

# Toward the Substitution of Invasive Electroencephalography in Epilepsy Surgery

Andrew C. Papanicolaou,\* Ekaterina Pataraiia,\* Rebecca Billingsley-Marshall,\*  
Eduardo M. Castillo,\* James W. Wheless,† Paul Swank,‡ Joshua I. Breier,\* Shirin Sarkari,\* and  
Panagiotis G. Simos§

**Abstract:** The authors compared the localization accuracy of interictal magnetoencephalography (MEG) with ictal and interictal invasive video electroencephalography (VEEG) in identifying the epileptogenic zone in epilepsy surgery candidates. Forty-one patients, 29 with temporal lobe epilepsy (TLE) and 12 with extratemporal lobe epilepsy (ETLE), participated. Only patients with interictal changes during the MEG recordings were included. A comparison of the accuracy of invasive VEEG and MEG seizure zone identification was based on the degree of overlap between the location of the actual surgical resection and the zone identified by each method, and the success of surgery in reducing seizure activity. No statistical differences were observed between the accuracy of invasive VEEG and MEG in determining the location of the seizure zone across TLE and ETLE cases. Invasive VEEG and MEG localization judgments were correct in 54% and 56% of the cases, respectively. Separate group analyses suggested that MEG may be less beneficial relative to invasive VEEG in ETLE than TLE cases. MEG is of statistically equivalent accuracy to invasive VEEG, despite the fact that its use has not reached optimal conditions. The authors predict the replacement of the more invasive procedure with MEG in the near future for TLE cases, subsequent to the optimization of the conditions under which preoperative MEG is performed.

**Key Words:** Magnetoencephalography, Epilepsy surgery, Invasive neurophysiology, Epileptogenic zone, Surgical outcome.

(*J Clin Neurophysiol* 2005;22: 231–237)

In the United States, approximately 2,000 patients undergo surgery for epilepsy every year (Engel et al., 2003). This rate

is increasing due to ongoing improvements in the diagnosis and surgical management of epilepsy and may reach the level of 2,000 to 5,000 cases per year, because many new patients are suitable for surgical management every year (Surgery for Epilepsy, NIH Consensus Statement Online). In the past 10 to 15 years, evidence has accumulated in support of the utility of magnetoencephalography (MEG) as a functional neuroimaging method suitable for mapping somatosensory (Kakigi et al., 2000; Papanicolaou et al., 2001), motor (Castillo et al., 2004), auditory (Nakasato et al., 1995; Pantev et al., 1995; Papanicolaou et al., 1990; Reite et al., 1994), visual (Seki et al., 1996), and language-specific cortex (Breier et al., 1999, 2001; Castillo et al., 2001; Simos et al., 1999; Szymanski et al., 2001), and is a possible substitute for the amobarbital sodium procedure (Wada test) in determining hemispheric dominance for language in patients with epilepsy (Breier et al., 1999, 2001; Papanicolaou et al., 2004). MEG has also been shown to be a reliable method of detecting aberrant brain activation profiles associated with developmental disorders like dyslexia (e.g., Simos et al., 2000). Moreover, evidence is accumulating regarding the role of MEG as an adjunct to video electroencephalography (VEEG) in identifying epileptogenic zones (Knowlton et al., 1997; Mamelak et al., 2002; Pataraiia et al., 2004; Wheless et al., 1999). In the past five years, we have been collecting prospective data on the efficacy of MEG as compared with other noninvasive diagnostic procedures. We have reported evidence that MEG has greater precision than scalp VEEG in epileptogenic zone identification. (Pataraiia et al., 2004). Similar evidence has been reported by other investigators (Stefan et al., 2003; Sutherling et al., 1990).

In this article, we report our findings regarding the relative efficacy of MEG recordings of interictal spikes compared to both ictal and interictal invasive VEEG recordings from both subdural grids and depth electrodes for the accurate identification of epileptogenic zones defined with respect to one-year postoperative outcome. Thus far, only a few studies have addressed in a systematic fashion the question of the diagnostic yield of MEG, because only those patients who

\*Division of Clinical Neurosciences in the Department of Neurosurgery, and the Departments of †Neurology and ‡Pediatrics, University of Texas – Houston Health Science Center, Houston, Texas, U.S.A.; and the §Department of Psychology, University of Crete, Greece

This study was supported in part by NINDS grant NS37941 to Andrew C. Papanicolaou, PhD, and by the Vivian L. Smith Center for Neurologic Research, Houston, Texas.

Address correspondence and reprint requests to Dr. Andrew C. Papanicolaou, Division of Clinical Neurosciences, Department of Neurosurgery, 1333 Moursund Street, Suite H 114, Houston, TX 77030, U.S.A.

Copyright © 2005 by Lippincott Williams & Wilkins

ISSN: 0736-0258/05/2204-0231

actually exhibited spikes during MEG recordings were included in published reports (e.g., Lamusuo et al., 1999) or only patients with frequent interictal spikes on scalp EEG were referred for MEG recordings (Wheless et al., 1999). The comparison between MEG and invasive VEEG is particularly important because whereas invasive VEEG recordings tend to be more accurate than noninvasive scalp VEEG recordings in identifying the epileptogenic zone, they carry the risk of intracranial infection or bleeding and require special facilities. If MEG is as accurate as invasive VEEG in predicting the true epileptogenic zone for some or all patients, then this noninvasive method of localization could become the preferred standard of care. In the present investigation, we sought to determine the relative accuracy of the two methods.

## METHODS

### Patients

All patients were evaluated at the Epilepsy Monitoring Unit of the Texas Comprehensive Epilepsy Program at Memorial Hermann Hospital from 1997 to 2001. All patients underwent epilepsy surgery during the same period of time. Twenty-nine patients had temporal lobe epilepsy (TLE) and 12 patients had extratemporal lobe epilepsy (ETLE). Follow-up information was available for up to 12 months postoperatively. Only the patients with interictal changes during the MEG recordings were included in the present sample. Table 1 shows clinical and demographic information of the 41 patients. Informed consent for the study was obtained from all participants and their parents or guardians, when applicable.

### Invasive VEEG Procedure

During invasive VEEG monitoring, depth electrodes and subdural strips or grids are tailored for each patient. EEG recordings were performed concurrently with 24-channel surface EEG. At least three typical seizures were recorded and reviewed to make a decision regarding localization of the epileptogenic zone. Skull x-rays and MRIs were taken postoperatively to assist in determining the precise anatomical location of each intracranial electrode. On the basis of these data, we specified which brain regions were considered epileptogenic for each individual using a prearranged division of the brain into possible surgical targets, as listed in the Appendix.

For the purposes of this study, the epileptogenic zone identified by invasive VEEG was defined in relation to the actual resected area, which itself was decided on by jointly considering data from surface and invasive VEEG procedures, MRIs, a neuropsychologic evaluation, single photon emission computed tomography, positron emission tomography, and Wada testing. The classifications of the epileptogenic zone, as determined by invasive VEEG, fell into three

categories: (a) perfectly overlapping: the predicted area was the same as the resected area; (b) partially overlapping: more extensive than the resected area, but included at least part of the resected area; and (c) nonoverlapping: different from the resected area.

### MEG Procedure

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 across participants. MEG was performed with a 148-channel whole-head MEG system (Magnes 2500WH, 4D Neuroimaging, San Diego, CA, U.S.A.) 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 to 20 System. MEG and EEG signals were amplified, filtered (band-pass 3–70 Hz), analog-to-digital converted (sampling frequency 508 Hz), and stored digitally for off-line data analysis.

### MEG-MRI Coregistration

To facilitate MEG-MRI coregistration of activity source locations, structural MRI scans were acquired with lipid markers placed on the nasion and inside the right and left auditory canals. These fiducial points were digitally localized (Polhemus, Colchester, VT, U.S.A.) before the MEG recording session. Fiducial locations were then coregistered onto the visually identified locations of the lipid markers on the patient's MRI. A three-dimensional model of the surface of the patient's scalp was also 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. The surface EEG recordings that had been obtained simultaneously with the MEG recordings were used to identify interictal epileptiform events and to rule out artifacts, such as those produced by body or eye movements or by cardiac and sleep-related activity. Single epileptiform events were used for source localization to avoid introducing artificial time delays by averaging variable spike populations. The location, orientation, and strength of the dipolar sources that best fit the measured magnetic fields was estimated using the equivalent current dipole model that is part of the 4D Neuroimaging software. The algorithm was applied only to magnetic flux distributions that showed clear and stable dipolar morphology. Magnetic flux data from 37 magnetometer sensors, encompassing both extrema of the dipolar surface distribution, were used in each calculation. For each epileptiform event, source solutions were examined every 2 milliseconds during a 200-millisecond window (100 milliseconds before and 100 milliseconds after the peak of the

TABLE 1. Clinical and Demographic Characteristics of All Participants

Patient No.	Age/Gender	Invasive EEG*	Interictal MEG <sup>†</sup>	Invasive EG <sup>‡</sup>	MEG <sup>§</sup>	Lobe	Follow-Up (mo)	Post-Operative Outcome <sup>  </sup>	Pathology
1	37/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	53	1	MTS
2	36/f	Partially overlapping	Perfectly overlapping	Incorrect	Correct	TLE	45	1	MTS
3	18/m	Partially overlapping	Perfectly overlapping	Indeterminate	Incorrect	ETLE	67	5	No changes
4	18/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	ETLE	16	3	Gliosis
5	28/m	Partially overlapping	Perfectly overlapping	Incorrect	Correct	TLE	68	1	MTS
6	18/m	Perfectly overlapping	Partially overlapping	Correct	Incorrect	TLE	44	1	MTS
7	7/f	Perfectly overlapping	Partially overlapping	Correct	Incorrect	ETLE	23	3	No changes
8	7/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	ETLE	37	1	Astroglia
9	35/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	38	2	MTS
10	46/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	66	1	MTS
11	16/m	Perfectly overlapping	Nonoverlapping	Correct	Incorrect	TLE	25	1	MTS
12	39/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	49	1	MTS
13	37/m	Perfectly overlapping	Perfectly overlapping	Incorrect	Incorrect	ETLE	45	5	Ependymoma
14	27/m	Perfectly overlapping	Perfectly overlapping	Incorrect	Incorrect	TLE	11	4	MTS
15	19/m	Perfectly overlapping	Nonoverlapping	Correct	Incorrect	ETLE	28	1	FCD
16	53/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	49	1	AVM
17	17/f	Perfectly overlapping	Perfectly overlapping	Incorrect	Incorrect	ETLE	35	5	Astroglia
18	30/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	62	1	MTS
19	37/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	45	1	MTS
20	42/f	Partially overlapping	Perfectly overlapping	Incorrect	Correct	TLE	54	1	MTS
21	13/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	19	1	MTS
22	16/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	34	1	MTS
23	35/m	Perfectly overlapping	Nonoverlapping	Correct	Incorrect	TLE	63	1	MTS
24	43/m	Partially overlapping	Perfectly overlapping	Incorrect	Correct	TLE	50	1	MTS
25	11/m	Partially overlapping	Perfectly overlapping	Incorrect	Correct	ETLE	10	3	Gliosis
26	25/f	Perfectly overlapping	Partially overlapping	Correct	Incorrect	ETLE	25	3	Gliosis
27	52/f	Partially overlapping	Perfectly overlapping	Incorrect	Correct	TLE	45	3	MTS
28	17/m	Perfectly overlapping	Perfectly overlapping	Incorrect	Incorrect	ETLE	74	5	No changes
29	15/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	ETLE	23	1	FCD
30	27/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	61	3	MTS
31	15/m	Non-overlapping	Perfectly overlapping	Incorrect	Correct	TLE	44	1	MTS
32	9/f	Partially overlapping	Nonoverlapping	Incorrect	Incorrect	TLE	37	3	MTS
33	18/m	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	19	1	MTS
34	50/m	Nonoverlapping	Partially overlapping	Incorrect	Incorrect	ETLE	23	1	Gliosis
35	17/f	Perfectly overlapping	Perfectly overlapping	Correct	Correct	TLE	36	1	Gliosis
36	38/m	Perfectly overlapping	Perfectly overlapping	Incorrect	Incorrect	TLE	28	5	MTS
37	13/m	Perfectly overlapping	Partially overlapping	Incorrect	Indeterminate	TLE	44	5	MTS
38	15/f	Partially overlapping	Partially overlapping	Indeterminate	Indeterminate	TLE	41	4	MTS
39	52/f	Nonoverlapping	Partially overlapping	Indeterminate	Indeterminate	TLE	42	4	Astrocytoma
40	21/f	Perfectly overlapping	Partially overlapping	Correct	Incorrect	TLE	41	1	MTS
41	54/f	Partially overlapping	Perfectly overlapping	Incorrect	Correct	TLE	44	1	MTS

EG, encephalography; f, female; m, male; TLE, temporal lobe epilepsy; ETLE, extratemporal lobe epilepsy; MTS, mesial temporal sclerosis; FCD, focal cortical dysplasia; AVM, arteriovenous malformation.

\*Invasive EEG results in comparison with the resected area.

<sup>†</sup>MEG results in comparison with the resected area.

<sup>‡</sup>Invasive EEG results in relation to postoperative outcome.

<sup>§</sup>MEG results in relation to postoperative outcome.

<sup>||</sup>Postoperative outcome according to Wieser et al. (2001).

interictal spike complex). The goal of this method was to find the best combination of equivalent current dipole 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 estimated current moment of the net neuronal population response of 400 nAm or less.

Classification of the epileptogenic zone as defined by MEG was performed in the same manner in which the epileptogenic zone was defined by invasive VEEG, that is,

with respect to the location of the actual resected area. Once again, the classifications of the epileptogenic zone, as determined with either MEG or invasive VEEG, fell into three categories: (a) perfectly overlapping: the predicted area was the same as the resected area; (b) partially overlapping: more extensive than the resected area, but included at least part of the resected area; and (c) nonoverlapping: different from the resected area.

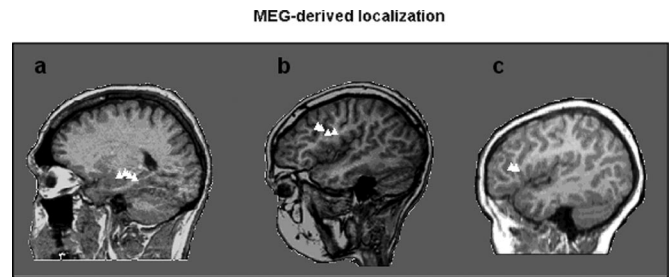
## Outcome Evaluation

To compare the accuracy of MEG and invasive VEEG in identifying the true epileptogenic zone, the localization of each method was further classified in relation to seizure outcome postoperatively. Seizure outcome was classified as successful (no seizures, only auras or one to three seizure days per year; Class 1–3 according to Wieser et al.'s 2001 classification) or unsuccessful (more than four seizure days per year to no improvement or even worsening; Class 4–6 by Wieser et al., 2001). The results were defined with respect to the region identified separately by each method as (a) *correct* if the predicted, localized epileptogenic area overlapped perfectly with the resected area and the patient was seizure-free postoperatively; (b) *incorrect* if the localized area was the same as resected area, but the patient was not seizure-free postoperatively, or the localized area was different from resected area (including only a partial overlap) and the patient was seizure-free postoperatively; and (c) *indeterminate* if the localized zone differed from the resected zone and the patient was not seizure-free postoperatively. Table 2 illustrates the means by which a value was assigned to the localization accuracy of each method for individual patients.

## RESULTS

Figure 1 shows MEG activity sources indicative of a temporal and a frontal seizure focus in individual cases included in the analyses.

The results for the entire group of 41 patients are shown in Table 3 below. With respect to postoperative outcome, MEG localization was correct in 23 of the 41 patients and



**FIGURE 1.** Magnetoencephalography-derived localization of interictal activity in three separate cases. (a) A patient (# 33) with mesial temporal sclerosis is shown with MEG localization of interictal dipoles (yellow triangles) in the mesial parts of left temporal lobe. The invasive VEEG also localized the seizure onset zone in the left mesial temporal area. Both methods showed a perfect overlap with the resected area and the patient is seizure-free since the operation. (b) A patient (# 29) with focal cortical dysplasia in frontal lobe is shown. The yellow triangles indicate the MEG dipole localization, which overlapped perfectly with the resected area. Invasive VEEG showed the seizure onset zone to be in the same area. The patient remains seizure-free after the resection. (c) A patient (# 28) who did not have obvious changes on the preoperative MRI is shown. The yellow triangles indicate the MEG localization of the epileptogenic zone in the frontal cortex. The same area was localized with invasive VEEG and resected. The patient had showed improvement with respect to seizure activity.

invasive VEEG localization was correct in 22 of the 41 patients. As shown in Table 3, the predictions were incorrect for 15 patients using MEG and 16 patients using invasive VEEG. Finally, there were three indeterminate cases for both MEG and invasive VEEG. No significant differences between the two methods were found in terms of their ability to predict the localization of the epileptic zone, and therefore, seizure outcome in individual patients (Bowker's Symmetry Test,  $S(3) = 0.07$ ,  $P = 0.99$ ).

We next attempted to determine whether differences emerged between the two methods when the TLE and ETLE cases were considered separately. Tables 4 and 5 show the localization accuracy of the two methods for the temporal and extratemporal cases, respectively.

As shown, when the TLE and ETLE groups were considered separately, MEG seemed to have a slight but nonsignificant ( $P > 0.40$ ) advantage over invasive VEEG for temporal cases, whereas the reverse was true for ETLE cases. However, when analyzed in this manner, the sample size of each group, particularly the ETLE group, was too small to draw general conclusions about the relative accuracy of the two methods.

## DISCUSSION

In this study of 41 epilepsy surgery candidates, MEG recordings resulted in statistically comparable rates of

**TABLE 2.** Determination of the Value Assigned to the Localization Accuracy of Each Method

MEG/invasive VEEG Localization	Outcome	Value Assigned
Perfectly overlapping	Successful ⇒	Correct
Perfectly overlapping	Unsuccessful ⇒	Incorrect
Partially overlapping	Successful ⇒	Incorrect
Partially overlapping	Unsuccessful ⇒	Indeterminate
Nonoverlapping	Successful ⇒	Incorrect
Nonoverlapping	Unsuccessful ⇒	Indeterminate

**TABLE 3.** Localization Accuracy of Invasive EEG (Interictal and Ictal) versus MEG Based on Postoperative Seizure Outcome

	Invasive VEEG (Interictal and Ictal)			Total
	Correct	Incorrect	Indeterminate	
MEG				
Correct	15 (36.6%)	8 (19.5%)	—	23 (56.1%)
Incorrect	7 (17.7%)	7 (17.7%)	1 (2.4%)	15 (36.6%)
Indeterminate	—	1 (2.4%)	2 (4.9%)	3 (7.3%)
Total	22 (53.7%)	16 (39.0%)	3 (7.3%)	41 (100%)

**TABLE 4.** Localization Accuracy of Invasive VEEG (Ictal and Interictal) versus MEG for Temporal Lobe Epilepsy Cases Based on Postoperative Seizure Outcome

	Invasive VEEG (Interictal and Ictal)			Total
	Correct	Incorrect	Indeterminate	
MEG				
Correct	12 (41.4%)	7 (24.1%)	—	19 (65.5%)
Incorrect	4 (13.8%)	3 (14.6%)	—	7 (24.1%)
Indeterminate	—	1 (3.4%)	2 (6.9%)	3 (10.3%)
Total	16 (55.2%)	11 (37.9%)	2 (6.9%)	29 (100%)

**TABLE 5.** Localization Accuracy of Invasive EEG (Interictal and Ictal) versus MEG for Extratemporal Lobe Epilepsy Cases Based on Postoperative Seizure Outcome

	Invasive VEEG (Ictal and Interictal)			Total
	Correct	Incorrect	Indeterminate	
MEG				
Correct	3 (25.0%)	1 (8.3%)	—	4 (33.3%)
Incorrect	3 (25.0%)	4 (33.3%)	1 (8.3%)	8 (66.7%)
Indeterminate	—	—	—	—
Total	6 (50.0%)	5 (41.7%)	1 (8.3%)	12 (100%)

accurate localization to those of invasive VEEG (both ictal and interictal). The lack of significant statistical differences between the two methods in their localization accuracy is, at this point in time, only suggestive of their equivalence. However, several aspects of these data suggest that MEG holds the potential to replace invasive VEEG, at least for some patients. MEG and invasive VEEG judgments were comparable in this study, despite several advantages that current standard invasive EEG acquisition holds relative to the conditions under which the MEG data were acquired. First, in this as well as many previously reported studies, only interictal MEG recordings were acquired. The invasive VEEG judgments, however, were based on both ictal and interictal recordings;

thus, potentially more information for localization was acquired as compared with the information available for the MEG judgments. Second, the MEG recordings were acquired over a 30-minute period, whereas the invasive VEEG recordings were acquired over a period of days, again potentially providing more information for localization than the MEG recordings. In fact, in 11 of the 41 patients, MEG judgments were based on as few as five interictal spikes. Third, the MEG judgments did not include supplemental clinical considerations, such as structural MRI findings, and were obtained routinely for all surgical candidates in the context of an ongoing investigation of the efficacy of MEG epileptogenic zone identification. In contrast, given the invasive nature of the

procedure, decisions to acquire invasive VEEG recordings were always prompted by supplemental clinical information and the subsequent VEEG judgments used in this study were based on the epileptologists' reports that had been made in the context of other clinical information about the location of the suspected epileptogenic focus. Finally, invasive VEEG was typically performed when patients were not taking their antiepileptic medication. In some cases, patients were administered clonidine during VEEG recordings to optimize the chances of capturing ictal events. In contrast, the MEG recordings were typically performed when the patient was still taking his or her antiepileptic medication (in all cases, the patients were at least on a reduced dose of their prescribed regimen). Thus, in light of these factors, one would expect invasive VEEG judgments to be more accurate than MEG judgments. Yet, despite these relatively advantageous conditions under which the invasive VEEG judgments were made, MEG judgments were no different statistically in their localization accuracy.

In order for MEG to replace the current standard procedure of invasive VEEG for some, if not all, candidates for epilepsy surgery, it is imperative to identify which patients would be profiting equally from both procedures, or from one more than the other, so that at least a subgroup of patients do not need to undergo the more invasive procedure. In this study we separately considered TLE versus ETLE cases to determine whether the two localization methods were comparable for each of these groups. Although no statistically significant differences were found, the percentage of correct localizations was higher for the TLE cases based on MEG compared with invasive VEEG, whereas the opposite was true for ETLE cases. Whether these results will hold—and become statistically significant—with a larger sample size remains to be shown. In the meantime, the conditions under which centers, including our own, acquire MEG information from patients should be optimized, just as invasive VEEG procedures have already been optimized. A direct comparison under optimal conditions for both methods is likely to reveal the patient characteristics associated with an equivalent benefit from each procedure, thereby eliminating the need for invasive VEEG at least in a subgroup of patients. A larger sample size of patients than those reviewed at our site alone may make it possible to recognize in advance which individuals will benefit most from a particular method.

In addition to lengthening the MEG recording time beyond 30 minutes to increase the possibility of capturing ictal events, and systematically administering clonidine for the same purpose, at least two other methods for potentially optimizing MEG conditions for localization deserve mention.

First, slow-wave activity may be used to aid estimates of the location of epileptogenic zones (Gloor et al., 1977; Schaul, 1981, 1990). In a previous study, our group (Ishibashi et al., 2002) examined the significance of focal, slow-wave and interictal spike activity detected using MEG in 29 patients who had mesial temporal lobe epilepsy (MTLE) not associated with structural brain lesions. The results indicated that although focal slowing of EEG background activity is generally considered to be a nonspecific sign of functional disturbance, abnormal interictal low-frequency magnetic activity (LFMA) in patients with MTLE should be conceptualized as a distinct electrographic phenomenon that is directly related to the epileptogenic abnormality. In our preliminary study (Ishibashi et al., 2002), the analysis of interictal LFMA improved the diagnostic utility of MEG in patients with MTLE who underwent surgical evaluation. In the present study, patients with heterogeneous pathologies were included and only spikes were used for epileptogenic zone identification, but in future investigations we plan to use, whenever possible, additional information regarding the epileptogenic zone furnished by LFMA.

A second feature of surface-recorded MEG activity that has been used by others to enhance prediction of epileptogenic zones is the orientation of the current dipoles (which are used to model intracranial sources). On the basis of dipole orientation, patients with MTLE can be classified into two types, namely those with predominantly anterior temporal vertical dipoles and those with anterior temporal horizontal dipoles (Baumgartner et al., 2000; Ebersole and Wade, 1991; Ebersole, 1991). Ebner and Hoppe (1995) have observed that EEG spikes with a similar dipolar distribution are indicative of mesial temporal lobe epilepsy. In a series of MEG studies, Ebersole and colleagues (Ebersole et al., 1995; Ebersole, 1997; Ebersole and Smith, 1995) found that anterior temporal vertical dipoles are associated with sources in the anterior superior temporal plane. Dipole orientation, therefore, may be added to analysis procedures to enhance the potential localization accuracy of epileptogenic zones on the basis of MEG recordings.

After only a limited number of years in development for clinical use, MEG has been shown to be of statistically equivalent accuracy compared with invasive VEEG, despite the fact that its use has not reached optimal conditions. MEG mapping of functional cortex has been shown to be as good as the Wada procedure for identifying language-specific cortex, and it is as accurate as extra- and intraoperative cortical stimulation mapping for somatosensory and language mapping. On the strength of the present findings, we believe we can reasonably offer the optimistic prediction that in the near future MEG is very likely to replace invasive VEEG in many if not all surgical candidates.

## APPENDIX

## Brain Region Classifications for the invasive VEEG and MEG Localizations of the Epileptogenic Foci

Anterior Temporal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Mid Temporal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Post Temporal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Mesial Temporal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Orbital Frontal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Fronto Polar	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Dorso Lat Frontal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Lateral Frontal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Mesial Frontal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Peri Rolandic	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Peri Sylvian	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Parietal	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral
Occipital	<input type="checkbox"/> Left	<input type="checkbox"/> Right	<input type="checkbox"/> Bilateral

## REFERENCES

- Baumgartner C, Pataria E, Lindinger G, Deecke L. (2000) Neuromagnetic recordings in temporal lobe epilepsy. *J Clin Neurophysiol* 17:177–89.
- Breier JI, Simos PG, Wheless JW, Constantinou JE, Baumgartner JE, Venkataraman V, et al. (2001) Language dominance in children as determined by magnetic source imaging and the intracarotid amobarbital procedure comparison. *J Child Neurol* 16:124–30.
- Breier JI, Simos PG, Zouridakis G, Wheless JW, Willmore LJ, Constantinou JE, et al. (1999) Language dominance determined by magnetic source imaging comparison with the Wada procedure. *Neurology* 53:938–45.
- Castillo EM, Simos PG, Venkataraman V, Breier JI, Wheless JW, Papanicolaou AC. (2001) Mapping of expressive language cortex using magnetic source imaging. *Neurocase* 7:419–22.
- Castillo EM, Simos PG, Wheless JW, Baumgartner JE, Breier JI, Billingsley RL, Sarkari S, Fitzgerald ME, Papanicolaou AC. (2004) Integrating sensory and motor mapping in a comprehensive MEG protocol. Clinical validity and replicability. *Neuroimage* 21:973–83.
- Ebersole JS. (1991) EEG dipole modeling in complex partial epilepsy. *Brain Topography* 4:113–23.
- Ebersole JS. (1997) EEG and MEG dipole source modeling. In: Engel J Jr., Pedley TA (ed) *Epilepsy: A Comprehensive Textbook*. Lippincott-Raven Publishers, Philadelphia, pp 919–35.
- Ebersole JS, Smith JR. (1995) MEG spike modeling differentiates basomesial from lateral cortical temporal lobe epilepsy. *Electroencephalogr Clin Neurophysiol* 95:20P.
- Ebersole JS, Squires KC, Eliashiv SD, Smith JR. (1995) Applications of magnetic source imaging in evaluation of candidates for epilepsy surgery. *Neuroimag Clin N Am* 5:267–88.
- Ebersole JS, Wade PB. (1991) Spike voltage topography identifies two types of frontotemporal epileptic foci. *Neurology* 41:1425–31.
- Ebner A, Hoppe M. (1995) Noninvasive electroencephalography and mesial temporal sclerosis. *J Clin Neurophysiol* 12:23–31.
- Engel J, Wiebe S, French J, et al. (2003) Practice parametertemporal lobe and localized resections for epilepsy. *Neurology* 60:538–47.
- Gloor P, Ball G, Schaul N. (1977) Brain lesions that produce delta waves in the EEG. *Neurology* 27:326–33.
- Ishibashi H, Simos PG, Castillo EM, Maggio WW, Wheless JW, Kim HL, Venkataraman V, Sanders DK, Breier JI, Zhang W, Davis RN, Papanicolaou AC. (2002) Detection and significance of focal, interictal slow wave activity for localization of the primary epileptogenic region using magnetoencephalography. *J Neurosurg* 96:724–30.
- Kakigi R, Hoshiyama M, Shimojo M, Naka D, Yamasaki H, Watanabe S, et al. (2000) The somatosensory evoked magnetic fields. *Prog Neurobiol* 61:495–523.
- Knowlton RC, Laxer KD, Aminoff MJ, Roberts TP, Wong ST, Rowley HA. (1997) Magnetoencephalography in partial epilepsyclinical yield and localization accuracy. *Ann Neurol* 42:622–31.
- Lamusuo S, Forss N, Ruottinen HM, Bergman J, Makela JP, Mervaala E, Solin O, Rinne JK, Ruotsalainen U, Ylinen A, Vapalahti M, Hari R, Rinne JO. (1999) [18F]FDG-PET and whole-scalp MEG localization of epileptogenic cortex. *Epilepsia* 40:921–30.
- Mamelak A, Lopez N, Akhtari M, Sutherling W. (2002) Magnetoencephalography-directed surgery in patients with neocortical epilepsy. *J Neurosurg* 97:865–873.
- Nakasato N, Fujita S, Seki K, et al. (1995) Functional localization of bilateral auditory cortices using an MRI-linked whole head magnetoencephalography (MEG) system. *Electroencephalogr Clin Neurophysiol* 94:183–90.
- Pantev C, Bertrand O, Eulitz C, et al. (1995) Specific somatotopic organizations of different areas of the human auditory cortex revealed by simultaneous magnetic and electric recordings. *Electroencephalogr Clin Neurophysiol* 94:26–40.
- Papanicolaou AC, Baumann SB, Rogers RL, Saydjari C, Amparo EG, Eisenberg HM. (1990) Localization of auditory response sources using MEG and MRI. *Arch Neurol* 47:33–7.
- Papanicolaou AC, Simos PG, Breier JI, Wheless JW, Mancias P, Baumgartner JE, et al. (2001) Brain plasticity for sensory and linguistic functions: A functional imaging study using magnetoencephalography with children and young adults. *J Child Neurol* 16:241–52.
- Papanicolaou AC, Simos PG, Castillo EM, Breier JI, Sarkari S, Pataria E, Billingsley RL, Buchanan S, Wheless J, Maggio V, Maggio WW. (2004) Magnetocephalography non-invasive alternative to the Wada procedure. *J Neurosurg* 100:867–76.
- Pataria E, Simos PG, Castillo EM, Billingsley RL, Sarkari S, Swank PR, Breier JI, Maggio V, Wheless JM, Papanicolaou AC. (2004) Does MEG improve standard noninvasive electrophysiological methods in presurgical epilepsy evaluation? *Neurology* 62:943–8.
- Reite M, Adams M, Simon J, et al. (1994) Auditory M100 component. Irelationship to Heschl's gyri. *Cogn Brain Res* 2:13–20.
- Seki K, Nakasato N, Fujita S, et al. (1996) Neuromagnetic evidence that the P100 component of the pattern reversal visual evoked response originates in the bottom of the calcarine fissure. *Electroencephalogr Clin Neurophysiol* 100:436–42.
- Schaul N. (1990) Pathogenesis and significance of abnormal nonepileptiform rhythms in the EEG. *J Clin Neurophysiol* 7:229–48.
- Schaul N, Lueders H, Sachdev K. (1981) Generalized, bilaterally synchronous bursts of slow waves in the EEG. *Arch Neurol* 38:690–2.
- Simos PG, Breier JI, Wheless JW, Maggio WW, Fletcher JM, Castillo EM, Papanicolaou AC. (2000) Brain mechanisms for readingthe role of the superior temporal gyrus in word and pseudoword naming. *Neuroreport* 3:2443–7.
- Simos PG, Papanicolaou AC, Breier JI, Wheless JW, Constantinou JE, Gormley WB, et al. (1999) Localization of language-specific cortex by using magnetic source imaging and electrical stimulation mapping. *J Neurosurg* 91:787–96.
- Stefan H, Hummel C, Scheler G, Genow A, Druschky K, Tilz C, Kaltenhauser M, Hopfengartner R, Buchfelder M, Romstock J. (2003) Magnetic brain source imaging of focal epileptic activity synopsis of 455 cases. *Brain* 126:2396–405.
- Surgery for Epilepsy. (1990) NIH Consensus Statement Online, Mar 19–21; 8:1–20.
- Sutherling WW, Barth DS. (1990) Magnetoencephalography in clinical epilepsy studies. The UCLA experience. *Adv Neurol* 54:231–45.
- Szymanski MD, Perry DW, Gage NM, Rowley HA, Walker J, Berger MS, et al. (2001) Magnetic source imaging of late evoked field responses to vowelstoward an assessment of hemispheric dominance for language. *J Neurosurg* 94:445–53.
- Wheless JW, Willmore LJ, Breier JI, Katakaki M, Smith JR, King DW, Meador KJ, Park YD, Loring DW, Clifton GL, Baumgartner J, Thomas AB, Constantinou JE, Papanicolaou AC. (1999) A comparison of magnetoencephalography, MRI, and V-EEG in patients evaluated for epilepsy surgery. *Epilepsia* 40:931–41.
- Wieser HG, Blume WT, Fish D, et al. (2001) ILAE Commission Report. Proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. *Epilepsia* 42:282–6.