INTRODUCTION

Temporal lobe epilepsies (TLE) are the most common type of focal epilepsies. A distinction based on the seizure onset zone into mesial and lateral neocortical TLE has been suggested. The determination of mesial or lateral neocortical TLE is very important because it is closely relevant to the natural prognosis of the disease and the subsequent strategies of treatment. In patients with mesial TLE, seizures are frequently resistant to antiepileptic drugs and finally 30-50% of patients remain medically intractable. Epilepsy surgery has been a valuable treatment for those patients and 70-90% of them are free from seizures after operation.
In patients with medically intractable epilepsies, a thorough presurgical work-up is essential to localize the epileptogenic zone and to evaluate functional brain areas relevant to the seizure focus. Presurgical evaluation includes intensive video-scap EEG monitoring, magnetic resonance (MR) imaging, single-photon emission computerized tomography (SPECT), positron emission tomography (PET), and neuropsychological assessment. Good surgical outcome can be expected in patients with convergent localization from these investigations. However, these studies provide inadequate information in a significant number of patients, and thus invasive intracranial EEG recordings with depth or subdural electrodes have to be performed. These invasive procedures, however, carry significant risks.

Magnetoencephalography (MEG) is a non-invasive tool for localization of epileptic activity. In contrast to surface EEG, MEG signals are not affected by extracerebral tissues, thus MEG may localize the spike sources more accurately. Although many articles have described MEG findings in TLE patients, relatively few studies reported the MEG features and clinical impact of MEG in clearly defined temporal lobe syndromes. We therefore studied mesial TLE patients who have been free from seizure after anterior temporal lobectomy (ATL). The aims of this study are to determine the MEG dipole patterns of interictal spikes in mesial TLE, and to see the agreement between MEG source localizations and the resection region of tailored ATL.

METHODS

Patients

We conducted MEG recordings in 16 patients with unilateral mesial TLE diagnosed by intensive presurgical evaluation in the Epilepsy Monitoring Unit of Taipei Veterans General Hospital between December 2000 and April 2002. Of these patients, 9 (5 women, 4 men; age 24-40 years) who have been seizure free after ATL were selected for the present study.

Presurgical evaluation

Our presurgical evaluation included intensive video-scalp EEG monitoring, brain MR imaging, PET, ictal and postictal SPECT, neuropsychological assessment, and tests of language and memory with intracarotid amobarbital injection. Seizures were documented according to the International League Against Epilepsy classification. All patients had typical clinical semiology of mesial TLE and evidence of unilateral mesial temporal lobe sclerosis (MTS) on MR imagings (left MTS in 4 patients and right MTS in 5). Ictal and interictal EEG showed clear lateralization of anterior temporal seizure focus in each patient. ATL with tailored resection was performed in patients under general anesthesia, guided by intraoperative electrocorticography and recordings from depth electrodes aimed freehand at the amygdala and hippocampus.

MEG/EEG recordings

MEG recordings were conducted in a magnetically shielded room with a whole-scalp 306-channel neuro-magnetometer (Vectorview, 4-D Neuroimaging, San Diego, USA) comprising 102 identical triple sensor elements. Each sensor element consists of two orthogonal planar gradiometers and one magnetometer coupled to 3 SQUIDs (superconducting quantum interference devices) and thus provides three independent measures of the magnetic fields. During the recordings, the patient sat comfortably with the head supported against the helmet-shaped bottom of the magnetometer. In this study, we only applied signals recorded by the 204 planar gradiometers for further analysis.

The exact location of the head with respect to the sensors was determined by measuring magnetic signals produced by currents and led to four head indicator coils placed at known sites on the scalp. The locations of the coils with respect to anatomical landmarks on the head were determined with a 3-dimensional (3-D) digitizer to allow alignment of the MEG and MR image coordinate systems. MR images of the patient’s brain were acquired before and after surgery with a 3-T Bruker Medspec300 scanner (Germany). For scalp EEG recordings, 19 gold-disk electrodes were placed according to the International 10-20 System with the addition of bilateral cheek electrodes.

All patients were informed of the MEG measure-
ment schedule at least one day in advance and instructed told to keep themselves relatively deprived of sleep before the measurement. During simultaneous MEG and EEG recordings, patients were allowed to fall asleep with their eyes closed. Spontaneous signals were recorded for 3-4 min in each session. Totally, 10-12 recording sessions were obtained. Head position was measured immediately prior to each session. The raw data were bandpass filtered between 0.03 and 130 Hz, sampled at a digitization rate of 400 Hz, and stored in magnetic optical disks for off-line analysis.

We followed up MEG recordings 6-12 months after epilepsy surgery.

**Spike identification and source modeling**

Interictal spikes were collected during off-line visual search on MEG and EEG channels. For EEG spike recognition, Cz reference, transverse bipolar, and longitudinal bipolar montages were applied to identify the unequivocal epileptic spikes. For MEG spike recognition, we divided the 204 gradiometer channels into 8 regions with 24-26 channels in each and looked for spike activities region by region. Sharp MEG signals clearly distinguishable from ongoing background activities, seen on at least 3-5 nearby channels of the individual region, were selected and then regarded as MEG spikes if clear magnetic dipole patterns were selected and then regarded as MEG spikes if clear magnetic dipole patterns were identified with reasonable localization in temporal structures. We rejected those sharp signals suspected of contribution from heart beating, eye movements, physiological rhythmic discharges, or vertex sharp activities during sleep. We applied MEG equivalent current dipole (ECD) modeling to localize those spikes appearing simultaneously on both MEG and EEG recordings.

A segment of 400-500 ms duration with an interictal spike complex was selected to localize the cortical generator. Deflections around the spike complex were first visually searched to select the time windows and cortical areas of interest for further analysis. During these time windows (from the beginning of the deflection to its return to the baseline level) the magnetic field patterns were visually surveyed in 2 ms steps to create the initial guess of the number of active sources within that time period and to estimate the stability of the dipolar magnetic field pattern. The ECDs, best describing the measured data, were found by a least-squares search using subsets of 40-60 channels around the maximum spike signals. These calculations resulted in the 3-D locations, orientations, and strengths of the ECDs in a spherical conductor model, which were based on this patient’s MR images.

We evaluated the dipole model by calculating goodness-of-fit and only ECDs explaining more than 80% of the field variance at selected time period over a subset of MEG channels were used for further analysis.

After identifying the single dipole, we extended the analysis period to the entire measurement epoch and took all channels into account in computing a time-varying multi-dipole model. The strength of the previously found ECD was allowed to change as a function of time while its orientation and location were kept fixed. To evaluate the validity of the dipole model, we compared the measured signals with responses predicted by the model. If signals of some brain region were left inadequately explained by the model, the data were reevaluated for more accurate estimation of the generators. This approach, explained previously in detail, has been successfully applied in previous MEG studies. In the present study, because single ECD well explained most measured signals, we used a single ECD as the neural source of individual spike activity.

**Data analysis**

Patients with inadequate spike sampling (<10 spikes during presurgical MEG measurement) were excluded from this study. We calculated the locations and strengths of the spike dipoles in each patient obtained during the 30-40 min recordings. As described previously, the point where the central sulcus reaches the Sylvian fissure was considered as the anatomic boundary between anterior and posterior temporal lobes.

According to the narrower intersection angle between the horizontal plane and the dipole vector identified on the sagittal slices of MR images, the orientation of the individual spikes was defined as either horizontal (< 45°) or vertical (≤ 45°).

**RESULTS**

We presented data from 5 out of the 9 patients stud-
ied because of an inadequate spike sampling in the others. Table shows the general information of the 5 patients with mesial TLE who have been free from seizures after ATL. The outcome after epilepsy surgery was assessed according to Engel’s classification[47]. Bilateral independent spikes were found preoperatively in 3 out of the 5 patients, but we only demonstrated the analysis results from spikes on surgical side. Postsurgical follow-up of MEG recordings did not show epileptic discharges.

Most spikes in our patients with mesial TLE were seen simultaneously in both MEG and EEG recordings (M/E- spikes), although some were preferentially identified in either MEG (M- spikes) or EEG (E- spikes). Figure 1 shows the M/E-, M-, and E- spikes of Patient 1. The M/E- spike marked with the shadowed bars was found over the MEG and EEG channels of the right temporal region.

Figure 2 shows the spatial distribution of the interic-
The magnetic signals were largest in the right anterior temporal channels. The upper part of the insert shows the enlarged spike waveform (solid signal) in comparison with the predicted signal (dashed signal) calculated from single ECD model. The magnetic field pattern of the ECD at the spike peak (vertical line) was shown in the lower part of the insert. The arrow indicates the location and orientation of the ECD with respect to the helmet-shaped sensor array viewed from the right.

Figure 3 shows the spike localization superimposed on the MR images of Patient 1. The patient has been seizure free after surgery for 17 months and no spikes were identified on 1-year postoperative MEG recordings. The superimposition of the preoperative spike coordinates on the postoperative MR images showed that the spike was clearly localized within the resection area.

As a whole, 86% (68-100%) of preoperative spike dipoles in the 5 patients were localized within the resection demarcation of ATL.

Figure 4 shows the dipole locations of some consecutive spikes superimposed on MR images in all patients. The dipole orientation was horizontal for 86% (83-94%) of interictal spikes in Patients 1-4 and vertical for 86% of interictal spikes in Patient 5.

**DISCUSSION**

To characterize the spike dipole localization in mesial TLE, we included only patients in whom the seizure focus has been definitely identified by intensive presurgical work-up and removed by ATL (seizure and spike free after surgery). We found that the characteristic spike dipoles in mesial TLE were localized in anterior temporal area with horizontal orientation. Although the dipole locations were not exactly situated in mesial temporal structure, the locations of most spikes in anterior...
temporal area were correlated well with the resection demarcation of standard ATL.

Our simultaneous MEG and EEG recordings showed that interictal spikes of mesial TLE were found either simultaneously in both modalities or preferentially in only one modality, in line with previous reports\(^{(23,32,38)}\). In the present paper, the results of dipole analysis were based on those spikes simultaneously identified on both MEG and EEG channels. The modality-related spike presentation will be analyzed later.

Identification and localization of epileptic discharges play important roles in the determination of the epileptogenic focus and the subsequent ablative surgery\(^{(48)}\). In our study, we applied single-ECD model to localize the spike sources. Individual spikes were successfully modeled with single-ECD model validated by the good agreement between measured spikes and predicted signals (see Fig 2). Although the single-ECD approach cannot offer a thorough evaluation for extended areas of activation\(^{(49)}\), previous studies have found this method clinically useful in the localization of focal epileptic activity\(^{(17,18,25,26,30,33,34,37)}\).

As shown in Fig 3, the typical interictal spike of Patient 1 with mesial TLE was localized in the right anterior temporal region, but not exactly situated in the mesial temporal structure. The non-mesial localization in mesial TLE was in line with previous reports\(^{(32,33,50,51)}\) suggesting the limitation of MEG localization for deep sources\(^{(33,33)}\) or the presence of neocortical spike activities propagated from mesial structures\(^{(16,33,33)}\). Knowlton and his colleagues\(^{(39)}\) also reported the non-mesial spike source in one MTS patient who had simultaneous discharges from mesial and lateral ECoG electrodes. Thus, non-mesial spike localization in mesial TLE may be related to the relatively extended activation involving both mesial and lateral temporal structures\(^{(39)}\). This interpretation has been supported by one recent study using simultaneous MEG and invasive EEG recordings\(^{(32)}\) showing that an extended activation area (6-8 cm\(^2\)) over

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**Figure 4.** Locations of consecutive interictal spikes in Patients 1-5 superimposed on preoperative brain MR images. R: right; L: left; A: anterior; P: posterior.
both mesial and lateral electrodes is required to produce a clear spike signal detectable extracranially by MEG.

Considering the limitation of the pinpoint-like assumption of ECD source modeling, we analyzed consecutive multiple spikes to determine the irritative zone. As displayed in Fig 4, the spikes were mostly localized in the anterior temporal region, although not exactly in mesial temporal structure. We also evaluated the anatomical relationship between preoperative spike dipoles and resection territory based on postoperative MR images. Most spike sources (91%) were located within the tailored resection margin, whereas some were found in more posterior region, in line with one recent study(33). Nevertheless, our patients became seizure free and spike free after surgery. Thus, irritative zone defined by interictal spike localization is usually more extensive than the actual epileptogenic area(52), suggesting the remote propagation phenomena of interictal spikes(16,33,50,52).

Previous studies have reported that MEG dipole analysis might be of help to differentiate patients with mesial and lateral neocortical temporal foci(41,49). Anterior temporal horizontal (ATH) and anterior temporal vertical (ATV) dipoles were correlated with mesial temporal onset, whereas posterior temporal vertical dipoles were compatible with lateral neocortical temporal onset. In our study in 5 patients with well-documented mesial TLE, most spikes were localized in the anterior temporal region, whereas the dipole orientation was mostly horizontal in Patients 1-4 or vertical in Patient 5. Our ATH and ATV dipoles were in agreement with the characteristic MEG dipole patterns reported previously in mesial TLE patients(40,49).

In conclusion, the MEG spike sources of mesial TLE are typically localized in the anterior temporal region with horizontal or vertical the orientations, although they may not be exactly localized in mesial temporal structure. Further studies with comparisons between mesial and neocortical TLE may help to clarify the preoperative evaluation value in these patients.

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