The role of magnetoencephalography in epilepsy surgery

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Epilepsy surgery requires the precise localization of the epileptogenic zone and the anatomical localization of eloquent cortex so that these areas can be preserved during cortical resection. Magnetoencephalography (MEG) is a technique that maps interictal magnetic dipole sources onto MR imaging to produce a magnetic source image. Magnetoencephalographic spike sources can be used to localize the epileptogenic zone and be part of the workup of the patient for epilepsy surgery in conjunction with data derived from an analysis of seizure semiology, scalp video electroencephalography, PET, functional MR imaging, and neuropsychological testing. In addition, magnetoencephalographic spike sources can be linked to neuronavigation platforms for use in the neurosurgical field. Finally, paradigms have been developed so that MEG can be used to identify functional areas of the cerebral cortex including the somatosensory, motor, language, and visual evoked fields.

The authors review the basic principles of MEG and the utility of MEG for presurgical planning as well as intraoperative mapping and discuss future applications of MEG technology. (DOI: 10.3171/FOC/2008/25/9/E16)

KEY WORDS • children • epilepsy surgery • magnetoencephalography

PEDIATRIC epilepsy surgery is a constantly evolving field that offers patients with drug-resistant epilepsy a better chance for seizure control without causing additional morbidity. Over the years, advances in the knowledge of neuromagnetism have allowed for the integration of MEG data with MR imaging to produce magnetic source images. Magnetoencephalography has proven to be a valuable presurgical tool in identifying the epileptogenic zone and eloquent brain cortex, and in predicting surgical outcomes in a subset of children with intractable epilepsy.27,28,48,55

An Overview of MEG

Introduced in 1968,1 MEG is a technique that allows for the measurement of extracranial magnetic fields generated by massive synchronized intraneuronal electric currents. Magnetoencephalography uses a “superconducting quantum interference device” (SQUID)34,39 to amplify small magnetic fields generated by intracranial neuronal activity. The flow of electrical current in this activity must be parallel to the surface of the skull so that a perpendicular magnetic field can be generated and detected by MEG sensors. Current MEG systems use multiple detector coils arranged over the convexity of the skull to record magnetic fields over almost the entire brain.20

Abbreviations used in this paper: CSF = cerebrospinal fluid; EEG = electroencephalography; fMR = functional magnetic resonance; MEG = magnetoencephalography; MEGSS = MEG spike source; SAM = synthetic aperture magnetometry; SEF = somatosensory evoked magnetic field; VEEG = video EEG.

Comparison of MEG and EEG

The question of whether MEG has advantages over EEG has been widely discussed.29,35,56,65 Although both EEG and MEG are based on analysis of synchronized electrical discharges originating from cortical pyramidal cells, MEG has several advantages over conventional scalp EEG. The techniques of EEG and MEG can be compared as follows.10,15,49

Neuronal Currents. Magnetoencephalography primarily detects the magnetic fields induced by intracellular currents, whereas scalp EEG is sensitive to electrical fields generated by extracellular currents.

Orientation of Currents. 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.

Sensitivity. Epileptiform spikes detected by MEG are 1/1,000,000 times smaller than environmentally generated magnetic noise. Hence, to be able to capture the weak magnetic signal, the biomagnetometer must be housed in a shielded room with high-permeability metals to reduce competing ambient magnetic noise.70

Detected Field. Magnetoencephalography requires 3–4 cm2 of synchronized cortical epileptic activity to detect an epileptic spike,38,46 whereas at least 6–20 cm2 of synchronized cortical area is needed for scalp EEG spike detection.31,49

Conductivity. Magnetic fields are theoretically not distorted by the tissue conductivity of the scalp, skull, CSF, and brain; in contrast, electrical fields may be distorted by the skull and CSF.

Accuracy of Source Localization. Magnetoencephalo-
Graphy provides better spatial resolution of source localization (2–3 mm) than EEG (7–10 mm).31,49

**Electrodes and Sensor Coils.** For EEG, electrodes are placed on the scalp. Magnetoencephalography is performed using a dewar that contains multiple sensor coils, which do not touch the patient’s head.

**Ictal Recording With Head Movement.** Because epileptic seizures may be associated with head movements, MEG may lose the precise localization of epileptic sources. Although the ictal wave form can still be recorded, the sensors are inaccurate and superimposition on MR images may not be worthwhile.85

**Signal-To-Noise Ratio.** A recent study comparing the signal-to-noise ratios of hypothetical sources in different areas of the brain indicated an advantage for MEG over EEG in the study of neocortical epilepsies, although the estimated signal-to-noise ratios were comparable in the temporal lobe.12

**Analysis.** Magnetoencephalographic data can be analyzed by source modeling techniques, which allow for localization in 3 dimensions.2,14 Although source modeling techniques are available for scalp EEG, MEG source modeling is generally simpler and more accurate for technical reasons.5

**Cost.** The MEG technology and appropriate source analysis software is several times more expensive than the most sophisticated EEG device.32

The Utility of MEG for Presurgical Evaluation

**Localization of the Epileptogenic Zone.**

Different strategies are used to determine the epileptogenic zone.2,29 The Subcommission for Pediatric Epilepsy Surgery of the Commission on Neurosurgery of the International League Against Epilepsy (ILAE) has recently published guidelines for the presurgical evaluation of children with epilepsy based on a survey collecting data from 543 patients in 20 pediatric epilepsy programs in the US, Europe, and Australia.24,37 The guidelines suggest that in addition to initial evaluation by an experienced clinician, EEG (including sleep recording) and MR imaging are mandatory. While VEEG recording is strongly recommended in all children, 80% of the centers used ictal-SPECT, 85% used FDG-PET, 70% used fMR imaging for language localization, 35% used MEG/magnetic source imaging, and 50% performed an intracarotid amobarbital procedure (Wada test). Only 3 centers used all presurgical tests. Neuropsychological and neuropsychiatric evaluations are also recommended.24

At the Hospital for Sick Children in Toronto, children with intractable epilepsy are considered candidates for surgery following analyses of seizure semiology, prolonged scalp VEEG recordings, MR imaging, and the distribution of MEGSSs.25,65 Neuropsychological evaluations are performed in cooperative school-aged children to determine preoperative verbal and memory function. Language dominance is determined by neuropsychological testing, fMR imaging, and MEG. In atypical cases with bilateral or ambiguous language findings, we perform a Wada test.60,64

The relationship between ictal and interictal findings and clinical presentation on scalp VEEG and MEG results should be correlated to initiate the map of the epileptogenic network.43 Concordant lateralization of the scalp VEEG findings and the MEGSSs can point to the primary epileptogenic hemisphere and identify those children who are candidates for surgical treatment. Discordant data from the scalp VEEG results and MEGSSs typically indicate that the epileptogenic zone cannot be lateralized, and in such cases surgical candidacy for local resection becomes less likely.44

The distribution of MEGSSs is defined by their number and density. In our center, we have defined “clusters” as comprising 20 or more spike sources within an area 1-cm in diameter; “small clusters” consist of 6–19 spike sources within 1 cm, and scatters consist of < 6 spike sources, irrespective of the distance between sources (Fig. 1).28 It has been our experience that, defined in this fashion, a single cluster frequently correlates with the seizure onset zone, part of the symptomatic zone, and the active irritative zone on intracranial VEEG recording.55

The utility of interictal MEG for localizing the epileptogenic zone has been demonstrated on the basis of postsurgical seizure freedom.48,50,65 Magnetoencephalography has been used both in children with lesional epilepsy26 and children with nonlesional epilepsy.58 In cases of malformations of cortical development, the removal of both the MEG spike cluster and the MR imaging lesion are essential for favorable outcomes. In cases of tumors with extramarginal MEGSSs, lesionectomy alone yields a favorable outcome.28 In nonlesional cases, the seizure outcome after resection of MEGSSs has been reported to be successful when the ictal onset zone was restricted on the intracranial VEEG. Postoperative seizure freedom was less likely to occur in children with bilateral clusters of MEGSSs or only scattered MEGSSs, multiple seizure types, or incomplete resection of the proposed epileptogenic zone.39,58

**Functional Mapping.**

In cases in which the epileptogenic zone is near eloquent regions of the brain, precise delineation of these functional areas is required to avoid neurological deficits.67

Localization of the Primary Sensorimotor Cortex. The primary motor cortex, somatosensory cortex, and central sulcus cannot be reliably identified by visual inspection alone. This may be due to displacement of the Rolandic region structures by tissue compression, brain edema,13 or epilepsy that can cause functional reorganization of neuronal pathways, especially in the developing brains of children.13 Direct cortical stimulation and assessment of so-
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Matosensory evoked potentials are considered to be the most accurate methods for the localization of the central sulcus.\textsuperscript{33,37} Localization of the central sulcus by MEG can be obtained by the determination of the SEF. The SEF has been validated as being accurate in approximately 90% of cases through the use of direct cortical stimulation and somatosensory evoked potential phase reversals through electrocorticography in adults.\textsuperscript{17,18,61} Interestingly, the SEF can be reliably studied in infants and young children with epilepsy even while they are receiving total intravenous anesthesia.\textsuperscript{6}

Language Lateralization. Language lateralization can be determined by means of MEG using various language paradigms such as word recognition tasks,\textsuperscript{34} silent reading,\textsuperscript{26} picture naming, and verb generation.\textsuperscript{7} An 89-95% concordance rate has been found between MEG language mapping and results from Wada testing.\textsuperscript{53} Magnetoencephalographic language studies in patients with chronic seizure disorders of left hemispheric onset have demonstrated atypical language organization. In these children, right hemispheric language competence on nonverbal functions is frequently found.\textsuperscript{7,26} It should be noted that normative MEG language data obtained in healthy children are still somewhat scarce,\textsuperscript{41,59} although the localization of auditory evoked potentials\textsuperscript{52} and the effect of age on language perception have been studied.\textsuperscript{52}

Visual Evoked Field Determination. Magnetoencephalography has been used for preoperative visual field detection in children and adults with occipital seizures.\textsuperscript{7} This paradigm is helpful in determining the relationship between the visual cortex and brain lesions. The localization of the visual evoked field on MEG should always prompt consideration of a surgical approach that would retain the visual pathways.\textsuperscript{21}

Applications of MEG in Intracranial VEEG

Creating the Neurosurgical Map

The co-registered MEG data are overlaid onto axial 3D fast spoiled gradient and T1-weighted volume MR images, generating a high-resolution magnetic source image.\textsuperscript{18} We design subdural electrode grids for individual patients to cover the interictal MEGSSs, areas from which ictal and interictal scalp VEEG data have been obtained, and regions of functional cortex.\textsuperscript{97} The size of the individual intracranial subdural electrode array is prepared from data derived from 3D MR imaging, MEG SEF, and MEGSSs.\textsuperscript{27}

Neuronavigation

Magnetoencephalographic data are incorporated into the neuronavigation system to obtain a 3D localization of the MEGSSs and somatosensory, auditory, and visual evoked magnetic fields. This information is then co-registered to the cerebral cortex at the time of surgery.\textsuperscript{50} The neuronavigation system guides neurosurgeons in the placement of the subdural grid to cover the locations of the SEF and margins of the MEGSSs, which are marked with letters during the procedure. Intraoperative digital photographs are then taken of the surgical field for future use in the development of the surgical plan once enough seizures have been captured.\textsuperscript{62}

Determining the Extent of Resection

After the intracranial electrodes are implanted for extraoperative recording of seizures, the patient routinely undergoes a brain CT scan within 24 hours. Data from the postoperative CT in terms of grid localization are fused with the preoperative magnetoencephalographic data to map the subdural grid to the region of interest on the cerebral cortex.

The ictal onset zone, the symptomatic zone, and the irritative zone are identified by the intracranial VEEG recording and mapped to the appropriate regions under the subdural grid.\textsuperscript{60} After several habitual seizures are captured, the area to be resected is mapped by taking into consideration the ictal onset zone, the irritative zone, and MEGSSs. The final neurosurgical map is produced taking into account the potential for seizure control, possible functional deficits, and the patient’s quality of life.\textsuperscript{47}

The Role of MEG After Failed Epilepsy Surgery

Persistent seizures occur in 20–60% of patients following resection procedures for intractable epilepsy.\textsuperscript{15,41,42,63} The majority of patients have recurrent or persistent seizures emanating from the same location of the brain because of insufficient initial resection, activation of mesiotemporal structures in temporal lobe epilepsy,\textsuperscript{12,72,73} or the development of an independent zone of epileptogenesis nearby.\textsuperscript{53} Brain shifts following resection may cause gross distortions of topographic anatomy in these patients.\textsuperscript{7} In this situation, MEG is superior to scalp EEG, because the magnetic field is not distorted by skull defects and CSF collections, which may cause false localization on scalp EEG.\textsuperscript{55} Magnetoencephalography has been used to successfully localize the residual epileptogenic zone in patients with late-onset recurrent seizures in whom MR imaging reveals no residual abnormality and ictal scalp EEG is not lateralizing.\textsuperscript{21}

The Utility of MEG in Epilepsy Surgery: Illustrative Case

A 4-year-old previously healthy boy had episodes of auditory and visual hallucinations that occurred during sleep as he awoke. The parents noted eye deviation to the right side followed by eye twitching with sparing of consciousness during wakefulness and sleep. These events increased in frequency up to multiple events per hour.

A CT scan of the brain demonstrated no abnormality.

![Fig. 2. Axial FLAIR MR images showing abnormal signal in the subcortical white matter in the right mesial occipital region (white arrows).]
Scalp VEEG showed electroclinical seizures arising from the right occipital region and propagating to the right parietal region. An MR imaging study of the brain showed abnormal signal with cortical thickening over the right calcarine cortex and parietal lobe suggestive of focal cortical dysplasia (Fig. 2). Magnetoencephalography showed a cluster of dipole sources in the right mesial parietooccipital region (Fig. 3).

Eleven months later, the boy’s seizures became refractory to treatment with multiple antiepileptic drugs. He underwent placement of a right temporoparietooccipital grid and 2 depth electrodes to the superior and inferior margins of the clustered MEGSSs and 1 interhemispheric strip electrode covering the calcarine cortex (Fig. 4). The patient experienced 4 electroclinical seizures consisting of eye twitching during 4-day intracranial VEEG monitoring period. The ictal onset zone was localized to the right mesial occipital region and right parietooccipital junction close to the midline, spreading to the lateral parietal and occipital regions. He underwent a right occipital lobectomy and a corticectomy over the right parietal region posterior to the sensory cortex. A postoperative right homonymous hemianopsia was expected and found. The final neuropathological diagnosis was focal cortical dysplasia with balloon cells. As of this writing (6 months after surgery), the child continues to be treated with antiepileptic medication and remains seizure free.

Future Applications of MEG Technology

Several methods are being developed to advance the analysis of the 3D magnetic-field data collected by multiple sensor coils for improvement of the localization of epileptic foci and eloquent cerebral functions. In the future, when interictal epileptiform discharges on scalp EEG show a diffuse hemispheric distribution or bilateral synchronous spike waves, dynamic statistical parametric maps and gradient magnetic-field topography may be used to demonstrate dynamic changes of epileptic spikes moving within the epileptic zone. Today, spatial filtering can be applied to MEG data by means of SAM. The SAM virtual sensor analysis reveals morphological characteristics, location, and distribution of epileptiform discharges similar to those shown by subdural EEG recordings. Noninvasive localization of the primary motor cortex and language function can be reliably carried out using SAM, providing a robust and accurate measurement of cortical functions for the purpose of surgical guidance.

Ideally, what would be extremely useful would be the development of MEG technology to map ictal data onto the neurosurgical map. As MEG technology improves and as software design advances to take into account such factors...
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as head movement during seizure onset, the precise identification of the ictal onset zone by MEG may become a reality.

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