MEG Source Imaging in the Presurgical Work-up

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American Epilepsy Society | Annual Meeting
Disclosure

Eisai
Lundbeck
UCB

Clinical trials
Consultant
Honoraria

American Epilepsy Society | Annual Meeting
Learning Objectives

• Attendees will be able to describe which surgery candidates benefit from MEG

• Attendees will be able to explain how MEG should be used in surgical decision-making
Clinical Value of Functional Imaging in Epilepsy Surgery

- Epilepsy surgery clinical context–stakes are uniquely high (effect size is very large)
- Impact of a test (MEG) must account for and distinguish between two important effects:
  1. Patient selection based on test sensitivity and specificity
  2. Effect on cure rate
  3. Go-no go
Epilepsy Surgery Candidates
Video-EEG (VEEG), standard imaging (MRI)

- Functional Imaging: MEG, FDG-PET, Ictal SPECT

No Surgery

Surgery

Standard Invasive Tests: ICEEG and Wada
Role of MEG: Localization of Spike Sources

Before beginning one has to accept the premise that accurate localization of interictal spikes can help localize epilepsy.
MEG Compared to EEG Issues

1. Number of channels (spatial resolution)
2. Differential sensitivity (source orientation)
3. Signal-to-noise
4. Simplicity of model
5. Skull filtering, e.g. HFO detection
6. Volume conduction distortion
EEG compared to MEG
Epilepsy MEG Study Sensitivity

Patarai et al.  
Neurology 2004:62:943-948  
n=82  
VEEG 71%  
-29% non-localizing  
MEG 79%  
-21% no MEG spikes-

Stefan et al.  
Brain 2003:126:2396-2405  
n=455  
MEG 70-78%  
-19.5% no MEG spikes  
-10.1% artifacts or technically unusable
Epilepsy MEG versus EEG Spike Sensitivity

- Temporal Lobe
  - Mesial-basal versus temporal polar
  - Lateral neocortical versus intrasylvian
- Extratemporal Lobe
  - Convexity versus inter-hemispheric fissure
  - Basal frontal or occipital
Epilepsy MEG versus EEG Spike Sensitivity

Patients of Interest

Difficult, complex, confusing ... but those that are strongly suspected to be of unifocal onset.

1. Normal MRI (ambiguous, questionable, subtle)
2. Ictal EEG non-localizing
3. Semiology does not agree with EEG or MRI
Epilepsy Subgroups

1. Neocortical temporal
2. Extra-temporal lobe
3. Secondary bilateral synchrony
4. Post surgical / repeat surgery evaluation
5. Lesions of uncertain relationship to epileptogenic tissue (functional significance)
Secondary Bilateral Synchrony

Chang et al. J Neurosurg, (2009), 111:1248-1256
Repeat Surgery Evaluation
Repeat Surgery Evaluation
Diagnostic Yield

1. Detection of spikes in routine study (~60 minutes of interictal recording)
2. Sensitivity and specificity with respect to prediction of intracranial EEG
3. Prediction of surgical outcome
Relative Predictive Value of ICEEG

Sens. 50-62%
Spec. 50-69%

PPV 70-89%
NPV 24-53%
Tight Spike Clusters and prediction of ICEEG Localization / surgical outcome

n=23 ICEEG cases, 17 were localized.
-11/17 (70%) had greater than 6 or more densely clustered spikes.
-MEG guided electrode placement that otherwise would not been covered in 3 (13%) patients.

n=22 ICEEG children cases (MRI negative)
-MEG single clusters agree with localized ICEEG and surgical outcome.
Conclusively localized MEG study association with Engel I outcome independent of MRI and VEEG

<table>
<thead>
<tr>
<th>Diagnostic Value</th>
<th>MSI, (CI) (n = 62)</th>
<th>Diagnostic MSI (CI)(^a) (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>55% (44.2–63.7)</td>
<td>72% (59.1–82.7)</td>
</tr>
<tr>
<td>Specificity</td>
<td>75% (57.4–88.4)</td>
<td>70% (50.8–84.8)</td>
</tr>
<tr>
<td>PPV</td>
<td>78% (62.1–89.7)</td>
<td>78% (63.5–88.8)</td>
</tr>
<tr>
<td>NPV</td>
<td>51% (39.4–60.6)</td>
<td>64% (46.1–77.1)</td>
</tr>
</tbody>
</table>

\(^a\)Nondiagnostic MSI (no spikes) cases excluded.
MSI = magnetic source imaging; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.

Knowlton et al. *Ann Neurol* 2008;64:35–41
Prediction of Outcome: TLE

- AT vs non-AT associated with better surgical outcome.

Effect on surgical decision-making

M-Period Patients who went to surgery (n=104)

<table>
<thead>
<tr>
<th>code</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) agreement</td>
<td>56</td>
</tr>
<tr>
<td>(2) additional info</td>
<td>25</td>
</tr>
<tr>
<td>(3) influenced surgery</td>
<td>11</td>
</tr>
<tr>
<td>(-1) no contribution</td>
<td>10</td>
</tr>
<tr>
<td>(-2) disagree</td>
<td>2</td>
</tr>
</tbody>
</table>

Stefan et al. Brain 2003:126:2396-2405
Effect on surgical decision-making

1. Modify ICEEG electrode coverage
2. Change from ICEEG to no surgery
3. No surgery to ICEEG
4. ICEEG (second stage modification)

- Non-redundant information 33%
- Changed ICEEG 23%
- Changed surgical decision 20%

Suthering et al. Neurology 2008;71;990-996
Effect on ICEEG (outcome)

Prospective cohort with initial blinding of MEG results:
Changed ICEEG sampling in 18/77 (23%) cases
[Dependent on local practice strategy—extent / density of sampling]

Effect on outcome can only be inferred in a minority of cases in which surgery was modified
--8% of the total cases.

[Does not reflect sampling optimization effect—centering of electrode array]

Effect on ICEEG (outcome)

- n=6/20 with neocortical epilepsy
- 5/6 MEG ictal localization at least as good as IC-EEG
  (superior in two based on outcome)
- 3/6 ictal MEG superior to interictal MEG

- n=6/13 with temporal and extratemporal epilepsy
- all six interictal MEG findings confirmed by ictal MEG
Scalp Detectable HFOs

Frequency and spatial characteristics of high-frequency neuromagnetic signals in childhood epilepsy

Noninvasive localization of epileptogenic zones with ictal high-frequency neuromagnetic signals

Case report

Interictal scalp fast oscillations as a marker of the seizure onset zone


Neurology 2011;77;524; Published online before print July 13, 2011;
DOI 10.1212/WNL.0b013e318228bee2
Conclusions

1. MEG can accurately localize spikes in most instances when specific *assumptions* about the source(s) are valid.
2. The spikes that are localized with MEG are a subset of those that can be detected with ECoG and SEEG.
3. This subset of spikes, when tightly clustered, are associated with successful yield of localized ICEEG and surgical outcome.
4. MEG can allow more patients to receive surgery.
Impact on Clinical Care and Practice

- Understanding the role of MEG in the presurgical evaluation allows judicious use of this special, but expensive test.

- MEG can increase the number of patients who can proceed to surgical treatment.

- MEG may improve targeting (and by inference, the outcome) of the epileptogenic zone in certain patient populations.
Future

1. Determination of whether advanced spatio-temporal modeling methods provide additional accuracy for complex sources
2. \( H_0: \) ESI = MSI when real head modeling techniques are used with comparable spatial sampling (well developed boundary element models and high density EEG).
3. \( H_1: \) MEG > EEG in detection of HFOs at the scalp.