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Dynamic seizure imaging in patients with extratemporal lobe epilepsy

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Abstract— **Epilepsy is a common neurological disease that affects about 50 million people worldwide. Extratemporal lobe epilepsy, which represents an important type of epilepsy, may involve seizure activity in various lobes and the surgical treatment in these patients tends to have less favorable surgical outcome. Noninvasive seizure imaging in drug-resistant patients is of vital importance to image the seizure onset zones (SOZs) and understand the mechanisms for an improved treatment plan. In this study, we directly imaged the seizure sources in 8 extratemporal lobe partial epilepsy patients from noninvasive EEG. The surgically resected regions and SOZs identified from intracranial EEG (iEEG) recordings were used to evaluate the source imaging results. All of the eight patients underwent resective surgery and the estimated seizure sources were co-located with the resection zone. Seven of the patients had iEEG recordings available and the source imaging results were concordant with the SOZs marked on the intracranial recording grid. The present results suggest that dynamic seizure imaging could be potentially useful to image the SOZs of extratemporal lobe seizures and help the pre-surgical planning of epilepsy patients.**

I. Introduction

Epilepsy affects about 50 million people in the world and 30% of the patients cannot control their seizures effectively with the currently available antiepileptic drugs [1]. Surgical treatment removing the epileptogenic foci is one of the last practical options [2]. Intracranial monitoring has been intensively used in routine clinical settings and it is considered as the gold standard to identify the seizure onset zones for surgical planning [3]. However, due to the risk factors of this highly invasive procedure and the limited intracranial recording facilities in the healthcare system, it is desirable to have noninvasive modalities to help image and study the epileptic brains in epilepsy patients.

EEG has been routinely used in hospital monitoring to diagnose epilepsy and other neurological diseases. Recent advancement in EEG source imaging has also helped to noninvasively study the underlying brain activity in addition to the traditional EEG trace examination. Many studies have shown that interictal spikes could be successfully used to lateralize or localize the seizure onset zone [4-7]. Temporal lobe epilepsy is the most commonly studied epilepsy type, while few investigations have taken into account the extratemporal lobe epilepsy [8, 9]. The source imaging in ictal EEG remains a challenge due to the diverse ictal patterns and possible moving artifacts [10-12]. In this study, we have investigated imaging the SOZs of extratemporal lobe epilepsy from noninvasive ictal EEG and validated the imaging results as compared with the surgical resection and intracranial EEG recordings.

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II. Methods

A. Patients and data acquisition

The schematic diagram of this study is shown in Fig. 1. Eight medically intractable epilepsy patients were included in this study. All the patients had seizures captured during the long-term EEG recording. Both the pre-operative MRI and post-operative MRI images were acquired in these patients. All the patients underwent resective surgery and seven of them had intracranial recordings. The patients were studied under the approved protocol by the Institutional Review Boards of the University of Minnesota and the Mayo Clinic.

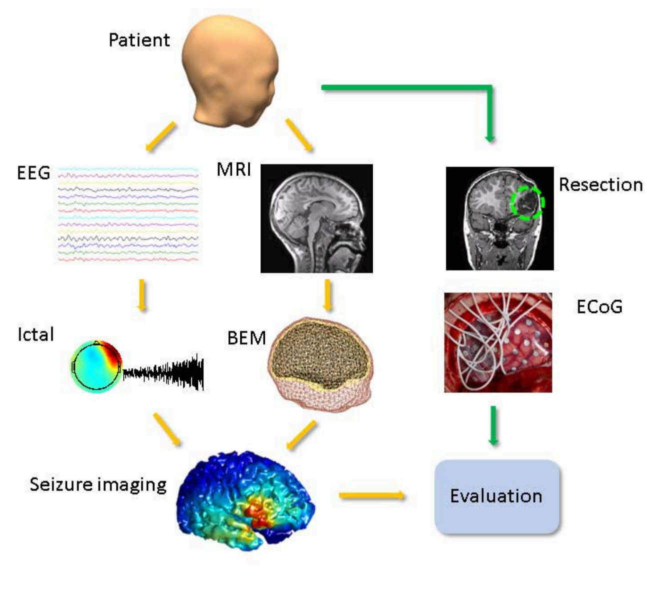

Figure 1. Illustration diagram of seizure source imaging and study design.

The scalp EEG was recorded prior to the patient surgery in a long-term video EEG monitoring. The EEG was sampled at 200 Hz and band-pass filtered between 1-70Hz. The recorded EEG had 32 channels and the recording electrodes were placed according to the modified 10-20 system. The scalp EEG was reviewed by experienced epileptologists and seizures were marked from the EEG data. High resolution structural MRI was scanned in all of these patients before their surgery and these MRI images (voxel size: 0.9375* 0.9375* 1.0 mm^3) were acquired from a 1.5 Tesla or 3 Tesla GE Signa scanner (General Electric Medical Systems, Milwaukee, WI). Individual realistic boundary element method (BEM) head models with three layers were segmented from the structural MRI in Curry software (Compumedics, Charlotte, NC).

B. Dynamic seizure imaging

The dynamic seizure imaging (DSI) approach [13] was used to extract spatio-temporal ictal features and reconstruct the seizure sources on cerebral cortex. The scalp EEG represents mixed activities including functional brain activity, baseline activity, and artifacts. The EEG can be decomposed into independent components (ICs) with spatial maps and temporal activation [13-15]. The source separation can be accomplished by independent component analysis (ICA) as following,

$$\Phi = \mathrm{WMT} = \sum_{i=1}^{N_C} w_i M_i T_i \qquad (1)$$

where Φ is the measured EEG, N_c is the number of ICs, w_i is the *i*th weighting, M_i and T_i are the *i*th spatial map and temporal activation, respectively.

Artifact components of eye blinks and other motions were rejected from the ICs [16]. Ictal components with temporal-spectral features were selected for the source imaging. Spectrogram correlations between IC and ictal EEG were used to find the significant ictal components. The IC components with less than 80% dipolar fitting variances were rejected from the source analysis [14, 15]. The ictal EEG Φ can be represented by the N_s seizure components. By solving the inverse problem, the estimated source activities $\hat{S}$ can thus be expressed as

$$\hat{S} = A^{-1}\Phi = A^{-1}\left(\sum_{i=1}^{N_S} w_i M_i T_i\right) = \sum_{i=1}^{N_S} w_i \left(A^{-1} M_i\right) T_i \approx \sum_{i=1}^{N_S} w_i \hat{S}_i T_i \qquad (2)$$

where A is the lead field matrix, $\hat{S}_i = A^{-1} M_i$ is the estimated source for *i*th IC. The source distribution could then be reconstructed by combining the IC sources in the source domain. Cortical current density (CCD) model with unconstrained orientations [17] and minimum norm estimation [18] were used to image the sources. The cortex with two-millimeter resolution was extracted from structural MRI (Curry, Compumedics, Charlotte, NC) and the lead field matrix was computed from the individual realistic BEM model. The BEM model had three layers (scalp, skull, brain) and the conductivity values were chosen as 0.33 S/m, 0.0165 S/m, and 0.33 S/m [19].

C. Evaluation of seizure imaging results

The source imaging was conducted on the eight patients and the DSI results were evaluated with the surgically resected region and seizure onset zone (SOZ) determined by intracranial EEG (iEEG) of the patients. The estimated seizure sources were on the cerebral cortex and the source location with source maximum was used for the estimated source. All patients had surgery and post-operative MRI images. The resection zones were obtained from post-operative MRI and used to validate the estimated sources. Concordant results were obtained if the maximal source was inside the resection. In the seven patients with intracranial recordings, we compared the estimated results with the SOZs of iEEG. The ECoG electrodes were one centimeter away from each other and the electrode locations were obtained from CT images. The distance between the maximal estimated source and its closest SOZ electrode was evaluated for the patients with intracranial recordings.

III. Results

Eight drug-resistant patients with extratemporal lobe epilepsy were studied. Seizure sources were compared with surgically resected regions in all patients and with iEEG-SOZ in the seven patients who had intracranial recordings.

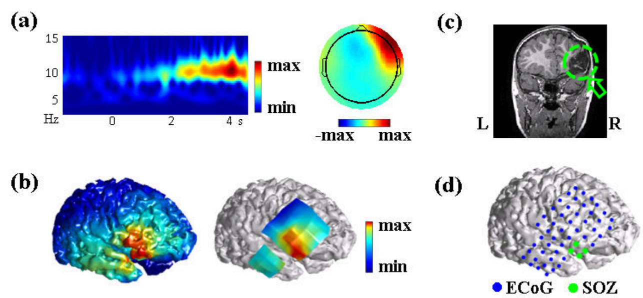

Figure 2. Seizure imaging results in one patient. (a) Time-frequency representation and spatial map of one seizure component. (b) DSI seizure onset results displayed on cortex (left) and ECoG grid (right). (c) Surgical resection shown on post-op MRI image. (d) Clinically marked SOZ.

Fig. 2 shows seizure imaging in one patient and the DSI results are compared with the surgical resection and the SOZ determined by iEEG. Multiple seizure components were extracted and the ictal component with the earliest seizure activity is demonstrated in Fig. 2a. The seizure is characterized as alpha activity as shown in the time-frequency representation (TFR), and the scalp map indicates that the activity is located in the right fronto-temporal area. The estimated DSI results over whole cortex (Fig. 2b, left) suggest that the seizure onset is in the right lateral frontal region. This patient underwent intracranial monitoring and the intracranial electrodes were implanted over right frontal and right temporal lobe. The DSI results overlapping with intracranial electrodes are projected and displayed on the intracranial grid (Fig. 2b, right). The post-operative MRI in Fig. 2c suggests that resective surgery was performed on the right frontal lobe of the patient. The SOZ of intracranial EEG marked on Fig. 2d shows that the seizure onset activity is located at the posterior part of right frontal grid. The DSI results are located in the right frontal region and they are concordant with the resection and SOZ of intracranial monitoring.

The DSI results and comparison with surgical resection and SOZ in another patient are shown in Fig. 3. Multiple seizure components were extracted and the seizure component with the earliest seizure activity is shown in Fig.

3a. The seizure is characterized as theta activity as shown in TFR, and the spatial map suggests the parieto-occipital location of the activity. The DSI results on the cortical layer and intracranial grid (Fig. 3b) indicates occipital seizure sources. The post-operative MRI image in Fig. 3c shows that the resective surgery was performed on the occipital lobe of the patient. The SOZ marked in Fig. 3d suggests that the seizure onset activity is located in the posterior part of left occipital grid. These results suggest that the DSI results in the left occipital lobe are co-localized with the surgically resected region and the SOZ delineated from iEEG.

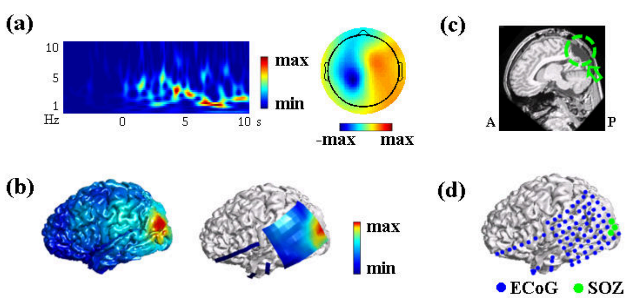

Figure 3. Seizure imaging results in another patient. (a) Time-frequency representation and spatial map of one seizure component. (b) DSI seizure onset results displayed on cortex (left) and ECoG grid (right). (c) Surgical resection shown on post-op MRI image. (d) Clinically marked SOZ.

Table I shows the seizure source imaging results in all the eight epilepsy patients. The DSI results are concordant to the surgical resection if the estimated maximal source is inside the surgically resected region. In six of the eight patients, the estimated source maxima were located within the surgical resection. The DSI source maxima of the other two patients were in close vicinity to the boundary of resected region. Seven epilepsy patients underwent intracranial monitoring. In five patients, the DSI results were only having one electrode distance from the iEEG-SOZ. The result with one electrode distance to SOZ may be caused by the localization error and it may also be explained by the limited coverage of intracranial EEG because iEEG may not fully capture the activity between two iEEG electrodes. These results show that the DSI imaged sources are in concordance with the surgically resected region and the intracranial monitoring of the patients.

IV. Discussion

EEG has been used as an important tool to noninvasively capture the electrophysiological activity with high temporal resolution at millisecond scale. While intracranial recordings are usually covered over certain limited areas of human brain, scalp EEG has the advantage of covering the whole head and it can track the local brain activation and global brain networks. The recent advancement in EEG source imaging techniques has further expanded the usage of EEG from traditional waveform inspection to noninvasive study of the underlying brain activation. Efforts have been made to image seizure sources in epilepsy patients [10, 12, 20-22]. However, it remains difficult to accurately localize ictal sources because the seizure EEG may include moving artifacts and noises. The variation of seizure activity across time, space and frequency makes it more challenging to image the seizure sources. The dynamic seizure imaging approach was recently developed to track the spatio-temporal activation of seizures [13]. The DSI approach provides a way to extract features of seizure activity and reconstruct the spatio-temporal imaging results without handling the inverse problem on the large amount of EEG time points. In this study, the DSI approach was applied in eight epilepsy patients and the imaged ictal sources were in concordance with the surgically resected region and SOZ of intracranial monitoring.

The brain activation can be noninvasively estimated from EEG source imaging method by constructing the head models and volume conducting models [4, 6, 23]. Individual realistic BEM models were obtained in this study from patient MRI images and they were used for imaging EEG source to enhance the spatial resolution. Previous studies have suggested that more accurate source imaging results can be achieved in realistic head models compared to spherical models [7]. Additional information such as anisotropic conductivities [6] and fMRI constrains [24-26] can also be used to further improve the EEG source analysis results.

TABLE I. SOURCE IMAGING RESULTS IN ALL PATIENTS

Pt	Location of source maximum	Comparison to Resection	Comparison to iEEG-SOZ
1	R posterior frontal	*	+
2	L occipital	*	+
3	L posterior frontal	**	++
4	L superior frontal	*	+
5	R superior frontal	*	+
6	R superior frontal	*	+
7	R anterior frontal	*	++
8	L parietal	**	N/A

Left (L), Right (R); *: Source maximum is located inside surgical resection; **: Source maximum is close to surgical resection; +: Source maximum is located around 1 electrode distance to SOZ; ++: Source maximum is located within 3 electrode distances to SOZ.

It has been challenging to lateralize and localize seizure onset zone in patients with extratemporal lobe epilepsy [8]. The epileptogenic foci and the functional cortical region may overlap with each other, which makes it more difficult to plan successful surgery in extratemporal patients without impairing functioning cerebral cortex. It is thus crucial in extratemporal lobe patients to accurately distinguish the epileptogenic zone and functioning brain regions. Among the eight studied patients, the DSI seizure onset results of six patients were inside the resection zone. The DSI result in one patient was within 3 electrode distances to the iEEG-SOZ, but the estimated source maxima was still inside the resection zone which included the resected SOZ and the resected surrounding regions. In the other two patients with frontal and parietal lobe epilepsy, the DSI sources were not inside the resection zone but in close vicinity to the resection boundary. This small location discordance may be caused by the localization error of source imaging and it may also be the result of the limited resection size in the critical functioning cortex. Although it is essential to resect the whole epileptogenic zone to achieve a successful surgical outcome, resective surgery needs to be cautious in extratemporal patients to prevent from damaging functional cerebral cortical regions. Application of DSI in identifying functioning brain regions could further assist in distinguishing eloquent cortex from pathological regions of the patients.

In conclusion, we have studied dynamic seizure imaging in eight extratemporal lobe epilepsy patients. Our results indicate time-frequency seizure features can be extracted and used to localize and image brain regions generating seizures. The estimated sources were found concordant with the surgically resected regions and seizure onset zones as determined from intracranial EEG recordings in the patients. These promising results suggest that innovation in source imaging and localization may lead to enhanced management of intractable epilepsy through direct seizure imaging from noninvasive EEG recordings.

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