Magnetoencephalography and its usefulness in epilepsy surgery

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About 10% to 20% of all epileptic patients ultimately suffer from medically intractable epileptic seizures. Epilepsy surgery has been considered as a useful treatment option for these patients. A successful outcome from surgery is a seizure-free state without imposition of neurological deficit. Thus, the goals of presurgical workup include the delineation of the epileptogenic zone and the identification of the nearby brain area with eloquent function. Noninvasive evaluation consists of intensive video-EEG monitoring, magnetic resonance imaging, single photon emission tomography, positron emission tomography, magnetic resonance spectroscopy, and neuropsychological test. For those patients with no convergent localization information, invasive EEG recordings with subdural or depth electrodes are indicated. However, these procedures carry significant risk. Magnetoencephalography (MEG) is a totally noninvasive tool to measure the cerebral magnetic fields generated by intraneuronal currents. The advent of whole-scalp MEG systems facilitates simultaneous measurement of the entire brain activities. MEG has been used to localize the irritative focus and surrounding brain areas with eloquent function, such as sensorimotor cortex. Thus, MEG offers a noninvasive evaluation to help the planning of invasive recordings and surgical treatment. In this article, we will review the basics of MEG and then discuss its applications in the evaluation for epilepsy surgery. Illustrated figures were obtained in our own patients measured with a whole-scalp neuromagnetometer (Vectorview™, 4-D Neuroimaging).

Key words: **Magnetoencephalography; Epilepsy surgery; Spike; Localization**

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The prevalence of epilepsy has been estimated to be 5 to 9 cases per 1,000 persons. Approximately 60% to 70% of all patients with epilepsy enter satisfactory remission on antiepileptic drugs (AED). About 10% to 20% of all patients ultimately suffer from intractable epileptic seizures despite using optimal AED. Epilepsy surgery has been considered as a useful treatment option for these patients.

The goal of epilepsy surgery is to abolish the seizures by removing the epileptogenic focus without neurological or psychological deficits caused by the operation [1,2]. Thus, a thorough presurgical evaluation of both the epileptic focus and essential brain areas is very important. Noninvasive presurgical evaluation consist of intensive EEG video monitoring, magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission tomography (SPECT), magnetic resonance spectrooscopy (MRS), neuropsychological examination, and WADA (intracarotid amobarbital) test. Patients can undergo epilepsy surgery if these studies yield converging information. When noninvasive work-up does not show adequate information, invasive EEG recordings with subdural or depth electrodes are indicated. However, these methods carry significant risk, and do not necessarily yield conclusive information.

Magnetoencephalography (MEG) is a totally noninvasive technique with super-conducting quantum interference device (SQUID) magnetometers to detect cerebral magnetic fields generated by intraneuronal electric currents [3]. The advent of whole-scalp MEG systems makes it feasible to simultaneously record cerebral activity from the entire brain [4]. Source analysis based on equivalent dipole models has been used to localize epileptic foci and delineate functionally eloquent cortical areas [5-9]. We will review the basics of neuromagnetic field and source analysis, and then give practical examples to highlight the usefulness of MEG in epilepsy surgery.

BASICS OF MEG

Generation of neuromagnetic fields

The brain activity most relevant to neuromagnetic fields is the postsynaptic intracellular potential. Its relatively sustained duration (tens of milliseconds) and slow build-up explain the observed frequent content of MEG signals. Synchronized activation of at least thousands of pyramidal cells generate cerebral magnetic fields which can be measured outside the head with very sensitive magnetometers. In contrast, the action potential does not provide substantial contribution to the formation of measured generate magnetic fields because it is briefly travelling with depolarization and repolarization waves close to each other.

Comparison between MEG and scalp EEG

The apical dendrites of pyramidal cells lie parallel to each other and perpendicular to the cortical surface. Synchronized activation in the fissural cortex generates tangential current measurable by both MEG and scalp EEG. However, radial current is magnetically silent outside of the head, and thus it can be measured with scalp EEG but not with MEG. The selective sensitivity of MEG to tangential currents make the localization of neuronal sources more specific. Moreover, the distortion effect of skull and scalp on electric potentials hinders the exact localization of intracerebral activation sources based on scalp EEG recordings. These structures do not affect MEG measurement because they are practically transparent to magnetic fields. Thus, it is more feasible to obtain accurate source localization with MEG recordings.

Whole-scalp MEG

Several whole-scalp MEG systems are nowadays operative in hospitals and research institutes all over the world. The MEG system in Taipei Veterans General Hospital is a whole-scalp 306-channel neuromagnetometer (Vectorview™, 4-D Neuroimaging) (Fig. 1), which comprises 102 identical triple sensor elements [10]. Each sensor element consists of two orthogonal planar gradiometers and one magnetometer coupled to a multi-SQUID and thus provides three independent measurements of the magnetic fields. The measurements are performed in a magnetically shielded room to reduce the effect of environmental noise. The exact location of the head with respect to the sensors is found by measuring the magnetic signals produced by currents led to four indicator coils placed at known sites on the scalp. The locations of the coils with respect to anatomical landmarks on the head are determined with a 3-dimensional digitizer to allow alignment of the MEG and the MRI coordinate systems. In our hospital, MR images of the subject's brain are acquired with a 3-T Brucker Medspec300 scanner (Germany).

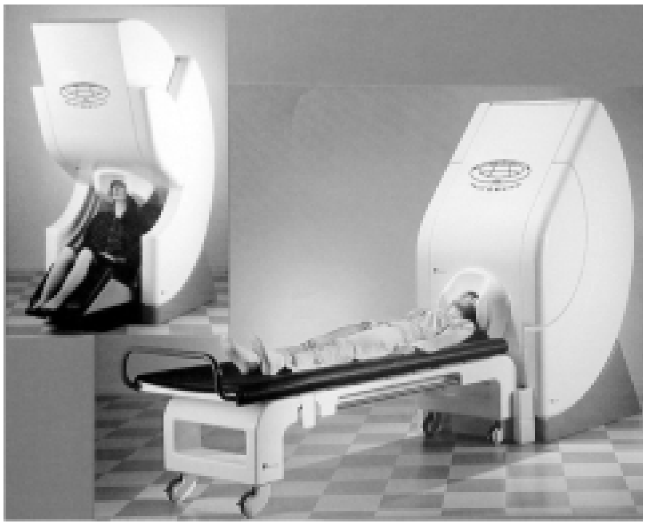

Figure 1. Whole-scalp 306-channel MEG system (Vectorview™). Helmet-shaped coverage facilitates the simultaneous recordings of neuronal activity over the entire brain. The subject can be in supine or sitting position during MEG measurement.

Source estimation

The interpretation of MEG data can be improved by solving the inverse problem of clinical neurophysiology [11]. Because there is no unique solution, certain model restrictions have to be defined about the current sources and the volume conductor. The most widely applied source model is the equivalent current dipole (ECD) indicating a patch of activated cortex. Regarding the volume conductor, spherical models are commonly used because it is simpler and analytic solutions are available. The ECD that best accounts for the measured signals can be calculated on the basis of the measured magnetic field distribution. As a

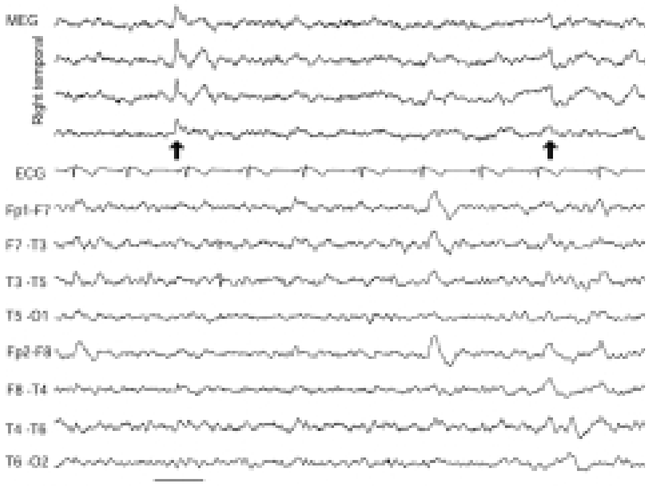

Figure 2. Simultaneous MEG and scalp EEG signals in a 30-year-old female patient with medically intractable partial epilepsy. Two interictal spikes (arrows) were found in the 4 MEG channels selected from right temporal region. No corresponding spike activity was found on EEG channels. ECG indicates electrocardiography. The passband is 0.5 - 50 Hz.

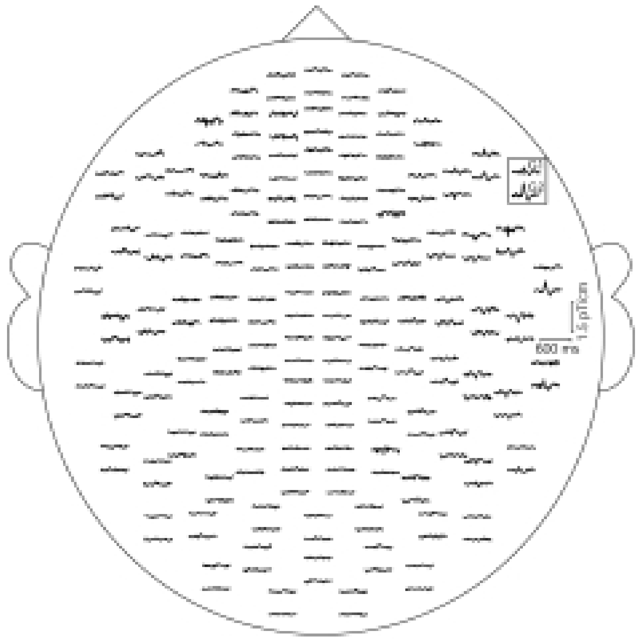

Figure 3. Distribution of interictal spikes in the whole-scalp MEG recording of a 40-year-old male patient with medically intractable partial epilepsy. The head is viewed from the top. Each trace pair illustrates signals recorded by the two orthogonal gradiometers (G1 and G2). The passband is 2 - 50 Hz.

result we can obtain the 3-D location, orientation, and strength of the ECD in a spherical conductor model. The ECD can then be superimposed on the subject's own MRI to see the source location with respect to anatomical structures.

MEG STUDIES IN EPILEPSY SURGERY

We will review the useful applications of MEG in focal epilepsy on the basis of previous studies and our own data.

Identification of interictal spikes in MEG and scalp EEG

The comparison between MEG and scalp EEG in source localization of interictal spikes has been reported in some previous studies [7,12-16]. Some studies showed good agreement of MEG and EEG in spike source localization, but the others reported apparent difference between the two modalities. The controversies may be partly related to the fact that MEG is selectively sensitive to tangential dipole sources, whereas scalp EEG can record both tangential and radial sources. Further, some information of tangential sources can be lost in scalp EEG. Recent studies in proven temporal lobe epilepsy showed that MEG spike source localization was more accurate and anatomically reasonable than that of EEG. Figure 2 shows simultaneous MEG and scalp EEG recordings in a 30-year-old patient with temporal lobe epilepsy. Two interictal spikes are seen on the MEG with no corresponding spike activity on EEG. Our results indicate that simultaneous MEG and EEG recordings facilitate the yield of spike identification.

Differentiation between mesial and lateral temporal lobe seizures

The identification of mesial versus lateral temporal seizure onset is important for surgical consideration and planning. Distinct patterns of interictal spike sources in temporal lobe epilepsy have been reported in previous MEG studies [9,17]. Anterior temporal horizontal dipoles were associated with mesial temporal lobe foci, whereas posterior temporal vertical dipoles corresponded to lateral temporal or other extratemporal foci. Anterior temporal vertical dipoles could be correlated with anterior and perhaps mesial temporal foci [17]. Figure 3 shows the MEG spike distribution in a 40-year-old male patient with right mesial temporal sclerosis. The spike signals are distributed in the right anterior temporal region. Further MEG analysis shows the horizontal dipole localized in

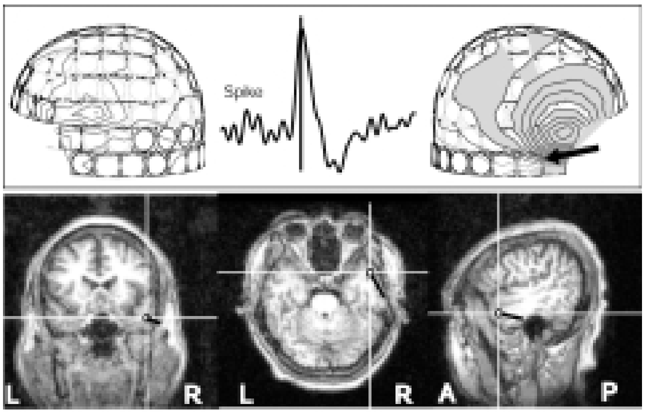

Figure 4. Upper: magnetic field patterns during a single time moment of one spike in the patient shown in Fig. 3. The sensor array is viewed from the left and right. The shadowed areas indicate magnetic flux into the head. The arrow shows the site and orientation of the dipole required to account for the field pattern. Lower: dipole source localization for the interictal spike on coregistered MR images. R = right; L = left; A = anterior; P = posterior.

the anterior region of right temporal lobe (Figure 4). PET and ictal video-scalp EEG studies also showed convergent information. Thus, he underwent right anterior temporal lobectomy and has been free from seizures for 10 months after surgery.

The locations of spike dipole sources are not exactly confined in mesial region, but the horizontal orientations are highly consistent for different spikes, in line with previous observations [9,17]. Figure 5 shows vertical spike dipoles in the posterior temporal region of a 31-year-old female patient with lateral temporal lobe epilepsy. Thus, MEG analysis of interictal spikes is useful to differentiate patients with lateral and mesial temporal seizure foci. Moreover, MEG can be used to study spike propagation between mesial and lateral temporal lobe regions [5,18].

Localization of irritative zones and functionally eloquent areas in extratemporal epilepsy

Localizations of seizure focus in extratemporal epilepsy (ETE) are generally much more demanding than in temporal lobe epilepsy [19,20], and invasive recordings are usually necessary for accurate information in patients with ETE. Irritative zones defined by interictal spikes are important information for the localization of epileptogenic zones and for the prognosis of surgical outcome [21]. MEG can provide a noninvasive evaluation of irritative zones in these patients [8,13,14,17,22]. Figure 6 shows the locations of interictal spikes in a 18-year-old male patient with tonic seizures characterized by sudden tonic stretching of both arms and vocalization. MRI shows no focal structure lesion. The irritative zones are located in the left frontocentral region anterior to the central sulcus. The primary hand somatosensory cortex, determined by right median nerve stimulation, is located lateral to the seizure focus. Thus, MEG is useful to localize the irritative zones and nearby functional areas frontal lobe epilepsy. These data are important for subsequent ablative surgery or further planning of invasive studies.

Reevaluation of patients with persistent seizures after previous epilepsy surgery

Figure 7 shows the MEG spike localization in a 11-year-old female patient who continued to suffer from seizures after surgical resection of an astrocytoma in the right temporal lobe 2 years earlier. Irritative foci are localized to the resection margin of the previous surgery. The results of MEG study will facilitate planning of second epilepsy surgery. Thus, evaluation of patients with persistent seizures after resection surgery is another important application of MEG [9,23].

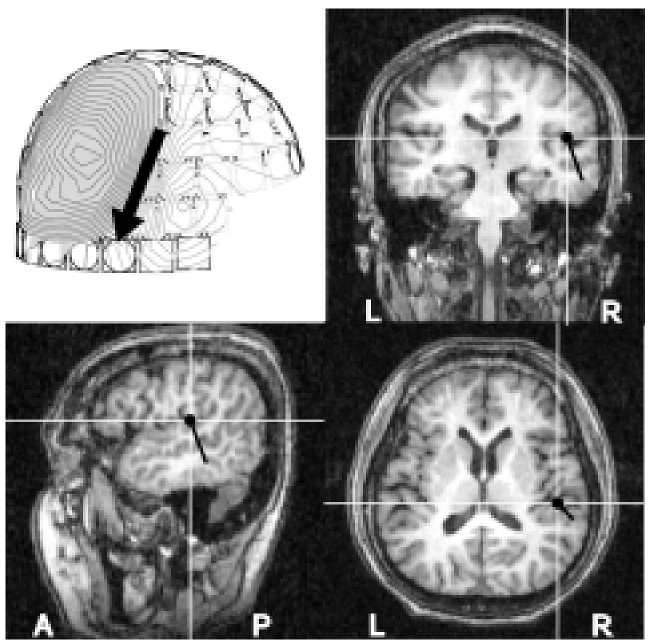

Figure 5. Magnetic field pattern (upper left) and dipole source localization of an interictal spike in a patient with complex partial seizures. The sensor array is viewed from the right. The shadowed areas indicate magnetic flux into the head and the arrow shows the site and orientation of the dipole required to account for the field pattern. R = right; L = left; A = anterior; P = posterior.

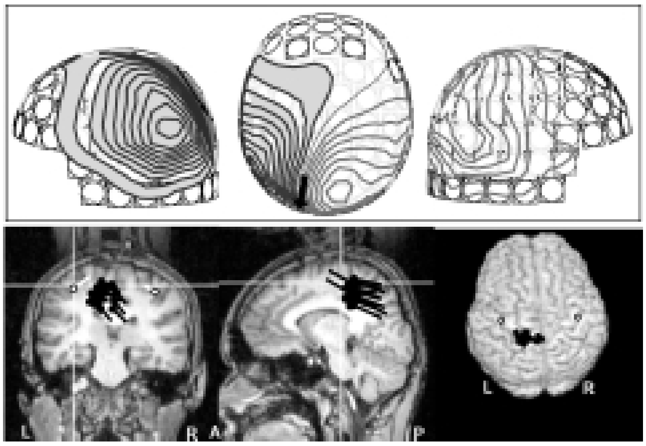

Figure 6. Upper: magnetic field patterns of one spike in a 18-year-old male patient with tonic seizures. The sensor array is viewed from the left, top, and right. The shadowed areas indicate magnetic flux into the head. The arrows show the sites and orientations of the dipole required to account for the field pattern. Lower: dipole source localizations for the interictal spikes (black) and primary somatosensory cortices (white) on coregistered MR images and surface rendering. R = right; L = left; A = anterior; P = posterior.

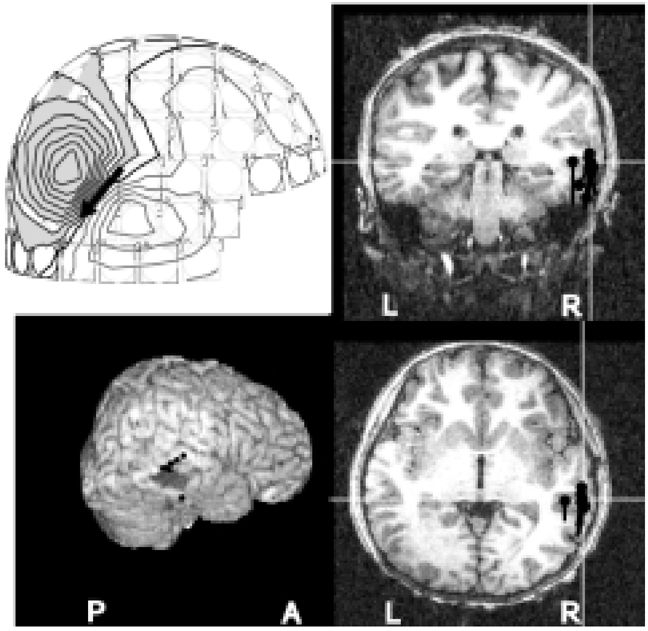

Figure 7. Magnetic field pattern (upper left) and dipole source localizations of interictal spikes on MRI images and surface rendering in a 11-year-old female patient with refractory seizures. She had undergone resection of a tumor in the right temporal lobe, but continued to suffer from seizures. MEG spike dipoles are localized in the resection margins of previous surgery. R = right; L = left; A = anterior; P = posterior.

CONCLUSIONS

Simultaneous MEG and scalp EEG recordings help to enhance the detection yield of interictal spikes in epileptic patients. MEG is potentially better than EEG for the localization of interictal spikes because skull and scalp do not distort magnetic fields. In addition, MEG records nearly pure tangential dipole activity, whereas EEG measures a mixture of radial and tangential components. Accordingly, the results of MEG dipole modeling by inverse dipole solutions should be more accurate.

For temporal lobe epilepsy, MEG study provides dipole orientations and locations of interictal spikes and thus help to differentiate between mesial and lateral seizure onset. The relavant information is important for treatment planning. For extratemporal epilepsy, MEG can delineate the location of the irritative zone and define its anatomical relation to brain lesions and functionally eloquent areas. The results are very helpful for planning of surgical procedures and placement of subdural electrodes. Besides, MEG offers a noninvasive reevaluation of the irritative zone in patients with recurrent seizures after previous epilepsy surgery. MEG is better than EEG in these patients because magnetic fields are not influenced by skull and dural defects caused by prior operation.

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簡介腦磁圖及其在癲癇手術之評估應用

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平均每一百名癲癇患者當中有十至二十位無法單獨靠抗癲癇藥物獲得良好治療，而長期遭受反覆癲癇發作，部份個案可以藉由手術方法將癲癇病灶摘除而改善病情。成功的癲癇手術將使患者之癲癇不再發作或發作次數顯著減少，並且沒有因手術而造成之神經功能損傷。

為確保癲癇手術之成功，在術前需要有周詳的檢查評估以確認癲癇病灶所在的部位及其鄰近重要腦功能區位。常規術前評估方法包括：長時間之錄影暨頭皮腦電圖記錄、磁振造影掃描、單光子放射斷層檢查、正子放射斷層檢查、磁振頻譜分析以及神經心理檢查等。如果這些檢查仍無法獲得確切資料，患者可能需接受較具危險性的顱內腦電圖記錄檢查。

腦磁圖是一種完全不具有傷害性的腦功能檢查方法，原理是藉由高敏感性之磁場感應記錄器在頭皮表面測量腦部磁場。全頭型腦磁圖儀具有很多磁場感應記錄器，可以在同一時間偵測整個腦部不同部位之興奮狀況，應用腦磁圖檢查癲癇患者可以協助確認癲癇病灶，並釐清病灶與其鄰近功能區位之位置相關性，有助於導引顱內記錄電極正確的擺置，以及後續手術執行計劃之擬定。

本文將回顧有關腦磁圖的基本知識，並討論腦磁圖在癲癇手術評估的應用。

關鍵詞：腦磁圖、癲癇手術、癲癇棘波、定位