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# Does magnetoencephalography add to scalp video-EEG as a diagnostic tool in epilepsy surgery?

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**Abstract—Objective:** The authors evaluated the sensitivity and selectivity of interictal magnetoencephalography (MEG) versus prolonged ictal and interictal scalp video-electroencephalography (V-EEG) in order to identify patient groups that would benefit from preoperative MEG testing. **Methods:** The authors evaluated 113 consecutive patients with medically refractory epilepsy who underwent surgery. The epileptogenic region predicted by interictal and ictal V-EEG and MEG was defined in relation to the resected area as perfectly overlapping with the resected area, partially overlapping, or nonoverlapping. **Results:** The sensitivity of a 30-minute interictal MEG study for detecting clinically significant epileptiform activity was 79.2%. Using MEG, we were able to localize the resected region in a greater proportion of patients (72.3%) than with noninvasive V-EEG (40%). MEG contributed to the localization of the resected region in 58.8% of the patients with a nonlocalizing V-EEG study and 72.8% of the patients for whom V-EEG only partially identified the resected zone. Overall, MEG and V-EEG results were equivalent in 32.3% of the cases, and additional localization information was obtained using MEG in 40% of the patients. **Conclusion:** MEG is most useful for presurgical planning in patients who have either partially or nonlocalizing V-EEG results.

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The localization of the epileptogenic zone is most commonly defined with video-electroencephalography (V-EEG) using scalp electrodes, and when necessary, intracranial electrodes. However, scalp V-EEG can be nonlocalizing, while invasive recordings carry risks of intracranial infection or bleeding and require special facilities. Several noninvasive, functional brain imaging techniques have been developed to improve the localization of the epileptogenic zone. These include MR spectroscopy (MRS),<sup>1,2</sup> PET,<sup>3,4</sup> interictal and ictal SPECT,<sup>5-7</sup> and a variety of sophisticated EEG source localization models.<sup>8-12</sup> Although each of these methods has particular strengths, none has emerged as the best method for localization.<sup>13</sup>

Magnetoencephalography (MEG) was developed with the goal of providing unique and nonredundant localization information. MEG has excellent temporal resolution, and has been shown in several studies to be a useful technique for localizing ictal and interictal events.<sup>14-21</sup> However, all of these studies tar-

geted a specific subgroup of patients, resulting in relatively small sample sizes. Therefore, the contribution of MEG to the localization of the epileptogenic zone is still an open question.

In the present study we obtained MEG data from a large series of consecutive patients with drug-resistant epilepsy who were referred to our site for a presurgical evaluation. There were four objectives of the study: first, to determine the overall utility of MEG in patients with various epileptogenic substrates who underwent a comprehensive presurgical evaluation; second, to evaluate the equivalence of MEG compared with prolonged ictal and interictal scalp V-EEG monitoring; third, to determine whether MEG provides more specific, consistent, or conflicting information regarding location and extent of the epileptogenic zone compared with interictal and ictal scalp-EEG methods; and fourth, to determine which patient subgroup might benefit the most from undergoing preoperative MEG testing.

**Methods. Patients.** A total of 113 patients with drug-resistant epilepsy participated. All were evaluated at the Epilepsy Monitoring Unit of the Texas Comprehensive Epilepsy Program, Memorial Hermann Hospital in Houston, TX, between 1997 and 2001.

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They underwent an extensive presurgical evaluation, including prolonged V-EEG monitoring and a high resolution MRI scan using a predefined epilepsy protocol. In some patients interictal and ictal SPECT, PET, formal neuropsychological testing, and intra-arterial amobarbital testing for lateralization of language and memory function were performed.

**Video-EEG monitoring.** Scalp V-EEG monitoring was performed with a commercially available monitoring system (XLTEK, Toronto, Canada) for an average of 5 days. Scalp EEG was recorded from gold-disc electrodes placed according to the extended International 10–20 System with additional bilateral anterotemporal and sphenoidal electrodes as needed. Frequency and location of interictal spikes were assessed visually over the entire recording time. Ictal EEG changes were classified with respect to lateralization, location, morphology, and temporal evolution. At least three of each typical seizure type were recorded. All EEG were interpreted by board-certified clinical neurophysiologists (J.W.W. and V.M.).

**MEG recordings.** In the context of a prospective study, simultaneous MEG and scalp-EEG recordings were performed in all patients for 30 minutes. Aside from sleep deprivation the previous night, no seizure elicitation procedures were used. MEG was performed with a 148-channel whole-head MEG system (Magnes 2500WH, 4D Neuroimaging, San Diego, CA) in a large magnetically shielded room (Vacuumschmelze GmbH, Hanau, Germany). Simultaneous scalp-EEG was recorded from 20 gold-disk electrodes placed according to the International 10–20 System. MEG and EEG signals were amplified, filtered (band-pass 3 to 70 Hz), analog-to-digital converted (sampling frequency = 508 Hz), and stored digitally for off-line data analysis. Informed consent for the study was obtained from all participants and their guardians, when applicable.

**MEG-MRI coregistration.** In order to facilitate registration of activity source locations onto structural MRI scans, the latter were performed with lipid markers placed on the nasion and inside the right and left auditory canals. These fiducial points were digitally localized (Polhemus, Colchester, VT) before the MEG recording session. Fiducial locations were then coregistered onto the visually identified locations of the lipid markers on the patient's MRI. The skull shape was derived from a three-dimensional model of the surface of the patient's scalp, which was acquired before the MEG recording session.

**Localization of interictal MEG events.** The MEG recordings were reviewed and classified by a clinical neurophysiologist (E.P.), who was blind to the patients' clinical information. Simultaneous surface EEG was used to identify interictal epileptiform events and to rule out artifacts, such as those produced by body or eye movements, cardiac, and sleep-related activity. We used single epileptiform events for source localization in order to avoid introducing artificial time delays by averaging variable spike populations. Calculation of the location, orientation, and strength of the dipolar sources that best fitted the measured magnetic fields was performed using the single, moving, equivalent current dipole (ECD) model that is part of the 4D Neuroimaging software. The algorithm was applied to magnetic flux distributions that showed clear and stable dipolar morphology. For each calculation, magnetic flux data from 37 magnetometer sensors were used, encompassing both extrema of the dipolar surface distribution. For each epileptiform event source solutions were examined every 2 msec during a 200 msec window (100 msec before and 100 msec after the peak of the interictal spike complex). The goal of this method was to find the best combination of ECD location, strength, and orientation parameters. A dipole solution was considered acceptable if it was associated with a correlation coefficient of 0.95 or greater, global field power (or root mean square of the magnetic flux in the set of 37 magnetometer sensors entered in the analysis) of 400 fT or greater, and an ECD product moment of 400 nAm or less.

**Data coding.** All patients included in this study underwent surgical treatment. In all cases a consensus decision regarding the location and extent of the area to be resected was reached by jointly considering data from surface V-EEG, MRI, neuropsychological evaluation, SPECT, PET, Wada testing, and invasive V-EEG monitoring, when performed. During the time period in which these patients participated in the current study, the MEG data were considered to be experimental and therefore were not included in the preoperative consensus decision.

For the purpose of data coding in the context of the present study, and in order to minimize the influence of potential confounding variables (different neurosurgeons, postoperative complications, or change in antiepileptic drugs postoperatively) on the postoperative seizure outcome, we decided to define the epileptogenic region predicted by each method—interictal scalp V-EEG, ictal scalp V-EEG, and interictal MEG—in relation to the resected area based on the consensus decision. Thus, for each method the results were coded as follows: the predicted area could be the same as the resected area, different from the resected area (non-overlapping), more extensive than the resected area, and finally, nonlocalizing, if the method failed to provide localization information.

**Identification of the epileptogenic zone on the basis of the interictal and ictal scalp V-EEG data.** The concordance between the scalp-EEG results and the resected epileptogenic zone was rated as follows: perfect overlap when the predicted zone for both interictal and ictal scalp V-EEG was the same as the resected region; partial overlap when the predicted zone by one of the methods (either interictal or ictal scalp V-EEG) was the same as the resected zone, but the predicted zone by the other method (either interictal or ictal scalp V-EEG) was larger than the resected zone; nonlocalizable when the delineation of the epileptogenic zone was not possible based on the interictal and ictal scalp V-EEG.

**Identification of the epileptogenic zone on the basis of the interictal MEG data.** The concordance between MEG results and the resected region was determined as follows: perfect overlap when the predicted zone was the same as the resected zone; partial overlap when the predicted zone was larger than the resected zone; no overlap when the predicted zone was different from the resected zone; no interictal changes when no prediction was possible due to an insufficient amount or amplitude of epileptogenic activity, or when there was a poor signal-to-noise ratio due to magnetic artifacts.

**Statistical analysis.** The localization data for each presurgical evaluation method (interictal and ictal V-EEG and MEG) were compared using Bowker's Test for Symmetry,<sup>22</sup> which assessed the probability that MEG improved the localization decision, relative to chance alone, compared with the other methods.

**Results. Patients.** Data from 31 of the 113 patients were unusable (due to presence of large magnetic artifacts in 16 cases and loss of clinical information during a flood that affected the Texas Medical Center in June 2001 in 15 patients). The final data set included complete clinical, scalp and invasive V-EEG data, and MEG results for 82 patients. There were 41 female and 41 male patients with a mean age of 25.3 years (range 1.2 to 54 years). The age at seizure onset varied between infancy and 45 years (mean 8.6 years) and the duration of seizures ranged from 1 to 30 years (mean 14.6 years) (see table E-1 on the *Neurology* web site; [www.neurology.org](http://www.neurology.org)).

**Identification of the epileptogenic zone on the basis of the interictal and ictal scalp V-EEG data.** There was a perfect overlap between the interictal and ictal scalp V-EEG results and the resected region in 28 patients (34.1%) and a partial overlap in 30 patients (36.6%). In 24 patients (29.3%) the interictal and ictal scalp V-EEG did not provide sufficient localization information.

**Identification of the epileptogenic zone on the basis of the interictal MEG data.** There was a perfect overlap between the MEG localization data and the resected region in 47 patients (57.3%), a partial overlap in 12 patients (14.6%), and no overlap in 6 cases (7.3%). In 17 patients (20.8%) no interictal MEG changes were registered. Data from these patients were not included in further analyses. Thirteen of these 17 patients had temporal lobe epilepsy (TLE: 76.5%), comprising 25% of all of the TLE patients in our sample. Four patients who had no interictal changes during the MEG recordings had extra-temporal lobe epi-

**Table 1** Agreement of interictal MEG and noninvasive V-EEG with the resected region: patients with > five interictal spikes in MEG

Noninvasive EEG (interictal and ictal)	MEG			
	Perfect overlap	Partial overlap	No overlap	Total
Perfect overlap	21 (32.3)	3 (4.6)	2 (3.1)	26 (40.0)
Partial overlap*	16 (24.6)	3 (4.6)	3 (4.6)	22 (33.8)
Nonlocalizable	10 (15.4)	6 (9.2)	1 (1.5)	17 (26.2)
Total	47 (72.3)	12 (18.5)	6 (9.2)	65 (100)

Values are n (%).

\*  $p < 0.01$ .

MEG = magnetoencephalography; V-EEG = video-EEG.

lepsy (ETLE: 23.5%), comprising 13.3% of all ETLE patients in the sample.

*Comparison of noninvasive interictal and ictal EEG with interictal MEG.* The relative capacity of noninvasive EEG and MEG to localize the epileptogenic zone was examined in 65 patients for whom localization information was available for both methods. The results are presented in table 1. The group of patients with interictal changes during the MEG study included patients who showed a very small number of spikes (less than 10, but more than 5). In order to examine whether the number and morphology of interictal events affected the localization accuracy of MEG, we tabulated data from patients ( $n = 45$ ) with at least 10 interictal events that had a similar waveform morphology and scalp distribution (table 2). As shown in tables 1 and 2, the distribution of cell counts was very similar in this smaller group as compared with the larger sample of 65 patients, with only one exception: the proportion of cases for which the MEG-based epileptogenic zone was partially overlapping with the resected region increased slightly (Symmetry test,  $\chi^2[2] = 15.56$ ,  $p < 0.01$ ; see table 2). We therefore decided to include all 65 patients who had at least five spikes with similar morphology during the MEG recordings in subsequent analyses (see figure E-1 on the *Neurology* web site; [www.neurology.org](http://www.neurology.org)). A comparison for the entire group of 65 patients as a function of the location of the resected region is provided in table 3, with patients diagnosed with TLE and ETLE shown separately.

*Does MEG augment the results from the scalp V-EEG in the presurgical evaluation?* We next addressed the question of whether the MEG data would have significantly

improved the accuracy of the delineation of the epileptogenic zone, beyond the information provided by noninvasive V-EEG. Localization was deemed to be improved when the MEG results could have localized the epileptogenic zone correctly (as compared to the resected area) in those patients for whom interictal and ictal V-EEG results were either mutually conflicting (identifying the resected region with reduced confidence) or were utterly inconclusive (nonlocalizing). Conversely, information provided by the MEG results would not have affected the localization judgment under each of the following conditions: 1) when the MEG and scalp V-EEG results both delineated the epileptogenic zone correctly, 2) when both methods delineated the resected zone only partially, or 3) when localization was not possible on the basis of the scalp V-EEG results, and the epileptogenic zone indicated by the MEG results overlapped only partially with the resected region. Finally, it was deemed that the MEG results would have adversely affected surgical planning when 1) the resected zone was accurately identified by the V-EEG results and only partially or falsely localized by the MEG results, or 2) the ictal and interictal V-EEG results provided conflicting information and the resected zone was therefore only partially delineated, but it was nonlocalizable from the MEG results. These data are tabulated in table 4.

Out of 22 patients for whom the scalp V-EEG ictal and interictal data would have resulted in the partial delineation of the resected area, the MEG data would have contributed to a more accurate determination of that zone in 16 patients (72.8%). The MEG study would not have changed the localization decision in 3 of the 22 patients (13.6%), and the MEG-defined epileptogenic zone was

**Table 2** Agreement of interictal MEG and noninvasive V-EEG with the resected region: patients with > 10 interictal spikes in MEG

Noninvasive EEG (interictal and ictal)	MEG			
	Perfect overlap	Partial overlap	No overlap	Total
Perfect overlap	14 (31.1)	2 (4.4)	—	16 (35.5)
Partial overlap*	16 (35.6)	2 (4.4)	2 (4.4)	20 (44.4)
Nonlocalizable	4 (8.9)	4 (8.9)	1 (2.3)	9 (20.1)
Total	34 (75.6)	8 (17.7)	3 (6.7)	45 (100)

Values are n (%).

\*  $p < 0.01$ .

MEG = magnetoencephalography; V-EEG = video-EEG.

**Table 3** Agreement of interictal MEG and noninvasive V-EEG with the resected region in patients with temporal (TLE) and extratemporal lobe epilepsy (ETLE)

Noninvasive EEG (interictal and ictal)	MEG			Total
	Perfect overlap	Partial overlap	No overlap	
<b>TLE</b>				
Perfect overlap	15 (38.5)	3 (7.7)	2 (5.1)	20 (51.3)
Partial overlap	13 (33.3)	1 (2.6)	2 (5.1)	16 (41.0)
Nonlocalizable	2 (5.1)	1 (2.6)	—	3 (7.7)
Total	30 (76.9)	5 (12.8)	4 (10.3)	39 (100.0)
<b>ETLE</b>				
Perfect overlap	6 (23.1)	—	—	6 (23.1)
Partial overlap	3 (11.5)	2 (7.7)	1 (3.8)	6 (23.0)
Nonlocalizable	8 (30.8)	5 (19.2)	1 (3.8)	14 (53.8)
Total	17 (65.4)	7 (26.9)	2 (7.7)	26 (100.0)

Values are n (%).

MEG = magnetoencephalography; V-EEG = video-EEG.

more extensive than, or did not include, the resected region in the remaining 3 patients (13.6%). Improvement of the localization based on the MEG data were significantly better than expected based on chance alone,  $\chi^2(2) = 15.4$ ,  $p < 0.01$ . Moreover, the MEG data would have made a significant contribution to the delineation of the resected region in 58.8% of the patients for whom the V-EEG results failed to provide any localization information.

MEG would have provided additional localization information in 40% of the cases in our sample, and it would have corroborated the scalp V-EEG results in 47.7% of the cases. It should be noted, however, that the MEG results alone would have misidentified the resected region in 12.3% of our patients. A large proportion of the patients with inconsistently localized or nonlocalizing scalp V-EEG results underwent invasive recordings (18 of 22 patients with inconsistently localized results and 11 of 17 patients with nonlocalizing results). Additional localization information would have been available from the MEG results for 75% of the patients with inconsistently localizing V-EEG results and for 80% of the patients with nonlocalizable scalp V-EEG results. These results were similar for patients with ETLE and TLE.

**Discussion.** The primary goal in planning surgical resections for patients with drug-resistant epilepsies is the delineation of the epileptogenic zone, that is, establishing whether all of the patient's seizures originate from one region and defining the location and extent of that region. The presurgical evaluation of patients with medically refractory epilepsy is often lengthy and expensive, and in a significant percentage of patients, it is nonlocalizing. Only in approximately 25 to 50% of patients with medically intractable epileptic seizures can the presurgical evaluation be achieved noninvasively in a safe and cost-effective manner.<sup>23,24</sup> The goal of this study was to conduct a critical assessment of the potential utility of MEG. To date, only a few studies have addressed the question of the diagnostic yield of MEG because typically only those patients who actually showed interictal epileptiform activity during the MEG study have been reported.<sup>18</sup> Moreover, in many centers, only patients with frequent interictal spikes on scalp-EEG are referred for a MEG study.<sup>25</sup> This

**Table 4** Potential contribution of MEG data to the identification of the resected region

Noninvasive EEG (interictal and ictal)	MEG			Total
	Improvement	No change	Misidentification	
Perfect overlap		21 (80.8)	5 (19.2)	26 (40)
Partial overlap*	16 (72.8)	3 (13.6)	3 (13.6)	22 (34)
Nonlocalizable	10 (58.8)	7 (41.2)		17 (26)
Total	26 (40.0)	31 (47.7)	8 (12.3)	65 (100)

Values are n (%).

\*  $p < 0.01$ .

MEG = magnetoencephalography.

highlights the problem of the limited recording time inherent in current MEG technology as compared to EEG methods, where prolonged recordings can easily be obtained during intensive video-EEG monitoring. Although some patients may tolerate longer and multiple MEG measurements, a significant prolongation of recording time is impractical in routine clinical practice.

In the present study all patients who were considered for epilepsy surgery underwent MEG study. The proportion of the patients showing a sufficient number of spikes during the 30-minute MEG recording session was 79.2%. The proportion of ETLE patients for whom interictal events were registered was slightly higher than the proportion of TLE patients (86.7% vs 75%). These results are similar to previous reports, where the proportion of randomly selected patients showing epileptiform discharges during MEG recordings ranges from 53 to 73%.<sup>16,17,26</sup> By comparing results from patients with frequent spikes to those of patients with infrequent spikes during the MEG acquisition, we found that even a small number of spikes with a similar morphology (but not less than five) was adequate to make a localization decision.

Only a small number of studies have addressed the question of the localization value of MEG. In our previous report, the localization accuracy of MEG was compared with MRI, scalp V-EEG, and invasive EEG, based on the outcome of a surgical resection.<sup>19</sup> MEG was second (57%) only to ictal invasive EEG (62%) in predicting a good surgical outcome. In that report, the surgical resection was based on the invasive EEG findings. In order to avoid the possible influences of postoperative complications or the potential biases of individual surgeons that can be inherent in using surgical outcome as a gold standard for the predictive value of each method, here we focused instead on the resected region that was determined by a consensus decision during the presurgical evaluation.

In the present study, we showed that on the basis of MEG study alone, the correct localization of the resected region would have been possible in 72.3% of the patients for whom at least five interictal spikes of similar morphology were registered during the 30-minute MEG recordings. These results were significantly better than the proportion of correct localizations that were made based on the noninvasive V-EEG results (40%). The utilization of the MEG results would have potentially led to fewer patients undergoing placement of subdural or depth electrodes.

The accurate delineation of the resected zone by MEG was slightly higher in the TLE (76.9%) than the ETLE patients (65.4%), corroborating the results of earlier studies with far fewer patients.<sup>17,18,25</sup> The present results highlight the suitability of MEG for the evaluation of ETLE patients, given that MEG correctly identified the location of the resected region in ETLE patients for whom scalp interictal and ictal

V-EEG results were either mutually contradicting (11.5%), and therefore only partially overlapped with the resected region, or simply inconclusive (30.8%).

There was perfect agreement between the MEG and V-EEG results in 32.3% of the 65 patients in the present series. In this group of patients, therefore, MEG studies would not have provided additional localizing information beyond the results obtained from V-EEG monitoring. However, MEG correctly identified the resected region in over half (58.8%) of the patients in this study who had nonlocalizing scalp V-EEG results. The accurate delineation of the resected zone from the MEG results was even higher for the patients who had inconsistently (or partially) localizing V-EEG results (72.7%). Thus, the potential contribution of MEG would have been greatest in patients with inconsistently localizing V-EEG results. We recommend that MEG studies should be carried out, in the very least, for patients in whom noninvasive V-EEG results are either partially localizing or nonlocalizing.

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E. Pataraiia, P.G. Simos, E.M. Castillo, R.L. Billingsley, S. Sarkari, J.W. Wheless, V. Maggio, W. Maggio, J.E. Baumgartner, P.R. Swank, J.I. Breier and A.C. Papanicolaou  
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