Surgical approaches to epilepsy

Surgical treatment for epilepsy is the only currently available treatment that provides the patient with the possibility of becoming seizure free and off anticonvulsants. This article describes many of the recent advances in the field of epilepsy surgery that are used by the epilepsy team to render patients seizure free without neurological or cognitive deficit. In particular, this article discusses the role of magnetoencephalography, recent advances in MRI techniques for preoperative brain mapping, invasive electrode recording and neuronavigation for the work-up of patients prior to definitive surgical treatment. We then discuss the outcome following different epilepsy surgical procedures, including vagal-nerve stimulation, multiple subpial resections and corpus callosotomy. Finally, we describe techniques that do not currently have an established role but hold promise in the treatment of epilepsy. These techniques include deep-brain stimulation and additional forms of neural stimulation for the patient with epilepsy.

KEYWORDS: corpus callosotomy ▪ deep-brain stimulation ▪ epilepsy surgery ▪ hemispherectomy ▪ invasive monitoring ▪ magnetoencephalography ▪ neuroimaging

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Epilepsy is a devastating condition with a lifetime incidence of 3.2% and a prevalence of five to ten per 1000 people [1]. Medical treatment with antiepileptic medication controls seizures in approximately 60–70% of patients [2]. The remaining patients endure frequent seizures with the concomitant problems of intellectual decline, neurological deficits and the risk of sudden unexplained death. The incidence of sudden unexplained death has been estimated to be 24-times greater than the general population [3]. Resective surgery has the potential to render patients seizure free whilst preserving cognitive and neurological function. Adjunct surgical strategies, such as vagal-nerve stimulation (VNS), aim to reduce seizure frequency and severity but are unlikely to be curative. This article discusses some of the recent advances in the field of epilepsy surgery.

Who is a candidate for epilepsy surgery?

Approximately 60% of all patients with epilepsy have focal epilepsy [4]. Of those, 15–20% are not adequately managed with anticonvulsants. These patients should be considered for epilepsy surgery.

The diagnosis of medically intractable epilepsy is made when anticonvulsants fail to avert seizures to the point that quality of life is impaired for the individual [5]. Historically, patients were required to have tried many antiepileptic drugs without sucess to control seizures prior to consideration of surgical resective procedures. With improvements in the safety of neurosurgical intervention and an increasing awareness of the long-term side effects of many antiepileptic medications, there has been a shift, particularly in centers where epilepsy surgery is practiced commonly, to perform these procedures at an earlier stage. The long-term adverse effects of antiepileptic medications in children are of particular concern. Accordingly, many units are aggressively evaluating children following the onset of a seizure syndrome. In children with specific epilepsy syndromes, such as Sturge–Weber syndrome, the natural history is very well characterized such that epilepsy surgery is often advocated at an early time-point, even if the intractability of the seizure disorder has not been reached.

Criteria for consideration of epilepsy surgery include medical intractability to the point where activities of daily life are compromised, where neurophysiological and anatomical lateralization and localization is possible with a good likelihood of significantly improving seizure control, and where the proposed surgery is unlikely to leave the patient worse off, both cognitively and neurologically.

The goals of resective epilepsy surgery

In summary, the aim of resective epilepsy surgery is to render the patient seizure free and free of medication without inflicting a new deficit, be it neurological or cognitive, to the patient. As such, the aim of preresection investigations is to:

- Identify the area of the brain that is responsible for seizure generation – the so called epileptogenic zone
- Identify and preserve eloquent cortex where feasible
- Reduce the incidence of sudden unexplained death
- Improve neuropsychological outcomes

Identification of the epileptogenic zone

The epileptogenic zone is not usually isolated using any one particular investigation; rather, estimations are made based on a combination of preoperative electrophysiological, structural and functional investigations.

Modalities commonly utilized to identify the epileptogenic zone are detailed in Table 1. In the next sections, we will discuss some of the more recent advances in preoperative localization of the epileptogenic zone and eloquent cortex, including the more common electrophysiological investigations used to identify the epileptogenic zone, and then the techniques used for anatomical and functional localization. The article concludes with a discussion of the more common surgical procedures used in epilepsy surgery.

Electrophysiological investigations

EEG & video EEG

EEG has been the cornerstone for localization and lateralization of the epileptogenic zone for decades. EEG reflects correlated synchronous synaptic activity of the cerebral cortex and provides lateralizing information on the epileptogenic zone by identifying inerictal and ictal activity. In many units, it is common practice for all patients who are being considered for a surgical treatment of their epilepsy to have video EEG recording to provide ictal and interictal electrophysiological data that can be correlated with seizure semiology.

Table 1. Modalities commonly utilized to identify the epileptogenic zone.

Type	Modality
Clinical	Semiology Physical and neurological examination
Neurophysiological	EEG (interictal) EEG (ictal) MEG Invasive monitoring (ECoG)
Functional	fMRI EEG-fMRI SPECT (ictal/interictal) PET (interictal) MEG Evoked potentials: somatosensory and visual Intracarotid amobarbital procedure (Wada test) Direct cortical stimulation

ECoG: Electrocorticography; fMRI: Functional MRI; MEG: Magnetoencephalography.

Magnetoencepholagraphy

Magnetoencephalography (MEG) is a noninvasive technique used to assist in the identification of the epileptogenic zone and also to localize the eloquent cortex. MEG measures extracranial magnetic fields generated by massive synchronized intraneural electric currents [6]. MEG uses a superconducting quantum interference device to amplify small magnetic fields generated by intracranial neuronal activity. The flow of electrical current must be parallel to the surface of the skull so that a perpendicular magnetic field can be generated and detected by MEG sensors. It has potential advantages over interictal EEG in the following ways [6]:

- Magnetoencephalography may be more sensitive than scalp EEG in detecting electrical discharges. This is mainly because magnetic fields are less attenuated by bone and scalp than electrical fields;
- The smallest area of cortex over which synchronized epileptiform cortical discharge is required to detect a spike is 3–4 cm^2 for MEG as opposed to 6–20 cm^2 for scalp EEG [6];
- The spatial resolution for detecting epileptiform spikes is superior for MEG compared with EEG [7].

Knowlton provides a good overview of the use of MEG for localizing the epileptogenic zone [8].

It should be stressed that MEG is not ideal at detecting ictal activity as any head movement that might occur during seizures will degrade spatial resolution. Although MEG is more sensitive in detecting currents that are tangential to the surface of the scalp, EEG is sensitive to tangential and radial neuronal activities. In our unit, we use a combination of MEG, and ictal and interictal video EEG to assist in the localization of the epileptogenic zone. Concordance between the scalp video EEG and MEG findings provides strong noninvasive evidence that surgical resection will be successful [9].

The density of spike sources for a given area seen on MEG has been demonstrated to be a good predictor of outcome after epilepsy surgery [10]. We have defined a MEG spike cluster as at least 20 spike sources within an area that is 1 cm in diameter; small clusters consist of six to 19 spike sources within 1 cm and scatters consist of six spike sources, irrespective of the distance between sources (Figure 1). A solitary 'tight' spike cluster frequently correlates with the seizure onset zone and the active irritative zone on intracranial video EEG recording. For lesional epilepsy, resection of the MEG cluster and the lesion provide the greatest chance of seizure freedom [11]. For nonlesional epilepsy, (i.e., where MRI demonstrates no abnormality, very subtle abnormalities or multifocal abnormalities, following invasive electrode recording) resection of the MEG cluster resulted in favorable postoperative seizure outcome, although not as good as for lesional epilepsy [12]. Predictors of good outcome included concordance between MEG and invasive recordings, MEG spike clusters, single seizure types and complete resection.

Magnetoencephalography has also been demonstrated to be a useful adjunct in the identification of the epileptogenic zone where other studies have not elucidated the ictal onset zone. In one study, the authors found that MEG supplied additional information in 35% of surgical cases that was not available using other conventional techniques. In this study, MEG was critical in decision-making in 10% of cases [13].

Specific clinical situations where MEG provides information that is not available using noninvasive techniques include evaluation of patients who continue to have seizures despite undergoing seizure surgery [14]. Scalp EEG suffers from artifacts as a result of skull defects, dural scarring and surface cerebrospinal fluid collections, making interpretation more difficult. MRI can also be difficult to interpret as anatomy has been disrupted. In these problematic situations, MEG can provide the electrophysiological and anatomical location of the remaining epileptogenic zone.

Tuberous sclerosis patients may have a number of epileptogenic zones. A novel application of MEG called synthetic aperture magnetometry kurtosis can localize complex epileptic zones in children with tuberous sclerosis whose seizures may originate from multiple cortical tubers [15]. This technique may help identify the most likely location of the epileptogenic zone.

Magnetoencephalography can also be used for anatomical localization of eloquent cortex. The somatosensory-evoked field from median-nerve stimulation is a well-characterized method for identifying the primary somatosensory cortex and, thus, the central sulcus (Figure 2) [16]. Functional data from MEG can now be used to map the auditory and motor cortex, and the visual evoked field prior to surgery.

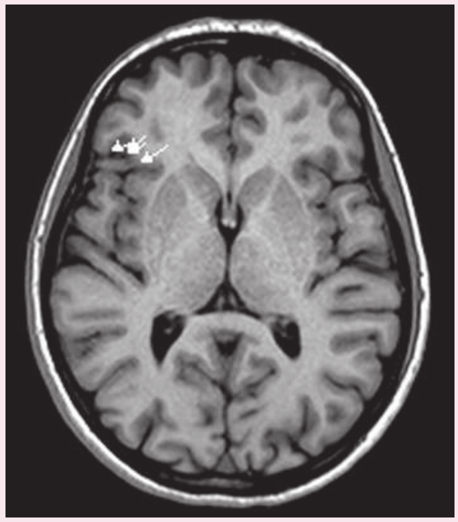

Figure 1. Magnetoencephalography showing a cluster in the right inferior frontal gyrus. This patient had a resection in the area of the magnetoencephalography cluster and has been rendered seizure free. White triangle and lines indicate the magnetoencephalography spike focus location.

One of the important drawbacks of MEG is its cost. It is not currently widely available throughout the world. At present, there are MEG scanners in clinical use for the preoperative planning of patients with epilepsy in the UK. If future studies demonstrate a clear clinical benefit for the use of MEG compared with other tests it is likely that the cost will start to reduce.

Anatomical localization

■ MRI & other forms of structural imaging

MRI is the cornerstone of structural imaging, employed in patients with medically intractable epilepsy. It is recommended that MRI be performed in every patient with epilepsy, and the scans should be evaluated by experts in epilepsy imaging who have access to the pertinent clinical and electrophysiological findings. Epilepsy sequences often include T_1- and T_2-weighted imaging, proton density and fluid-attenuation inversion-recovery sequences in the majority of cases.

Most major epilepsy centers now use 3-Tesla (T) MRIs for the preoperative surgical evaluation of patients with epilepsy. In 20% of patients with medically intractable epilepsy,

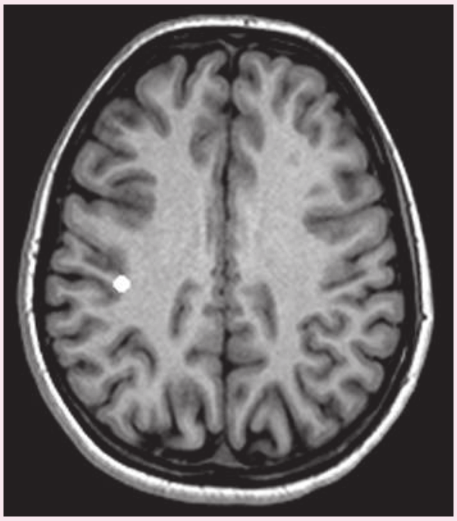

Figure 2. Magnetoencephalography on the patient shown in Figure 1, identifying the somatosensory-evoked field.
The somatosensory-evoked field (white circle) correlates well with intraoperative mapping of the rolandic fissure.

3-T MRI identifies cortical lesions, where structural pathology was not clearly evident on 1–1.5-T MRI scans [17].

MRI data have been analyzed using various computer-assisted methods in order to identify more subtle abnormalities. Techniques, including voxel-based imaging to identify differences in the distribution of regions of interest, such as gray matter, or for measuring hippocampal volumes are frequently used [18]. These techniques are useful in the identification of subtle cortical dysplasia.

Another important structural imaging technique is diffusion-tensor imaging or tractography (Figure 3). In this technique, white matter tracts are imaged based on the anisotropic movement of water molecules along axons. For example, tractography has been used to identify Meyer's loop prior to temporal lobectomy, in order to minimize the risk of visual-field deficits [19].

Functional localization

Magnetic resonance spectroscopy is a means of identifying regional metabolic rate. Regions of abnormal development are often hypometabolic. Magnetic resonance spectroscopy has been demonstrated to lateralize the epileptogenic zone in patients with focal cortical dysplasia [20].

Functional MRI has a number of applications for epilepsy surgery, particularly in the identification of eloquent cortex such as the primary motor area. Functional MRI identifies accentuations in regional cerebral blood flow in response to specific paradigms. It has been used for motor mapping, language mapping (Figure 4), mapping of the somatosensory cortex and memory function. Functional MRI has been shown to have a greater than 90% concordance when compared with the Wada test for language lateralization, with the majority of remaining patients demonstrating language codominance [21]. It is rapidly becoming the investigation of choice for identifying language dominance.

Ictal SPECT is a technique whereby a radioactive tracer is injected at the time of a seizure onset, either using technetium-99m hexamethylpropyleneamineoxime or technetium-99m bicisate as common reagents. On first pass, the tracer enters neurons and is retained there. It takes 1–2 min for maximal intraneuronal tracer concentrations to be achieved and 4 h for the tracer to dissipate; as such, ictal SPECT imaging shortly following a seizure provides a regional cerebral blood-flow map at a time that is potentially very close to seizure onset. The timing of injection is critical for obtaining appropriate images. The seizure-onset zone often has increased regional cerebral blood flow compared with other areas. Interictal SPECT may demonstrate areas of hypoperfusion in the region of the epileptogenic zone. As a result, it must be viewed in combination with the corresponding ictal SPECT. Resection of the subtracted ictal SPECT abnormality coregistered to MRI has been demonstrated to improve the outcome of surgical resection [22].

Surgical approaches to identify the epileptogenic zone: invasive electrode recording

Following assessment of the preoperative investigations, the neurosurgeon, in conjunction with the epileptologist, needs to determine whether further delineation of the epileptogenic zone and functional regions of the brain are required. If so, then invasive electrode recording is frequently performed. Invasive electrode recording is usually appropriate when noninvasive data are inconclusive as to the precise location of the epileptogenic zone and its relation to the eloquent cortex. It is important to note that localization of eloquent cortex, such as language, motor function and sensory function, can also be mapped intraoperatively during resective surgery, thus, precluding the requirement for invasive monitoring (e.g., by performing an awake craniotomy). However, the absence of a structural lesion on MRI frequently mandates invasive recording.

Invasive electrode recording is used in approximately 25–40% of cases reviewed by epilepsy surgical teams [23] and, therefore, noninvasive preoperative investigations provide adequate information prior to resection in the majority of patients.

Invasive recordings are obtained by subdurally placed grids or strips and/or depth electrodes. Image guidance is increasingly being utilized during invasive electrode recordings for accurate placement of the electrodes. The size of the craniotomy is determined by the estimated size of the epileptogenic zone based on the preoperative investigations. At the Hospital for Sick Children, we cover the MEG cluster, the structural lesion (if present) and any surrounding eloquent cortex (FIGURE 5). We believe that MEG should be used in conjunction with invasive recordings and is not a replacement for accurate localization of the epileptogenic zone. Large craniotomies will facilitate the maximum amount of electrophysiological data that can be captured. We frequently place depth electrodes into noneloquent structural lesions or into MEG spike cluster regions.

The advantages of invasive recordings, compared with scalp EEG, include superior spatial resolution, superior detection of low-amplitude epileptogenic activity, ability to identify ictal and interictal activity, and ability to functionally map eloquent cortex.

As the patient can only safely undergo electrode recordings for a period of 1–3 weeks, it is important to obtain as much ictal data as possible, so anticonvulsants are frequently withdrawn prior to surgery. Functional mapping requires direct stimulation of specific electrodes on the grid or on the depth electrode. Language should be mapped extraoperatively with the assistance of a neuropsychologist. Motor and sensory mapping are also performed in the extraoperative setting.

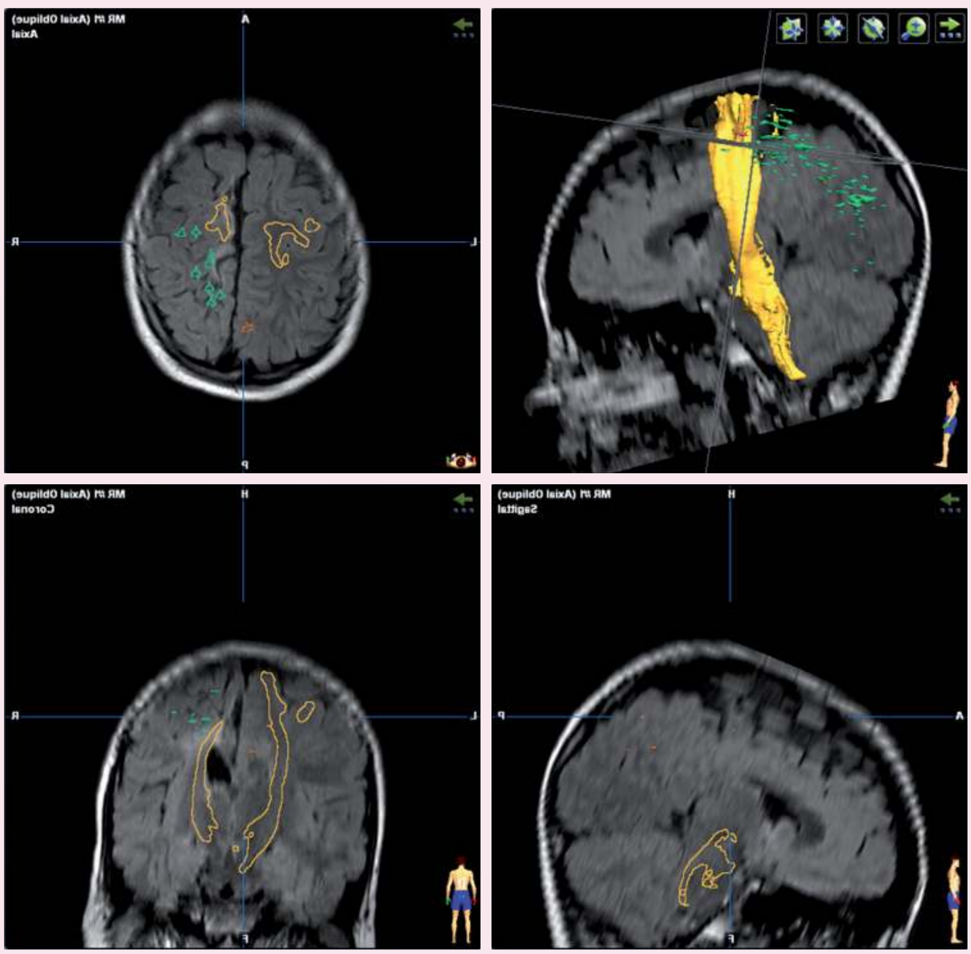

Figure 3. Diffusion tensor imaging showing the corticospinal tract in yellow with the superimposed magnetoencephalography spikes in green. This image can be superimposed on the neuronavigation system to accurately localize the corticospinal tract intraoperatively.

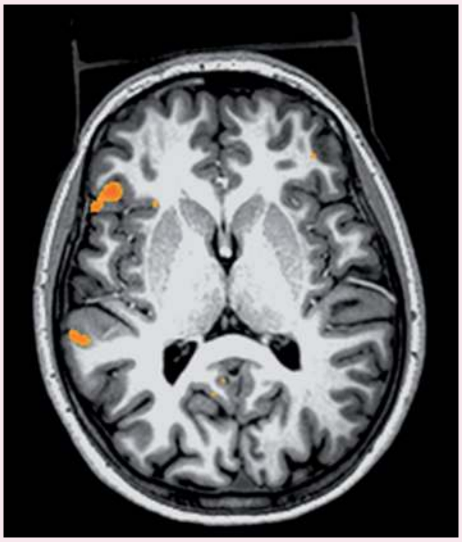

Figure 4. Functional MRI of the patient in FIGURE 1 showing the location of Broca's area. It appears to be located directly at the magnetoencephalography spike cluster.

Recently, we have been using high-frequency (γ-band) oscillations during invasive electrode recording. This technique is more precise in terms of functional mapping, both spatially and temporally [24], than typical spike detection computer software, and has been demonstrated to accurately localize the epileptogenic zone [25].

Neuronavigation

The advent of neuronavigation has led to increased accuracy of lesion and epileptogenic zone depiction prior to resection in many patients undergoing epilepsy surgery. Neuronavigation enables the neurosurgeon to coregister preoperatively acquired data, usually in the form of a volumetric T_1-weighted MRI, with the spatial position of the patient in the operating room. It is important that the head does not move relative to the reference device. This can be achieved using pin immobilization with a reference frame attached to the bed, by attaching the reference frame directly to the patient's skull or by using a skin marker. Electromagnetic neuronavigation techniques that preclude the requirement for rigid fixation either to bone or using pins are now commercially available (StealthStation Axiom®, Medtronic, USA). This may be especially applicable in children where skull thickness often means that pin immobilization is potentially hazardous.

One important limitation of neuronavigation is intraoperative brain shifting. The degree of brain shift following craniotomy has been calculated at 8 mm in the vertical direction and 10 mm in the horizontal direction [26]. Real-time imaging techniques, such as intraoperative MRI, overcome this limitation. However, intraoperative MRI has not yet been demonstrated to improve accuracy during epilepsy resection compared with conventional techniques and is not readily available in most institutions. Intraoperative ultrasonography provides a more pragmatic alternative for checking neuronavigation accuracy. Another important advance is the fusion of multiple imaging modalities with the MRI dataset, allowing accurate localization of epileptogenic and functional areas intraoperatively.

Magnetoencephalography, in itself, provides electrophysiological data that can easily be superimposed on to anatomical datasets such as MRI. Fusion into a neuronavigation system has been widely practiced [27], and is often the determinant of the size and location of the grid when contemplating invasive recordings (FIGURE 6). There is growing evidence that the MEG data on functional localization of the somatosensory-evoked field correlate well with intraoperative maps of sensory- and motor-evoked potentials, and electrocortical stimulation [27].

Surgical resective procedures & outcome

Based on all the data obtained from noninvasive and invasive investigations, the epilepsy team evaluates whether or not the patient is a surgical candidate for resective (potentially curative) surgery. Surgical resection involves removal or disconnection of the epileptogenic zone.

Outcome following surgical resection is increasingly being studied. This relates not only to seizure outcome, but also to functional outcome in terms of motor or sensory deficits, language problems, memory deficits and psychological wellbeing. Tilez-Zenteno *et al.* performed a meta-analysis investigating long-term outcomes following epilepsy surgery [28]. It is important to note that there are some more recent reports of different outcomes. From these data, it is clear that the outcomes of surgery are impressive when considering that the alternative would have been medical intractable epilepsy.

Temporal-lobe epilepsy

Temporal-lobe epilepsy is the most common focal seizure disorder in adults, with mesial temporal sclerosis being the most common pathological entity. The overall rate of seizure freedom following temporal lobectomy for epilepsy has been reported to be between 74 and 82% [29]. The best outcome is seen in patients with temporal neoplasms (88–92%), followed by patients with gliosis (86%) and mesial temporal sclerosis (70%). with poorer control seen in patients with cortical dysplasia [29]. There are a number of different surgical approaches for the management of temporal-lobe epilepsy. One of the controversies is whether to perform temporal lobectomy or selective amygdalo hippocampectomy. Schramm *et al.* reviewed 53 papers on temporal-lobe epilepsy surgery and concluded that seizure outcome was not significantly different between the two groups, but that neuropsychological outcome was significantly improved in patients who underwent a selective amygdalo hippocampectomy compared with lobectomy in the adult population [30]. For lesional temporal-lobe epilepsy, the aim should be to completely resect the lesion. There is still some controversy regarding whether the mesial structures should be resected in cases that abut but do not involve the hippocampus or amygdala. Our approach has been to perform a temporal lesionectomy as the first procedure. If seizures persist, and are found on follow-up to be caused by the mesial structures, then repeat procedure is occassionally performed to resect these structures.

Extratemporal resections

Most patients with extratemporal resections will have a period of invasive electrode recordings because the epileptogenic zone is often not as well defined as in temporal-lobe epilepsy. The outcome for extratemporal-lobe resections is in the region of 60% [31]. Predictors of success include a greater extent of surgical resection, structural pathology on MRI, and concordant structural and electrophysiological imaging. For patients with cortical dysplasia seizure freedom, outcomes are reported to be in the region of 40–70% and are inversely related to the length of follow-up [32].

Seizures emanating from the peri-rolandic area have historically precluded any type of surgical resection. Our experience is that resection of the rolandic cortex for intractable epilepsy is often possible [33]. However, this requires accurate mapping of regions of functional cortex with invasive recordings and a complete mapping of the epileptogenic zone. Intraoperative electrophysiology with direct cortical stimulation to localize motor function (FIGURE 7A) and assessment of phase reversal to identify the central sulcus is

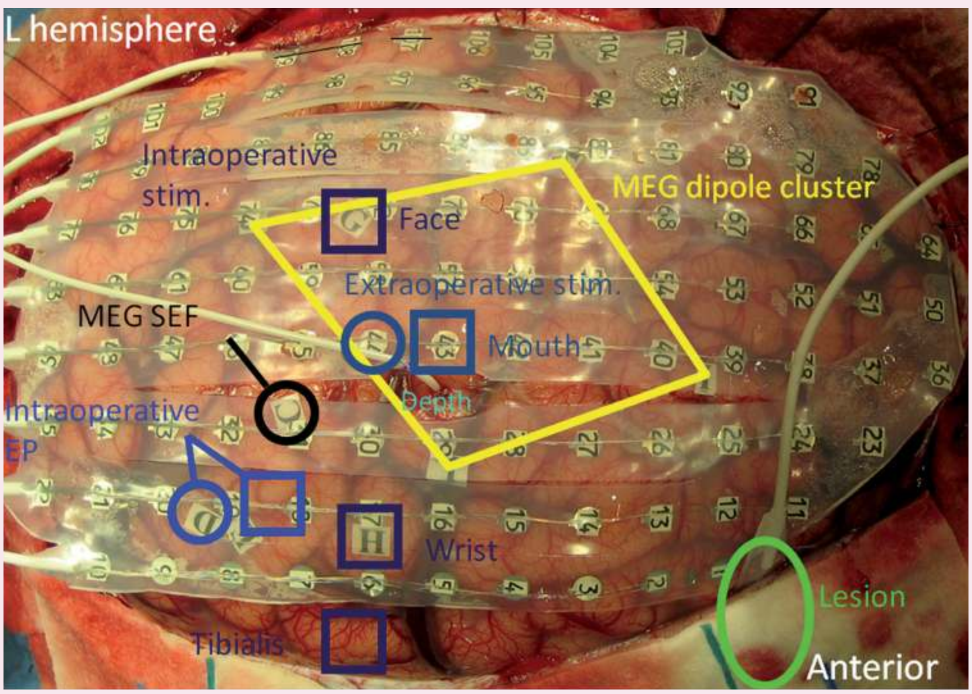

Figure 5. A typical intraoperative image showing a subdural grid and a depth electrode. The location of the MEG spike cluster is superimposed on the image (to help identify the interictal zone [yellow polygon]), the SEF (to help identify motor cortex [black circle]), the intraoperative location of motor hand function (light blue square) next to sensory hand (light blue circle), as measured looking for phase reversal using a strip of four electrodes, and the location of hand, foot and face function based on postgrid insertion stimulation (dark blue squares). The lesion was located in the parafalcine area. Two subdural strips in the fronto-central region are also noted.
EP: Evoked potentials; L: Left; MEG: Magnetoencephalography; SEF: Somatosensory-evoked field; Stim.: Stimulation.

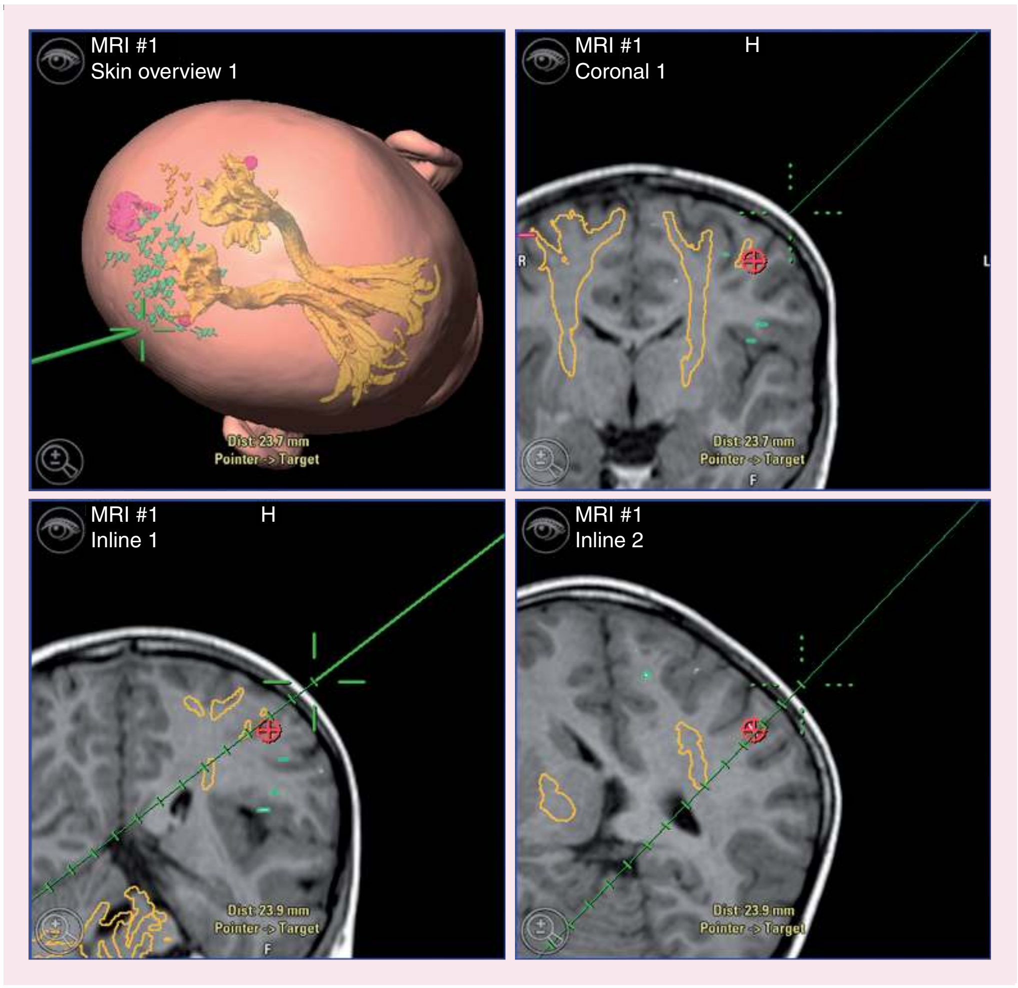

Figure 6. Image guidance using BrainLAB (BrainLAB Inc., IL, USA). The MRI scan has been fused with diffusion tensor imaging and magnetoencephalography. The lesion has been highlighted using thresholding tools and is colored pink, somatosensory-evoked field is represented by the red circle with cross hairs and the magnetoencephalography dipoles are represented in green.

an essential adjunct to localize the primary motor cortex using a train-of-five stimulation technique (Figure 7B). If eloquent cortex is involved in the epileptogenic zone and surgical resection is recommended to control severe, life-threatening seizures, then extensive counseling is performed in advance of these procedures [33]. Compared with adults, younger children seem to have a much greater capacity to recover from resection of the eloquent cortex, although complete recovery of fine motor function, particularly of the hand, is unusual.

Multilobar disconnections & hemispherectomy

Disconnections, as opposed to resections, are frequently performed in patients with epileptogenic zones spanning several lobes in the same hemisphere. Pathologies that warrant such procedures include Rasmussen's encephalitis, hemimegalencephaly, central neonatal infarction, Sturge–Weber syndrome (Figure 8) and hemispheric cortical dysplasia. In our center, we typically performed peri-insular hemispherotomies.

Outcome, in terms of seizure freedom, has been reported to be 56.5% in patients with cortical dysplasia, 77% in patients with Rasmussen's encephalitis, 82.1% in patients with Sturge–Weber syndrome, 76% in patients with vascular insults and 77.3% in patients with hemiatrophy [34]. Patients under the age of 3 years who are undergoing hemispherectomy recover from their hemiparesis quite readily and are usually community ambulators. Fine finger movements, as controlled by the corticospinal tract, improve less quickly, if at all. The incidence of hydrocephalus following hemispherectomy range from 0 to 28%, with mortality rates of 0–5.7%. Blood loss and superficial cerebral hemosiderosis have been reduced significantly when utilizing disconnective procedures, as opposed to hemidecortications or anatomic hemispherectomy.

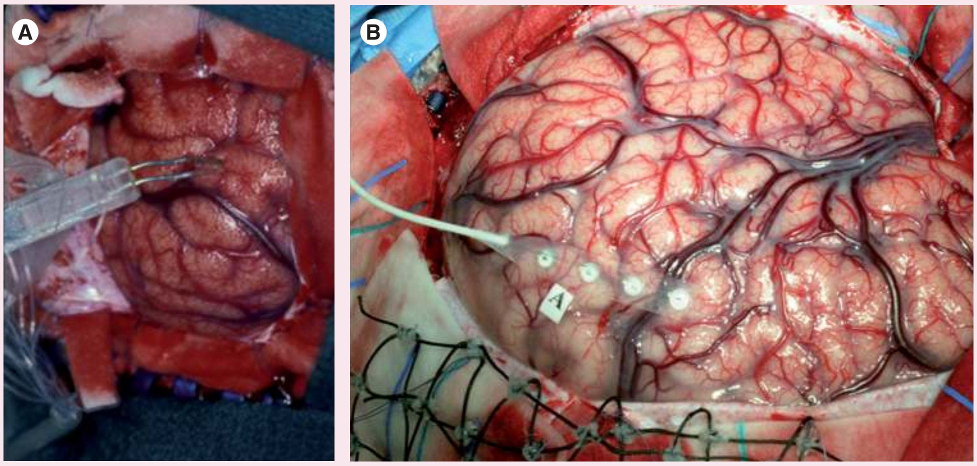

Figure 7. Intraoperative image demonstrating the method by which the primary motor cortex is identified. (A) Direct cortical stimulation and **(B)** the phase-reversal techniques are employed.

Nonresective surgical procedures

Many patients are not candidates for surgical resection as the epileptogenic zone is located in both hemispheres or because the epileptogenic zone is part of eloquent cortex that is construed as indispensable for quality of life. Three palliative procedures have been commonly employed. They include VNS, corpus callosotomy and multiple subpial transections (MSTs).

Vagal-nerve stimulation

It is not clearly understood how VNS reduces seizure frequency and severity. Theories include increased activation of inhibitory neurons, thus, leading to hyperpolarization of large areas of cortex, increasing the seizure threshold. The locus coeruleus and the dorsal raphe nucleus are believed to be the anatomical locations of excitation [35]. There is now good evidence supporting the use of VNS for intractable epilepsy. A meta-analysis has demonstrated a 44.1% reduction in seizure frequency with a follow-up of more than 3 years [36]. These positive effects are frequently sustained over time. Figure 9 shows the stages of insertion of a VNS.

Corpus callosotomy

Corpus callosotomy blocks interhemispheric spread of secondary generalized seizures. It is particularly useful in patients with atonic seizures but has also been used for patients with tonic–clonic and tonic seizures. It is not seen as a curative procedure but more as a technique to reduce seizure frequency and severity. Figure 10 shows the pro- and postoperative mid sagittal MRI scan of a patient who has had a corpus callosotomy.

Satisfactory seizure control (>50% reduction in seizures) has been reported to be between 66.2 and 79.5% [37]. Operative complications include disconnection syndromes, which tend to be more common in older patients, and pericallosal artery injuries, which lead to distal ischemia.

Extent of callosotomy has been studied. There is evidence that sectioning of the anterior callosum only increases the likelihood of seizures and a lower IQ; however, the neuropsychological sequellae in the form of disconnection syndromes is lower [37]. It is felt that preservation of the splenium and a younger age at operation reduces the incidence of disconnection syndromes [38].

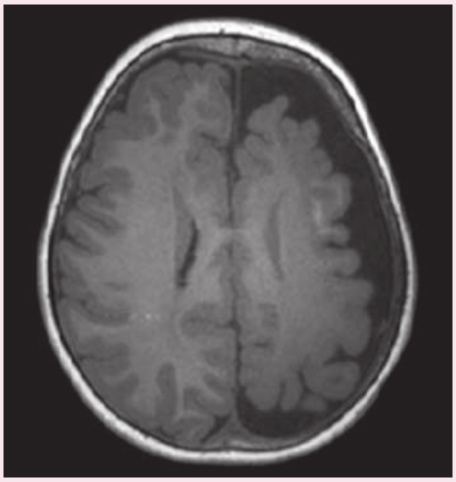

Figure 8. Preoperative MRI scan of a patient with Sturge–Weber syndrome who underwent a functional hemispherectomy. Note the cortical atrophy and subcortical calcification. The patient was having 80 seizures per day but became seizure free on anticonvulsants following hemispherectomy.

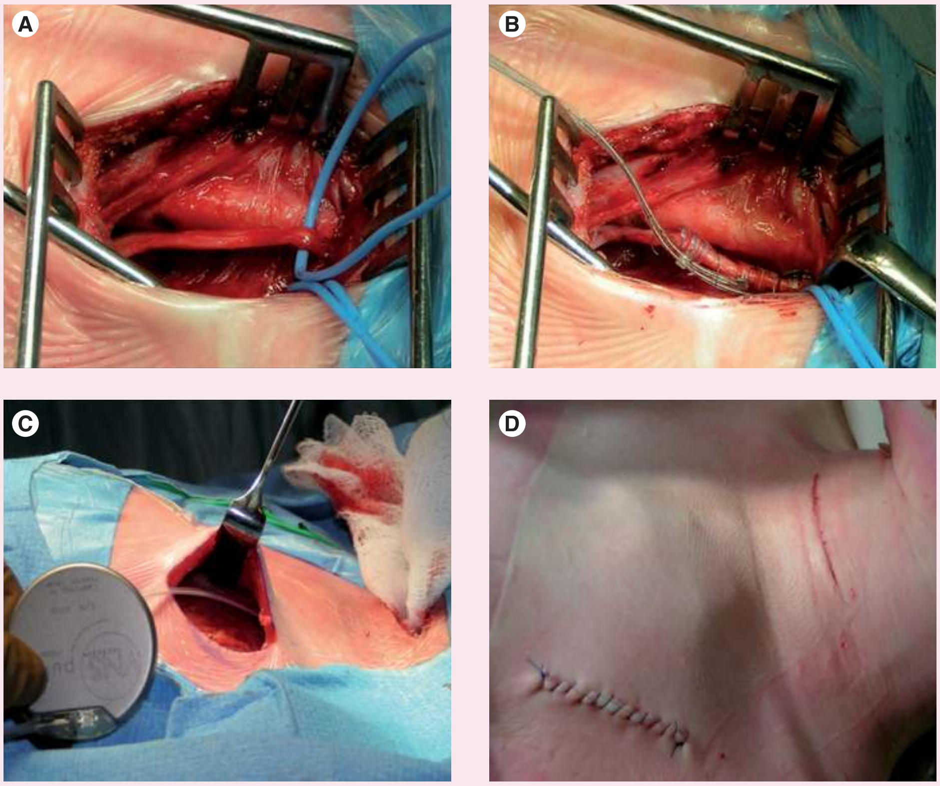

Figure 9. Intraoperative images during insertion of a vagal-nerve stimulator. (A) The left vagus nerve is identified and isolated from within the carotid sheath, **(B)** the coils of the electrode are wound around the nerve and **(C)** the battery is placed in an infraclavicular subcutaneous pocket; **(D)** the postoperative incisions are shown.

Multiple subpial transections

The rationale for MSTs is that functional cortical units are orientated vertically whereas depolarization from the epileptogenic zone traverses horizontally. Thus, a vertically placed incision will stop the spread of epileptogenic spikes whilst preserving the functional unit. Indications for its use include seizures arising from eloquent cortex (Figure 11). A meta-analysis has demonstrated that MST has a long-term seizure-free outcome of only 16% [39]. MST has been advocated for Landau–Kleffner syndrome, a condition characterized by acquired epileptic aphasia or verbal auditory agnosia. There is some evidence that communication skills and behavior improves following surgery [40].

Future perspective

Cortical & deep-brain stimulation

Several studies have examined the effects of direct neurostimulation of cortical and subcortical structures on epilepsy control. Targets that are being evaluated include stimulation of the cerebellum [41], the thalamus [42], the hippocampus and direct stimulation of the cortex. To date, none of these studies has unequivocally demonstrated significant reduction in seizure frequency. The Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy (SANTE) trial of deep-brain stimulation in epilepsy was a multicenter double-blind study that recruited 110 patients [43]. Bilateral stimulation of the anterior nuclei of the thalamus significantly reduced seizure frequency and severity compared with controls, and the benefit persisted for the 2-year duration of the study.

Responsive neurostimulation is an emerging technology whereby cortical stimulation is delivered in response to the patient's individual seizure. This has been made possible owing to the advent of automated algorithms for detection of epileptiform activity [44]. A prospective controlled multicenter study is currently underway to examine this technique in more detail [101].

Radiosurgery

Radiosurgery has been attempted for mesial temporal epilepsy with seizure-free outcomes of 38% [45]. For hypothalamic hamartomas, the seizure-freedom outcome was 37% with a decrease in seizure frequency of a further 22% [46].

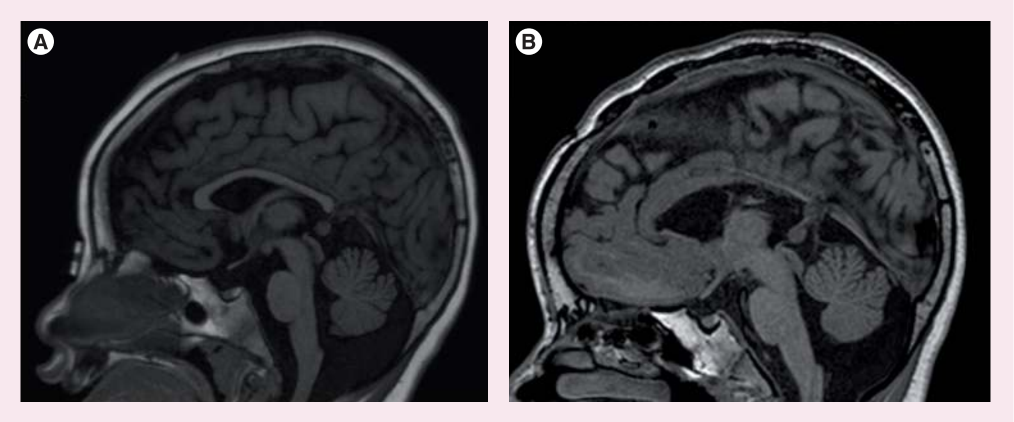

Figure 10. T_1-weighted mid-sagittal MRI scan showing a complete corpus callosotomy. **(A)** Pre- and **(B)** postoperative images demonstrate the completeness of the callosotomy, and the patient had marked improvement in his atonic seizures following this procedure.

Conclusion

Improved electrophysiological investigations and neuroimaging techniques have transformed the management of patients with epilepsy and identified more cases amenable to resective, and potentially curative, surgery. Intraoperative image guidance, neuromonitoring and improved functional localization have reduced the risks of postresection deficits.

Outcome analysis following surgical procedures, including seizure and functional outcomes, are becoming more important to quantify, and are particularly pertinent when counseling patients prior to surgery. Responsive neurostimulation has the potential to offer an elegant method of stopping seizures directly, but will need further study.

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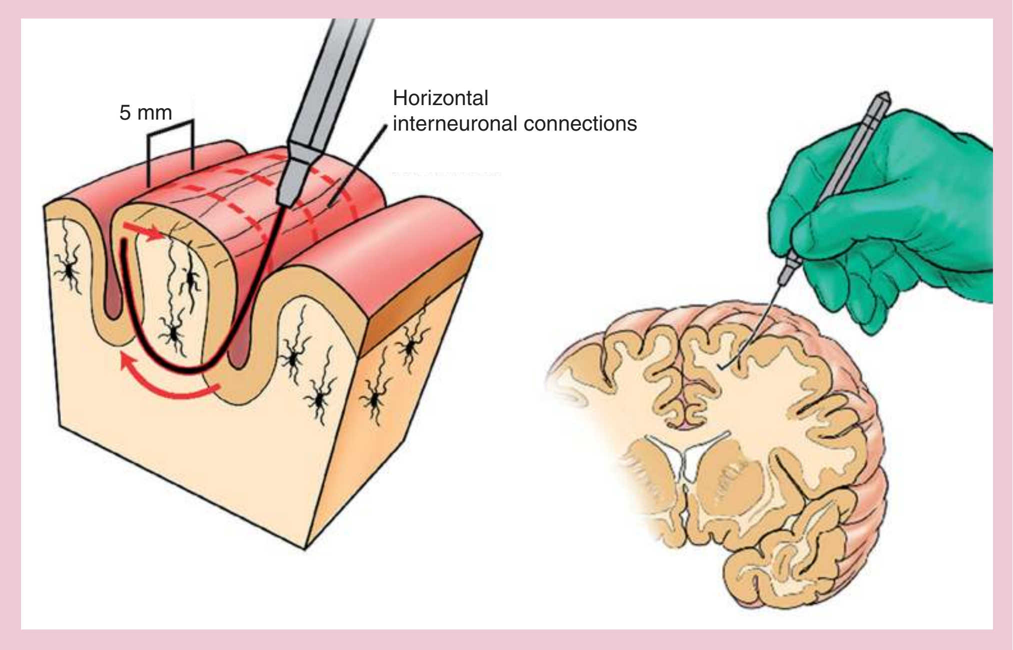

Figure 11. The principles of performing a subpial transaction. The instrument is inserted in the subpial plane and passed along a gyrus, disrupting horizontal interneural connections but preserving the vertical functional unit.

Executive summary

- Selecting candidates for epilepsy surgery is complicated and requires a great deal of multidisciplinary input.
- Magnetoencephalography has emerged as a useful adjunct in identification of the epileptogenic zone.
- 3-Tesla MRI assists in identification of subtle cortical abnormalities.
- Functional MRI, magnetoencephalography and neuropsychology are used for identification of the eloquent cortex.
- Invasive electrode recordings are required when the information from preoperative investigations does not clearly localize the epileptogenic zone and its association with the functional cortex.
- Neuronavigation and image fusion improve accuracy during invasive electrode recordings and during resective surgery.
- Neurostimulation has demonstrated promise in the treatment of epilepsy.

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