and pathophysiology of epilepsy allowed classification of the epilepsies and identification of surgically remediable syndromes. Over the past century, evaluation and treatment of epilepsy were refined, in large part, as a result of the development of diagnostic and localization technologies, including EEG, electrocorticography (ECoG), CT, MRI, frameless stereotaxy/neuronavigation, and intraoperative imaging.

In 1886, Horsley [17], working with Jackson and Ferrier, surgically removed posttraumatic scar and surrounding brain parenchyma successfully while treating a patient with focal epilepsy. In 1929, Berger [18] published the first work describing human scalp EEG recordings. Fischer and Lowenbach [19] were the first to demonstrate epileptiform spikes on EEG in 1934. Shortly thereafter, the application of ECoG for detection of the epileptogenic focus during surgery was reported by Foerster and Altenburger [20]. The hallmark of epilepsy, the interictal spike, was described in 1936 by Jasper [21] and Gibbs et al [22].

In 1934, Wilder Penfield and colleagues established the Montreal Neurological Institute (MNI). The MNI opened its laboratory of EEG and neurophysiology in 1939, the first of its kind dedicated to selecting epilepsy patients for surgery and providing the technology for intraoperative recordings. EEG was established as the primary modality for seizure localization in the pre- and intraoperative evaluation of epilepsy surgery patients. Penfield and Jasper [23] further advanced invasive EEG monitoring in 1954 through the use of chronically implanted epidural electrodes. This unique group established the multidisciplinary approach to the investigation, treatment, and follow-up of patients with epilepsy.

Microsurgical technique significantly improves surgical treatment of epilepsy. The operating microscope, introduced to neurosurgery in the early 1960s, provides magnification and superior illumination. This is of particular importance today, an era of minimalism, when operations to remove only MRI-defined abnormalities take

place through restricted surgical corridors. Microsurgical dissection allows removal of a target through anatomic cisterns with minimal injury to adjacent structures.

The introduction of CT brain imaging by Hounsfield in 1973 advanced the preoperative evaluation and localization of neurosurgical pathologic findings. Patient evaluation improved further when Lauterbur and Mansfield developed MRI, which permits multiplanar imaging with superior soft tissue resolution. MRI allows detection of subtle cortical abnormalities and excludes neoplastic, vascular, and infectious causes of seizures. Imaging resolution has improved localization of epileptogenic foci, reducing the need for invasive monitoring and allowing tailored surgical resections. Frameless stereotaxy, developed during the past decade, allows precise craniotomy placement and optimizes the surgical trajectory, thereby avoiding critical structures during dissection. Unfortunately, tissue dissection, cerebrospinal fluid loss, brain retraction, and gravity result in brain shift, invalidating localization coordinates based on preoperative images [24,25]. This problem, to some extent, fueled the development of intraoperative imaging systems that could not only correct for brain shift but provide a method of resection control during surgery.

Intraoperative MRI (iMRI) permits near-real-time updating of intracranial anatomy and surgical progress. iMRI, coupled with neuronavigation, optimizes each technology's complementary features. The utility of iMRI was recognized quickly, and the technique has been successfully applied to the full spectrum of neurosurgical disorders, including epilepsy. Through the introduction of high-resolution MRI systems, improved electrophysiologic monitoring, and iMRI, the concept of tailored resections targeting the epileptogenic focus has evolved.

Since 1999, all surgical procedures performed for treatment of epilepsy at the University of Calgary have used iMRI as an adjunct. This report focuses on the development of the iMRI system, together with the experience gained from 70 patients with intractable epilepsy.

Methods and materials

Technology

The iMRI system consists of a mobile, ceiling-mounted, 1.5-T magnet. The current system,

introduced in 1997, has been successfully used during 485 neurosurgical procedures, of which 70 (14%) were performed for intractable epilepsy.

The operating suite containing the iMRI system consists of two parts. The main operating room is 7.6 m \times 10.4 m. Attached is a small alcove measuring 2.4 m \times 3.8 m that houses the 5-tonne magnet. The magnet tracks along beams attached to the ceiling, allowing movement into the operating room to the anesthetized patient for imaging. The magnet returns to the alcove when imaging is complete, allowing a return to full operating room capacity (Fig. 1).

Lines on the operating room floor indicate areas of 5-G and 50-G, with the magnet in docked and imaging positions. These lines permit the operating suite to function like a typical neurosurgical operating room. The anesthesiologist is positioned opposite the alcove at the far end of the room, outside the 5-G line. The operating microscope, neuronavigation system, ultrasonic aspirator, and electrophysiologic monitoring or ECoG equipment are also moved outside the 5-G line during imaging.

The cantilevered operating table was designed specifically for this iMRI system. It is composed of MRI-compatible materials and is secured to the floor. Movements occur in six axes using hydraulics, optimizing patient positioning. The stationary

table eliminates risk associated with patient movement and aids with accuracy of the neuronavigation system. The radiofrequency (RF) coil consists of two parts. The bottom half is built into a Sugita type four-pin head holder that provides rigid immobilization (Fig. 2).

Images are obtained at different points throughout the procedure. Intraoperative surgical planning images are obtained after induction of anesthesia, patient positioning, and head fixation. Interdissection images are acquired at various stages of the surgical dissection. For imaging, a transparent C-arm drape is placed over the wound and the patient. The upper half of the RF coil is placed over the lower half of the coil, and the magnet is moved into position. On average, imaging and reregistration of the navigation coordinates take 30 minutes. Quality assurance images are acquired after wound closure but before reversal of anesthesia. These sequences confirm completion of the surgical objective, exclude acute complications, and eliminate the need for delayed postoperative imaging.

The 1.5-T magnet provides images that approach diagnostic quality and include T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), magnetic resonance angiography, diffusion-weighted imaging, or perfusion sequences. In general, gadolinium was not administered to the epilepsy cohort.

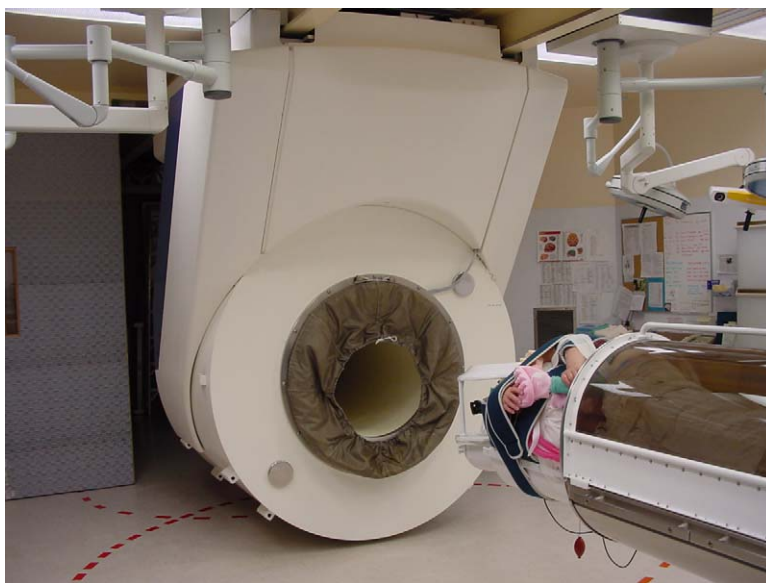


Fig. 1. The 1.5-T, 6-tonne, ceiling-mounted magnet is shown moving out of its alcove into imaging position.

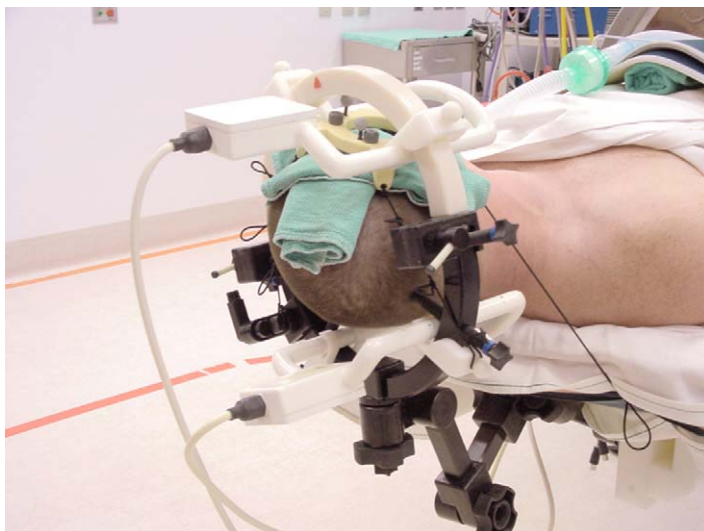


Fig. 2. Patient positioning for a selective amygdalohippocampectomy, with head fixation achieved using a Sugita type four-pin head holder with an integrated radiofrequency coil. The reference array for registration of surgical navigation coordinates is also shown.

Patient selection

The findings in 70 epilepsy patients include cortical dysplasia, ganglioglioma, gangliocytoma, pleomorphic xanthoastrocytoma (PXA), dysembryoplastic neuroepithelial tumor (DNET), and epilepsy without identifiable structural abnormalities on MRI. Patients with neoplastic or vascular lesions as a cause of seizures have not been included.

The patients underwent a complete history, physical examination, and seizure localization using EEG, MRI, and neuropsychologic evaluation. Amytal testing was performed when there was a question as to the functionality of the contralateral temporal lobe and language localization. Selective positron emission tomography, single photon emission computed tomography, and functional MRI (fMRI) were selectively acquired to provide confirmation of the seizure focus and its relation to eloquent cortex. Invasive monitoring using subdural electrode grids or strips was selectively employed before the definitive surgical procedure for confirmation of the epileptogenic focus.

Data, including age at seizure onset; age at surgery; side of surgery; surgical procedure; histopathology; seizure description; pre-, intra-, and postoperative imaging characteristics; and perioperative clinical evaluation results, were prospectively recorded. Patients were classified into four

groups: temporal lobe epilepsy (TLE), benign lesions (ganglioglioma, gangliocytoma, DNET, and PXA), cortical dysplasia, and corpus callosotomy. Surgical outcome was based on the Engel classification [26].

Results

Since 1999, 70 patients have undergone 70 surgical procedures for refractory epilepsy at the University of Calgary using iMRI (Table 1). Fifty-nine (84%) patients were adults (age >17 years), and 11 were pediatric patients (age <18 years). Of the 70 procedures performed, 62 (89%) were first operations and 8 were reoperations. TLE predominated in this series. Fifty-one (73%) patients underwent operations for TLE; of these 51 operations, 31 (44%) procedures were selective amygdalohippocampectomies (SelAHs). The 20 remaining procedures for TLE were more extensive temporal lobe resections, including eight (11%) reoperations for residual epileptogenic tissue. Nine (13%) patients underwent resections of benign brain lesions presumed to be the cause of their epilepsy. Resections for cortical dysplasia were performed in 7 (10%) patients. Three (4%) patients underwent corpus callosotomy for generalized epilepsy (Table 2). Eleven pediatric patients, with ages ranging between 12 months and 16 years, were treated for refractory epilepsy.

Table 1
Patient characteristics

	Totals (N = 70)	TLE (N = 51)		Benign lesion (N = 9)	Cortical dysplasia (N = 7)	Corpus callosotomy (N = 3)
		SelAH [31]	ATL [20]			
Age (y)	33 ± 13	35 ± 11	37 ± 13	22 ± 15	23 ± 20	24 ± 13
Gender						
Male	33	15	11	8	3	2
Female	36	16	9	1	4	1
Seizure type		Focal	Focal	Focal	Focal	Generalized
Preoperative evaluation						
MRI						
Normal		0	2 (10%)			
MTS		26 (84%)	13 (65%)			
Benign lesion				9		
Cortical dysplasia		1 (3%)	1 (5%)		7	
Other		4 (13%)	4 (20%)			
EEG		28	15	9	7	3
telemetry						
Invasive monitoring	18 (26%)	3	9	2	4	0
Previous operation	8 (11%)	0	8	0	0	0

Abbreviations: ATL, anterior temporal lobectomy; MTS, mesial temporal sclerosis; SelAH, selective amygdalo-hippocampectomy.

Procedures included five resections of benign lesions, three cortical dysplasia resections, two SelAHs, and one corpus callosotomy.

In most patients, surgical planning images were obtained (Table 3). Neuronavigation was registered based on these images in 38 (55%) patients. Sequences included T1-weighted images in all cases and T2-weighted or FLAIR images in select cases. Interdissection images were obtained in 69 (98.6%) patients. T1-weighted sequences

were obtained in all cases. Acquisition of other sequences, including T2-weighted and FLAIR images, was individualized to each case. Interdissection imaging revealed residual tissue in 18 (26%) cases, necessitating further resection. Interdissection images were sufficient in 51 (73%) cases demonstrating complete resection of the surgical target. Quality assurance images were obtained after 18 (26%) operations. The need for delayed postoperative imaging was eliminated in all cases. One acute complication, an operative site hematoma, was identified. The patient was redraped, the operative site was reopened, and the hematoma was evacuated.

The duration of imaging studies was approximately 30 minutes, adding, on average, 90 minutes to the procedural time.

Patient seizure outcomes were determined after surgery during the hospital stay and at 3, 6, and 12 months after surgery, followed by yearly clinical assessments thereafter (Table 4). All patients remained on their preoperative antiepileptic medication regimen until 1 year after surgery. At 1 year, tapering of medications was initiated based on each patient's outcome and seizure burden.

Table 2
Pathologic findings

Pathologic finding	Total (N = 70)
TLE	
Normal	8 (11%)
Mesial temporal sclerosis	37 (53%)
Other/gliosis	8 (11%)
Focal cortical dysplasia	7 (10%)
Benign lesions	9 (13%)
Ganglioglioma	4 (6%)
Gangliocytoma	3 (4%)
DNET	2 (3%)
Pleomorphic xanthoastrocytoma	1 (1%)

Table 3
iMRI

	Patients	Surgical planning	Interdissection	Residual tissue	Quality assurance	Neuronavigation
All procedures	70	65 (93%)	69 (99%)	18 (26%)	18 (26%)	39 (56%)
TLE	51 (73%)					
SelAH	31 (61%)	30 (97%)	30 (97%)	10 (32%)	10 (32%)	20 (65%)
ATL	20 (39%)	18 (90%)	20	4 (20%)	4 (20%)	7 (35%)
Cortical dysplasia	7 (10%)	5 (71%)	7	0	0	4 (57%)
Corpus callosotomy	3 (4%)	3	3	1 (33%)	1 (33%)	3
Benign lesion	9 (13%)	9	9	3 (33%)	3 (33%)	5 (56%)

Abbreviations: ATL, anterior temporal lobectomy; SelAH, selective amygdalohippocampectomy.

Of the 70 patients, 61 (87%) have had follow-up of 6 months or longer (mean duration = 21 months, range: 6–51 months). Fifty-nine patients underwent operations for TLE, cortical dysplasia, or benign lesions, with follow-up greater than 6 months. Of these, 41 (70%) remain seizure-free (Engel class I). Outcome for the remaining patients includes 10 (17%) in Engel class II, 4 (7%) in Engel class III, and 4 (7%) in Engel class IV.

Discussion

Epilepsy surgery and intraoperative MRI: current status

The application of iMRI to epilepsy surgery is new, first reported in 1999 [27]. Since that initial publication, only five papers devoted solely to this topic have appeared [28–32]. The reports are small case series documenting and describing the application of iMRI to epilepsy (Table 5).

The University of Calgary’s publication was a case series of 14 patients who underwent various operations for TLE and were monitored using the 1.5-T iMRI system. The utility of iMRI during epilepsy surgery was demonstrated by identification of unexpected residual tissue on interdissection imaging in 50% of patients. One acute postoperative hematoma was observed and removed before reversal of anesthesia [30].

Harvard University published a case series of 13 patients who underwent surgery using the General Electric (Waukesha, Wisconsin) Signa SP 0.5-T iMRI system for treatment of benign intracerebral lesions producing seizures. The use of iMRI during lesional epilepsy surgery was demonstrated to be safe and effective, providing guidance throughout the surgical procedure [32].

The University of Erlangen-Nuremberg has made two contributions to the literature. The first publication evaluated whether iMRI using the Magnetom Open 0.2-T iMRI system aided

Table 4
Surgical procedures and patient outcomes

			Seizure outcome: Engel class (follow-up >6 mo)			
	All patients	Patients (follow-up >6 mo)	Class I	Class II	Class III	Class IV
All procedures	70	59 (84%)	41 (70%)	10 (17%)	4 (7%)	4 (7%)
TLE						
SelAH	31 (33%)	30 (51%)	20 (67%)	7 (23%)	1 (3%)	2 (7%)
ATL	20 (29%)	15 (25%)	9 (60%)	1 (7%)	3 (20%)	2 (13%)
Cortical dysplasia	7 (10%)	7 (10%)	5 (71%)	2 (29%)		
Benign lesion	9 (13%)	7 (12%)	7 (100%)			
Reoperations for TLE	8/51 (16%)	8 (14%)	5 (63%)	1 (9%)	1 (9%)	1 (9%)
Corpus callosotomy	3 (3%)	2 (66%)				

Abbreviations: ALT, anterior temporal lobectomy; SelAH, selective amygdalohippocampectomy.

Table 5
iMRI during epilepsy surgery

Description	Year of publication	Authors	Source
Intraoperative MRI in epilepsy surgery	2000	Buchfelder M, et al	J Magn Reson Imaging 12:547–55
Optimizing epilepsy surgery with intraoperative MRI	2002	Kaibara T, et al	Epilepsia 43:425–9
Intraoperative magnetic resonance for the surgical treatment of lesions producing seizures	2002	Walker DG, et al	J Clin Neurosci 9:515–20
Use of iMRI in tailored temporal lobe surgeries for epilepsy	2002	Buchfelder M, et al	Epilepsia 43:864–73
Standardization of amygdalohippocampectomy with iMRI: preliminary experience	2002	Schwartz TH, et al	Epilepsia 43:430–6

surgery individualized to each patient. The series included 61 patients with pharmacoresistant epilepsy. iMRI provided a reliable assessment of the extent of the surgical procedure and a means for identification of residual tissue during surgery [29]. The second publication examined the utility of iMRI for immediate assessment of the extent of resection after operations for TLE. The case series of 58 patients using the same iMRI system provided a reliable evaluation of the extent of resection after temporal lobe procedures when compared with delayed postoperative studies [28].

The Neurological Institute of New Jersey reviewed a series of five patients to determine

whether iMRI using the PoleStar 0.12-T system was beneficial for standardization of amygdalohippocampectomy. The authors concluded that iMRI is a useful adjunct for the surgical treatment of mesial TLE and is a reliable method of standardizing complete hippocampectomy [31].

Based on this literature, it can be concluded that iMRI technology is safe and feasible. The benefit of iMRI in epilepsy surgery, however, has not been equivocally established. Further studies, including randomized clinical trials comparing epilepsy procedures performed with and without iMRI guidance, are necessary to provide objective evidence.

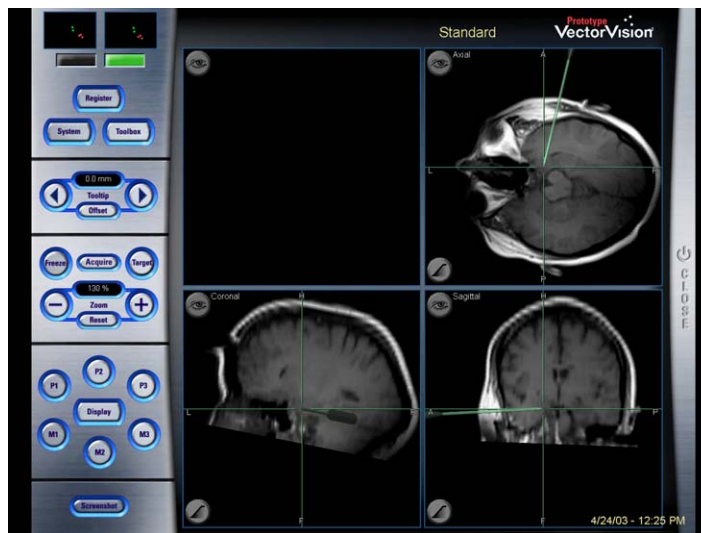


Fig. 3. Intraoperative surgical planning T1-weighted MRI scans registered to a frameless navigation system (BrainLab, Redwood City, California). The screenshot demonstrates the surgical trajectory.

Advantages of intraoperative MRI in epilepsy surgery

Surgical planning images update existing diagnostic studies with the patient anesthetized and positioned for surgery. Neuronavigational setup and coordinate registration occur at this time, thereby eliminating the need for patient transport for repeat diagnostic imaging and its associated cost. This stage optimizes craniotomy placement and target localization (Fig. 3).

Interdissection imaging provides resection control through visualization of intracranial contents, including the surgical target and normal brain parenchyma. The navigational system and the surgeon's anatomic knowledge are updated. Surgeons typically overestimate the amount of resection. In the present series, 18 (26%) cases demonstrated unexpected residual tissue during imaging, necessitating further resection.

The main indication for quality assurance imaging has been acute complication identification

and avoidance. This imaging sequence also eliminated the need for delayed postoperative image evaluation of the extent of resection.

Disadvantages of iMRI include economic costs and impact on surgical rhythm. The cost of iMRI technology, including installation cost and service contracts, has limited this technology to a few centers. Imaging during surgery disrupts rhythm and increases procedural time. On average, iMRI added 90 minutes to each case. Disruption of the surgical rhythm is not unlike that encountered during acquisition of traditional ECoG.

Epilepsy surgery and intraoperative MRI at the University of Calgary

Our experience has involved application of a 1.5-T iMRI system to a heterogeneous group of patients with TLE, cortical dysplasia, benign lesions producing seizures, and generalized seizure disorders treated by corpus callosotomy (Figs. 4, 5).

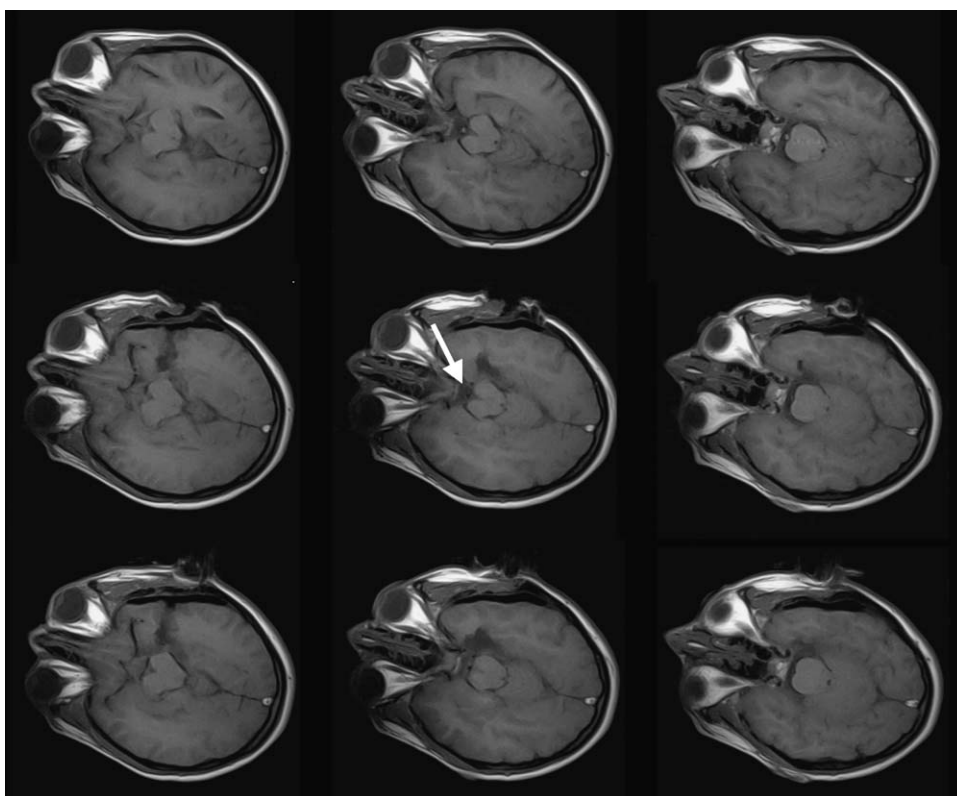


Fig. 4. Surgical planning (*upper row*), interdissection (*middle row*), and quality assurance (*lower row*) T1-weighted MRI scans from a patient with intractable temporal lobe epilepsy. The surgical planning study shows the targeted amygdala and hippocampus. Unsuspected residual amygdala (*arrow*) was present on the interdissection study and was removed before the quality assurance study.

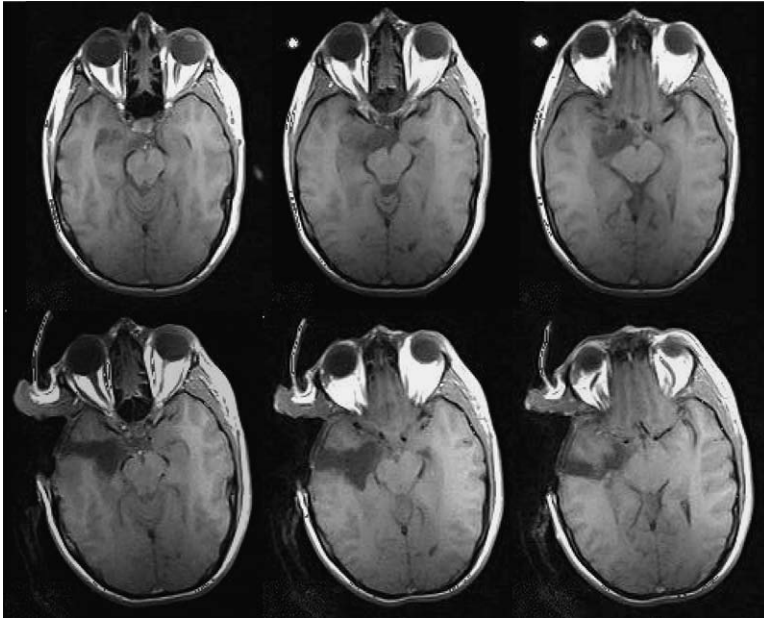


Fig. 5. Surgical planning (*upper row*) and interdissection (*lower row*) T1-weighted MRI scans from a patient with a dysembryoplastic neuroepithelial tumor of the right mesial temporal lobe causing intractable epilepsy. The surgical planning study demonstrates the hypointense lesion. The interdissection study demonstrates complete resection of the lesion.

The iMRI system has been applied to different types of epilepsy operations and is compatible with other technologies routinely used during the surgical management of epilepsy.

After introduction of the iMRI system, anterior temporal lobectomy (ATL) was the most common procedure performed for intractable epilepsy. Over time, the comfort level in performing selective procedures with iMRI guidance increased. Consequently, more selective and less invasive procedures are now performed.

Areas of cortical dysplasia are often subtle and are best identified using 1.5-T or higher iMRI systems. Single to noise, a prerequisite for image quality, is field dependent. Outcome after removal of cortical dysplasia and benign lesions associated with epilepsy is related to the extent of removal of the MRI abnormality. In the present series, dysplastic areas were occasionally visually indistinguishable from normal parenchyma, making iMRI and neuronavigation invaluable. ECoG, when used during these procedures, complemented the iMRI data by providing electrographic localization.

Corpus callosotomy was performed on three patients in an attempt to improve their quality of life. One of the disconnection procedures

benefited from interdissection MRI, which showed unexpected incomplete division of the body of the corpus callosum.

Approximately 20% to 50% of patients with TLE develop recurrent seizures after surgery. Reasons for failure include bitemporal EEG abnormalities, incomplete resection of abnormal tissue, and initially unidentified extratemporal lesions. Eight of our patients underwent repeat operations for recurrent seizures after temporal lobectomy. In all these cases, failure was related to incomplete resection of epileptogenic medial temporal lobe structures. It may be concluded that iMRI would decrease the likelihood of such patients.

Neuronavigation was frequently integrated with the iMRI. After interdissection imaging, the neuronavigation system was updated with newly acquired data, thereby restoring navigational accuracy and reducing the problem associated with brain shift. iMRI was particularly beneficial for patients undergoing selective resections of medial temporal structures, where residual tissue was identified in 50% of cases.

We decided to develop an iMRI system based on a moveable magnet for a number of reasons. The operating room looks and functions as a normal

surgical theater between imaging studies. MRI-incompatible surgical microscopes, neuronavigation systems, anesthesia and electrophysiologic equipment, and other surgical adjuncts can be accommodated. The potential for moving the magnet to an adjacent diagnostic room permits image acquisition on other patients. Technology sharing is important in a health care system burdened by escalating costs.

Based on the results described, our surgical results are comparable to those reported in the literature with respect to seizure control. We found iMRI of value for target localization and resection control. Given the nature of the disease process and the different factors that influence patient outcome, however, it will be difficult to unequivocally prove the benefit of iMRI during epilepsy surgery without a large randomized control trial.

Advancing epilepsy surgery means improving surgical efficacy. Further advancements in imaging techniques, and their fusion, will improve localization of the epileptogenic focus. Refinements of surgical techniques are necessary to optimize management of the epileptogenic focus with minimal disruption of normal brain parenchyma. Ultimately, surgical intervention in appropriately selected patients will maximally reduce seizure frequency while minimizing neurologic and neuropsychologic deficits. Incorporating surgical robotics into this environment will augment surgical precision and accuracy, allowing precise removal or modulation of abnormal tissue.

Summary

Despite the infancy of iMRI in epilepsy surgery and the paucity of literature on this topic, some conclusions may be reached. Although iMRI is a useful adjunct during epilepsy procedures, a randomized control trial is necessary to determine its true impact.

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