Magnetoecephalography-guided resection of epileptogenic foci in children

Clinical article

GREGORY W. ALBERT, M.D., M.P.H.,1,2 GEORGE M. IBRAHIM, M.D., PH.D.,3 HIROSHI OTSUBO, M.D.,4,5 AYAKO OCHI, M.D.,5,8 CRISTINA Y. GO, M.D.,4,5 O. CARTER SNEAD III, M.D.,4,5 JAMES M. DRAKE, M.B.B.CH.,3,6 AND JAMES T. RUTKA, M.D., PH.D.3,6

1Division of Neurosurgery, Arkansas Children' s Hospital; 2Department of Neurosurgery, University of Arkansas for Medical Sciences, Little Rock, Arkansas; 3Division of Neurosurgery and 5Department of Pediatrics, University of Toronto; and Divisions of 4Neurology and 6Neurosurgery, The Hospital for Sick Children, Toronto, Ontario, Canada

Object. Resective surgery is increasingly used in the management of pediatric epilepsy. Frequently, invasive monitoring with subdural electrodes is required to adequately map the epileptogenic focus. The risks of invasive monitoring include the need for 2 operations, infection, and CSF leak. The aim of this study was to evaluate the feasibility and outcomes of resective epilepsy surgery guided by magnetoencephalography (MEG) in children who would have otherwise been candidates for electrode implantation.

Methods. The authors reviewed the records of patients undergoing resective epilepsy surgery at the Hospital for Sick Children between 2001 and 2010. They identified cases in which resections were based on MEG data and no intracranial recordings were performed. Each patient’s chart was reviewed for presentation, MRI findings, MEG findings, surgical procedure, pathology, and surgical outcome.

Results. Sixteen patients qualified for the study. All patients had localized spike clusters on MEG and most had abnormal findings on MRI. Resection was carried out in each case based on the MEG data linked to neuronavigation and supplemented with intraoperative neuromonitoring. Overall, 62.5% of patients were seizure free following surgery, and 20% of patients experienced an improvement in seizures without attaining seizure freedom. In 2 cases, additional surgery was performed subsequently with intracranial monitoring in attempts to obtain seizure control.

Conclusions. MEG is a viable alternative to invasive monitoring with intracranial electrodes for planning of resective surgery in carefully selected pediatric patients with localization-related epilepsy. Good candidates for this approach include patients who have a well-delineated, localized spike cluster on MEG that is concordant with findings of other preoperative evaluations and patients with prior brain pathologies that make the implantation of subdural and depth electrodes somewhat problematic.

(http://thejns.org/doi/abs/10.3171/2014.8.PEDS13640)

Key Words • intractable epilepsy • magnetoencephalography • MEG • surgery

RESECTION of epileptogenic foci has become a widely accepted therapy for the treatment of medically refractory epilepsy in children. A recent review from the University of California, Los Angeles, found a 58% increase in the number of resections performed for epilepsy comparing the decade prior to 1997 to the decade after. Contrary to the experience in adult epilepsy surgery, many resections in children are extratemporal, accounting for over 50% of cases.7,12 This difference likely reflects the different pathologies encountered in children, including cortical dysplasia, tumors, tuberous sclerosis, Rasmussen encephalitis, and a number of congenital disorders.2,7,9,12 Temporal lobe resections in adults have proven to be more effective than best medical therapy in a randomized controlled trial.29 No such trial exists in children, but the available evidence suggests that while extratemporal resections are less effective than temporal lobectomy at controlling seizures, outcomes are still favorable with regard to seizure freedom14 and quality of life.15

Abbreviations used in this paper: EEG = electroencephalography; fMRI = functional MRI; MEG = magnetoencephalography; PET = positron emission tomography; SPECT = single-photon emission CT; VEEG = video EEG.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
MEG-guided resection of epileptogenic foci

The preoperative evaluation of pediatric patients with epilepsy is critical for proper localization of the seizure focus and maximization of outcome. The Pediatric Epilepsy Surgery Subcommission of the International League Against Epilepsy has proposed guidelines for the evaluation of surgical candidates, including interictal and video electroencephalography (VEEG), structural imaging with MRI and/or CT, functional imaging with single-photon emission CT (SPECT) or positron emission tomography (PET), and neuropsychological evaluation. Despite these recommendations, there remains institutional variability in the evaluation of these patients. At the Hospital for Sick Children, all patients undergo VEEG in the epilepsy monitoring unit, brain MRI with a 3-T scanner, functional MRI (fMRI), PET, and neuropsychological evaluation. In addition, magnetoencephalography (MEG) is performed on all patients at our institution.

Depending on the results of the noninvasive evaluation, subdural and depth electrodes may be implanted for further characterization of the epileptogenic focus. While these implanted electrodes can provide valuable information for the planning of operative resection, they may be associated with significant risks. Due to the implanted hardware and need for at least 2 operations, infection is a significant risk, reported to be as high as 2.4%. Other risks include CSF leak, intracranial hematoma, and cerebral edema.9,19

MEG is used at the Hospital for Sick Children as a guide for resection in a select group of patients in lieu of invasive monitoring. These patients all have localized spike clusters, as previously described. In addition, the results of other noninvasive evaluations are concordant with the MEG data. In these patients, resection may be undertaken in an attempt to avoid implantation of subdural and depth electrodes and proceed directly to resective surgery. Here we report a retrospective review of these cases to determine the success of this approach.

Methods

We reviewed the medical records of patients undergoing resection for the treatment of medically intractable epilepsy at the Hospital for Sick Children. We included patients who had localized spike clusters identified on MEG preoperatively. We excluded patients who underwent invasive electroencephalography (EEG) monitoring or who had seizures secondary to a well-defined lesion on neuroimaging, such as a neoplasm or vascular malformation, who would generally be immediately offered a 1-stage lesionectomy and would not be considered for invasive monitoring. We also excluded patients with mesial temporal sclerosis, given the overall favorable surgical outcome of this condition and the questionable utility of both MEG and invasive monitoring in this circumstance. Finally, we excluded patients for whom a resective strategy with curative intent was not considered. This included patients with hemispheric syndromes and children who underwent palliative procedures such as vagus nerve stimulator implantation and corpus callosotomy.

The records were reviewed for demographic information; details of the seizure history, including previous treatments; the surgical procedure performed and any associated complications; and outcome with regard to seizure control and need for additional interventions. Seizure outcome was recorded according to the Engel classification.3 Pathology reports and imaging studies were also reviewed.

This study was approved by the Research Ethics Board at the Hospital for Sick Children.

Results

We identified 16 patients who met the inclusion criteria. All patients underwent surgery between 2001 and 2010. These patients represent a minority of the epilepsy cases performed at the Hospital for Sick Children each year. Of these patients, 9 (56%) were male. The patients’ mean age at the time of surgery was 11.6 years (range 1.6–17.6 years).

All patients underwent preoperative evaluation including brain imaging by MRI and MEG (Fig. 1). Fifteen patients (93.7%) had clear structural lesions on MRI (Table 1). Most of these patients had either presumed cortical dysplasia or postoperative changes from previous surgery. Most of these previous surgeries were prior attempts at surgical control of epilepsy (Cases 7, 8, 10, and 15), although 1 patient had undergone previous resection of a dysembryoplastic neuroepithelial tumor (Case 13).

In each case, MEG helped to identify the suspected seizure focus. All patients included in this study had at least 1 localized spike cluster—defined in a previous publication as at least 6 dipoles with no more than 1 cm between sources.8 In the patients with abnormal MRI findings, the spike clusters were consistently spatially related to the lesion or abnormal finding.

Surgical procedures were tailored to the location of the MEG spike clusters (Fig. 2). Five patients underwent anatomical lobectomies. Two additional patients had temporal lobectomies with additional cortical resection as guided by MEG. The 5 patients with a history of surgery had extension of the previous resection (Table 1). There were no intraoperative complications. The neuropathological findings are listed in Table 2.

One patient was lost to follow-up 1 month after surgery. The remaining 15 children had a mean follow-up time of 2.4 years (range 7 months to 9 years). Of these patients, 4 (26.7%) had postoperative complications. These issues were minor and consisted of headaches, behavior changes, transient neurological deficit, and delayed wound healing with a stitch abscess. There were no deaths. Seizure outcomes were favorable. Ten patients (62.5%) were seizure free at follow-up (Engel Class I). One of these patients exhibited a “running-down” phenomenon, whereby seizure freedom was achieved in a delayed manner. An additional 3 patients (20%) had improvement in seizures (Engel Classes II and III). One patient had no change in seizures (Engel Class IVA) and an additional patient had worsening of seizures (Engel Class IVC). Both patients with Engel Class IV outcomes underwent subsequent surgery with intracranial electrode monitoring and additional resection. One of these children had ongoing seizures following the second attempt at resection.
Discussion

The American Clinical MEG Society has released a policy statement supporting the routine use of MEG in the evaluation of epilepsy. In addition, numerous studies have examined the utility of MEG in the preoperative evaluation of candidates for epilepsy surgery. In one study, MEG changed the surgical plan in 33% of patients. In some cases, the change entailed addition of electrodes, in others it involved placing unilateral rather than bilateral electrodes, and in a few cases MEG resulted in vagus nerve stimulation being performed rather than intracranial monitoring. Previous work from our institution demonstrated that interictal MEG accurately predicted the epileptogenic zone as determined by intracranial recording in 10 of 11 patients. MEG has also been used in the evaluation of patients with lesional epilepsy, recurrent epilepsy following a previous resection, refractory status epilepticus, insular/peri-insular epilepsy, and as part of the evaluation for hemispherotomy. In addition, previous reports have demonstrated more favorable seizure outcomes when the resection area includes the MEG spike cluster. A recent study from another institution demonstrated similar results for patients with extratemporal epilepsy. That series included 31 patients who did not undergo invasive monitoring, including several with temporal lobe epilepsy. Our series focuses on exclusively pediatric patients who would otherwise be candidates for invasive monitoring.

While the precise indications for invasive monitoring with intracranial electrodes vary between institutions, general guidelines include their use in patients with normal neuroimaging, cases in which the pathology involved is not likely to be fully delineated on imaging, cases with multiple lesions or lesions secondary to cerebral insults, cases in which scalp EEG does not adequately localize the seizure onset zone, and cases which require mapping of eloquent cortex. In our series, 1 patient had normal neuroimaging (Case 1) and 5 patients had lesions whose extent would likely extend beyond what is seen on imaging (cortical dysplasia in Cases 2, 5, 9, 12, and 14). One patient had heterotopias seen on neuroimaging (Case 4), but these were noted to be indistinct and difficult to visualize. The remaining patients all had prior cerebral insults. Many of these were from previous attempts at epilepsy surgery (Cases 7, 8, 10, and 15) or prior tumor resection (Case 13). An additional 4 patients had encephalomalacia or evidence of prior stroke (Cases 3, 6, 11, and 16). Therefore, all patients included in this series would have been candidates for intracranial electrode implantation if MEG was not available.

The 62.5% seizure-free rate in our cohort of patients compares favorably with previously published reports of outcomes in extratemporal epilepsy surgery. Recently pub-
MEG-guided resection of epileptogenic foci

Published series report seizure-free rates of 57%–74%. Most patients in our series derived some benefit in seizure control from the operation. Only 2 patients had Engel Class IV outcomes requiring additional surgical intervention.

The primary advantage of using MEG to guide resection for epilepsy is the avoidance of invasive monitoring. The use of intracranial electrodes is associated with several risks including CSF leak, cerebral edema, hemorrhage, infection, and blood loss requiring a transfusion. There were no infections or CSF leaks in our series. The primary disadvantages to routine use of MEG are the cost and limited availability of this technology. In addition, most MEG recordings are interictal, although occasionally ictal activity is recorded.

The decision to use MEG instead of intracranial electrodes is complex and depends on numerous factors. Certainly, the MEG data must be concordant with other available information including seizure semiology, VEEG, structural MRI, and PET when available.

### TABLE 1: Preoperative evaluation and operative procedure performed in each of the 16 cases*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Semiology</th>
<th>Scalp EEG</th>
<th>MRI</th>
<th>PET</th>
<th>MEG Clusters</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CPS</td>
<td>right temporal</td>
<td>normal</td>
<td>right temporal hypometabolism</td>
<td>right temporal, parietal inferior frontal spike cluster</td>
<td>temporal lobectomy</td>
</tr>
<tr>
<td>2</td>
<td>CPS</td>
<td>left posterior</td>
<td>left parietooccipital MCD</td>
<td>left occipital hypometabolism</td>
<td>left posterior spike cluster</td>
<td>resection of occipital pole &amp; lateral occipital cortex</td>
</tr>
<tr>
<td>3</td>
<td>CPS, SPS</td>
<td>right posterior</td>
<td>right-sided encephalomalacia</td>
<td>not performed</td>
<td>right parietooccipital spike cluster</td>
<td>parietooccipital clusterectomy</td>
</tr>
<tr>
<td>4</td>
<td>IS</td>
<td>left posterior</td>
<td>left occipital heterotopia</td>
<td>left posterior inferomedial temporal</td>
<td>perilesional occipital &amp; occipitotemporoparietal cluster</td>
<td>occipital lobectomy</td>
</tr>
<tr>
<td>5</td>
<td>CPS, sGTC</td>
<td>right frontal</td>
<td>right mesial frontal lobe MCD</td>
<td>not performed</td>
<td>right frontal lobe cluster</td>
<td>frontal lobectomy</td>
</tr>
<tr>
<td>6</td>
<td>sGTC, CPS</td>
<td>right frontotemporal</td>
<td>right diffuse encephalomalacia</td>
<td>not performed</td>
<td>right inferior frontal/peri-sylvian cluster</td>
<td>resection of frontooperateal/ superior temporal gyri/insula, amygdalohippocampectomy, frontobasal disconnection</td>
</tr>
<tr>
<td>7</td>
<td>CPS, sGTC</td>
<td>right frontal</td>
<td>right hemispheric cystic changes</td>
<td>not performed</td>
<td>left inferior frontal cluster</td>
<td>completion of frontal lobectomy</td>
</tr>
<tr>
<td>8</td>
<td>CPS</td>
<td>left frontal</td>
<td>left frontal gliosis</td>
<td>not performed</td>
<td>perilesional cluster, posterior to lesion</td>
<td>extension of prior resection (posteriorly)</td>
</tr>
<tr>
<td>9</td>
<td>SPS</td>
<td>left occipital</td>
<td>left occipital MCD</td>
<td>not performed</td>
<td>left occipital cluster</td>
<td>occipital lesionectomy</td>
</tr>
<tr>
<td>10</td>
<td>SPS</td>
<td>left centro-parietal</td>
<td>left frontal post-surgical changes</td>
<td>not performed</td>
<td>perilesional spike cluster</td>
<td>resection of frontal operculum</td>
</tr>
<tr>
<td>11</td>
<td>CPS, sGTC</td>
<td>left posterior temporal</td>
<td>left MCA infarct</td>
<td>not performed</td>
<td>left occipital, left parietal, &amp; left inferior frontal spike clusters</td>
<td>anterior temporal lobectomy, amygdalohippocampectomy, inferior frontoparietal topectomy, posterior temporal topectomy, anterior occipital topectomy</td>
</tr>
<tr>
<td>12</td>
<td>sGTC</td>
<td>right posterior</td>
<td>right parietooccipital MCD</td>
<td>not performed</td>
<td>right occipital spike cluster</td>
<td>occipital lobectomy</td>
</tr>
<tr>
<td>13</td>
<td>CPS, sGTC</td>
<td>perilesional discharges</td>
<td>right frontal post-surgical changes</td>
<td>not performed</td>
<td>peri–resection cavity spike cluster</td>
<td>superior temporal &amp; angular topectomies</td>
</tr>
<tr>
<td>14</td>
<td>IS</td>
<td>right frontal discharges</td>
<td>right frontal MCD</td>
<td>not performed</td>
<td>perilesional spike cluster</td>
<td>frontal lesionectomy</td>
</tr>
<tr>
<td>15</td>
<td>IS, CPS, sGTC</td>
<td>right hemisphere</td>
<td>right temporal gliosis</td>
<td>not performed</td>
<td>right temporal lobe spike cluster &amp; perilesional spike cluster</td>
<td>insular &amp; parietal lesionectomies</td>
</tr>
<tr>
<td>16</td>
<td>CPS</td>
<td>unclear origin</td>
<td>right hemispheric encephalomalacia</td>
<td>not performed</td>
<td>right frontal spike cluster</td>
<td>clusterectomy</td>
</tr>
</tbody>
</table>

* CPS = complex partial seizures; IS = infantile spasms; MCA = middle cerebral artery; MCD = malformation of cortical development; sGTC = secondarily generalized tonic-clonic seizures; SPS = simple partial seizures.
Techniques do exist for mapping of language and motor cortex with MEG, however the spatial resolution is limited. With these limitations, MEG-guided resection is appropriate in a small subset of patients. We estimate that 115 patients underwent implantation of subdural grids during the same time period. Intraoperatively, the MEG data may be fused with diffusion tensor imaging to predict the location of eloquent cortex. Intraoperative mapping may also be used for mapping of eloquent cortex during surgery.

Conclusions

In this study, we have demonstrated that the outcome in selected patients who undergo surgery based on MEG data is comparable to the outcome reported from resection based on data from invasive monitoring. In addition, there was a low complication rate, with no CSF leaks, infections, or intracranial hematomas, which can occur in patients undergoing invasive monitoring.

TABLE 2: Pathology results from resected tissue in 16 patients undergoing resective epilepsy surgery based on MEG data

<table>
<thead>
<tr>
<th>Pathology</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>cortical dysplasia</td>
<td>8</td>
</tr>
<tr>
<td>heterotopia</td>
<td>2</td>
</tr>
<tr>
<td>gliosis</td>
<td>5</td>
</tr>
<tr>
<td>postoperative changes</td>
<td>1</td>
</tr>
<tr>
<td>nondiagnostic/normal</td>
<td>2</td>
</tr>
</tbody>
</table>

* Two patients had multiple pathologies.

Acknowledgment

We would like to thank Ms. Maria Lamberti-Pascilli, R.N., for her assistance with the identification of these patients.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Rutka. Acquisition of data: Albert, Ibrahim. Analysis and interpretation of data: Rutka, Albert, Ibrahim. Drafting the article: Albert. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Albert.

References

MEG-guided resection of epileptogenic foci


