Advances in intracranial monitoring

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Intracranial monitoring using electroencephalography (IC-EEG) continues to play a critical role in the assessment of patients with medically intractable localization-related epilepsy. There has been minimal change in grid or electrode design in the last 15–20 years, and the surgical approaches for implantation are unchanged. Intracranial monitoring using EEG allows detailed definition of the region of ictal onset and defines the epileptogenic zone, particularly with regard to adjacent potentially eloquent tissue. Recent developments of IC-EEG include the coregistration of functional imaging data such as magnetoencephalography to the frameless navigation systems. Despite significant inherent limitations that are often overlooked, IC-EEG remains the gold standard for localization of the epileptogenic cortex. Intracranial electrodes take a variety of different forms and may be placed either in the subdural (subdural strips and grids, depth electrodes) or extradural spaces (sphenoidal, peg, and epidural electrodes). Each form has its own advantages and shortcomings but extensive subdural implantation of electrodes is most common and is most comprehensively discussed. The indications for intracranial electrodes are reviewed. (DOI: 10.3171/FOC/2008/25/9/E18)

Key Words • epilepsy surgery • intracranial monitoring • subdural grids • subdural strip electrodes

Essentials of Intracranial Monitoring for Epilepsy

Intracranial EEG monitoring plays a critical role in the assessment of patients with medically refractory partial epilepsy (or localization-related epilepsy).11,12,19,23,41 Controversies exist about the limits of IC-EEG, and the utilization of invasive monitoring differs significantly between centers, countries, and even geographic regions within a country.4,18 However, from a practical perspective, most large experienced tertiary centers apply similar principles in determining a patient’s candidacy for intracranial electrode placement, monitoring, and use. Due to advances in noninvasive imaging, intracranial electrodes are used in ~25–40% of surgical cases in most large epilepsy centers.12 Their use is higher in pediatric surgical patient series due to the propensity of children to harbor neocortical epilepsy and the inherent difficulties of localizing neocortical epilepsy noninvasively.15,17,18,22,26 Intracranial electrodes remain, at present, the gold standard for delineating the epileptogenic tissue that can be considered the region of the brain from which arises the abnormal electrical discharges that when propagated yield the clinically important seizure pattern.22,30,57 From a surgical perspective this may be considered the region of tissue that must be removed to ameliorate seizure activity. The decision whether or not to place electrodes in a patient, as well as the location and configuration of electrodes placed, arises from an organized review of all noninvasive studies in a patient at a multidisciplinary surgical planning conference. Seizure symptomatology, scalp EEG findings, and MR imaging results are uniform components of an evaluation, and noninvasive functional localization studies such as ictal-SPECT, subtraction ictal-SPECT coregistered to MR imaging, MEG, and FDG-PET may be added all or in part. The relative contribution and role for these studies has recently been reviewed.27,55

Intracranial grid monitoring is also critically important in defining eloquent function in the adjacent brain. Intracranial electrodes are typically placed during large craniotomies.15,40 Extensive exposure of the brain via craniotomy allows subdural grids to be placed directly over the convexity of the brain (Fig. 1). Under a continuous wash of lactated Ringer irrigation, smaller strip electrodes may be gently slid into regions not directly exposed by craniotomy that require sampling. As a result, extensive coverage of the neocortex can be achieved (Fig. 2). The decision of exactly which grids, strips, and depths to use arises from a working relationship between the epileptologist and the epilepsy neurosurgeon. The epileptologist determines the optimum extent of coverage based on noninvasive localization studies and makes recommendations and requests about the grid and depth electrodes that are used. The neurosurgeon...
Sphenoidal electrodes are less invasive if, however, there is discordance.

Depth electrodes are placed into the parenchyma of the brain and may be used alone or in conjunction with extensive subdural grid coverage. They may be placed using conventional frame-based stereotactic techniques (most commonly from an occipitotemporal approach to longitudinally sample the medial temporal lobe) or using frameless stereotactic techniques.

After using monitoring and stimulation to determine eloquence in the adjacent brain, a grid map is developed that becomes the road map for the secondary operation. At the time of the secondary operation the grid is exposed through the same surgical corridor and the epileptogenic region is defined, exposed, isolated, and resected while adjacent tissue is protected. Occasionally alternative techniques such as multiple subpial transections or subpial aspiration are undertaken if the epileptogenic region is also eloquent.

Intracranial Electrode Placement Indications

Temporal Lobe Epilepsy. Temporal lobe epilepsy is the most common form of epilepsy that is treated surgically.

The utilization of intracranial electrodes will vary between centers according to the experience of the surgeons with both noninvasive techniques for localization and their experience and confidence with intracranial recordings. For cases in which there is a clear MR imaging abnormality such as hippocampal sclerosis or atrophy, and there is concordant symptomatology for partial complex seizures, and good lateralization on scalp EEG, intracranial recording is not necessary. If, however, there is discordance in data such that EEG suggests unilateral onset but MR imaging reveals structural changes bilaterally, then monitoring both temporal lobes invasively appears to be warranted. Similarly if EEG localizes poorly and non-specifically but MR imaging shows unilateral structural changes (atrophy or sclerosis), then monitoring with invasive electrodes is likely to be warranted. If only the symptomatic lobe is confirmed by MR imaging and EEG, then it is very unlikely that intracranial recordings will significantly contribute to surgical decision-making.

The results of detailed neuropsychological studies may also affect the decision whether to use intracranial electrodes in TLE. There are two critical roles for neuropsychological tests in TLE. The first role is to aid in the determination as to whether ictal onset is bilateral or unilateral. This is particularly important when imaging results are normal. The second important role is to aid in the determination of whether temporal lobe involvement is primarily lateral (neocortical) or medial (limbic). A large verbal memory deficit in dominant-lobe TLE or a substantial disparity in verbal and nonverbal memory may suggest medial temporal lobe involvement and affect the extent of electrode placement, or may suggest a greater role for depth electrodes, which are better suited to monitor medial structures. In contrast, less verbal memory impairment may suggest a greater involvement of neocortical structures. This.
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finding may warrant greater exploration using extensive grid and strip electrodes but may spare the patient the need for a large medial temporal resection and its attendant risk for verbal memory insult.

Additional contributions of neuropsychological assessment may include evaluation of coping (with the stresses of surgery and recovery) and evaluation of changes in abilities after surgery, yet these issues do not play as direct a role in the decision-making process surrounding the use of intracranial electrodes. Intracranial monitoring can facilitate identification of good candidates for a temporal lobe resection that spares potentially eloquent structures such as the hippocampus and parahippocampal gyrus. This issue is particularly important for dominant-hemisphere nonlesional TLE in patients with relatively preserved memory function preoperatively, because such patients are at greatest risk for postoperative verbal memory decline.

An important consideration in the surgical approach to temporal lobe seizures is whether the seizures are characteristic mesial temporal lobe seizures or whether they arise from the temporal neocortex. A propensity to lateral or midtemporal spikes on EEG or symptoms consisting of a complex visual or auditory aura in the symptomatology may be indicators of temporal neocortical disease. Magnetic resonance imaging findings supporting a temporal neocortical origin may include disordered gray-white architecture or focal areas of visible dysplasia. In such cases, invasive temporal lobe monitoring using small subdural grids and strips is important in confirming neocortical disease as well as for defining a rational extent of resection.

Extratemporal Epilepsy. If localization-related seizures arise outside of the temporal region, then subdural grid monitoring is almost always needed in the absence of a clearly demonstrable lesion on MR imaging with concordant EEG. Even some lesional cases will be evaluated with intracranial electrodes because it has been clearly demonstrated that the region of epileptogenesis may extend well beyond the focal area of abnormality noted on MR imaging. Focal dysplasias and hamartomatous tumors such as dysembryoplastic neuroepithelial tumors and gangliogliomas are particularly inviting for more comprehensive evaluation, whereas tubers, hamartomas, and gliomas may be reasonably treated using a lesionectomy followed by a wait-and-see approach. A more extended discussion of specific indications in intracranial electrodes is available in several recent reviews.

Limitations and Risks of Intracranial Electrodes

Although intracranial grids have provided an unparalleled opportunity to study the anatomy of the epileptic human brain, there are significant limitations and risks associated with their use. These limitations and risks include cost, patient discomfort, patient immobility, risks for infection and bleeding, aseptic meningitis, limited time in which to monitor the patient, need for staged neurosurgical interventions, and some inherent limitations as to the localization of the epileptogenic cortex. Twenty percent of the estimated 2 million Americans with epilepsy have medically intractable disease, and these patients account for more than 75% of the overall costs of epilepsy diagnosis and treatment. Patient discomfort can be considerable due to the size of the cranial incisions and the need for extensive muscle dissection during electrode implantation. Exiting wires can become caught if the patient moves and place painful traction directly on the dura.

Proper cortical sampling requires extensive placement of electrodes across the cortex, but large or confluent veins or dural venous lakes may present a surgical obstruction to proper and desired placement. The tearing of surface draining veins and consequent risk of severe hemorrhage or

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<th>Author &amp; Year</th>
<th>Center Location</th>
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<th>% w/EDH</th>
<th>% w/SDH</th>
<th>% w/TND</th>
<th>% w/CSF Leak</th>
<th>% Rate of Infection</th>
<th>% w/Permanent Death/Disability</th>
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*Asan = Asan Medical Center; CHOP = Children’s Hospital of Philadelphia; CSF = cerebrospinal fluid; EDH = epidural hematoma; HSC = Hospital for Sick Children; MCG = Medical College of Georgia; ND = not discussed; SDH = subdural hematoma; TND = transient neurological deficit.
venous infarction is perhaps the most serious acute complication arising from use of subdural electrodes. Hemorrhages, however, can also arise in a more delayed and insidious fashion and are highly variable in their degree of clinical relevance. Table 1 outlines the reported incidences of infectious and hemorrhagic complications from 8 large case series reported within the last 15 years.

It is immediately evident that the incidence of complications varies considerably across these reports. There are a number of potential reasons for this variability. First, almost all of the series are retrospectively reported, which is a methodology notoriously inaccurate for its sensitivity. For example, some centers may perform postoperative CT scans at a greater frequency than others. Such a center would likely demonstrate greater sensitivity in the detection of asymptomatic hemorrhages. Other centers might routinely obtain cultures at the time intracranial electrodes are inserted. These centers might detect a higher rate of infection than those who utilize signs and symptoms of clinical infection to make the diagnosis. Furthermore, the number of patients at even the largest centers is small, which means that a small number of events can significantly impact the overall incidence rate. Several broad conclusions are evident, however. The incidence of hemorrhage in recent case series ranges from 0 to 14% and the incidence of infection ranges from 0 to 12%. As such, it appears reasonable to conclude that serious, potentially life-threatening hemorrhagic complications can and do occur, albeit at a low rate. Investigators at multiple centers allude to a learning curve and the importance of meticulous surgical technique and patient observation postoperatively to minimize the impact of these complications. Results are mixed as to whether prolonged monitoring and/or more electrodes are associated with higher risks of infection.16,24,40,56.

Perhaps the primary limitation to IC-EEG is that surface-based grid and strip electrodes best sample the surface cortex immediately on the convexity.29 Due to extensive sulci, approximately 60% of the cortex is below the surface. Deep regions of epileptogenic tissue may be difficult to localize because of the rapid spread of abnormal discharges. Due to the abundance of collateral projections found in neocortical tissue there is nearly immediate wide distribution of electrical activity from a deep epileptogenic region. The proper localization of such a focus may prove very challenging or impossible when only surface electrodes (subdural grids) are utilized, because the grid may detect a spread pattern rather than the primary region of ictal onset. Grid limitation in localizing epilepsy is further considered in later segments of this paper.

**Recent Advances, Issues, and Controversies in the Use of Intracranial Electrodes**

There have been essentially no substantive technical advances in intracranial electrode design in the last 10–15 years that have achieved widespread utilization in the epilepsy surgery community. Subdural grids are made of thin sheets of Silastic (medical grade silicone sheets) that have imbedded platinum electrodes at 1 cm intervals. Platinum is the preferred agent because it is the best-known conductor of electricity. These grids are available commercially from several manufacturers in North America (Ad-Tech Medical, PMT, and Integra) and a number of epilepsy centers use grids made in their own labs.2 Commercially available subdural grids come in a variety of shapes and configurations (Fig. 4). The largest widely available grid is an 8 × 8 configuration with the electrodes 1 cm apart. Other commonly used grid sizes are 4 × 8, 4 × 5, and 2 × 6. Strip electrodes typically employ a single row of electrodes with a variable number of contacts; examples include 1 × 4, 1 × 6, and 1 × 8 layouts. Other configurations include T-shaped grids and tapered grids (which are advocated by some groups for lateral temporal coverage). Most centers use commercially available grids because they have excellent performance profiles, are approved by the US Food and Drug Administration, and spare the infrastructure and resources necessary for grid manufacture on site. However, Backensto2 demonstrated a 62% cost savings when using grids created in-house compared with a commercially available product. They also cited the capability to individually customize grid design and configuration for an individual patient as a strong rationale supporting in-house manufacturing of subdural grids. Our group has utilized both in-house and commercially available products and have found both quite satisfactory. The ultimate choice of grid materials used at our center depends on surgeon preference.

Extradural electrode designs incorporate ball electrodes, bolts, pegs, and strips.38 Ross and colleagues38 described a percutaneous epidural screw electrode and Barnett et al.41 described a new peg-shaped electrode in a publication from 1990. There has otherwise been little technical change in the past 15 years. The primary reason why little effort has gone into electrode refinement appears to be that current electrodes provide good results and great strides have been made in amplifiers and EEG data acquisition systems, such that the overall process of IC-EEG is quite effective. Depth electrodes, sphenoidal electrodes, and foramen ovale electrodes are similarly available and have varied little recently in technical design from those used 20 years ago. Ives21 from the University of Western Ontario recently described a new silver/silver/chloride sphenoidal electrode that can be placed percutaneously in the subdermal space.
Evolution of Surgical Approaches: Technical and Conceptual Advances

The overwhelming majority of recent publications addressing surgical approaches for intracranial electrodes address the burgeoning field of deep brain stimulation rather than epilepsy. However, two major changes in surgical technique can be observed in the last 10–15 years. One change reflects technological advancement and the other represents an evolution in the surgical conceptual approach to a unique clinical problem. The major recent technological advance in the surgical approach to electrode placement involves the incorporation of frameless navigation systems into the surgical protocol. The second advance involves the role of multistaged epilepsy surgery.

Frameless navigation systems represent a real and significant advance in neurosurgery because they provide the surgeon real-time feedback and anatomical confirmation. Utilizing image fusion techniques, several different investigative groups have coregistered noninvasive functional imaging data such as MEG data or ictal-SPECT data onto the frameless platform. The practical result of this coregistration is that the surgeon receives real-time intraoperative feedback not only on anatomical information but also on the regions of the cortex that are implicated in epileptogenesis. This feedback can ensure that grids are optimally placed over the regions of brain most strongly implicated by noninvasive imaging and localization techniques (Fig. 5).

Otsubo and colleagues¹ from the Hospital for Sick Children in Toronto, Canada first reported the utility of frameless stereotaxy with scalp EEG electrodes on 3D CT scans in 1995. Eight patients who underwent epilepsy surgery were evaluated. Standardized scalp electrode placements using the 10–20 standardized system were utilized and several patients also had sphenoidal electrodes placed. Three-dimensional CT scans were obtained and coregistered successfully with the scalp and sphenoidal electrodes. This process enabled colocalization of EEG anomalies with underlying brain anatomy and formed the conceptual framework for later studies from this group.

In 2004, Holowka and associates² reported the utility of 3D reconstructed magnetic source images superimposed on the MR imaging-based ISG Wand Neuronavigation System in a series of 16 children undergoing epilepsy surgery. Interictal MEG data was superimposed on the ISG protocol MR imaging, resulting in real-time intraoperative capability to display dipole clusters on the exposed brain. Magnetoencephalography spike clusters were correlated with IC-EEG findings from subdural grids, and these results guided resection. Follow-up studies by Grondin et al.³ and Ochi and Otsubo⁴ extended the preliminary observations of the initial report and provided further experience and evidence to support the utility of these techniques.

Murphy and associates in 2004⁵ reported the superiority of frameless navigation systems compared with conventional frame-based navigation systems for the placement of depth electrodes in a series of 13 patients undergoing depth electrode implantation (5 also had subdural grids placed concomitantly). These authors found that frameless navigation systems provided a useful projection of the planned trajectory that enabled them to avoid high-risk areas for hemorrhage such as the sylvian fissure. They also found that the frameless system eliminated the obstruction frequently present in conventional frame-based stereotactic systems. They found this system particularly useful when simultaneously placing a subdural grid.

The Comprehensive Epilepsy Surgery Service at the University of Alabama at Birmingham has utilized MEG-guided grid placement since 2003 in both adults and children. We have used both StealthStation image guidance (Sofamor Danek/Medtronic) and Brain Lab VectorVision (BrainLAB Corp.) systems and found them to be equally effective (Fig. 6). We concur with the conclusions of the Toronto group that these techniques are useful in the placement of the grids (to avoid edge-of-grid phenomena) as well as in the interpretation of the IC-EEG and planning of the resection. We favor using the EEG findings and MEG findings cooperatively to optimize the region of resection to include areas of tightly clustered dipoles and regions of abnormal ictal EEG activity (Fig. 7).

Effect of Advances in Noninvasive Imaging: Limitations to Using IC-EEG as the Gold Standard

As detailed above, the use of intracranial electrodes still represents the gold standard in localization of epileptogenic tissue. Yet there are substantial limitations to utilizing IC-EEG as the gold standard. Knowlton and colleagues⁶ have elucidated these shortcomings in a pair of reports emanating from a large prospective 5-year trial that sought to collect observational data to assess the role of MEG, FDG-PET, and ictal-SPECT in epilepsy surgery candidates. In this prospective trial, 265 patients were evaluated and 169 patients met the criteria of medically intractable epilepsy with nonlocalizing MR imaging findings or ambiguous EEG-MR imaging correlation. Patients were studied using conventional 1.5T (or 3T) MR imaging and scalp video EEG as well as a variable combination of MEG, ictal-SPECT, and FDG-PET. The patient series was large and broadly selected, which potentially increases the applica-
bility of the results. Sensitivity, specificity, and positive predictive value were predicted for each imaging test in terms of its capacity for sublobar localization using IC-EEG. Several important findings emerged from this study. Magnetic source imaging consistently showed sensitivity, specificity, and positive predictive values higher than FDG-PET or ictal-SPECT. The greatest sensitivity was demonstrated when FDG-PET findings were combined with MEG values. Yet the most important conclusion emphasized by the authors pertained to the limitation of utilizing IC-EEG as the gold standard for localization. In a significant number of cases, the imaging test ultimately proved correct in localization but was considered a false negative result because of lack of concordance with IC-EEG. Seventy-two patients had seizures recorded with IC-EEG, yet the seizures in 17% of the patients could not be localized using implanted electrodes. This percentage is high for a gold standard, and most seizures were believed to arise as a result of an ictal focus deep within a sulcus. Electroencephalography clues to this disparity included nonfocal desynchronization and apparent attenuation. When assessed against surgical outcomes, imaging specificity was noted to rise for all modalities. An accompanying paper that assesses the same patient group from the perspective of surgical outcome draws similar conclusions. The aim of the study was to determine whether at this time and development any of the commonly applied functional imaging tests for localization could replace or augment IC-EEG. The authors concluded that modest concordance rates between noninvasive imaging studies preclude the replacement of IC-EEG, and that noninvasive studies have a very important function in augmenting IC-EEG. The authors cited cases of nonlocalizing IC-EEG in patients who became seizure-free following resection based upon imaging with attenuated or desynchronized EEG. Finally, each of the studies was found to make an independent contribution to localization and surgical decision making if conclusively positive (unequivocally localized).

Collectively this information emphasizes the limitations of IC-EEG as the gold standard for localization. Perhaps more importantly it represents an initial and important step in the development of the capability to recognize where noninvasive studies may augment and ultimately reduce the need for IC-EEG. As technological progress allows reduction in signal-to-noise ratios, a better understanding of MEG spike characteristics, and better estimates of the putative onset of ictal activity, it is likely that these less invasive, less costly, and less risk-inherent alternatives will gradually eclipse the preeminence currently held by intracranial electrodes in the localization of elusive epilepsy.

Conclusions

The potential role for meaningful surgical intervention for the treatment of medically refractory, localization-related epilepsy has never been as great as it is now. Yet the future holds greater promise. It appears likely that there will be continued refinement in intracranial electrode design and implementation. With Bluetooth and lay person satellite navigation as common as they currently are, it does not seem unbelievable to imagine wireless grids in the fore-
seemable future. Perhaps these intracranial electrodes could be implanted for a prolonged duration of monitoring that may even span into the outpatient realm. Advances in nanotechnology are likely to substantially refine the precision of intracranial monitoring and may ultimately allow prolonged and highly focal monitoring. At present there is minimal reported application of nanotechnology to the field of invasive monitoring. It appears virtually certain that noninvasive localization imaging will become more refined and the roles of noninvasive tests and intracranial electrodes will continue to evolve. It appears most likely that their relationship will remain an augmentative and cooperative one for the immediate future.

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Disclaimer

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References

34. Minkin K, Klein O, Mancini J, Lena G: Surgical strategies and
52. Weiner HL: Tuberous sclerosis and multiple tubers: localizing the epileptogenic zone. Epilepsia 45 (4 Suppl):41–42, 2004

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