Magnetoencephalography-directed surgery in patients with neocortical epilepsy

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Object. Magnetoencephalography (MEG) and magnetic source (MS) imaging are techniques that have been increasingly used for preoperative localization of epileptogenic foci and areas of eloquent cortex. The use of MEG examinations must be carefully balanced against the high cost and technological investments required to perform these studies, particularly when less expensive alternative localization methods are available. To help elucidate the value of MEG, the authors have critically reviewed their experience with whole-head MEG in the case management of patients undergoing epilepsy surgery.

Methods. The authors identified 23 patients with suspected focal epilepsy who underwent whole-head MEG and MS imaging at Huntington Memorial Hospital and, subsequently, underwent invasive intracranial electrode monitoring and electrocorticography (ECoG) to localize the zone of seizure origin for surgical resection. The results of the MS imaging were retrospectively stratified into three groups by the number of interictal spikes recorded during a 4-hour recording session: Class I (no spikes), Class II (≤ five spikes), and Class III (≥ six spikes). Class III was further subdivided according to the clustering density of the interictal spikes: Class IIIA represents a mean distance between interictal spikes of 4 mm or greater (that is, diffusely clustered) and Class IIIB represents a mean distance between interictal spikes of less than 4 mm (that is, densely clustered). The authors analyzed these groups to determine to what extent the results of MS imaging correlated with the ECoG-determined zone of seizure origin. In addition, they assessed whether the MS imaging study provided critical localization data and correlated with surgical outcome following resection. A statistical analysis of these correlations was also performed.

Of the 40 patients studied, 23 underwent invasive monitoring, including 13 with neocortical epilepsy, four with mesial temporal lobe epilepsy, and six with suspected neocortical epilepsy that could not be clearly localized by ECoG. Depth electrodes were used in nine cases, subdural grids in nine cases, depth electrodes followed by subdural grids and strips in four cases, and intraoperative ECoG in one case. Electrocorticography was able to localize the zone of seizure origin in 16 (70%) of 23 cases. In 11 (69%) of the 16 cases in which ECoG was able to localize the zone of seizure origin, the interictal spikes on the MS images were classified as Class IIIB (densely clustered) and regionally correlated to the MS imaging–determined localization in all cases (that is, the same lobe). In contrast, no Class IIIB cases were identified when ECoG was unable to localize the zone of seizure origin. This difference showed a trend toward, but did not achieve, statistical significance (p < 0.23), presumably because of the relatively small number of cases available for analysis. In three cases (all Class IIIB), MS imaging was used to guide invasive electrodes to locations that otherwise would not have been targeted and provided unique localization data, not evident from other imaging modalities, that strongly influenced the surgical management of the patient. The classification of findings on MS images into subgroups and subsequent statistical analysis generated a model that predicted that Class IIIB MS imaging data are likely to provide reliable information to guide surgical placement of electrodes, but all other data groups do not provide localization information that is reliable enough to guide surgical decision making.

Conclusions. Magnetic source imaging can provide unique localization information that is not available when other noninvasive methods are used. Magnetic source imaging appears most useful for cases of neocortical epilepsy. In particular, when an MS imaging study revealed six or more interictal spikes that were densely clustered in a single anatomical location, the MS image was highly correlated with the zone of seizure origin identified by ECoG. In these cases the MS imaging data may be useful to guide placement of intracranial electrodes.

KEY WORDS • magnetoencephalography • magnetic source imaging • electrocorticography • epilepsy • cortical mapping

Abbreviations used in this paper: ECoG = electrocorticography; EEG = electroencephalography; MEG = magnetoencephalography; MR = magnetic resonance; MS = magnetic source; PET = positron emission tomography; SPECT = single-photon emission computerized tomography.
emerged as the most superior method for localization. Evaluation often relies on the concordance of data between diagnostic modalities to direct the placement of intracranial grid electrodes. Electrocorticography through depth electrodes and/or subdural grid-and-strip electrodes remains the gold standard for localizing in patients with nonlesional neocortical epilepsy.

Magnetoencephalography was developed with the hope that it, too, might provide unique and nonredundant localization data. Because magnetic field strength is not significantly attenuated or dispersed by the skull and scalp, MEG, theoretically, can detect activity within the brain with better resolution than that provided by EEG. Magnetic source imaging is the term used to describe the imaging modality in which MEG-identified dipoles are coregistered with an MR image and then superimposed on the MR image to correlate dipole localization with anatomy. Because data obtained using MS imaging can be directly incorporated into surgical planning either by using visual inspection or by incorporation into a surgical navigation system, MS imaging has facilitated the utility of data provided by MEG as an intraoperative surgical adjunct. Despite the potential promise of MEG and MS imaging, this technique has remained relatively underused, largely due to the great expense and technical demands required to maintain and refine the associated technology.

Recently several groups reported a significant correlation between MS imaging–determined interictal spike dipoles and seizure foci in patients with epilepsy, which are principally based on surgical outcomes. These publications are the first population studies to suggest regional correlation of MS imaging with intracranial ECoG and the potential use of MS imaging for guiding the placement of intracranial electrodes. Because MEG typically measures interictal activity, whereas ECoG is used to localize both interictal and ictal activity, the true accuracy of MEG can only be ascertained if there is a precise correlation of seizure zone with MEG localization of interictal spikes in the individual patient. This is important because interictal activity may be seen in many locations, depending on when it is sampled, and may not directly correlate with seizure onset zone. Thus it is often uncertain whether an MEG study provided information that was essential to localize a seizure.

We now report our experience with whole-head MEG–MS imaging in the management of epilepsy. Careful correlation of the quality and location of MS imaging–determined interictal spike activity with invasive electrode ECoG-determined seizure onset was performed to identify those situations in which MS imaging provided valuable localization data and those situations in which it did not. Furthermore, we identified cases in which MS imaging provided nonredundant localization data crucial to surgical management.

Clinical Material and Methods

At our institution MEG–MS imaging is routinely used when noninvasive video-EEG inpatient telemetry, MR imaging, and PET scanning are insufficient to localize the seizure focus reliably in surgical candidates. All patients undergo an extensive workup before focal excisional surgery is considered, including neuropsychometric testing and an intracarotid sodium amyatal (Wada) procedure when indicated. The vast majority of these patients undergo additional noninvasive tests including SPECT scanning and MR spectroscopy. Magnetic source imaging is also routinely used to identify the primary sensorimotor cortex as a preoperative assessment for patients with intracranial mass lesions or neocortical epilepsy.

We prospectively studied 48 surgical candidates in whom MEG–MS imaging had been performed between October 1999 and January 2001. The study group consisted of 40 patients with localization-specific medically refractory epilepsy and eight patients with structural lesions in whom MS imaging was performed to determine the location of the primary sensorimotor cortex. For purposes of this report, analysis of cases was limited to 23 patients with medically intractable epilepsy who subsequently underwent intracranial ECoG monitoring. Before implantation, the type, number, and location of intracranial electrodes was determined by a consensus agreement between the neurologist (W.W.S.) and the neurosurgeon (A.N.M.), based on all available noninvasive data. In several cases in which the findings of MS imaging were judged to be compelling, this method was also used to focus the placement of electrodes. The extent of surgical resection was determined by data derived from the intracranial ECoG. The success of surgery was based on seizure outcome in the patient as well as the development of any new neurological deficits.

Methodology of MS Imaging

Patients underwent a conventional T1-weighted axial MR imaging. Studies were performed using a 0.3-tesla open magnet or a 1.5-tesla closed imaging system. Image acquisition parameters included the following: T1-weighted volume acquisition sequences; field of view of 240; slice thickness of 2 mm with no gap between slices; and in-slice resolution of 256 × 256 pixels. Images were acquired with the aid of fiducial markers that appear opaque on MR images; the markers were located over the nasion and the left and right preauricular points. Data obtained using MR imaging was transferred through an Ethernet connection to the MEG data-acquisition computer in American College of Radiology–National Electrical Manufacturer Association format for analysis using CTF software, and then to a second computer containing Curry (version 4.0) software.

Magnetoencephalography was performed in a whole-head neuromagnetometer containing 100 direct-current superconducting quantum interference devices. The configuration included 68 second-order coaxial gradiometers (diameter 1.5 cm, baseline 5 cm) and 32 reference gradiometers producing a third-order gradiometer configuration. The system noise was 7 to 10 fT/√Hz/channel. For interictal spikes, the MEG data were collected over a 4-hour period in 5- to 10-minute epochs. The digitization rate was 1250 Hz/channel and the bandpass was 1 to 300 Hz. The MEG data was spatially registered to the patient’s head by a headband containing three sensors coregistered with the MR imaging-compatible fiducial markers and tracked by a threerpace digitizer internal to the MEG dewar. Localization of the primary sensorimotor region was accomplished via pulsed electrical stimulation of the median nerves and, where indicated clinically, the posterior tibial nerves, by using shock stimulation at 3.1 Hz that was adequate to pro-
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duce a thumb or toe twitch, according to standard protocols.

Raw data were analyzed using a single equivalent dipole model in Food and Drug Administration–approved software, provided by the manufacturer of the neuromagnometer, to produce dipole locations and orientations for each single interictal spike. Alternate dipole modeling methods were also applied, but were not used for clinical application. The MR image was coregistered with the MEG data set by applying the software routine. Dipoles were superimposed on data obtained using MR imaging, producing MS images for review. The data were imported into the Curry software format, which also permitted segmentation of gray and white matter, skull, and skin.

Methods of Image Fusion and Image-Guided Surgery

An image-guided surgical navigation system was used in all subdural grid or strip placements. On the morning of surgery, patients underwent T1-weighted axial MR imaging of the brain according to a standard protocol, with gadolinium administered when clinically indicated. Fiducial markers that appear opaque on MR images were applied to the scalp before the MR image was obtained. The data obtained during MR imaging was imported into the surgical navigation system computer and fused to the previously acquired MS image by using a commercially available image-fusion program. At surgery, the patient’s head was secured to the operating room table by using three-point fixation, and the fiducial markers were registered to the surgical navigation system by using the fused MR–MS image as a reference. The MEG dipoles were then displayed on the intraoperative MR image by using a routine in the software that permitted manual registration of each MEG dipole as a color-coded label or “ticket.” For verification, the original data provided by MS imaging were simultaneously displayed on a separate computer through an Ethernet link to the MEG laboratory.

When subdural grids were placed, the surgical navigation system was used to plan the size and location of the craniotomy. If feasible, the flap was made large enough to incorporate the region of MS imaging spikes and the somatosensory response and language areas by using standardized protocols. At completion of monitoring, patients were returned to the operating room for removal of grids or depth electrodes, and subsequent resection when a seizure zone was identified. The surgical navigation system was employed in these procedures as well, along with inspection of digital photographs and cortical mapping results to ensure that the grids had not moved during monitoring. In some cases intraoperative ECoG and cortical stimulations were repeated to confirm intraoperative mapping results.

Analysis of the Role of MS Imaging in Focus Localization

For all patients a semiquantitative analysis of MS imaging data was performed. This analysis was undertaken in a retrospective fashion after the ECoG monitoring was completed. The number of interictal spikes on each MS image was counted and used to stratify the studies into four categories (Table 1): Class I if no interictal spike was recorded, Class II if five or fewer interictal spikes were recorded, and Class III if six or more interictal spikes were recorded. Class III studies were then subdivided into two groups based on the mean distance between adjacent interictal spikes. If the mean distance between any two contiguous interictal spikes was less than 4 mm, the clustering density was considered to be dense (Class IIIb), whereas if the mean distance between any two contiguous interictal spikes was greater than or equal to 4 mm it was considered to be diffuse (Class IIIa). The ECoG findings were then correlated to the stratified MS imaging classes to determine if the MS imaging results were predictive of being able to localize the zone of seizure origin with invasive monitoring. The cases were divided into those in which the ECoG clearly localized the zone of seizure origin and those in which it did not. When MS imaging dipoles were incorporated into the decision making to direct the placement of depth or subdural grid electrodes, the relationship between the MS imaging and ECoG findings were reviewed to determine critically whether the MEG provided localization information that was not apparent when other noninvasive measures were
TABLE 1

| Interictal Spike Stratification on MS Images and Correlation with Findings of ECoG |
|-----------------------------------------------|--------|--------|--------|
| Clustering Density† | Class    | No. of Cases | Depth Grid‡ | Total Depth Grid Total |
| Quantity* | Depth by ECoG | Not Localized by ECoG |
| none | I | 0 | 4 | 1 | 0 | 1 |
| few | II | 0 | 1 | 1 | 3 | 0 | 3 |
| many | IIIA | 0 | 1 | 1 | 2 | 0 | 2 |
| dense | IIIB | 3 | 8 | 11 | 0 | 0 | 0 |

*A None, 0; few, five or fewer spikes; many, six or more spikes per 4-hour recording session.
†Diffuse means greater than 4-mm mean distance and dense means less than 4-mm mean distance between interictal spike dipoles as measured by hand on coregistered MS imaging data sets.
‡Includes four cases in which depth electrodes were followed by subdural grid-and-stripe electrodes for final localization and one case in which intraoperative ECoG alone was used.

applied. A statistical comparison of cases in which localization was achieved using ECoG and those in which localization was not achieved using ECoG was performed using the one-tailed Student t-test.

Sources of Supplies and Equipment

Magnetic resonance imaging was performed using either a 0.3-tesla open magnet provided by Hitachi Medical Systems America, Inc. (Twinsburg, OH) or a 1.5-tesla closed magnet (Sigma) provided by General Electric Medical Systems (Milwaukee, WI). Curie software (version 4.0) was obtained from Neurosoft Inc. (El Paso, TX). The neuromagnetometer and CTF software were purchased from CTF Systems, Inc. (Port Coquitlam, BC). The Optical Tracking System image-guided surgical navigation system, Image Fusion program, bipolar Ojemann Cortical Stimulator, CRW stereotactic frame, and Stereoplan frame-based stereotactic planning program were obtained from Radionics, Inc. (Burlington, MA). The 16-contact cortical crown and the Spencer Depth Electrodes were acquired from Adtech Inc. (Racine, IL).

Results

Forty studies were performed in patients with medically refractory epilepsy, including seven cases of suspected temporal lobe epilepsy (four with possible neocortical onset), 25 cases of suspected neocortical frontal or parietal lobe epilepsy, and eight cases of nonlocalized epilepsy based on other studies. Twenty-three patients underwent subsequent video-EEG monitoring with intracranial electrodes. This group consisted of nine patients with subdural grids, nine patients with depth electrodes (and subdural strip electrodes in three cases), four patients with depth electrodes and subdural strip electrodes followed by a subdural grid, and one patient who underwent intraoperative ECoG only. In six patients (46%) with depth electrodes, intracranial ECoG failed to localize the seizure discretely and no further workup was pursued. In two patients electrodes were placed in non-standard targets directed entirely by spikes on MS images. These included one patient in whom there was a preponderance of interictal spikes in the posterior portion of the temporal lobe close to the temporoparietal junction, and one patient in whom there were spikes in the region of the parietooccipital junction.

Subdural grid-and-stripe electrodes were placed in 14 patients, including four who previously underwent depth electrode monitoring that demonstrated a neocortical zone of seizure onset. In patients in whom a dorsolateral grid was placed in the frontotemporal region, subtemporal and intrahemispheric strip electrodes were also placed. In two patients double-sided grids were placed in the interhemispheric fissure because of possible supplementary motor or mesial frontoparietal onset. In two patients with cystic cavities (one frontal and one parietal) evident on MR images, a series of subdural strip electrodes was placed inside the previous resection cavity to line the interior walls, because the MS images indicated maximum interictal spikes coming from the wall of the cavity.

Subdural grid ECoG localized the zone of seizure origin in all 14 cases. This includes one case in which intraoperative subdural ECoG alone was used. Resections were performed in all but one of these cases. In 10 patients (71%) a regional (that is, lobar) correlation was noted between the ECoG-determined zone of ictal onset and the interictal spike detected on MS imaging, but not an exact (that is, <2 mm) correspondence. In one patient the MS image proved quite disparate from the seizure localization determined using ECoG. In this case the MS image suggested an interhemispheric parietal lobe seizure focus, whereas ECoG identified a dorsolateral parietal lobe seizure focus. In three cases MS images provided localization data that were critical to the placement of the subdural grid, were not evident from other noninvasive monitoring, and demonstrated exact correlation with the zone of ictal onset defined by ECoG.

Magnetic Source Imaging–ECoG Correlations

Table 1 summarizes the results of stratifying the MS images based on the quantity and clustering density of interictal spikes on the MS imaging study, and comparing these groups in cases in which ECoG was able to localize the zone of seizure origin with cases in which it could not. Of the 17 cases in which the ECoG was able to localize the zone of seizure origin, the MS image was Class IIIB in 13 cases (76%), and Class I or II in only four cases (23%). In contrast, of the six cases in which location could not be achieved using ECoG, four (66%) were Class I or II and none was Class IIIB. These findings indicated that a subset of MS imaging studies in which six or more interictal spikes with dipoles located within less than 4 mm of each other were quite predictive of being able to localize a seizure by invasive monitoring. This finding was particularly notable in cases of neocortical epilepsy, in which Class IIIB MS imaging studies correlated with the ability to localize seizures by ECoG in eight of 11 cases. This finding, however, failed to reach statistical significance (p = 0.23, one-tailed Student t-test), possibly because of the relatively small sample size.

Magnetic Source Imaging–Determined Class and Surgical Outcome

A mean follow-up duration of 21 months (range 13–32...
months) was available for patients who underwent resection. Of 16 patients in whom the zone of seizure origin was well localized by ECoG, one declined resection because of a concern about possible injury to the leg primary sensorimotor cortex during resection. Among the 15 remaining patients, 11 were free of seizure, one experienced more than a 90% reduction in seizures, one claimed more than a 70% reduction in seizures, and in two patients the seizures were unchanged or worse. Thus 12 (80%) of 15 patients have been meaningfully affected by surgery. Among those patients becoming seizure free, in seven the MS images were Class IIIB, in one patient Class II, and in three patients Class I. In two of the three patients with poor surgical outcomes the MS images were Class IIIB. The surgical specimens revealed gliosis and ischemic neuronal changes in 13 patients, cortical heterotopia in one patient, and normal tissue in one patient. Among patients with gliosis, freedom from seizure was attained in eight patients, more than 90% reduction in seizures in two patients, more than 70% reduction in seizures in two patients, and no change in seizure frequency in one patient. One patient in whom normal tissue was identified is now seizure free and the patient with a heterotopia has experienced a 90% reduction in seizures. In all patients with Class III (A or B) MS imaging spikes there was pathological evidence of gliosis. Class I spikes were noted in two patients with gliosis, one patient with heterotopia, and one patient with normal tissue. Gliosis was also noted in one patient in whom Class II spikes were identified. No clear relationship between MS imaging findings and pathological surgical specimens could be established. This is perhaps due to the marked preponderance of cases with gliosis, making any meaningful analysis based on pathological subtype difficult.

**Illustrative Case**

**History.** This 36-year-old right-handed woman began to experience complex partial seizures at the age of 23 years. There was no significant birth trauma, no early childhood events such as febrile seizures or convulsions, and no developmental delays in this case. There was also no family history of seizures. The seizures were medically refractory from the time of onset despite trials of multiple anticonvulsant medications. Seizure frequency was approximately one to two/week. Typical seizures occurred without an aura. The patient would stare, blink her eyes, and mutter unintelligible words. Occasionally, she would suffer an injury to the left side. The seizures would last 20 seconds and there was minimal postictal somnolence. Seizure semiology suggested a possible frontal-lobe localization because of the brief nature of the seizure and the versive head movements.

**Examination.** Scalp video-EEG studies, which included the use of sphenoidal electrodes, captured multiple stereotypical seizures. These had a right anterolateral temporal onset with rapid propagation (<5 seconds) to the left sphenoidal electrodes and right orbitofrontal region. Frequent interictal spikes were recorded from the right temporal region. Neuropsychometric testing was nonlocalizing. An interictal SPECT scan yielded normal results. Aictal SPECT scan for which isotope was injected 3 minutes after seizure onset demonstrated relative hyperperfusion in the left temporal lobe, whereas an ictal SPECT scan for which tracer was injected within 1 minute after seizure onset demonstrated hyperperfusion in the anterior right temporal lobe.

The patient underwent a whole-head MS imaging study. A large population of interictal spikes were localized to the right posterior temporal lobe, in the region of the middle and superior temporal gyrus approximately 6 to 7 cm from the temporal pole (Fig. 1A–C). This region was located more posterior to the region of abnormality on the SPECT scan, but in the general region of the EEG-determined interictal spike activity. Depth electrodes had been placed in the patient to lateralize and localize the site of seizure origin more fully, and they were placed symmetrically in the bilateral amygdala, hippocampus, orbitofrontal region, anterior cingulate cortex, and supplementary motor cortex. In addition electrodes were placed in the posterior temporal lobe as guided by the interictal spike from the MS imaging data on the right side, with a contralateral symmetric placement on the left (Fig. 1D). Phase II depth electrode video-EEG monitoring demonstrated interictal spikes at the lateral contacts of the right posterior temporal depth electrode and seizures that originated in the temporal lobe, adjacent to the region of the lateral contacts of the posterior depth electrode, but demonstrated a rapid spread (<5 seconds) to the contralateral mesial temporal electrodes and on to the right mesial temporal region and orbitofrontal area. A Wada test indicated the left hippocampus could maintain memory function if the right hippocampus was removed.

Based on the extensive workup, it was hypothesized that the patient’s seizures had a neocortical lateral temporal origin, near the site of maximal interictal spike density on the MS image.

**First Operation.** The patient underwent a craniotomy for placement of a 64-contact frontotemporal grid, which was performed using a surgical navigation system to ensure that the grid covered and extended beyond the region of the interictal spike in the right posterior temporal lobe. Strip electrodes were also placed bilaterally in the subtemporal region, as well as in the region of the right lingual gyrus and left lateral temporal cortex. Electrocorticography reliably localized the onset of seizure to two contacts on the inferior temporal gyrus (contacts 3 and 4), which were located approximately 6 cm posterior to the temporal pole and slightly anterior and inferior to the site of the interictal spike identified by MS imaging (Fig. 1E). Seizures reproducibly started at these two contacts; they spread to the right mesial temporal lobe, and then on to the left mesial temporal and right dorsolateral frontal regions. The time from onset to spread to the right mesial temporal region was brief (<10 seconds) and the spread to the left side occurred within a few seconds afterward.

**Second Operation.** The patient underwent craniotomy for removal of the grid and a tailored right anterior temporal lobectomy that included the two contacts of seizure origin in the posterior temporal lobe, approximately 6.5 cm of the inferior temporal gyrus and 4 cm of the superior temporal gyrus. The resection included the anterior 2.5 cm of the hippocampus, inferior two thirds of the amygdala, and the entire uncus.
Postoperative Course. Postoperatively, the patient displayed no deficits and has been seizure free for 17 months. Because a more extensive temporal lobectomy was performed, rather than just a limited neocortical resection, we cannot definitively prove that resection of the zone of ictal onset would have provided adequate seizure control. Nonetheless, the MS imaging study clearly proved to be critical in carefully identifying the zone of initial ictal onset and in modifying the degree of lateral temporal resection, which in our opinion was crucial to achieving a seizure-free outcome in this case.

Discussion

The goal of this study was to analyze critically the use of MS imaging in the surgical management of epilepsy. Rather than report a series of cases in which there was a regional correspondence between MEG and ECoG, we focused on identifying subgroups of MS imaging studies that most correlated with subsequent ECoG localization of the zone of seizure origin, highlighting some cases in which MS imaging provides unique localization information not available from other noninvasive techniques. A critical analysis of cases is important because of the cost, technical constraints, and limited availability of MS imaging. As with all labor-intensive and costly medical technologies, such analyses are valuable to determine whether this technology is deserving of further investment in resources and research.

Using MEG or MS imaging as a clinical tool in the evaluation of patients with epilepsy or structural lesions in eloquent cortex is becoming increasingly popular. In recent years several groups have reported on their experiences with MS imaging or MEG for epilepsy.8,9,30–32,34,35 Wheless, et al.,35 compared the localization accuracy of MEG with MR imaging, scalp video-EEG, interictal ECoG, and ictal ECoG based on the outcome of a surgical resection. Using concordance analysis, they indicated that MEG was second only to ictal ECoG in predicting a good surgical outcome. No direct comparison between MEG and ECoG localizations was performed, however, and it is difficult to determine from that series how the MEG data were used during surgical decision making. Furthermore, because surgical resection was based on the ECoG findings, the analysis is inherently biased. Knowlton and colleagues9 evaluated the role of MEG data in a heterogeneous population of 22 patients, including six cases of mesial temporal lobe epilepsy, 14 cases of neocortical epilepsy, and two cases of multilobar epilepsy. Magnetoencephalography-identified interictal spikes were found in the resected lobe of 92% of the neocortical cases, leading to the conclusion that MEG was a
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useful tool for localizing neocortical epilepsy. Unfortunately, no direct comparison between the localization information provided by MEG and other invasive or noninvasive tests was made to determine directly if MEG provided unique and nonredundant localization data. Similarly, Lamusu, et al., reported on nine patients who underwent both MEG and [18F]fluoro-2-deoxy-D-glucose PET scanning. The efficacy of combined MEG and PET scanning in predicting seizure outcome was evaluated. The localizations provided by PET and MEG scanning agreed in all patients with good outcomes, whereas a discrepancy between these modalities was noted in the one patient with a bad surgical outcome. Because only six surgeries were performed and none of these patients underwent a subdural grid investigation prior to resection, it is difficult to determine if the MEG provided unique data that were important in the ultimate surgical resection and outcome.

Perhaps Minassian, et al., has provided the greatest evidence so far to support the utility of MEG. In a series of 11 children with neocortical epilepsy, the presence of MEG-defined interictal spikes were confirmed by intracranial ictal ECoG in which subdural grid electrode arrays were used. A regional correspondence (that is, the same lobe) was noted between MEG and ECoG in 10 of 11 patients and good seizure outcomes following surgery were achieved in nine of 11 patients. This is the first large series that demonstrated a strong regional correspondence between MEG-identified interictal spikes and seizure foci. The authors concluded that MEG imaging was useful in guiding the placement of subdural grids, but did not provide enough information to indicate the exact relationship between the spikes displayed by MS imaging and the seizure focus. Furthermore, in many reported cases, other noninvasive methods such as ictal SPECT scanning appeared to have provided similarly useful localization information.

Although these studies are valuable, their results focus on regional correlations between MEG or MS imaging and surgical outcome. From these reports one can conclude that the MEG data were generally not misleading, but it is much harder to conclude that it was critical to the focus localization or surgical outcome. It is not clear that MEG provided unique localization data that were otherwise lacking from other noninvasive tests or whether any subgroups could be identified in which the MEG study proved particularly valuable. Given the widespread availability of these other methods, it is essential to identify cases in which MEG data proved invaluable to the successful localization of a seizure focus.

Magnetic Source Imaging–Directed Placement of Invasive Electrodes

The results of this study validate the conclusions of previous authors and also extend the results they have reported by suggesting practical guidelines for the surgeon who treats epilepsy to incorporate MS imaging results into the placement of intracranial electrodes. The most significant finding of this series was that the quantity and quality of interictal spikes identified by the MS imaging study might be able to predict the likelihood that invasive intracranial recordings will be able to localize the zone of seizure origin. If multiple tightly clustered interictal spikes were identified by the MS imaging study (that is, Class IIIB), there was an 80% chance that invasive monitoring would localize the zone of seizure origin, and greater reason to focus the placement of electrodes in the the MS imaging results. In all other situations, the data obtained using MS imaging was not a reliable means to guide the placement of electrodes, and the likelihood of localizing the seizure onset zone by ECoG was far less. This finding may temper surgical decision making in cases otherwise considered borderline for invasive monitoring. We restrict this guideline to true MS imaging studies (that is, MEG studies that are coregistered with and superimposed on MR images) because, in our opinion, the ability to superimpose dipole localizations on the anatomic MR image is a critical element to accurate utilization of these data in surgical planning.

The stratification analysis provided in this paper is suboptimal in that it is not rigorously quantitative. A more rigorous statistical analysis of these results is currently underway to validate these findings and identify strict subgroups of MS imaging studies that predict seizure localization by ECoG (Merrifield, et al., in preparation). Applying these criteria to an independent, larger group of patients will be needed to verify this method and to provide a statistical basis for its validity. Nonetheless, these findings provide the neurosurgeon with a reasonable “rule of thumb” method to incorporate the results of MS imaging into surgical planning of invasive electrode monitoring.

Based on our results we propose the following algorithm for the use of MS imaging in the surgical workup of patients with medically refractory epilepsy. All patients in whom seizure semiology and noninvasive studies suggest a localization-specific neocortical seizure origin should undergo an MS imaging study. For patients with suspected mesial temporal lobe epilepsy, MS imaging is of significantly less value, and should not be considered to be a mandatory component of the preoperative workup. If the MS imaging study reveals no spikes, rarely occurring (< 5) spikes, or many diffusely distributed (> 4 mm mean distance) spikes, it is unlikely (< 50% likelihood) that ECoG will be able to localize the zone of seizure origin. In these cases a decision to proceed with invasive monitoring electrode placement should be made more cautiously based on other noninvasive measures, the patient should be counseled about the smaller likelihood of a successful localization, and the MS imaging data should not be used to guide the placement of electrodes. In contrast, if the MS imaging study reveals many interictal spikes that are tightly clustered (that is, Class IIIB), the ECoG is very likely to localize the zone of seizure origin and this supports proceeding to invasive recordings. Furthermore, in these cases, the MS imaging dipoles should be used to guide electrode placement when feasible.

Magnetoencephalography Can Provide Unique Localization Data

In this paper we have provided an illustrative case in which MEG–MS imaging data provided critical and unique localization information that was deemed a significant factor in the subsequent intracranial monitoring and surgical resection. In this case MS imaging identified posterior temporal neocortical spikes that directed the placement of depth electrodes. Confirmation of the MS imaging findings by depth electrode monitoring led to the placement of a sub-
dural grid and the identification of a lateral neocortical seizure focus that probably would have been missed in the absence of the MS imaging data. In this case the MEG–MS image provided localization information that was not evident from other noninvasive methods, the localization data were used to modify directly the invasive monitoring or surgical management, and the MEG findings were confirmed and/or verified by intracranial monitoring. We have observed this usefulness in several other cases, and believe that these cases may ultimately define the true utility of MS imaging in the preoperative workup of patients with symptomatic epilepsy. Otsubo et al., recently reported a case of similar value. They described a patient in whom MEG identified two discrete regions of interictal spikes. These data were used to guide the placement of a subdural grid, confirming the MEG findings and resulting in seizure-free outcome for the patient. In that case it was clear that MEG provided data that were not available from the MR images, PET or SPECT scans, or any other localization method. Similar to the cases that we report, that case defined a clear and unambiguous role for MEG and indicates avenues for more directed clinical investigation. It is these cases that ultimately define the greatest utility of MEG–MS imaging in seizure localization, and we believe that a careful examination of similar cases is an important avenue to advance the use of this technology in clinical practice.

Improved Source Localization Models and Methods

At present MEG–MS imaging seems particularly valuable in cases of suspected neocortical epilepsy, especially those cases in which there is a dorsolateral frontal onset. Significant research efforts are underway to improve methods of source localization of raw data provided by the MEG. Newer modeling programs, improved understanding of skull conductivity effects, improved sensor detection and superconducting quantum interference device arrays, and better methods for image coregistration are providing more accurate and realistic models of interictal spike activity. Simultaneous direct comparisons of intracranial ECoG with MEG should improve these results further and help modify modeling methods. Ultimately, these methods should provide an accurate means for noninvasive source localizations of both functional cortex and seizure foci. These data should directly translate into more successful focal excisional surgeries for epilepsy and tumors, and more complete preoperative determination of the benefit/risk ratios for a variety of neurosurgical procedures.

Furthermore, because MS imaging data are well suited to image-fusion techniques, it can be readily incorporated into surgical navigation systems, radiation treatment plans, and other site-directed therapeutic regimens. The increased safety, diminished operative time, and improved functional outcome that might be achieved should help justify the expense and technological investments in these methods. Further detailed descriptions of cases in which MEG data either corresponded with or failed to correspond with intracranial ECoG will be critical in efforts to refine this method and increase its availability for clinical care.

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References

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