Head modeling and cortical source localization in epilepsy

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***Abstract*— In this study, we developed numerical methods for investigating the dynamics of epilepsy from multi-scale EEG recordings acquired simultaneously from the scalp (sEEG) and intracranial subdural and/or depth electrodes (iEEG) in patients undergoing pre-surgical evaluation at the epilepsy center of the Mayo Clinic (Rochester, MN). The data are analyzed using independent component analysis (ICA), which identifies and isolates independent signal components from multi-channel recordings. A realistic individual head model was constructed for a patient undergoing pre-surgical evaluation. The forward problem of electro-magnetic source localization was solved using the Boundary Element Method (BEM). Using this approach, we investigated the relationships between noninvasive and invasive source localization of human electrical brain data sources. A difference of about 1 cm was observed between sources estimated from sEEG and iEEG measurements.**

I. INTRODUCTION

Epilepsy is one of the most common neurological disorders, affecting 50 million people worldwide, and in approximately 30% of these patients the seizures are not controlled by any available medical therapy. About 4.5% of all patients with epilepsy are thus potential candidates for surgical treatment. Epilepsy surgery has a good chance of success in this patient group, but only if the brain region generating seizures can be accurately localized and then safely removed. For this purpose, in selected cases, recordings are acquired using subdural and/or depth electrode (intracranial) pre-surgical evaluation. The aim of this study is to model and analyze the dynamics of epilepsy from multi-scale EEG recordings using simultaneous scalp (sEEG) and intracranial (iEEG) electrodes pioneered by Dr. Worrell at the Mayo Clinic. Independent component analysis is combined with source localization of the identified signal components. For accurate source localization, realistic head models are generated for the subjects undergoing pre-surgical evaluation, subjects for whom a part of the skull has been removed temporarily to implant the iEEG electrodes.

The head models are built to model the geometry and conductivity of brain, skull, and scalp, then potentials on the sensor locations are determined from a given dipole source in the model (i.e. forward problem). Source localization is then performed by searching for a source distribution whose forward solution best matches the measurements. Successful source imaging using EEG measurements of epileptic activity has two main challenges: A realistic, subject specific head model must be constructed, and the epileptiform discharges must be identified and isolated from the EEG background signal.

The accuracy of the head model used in electrical source imaging (ESI) affects the accuracy of the source localization significantly. A spherical head model may estimate the location of the seizure onset with up to 2–3 cm error [1]. Also, the influence of post-surgical defects in the skull and the influence on forward field computation of plastic sheet in which the subdural electrodes are embedded cannot be neglected [2]. When realistic head models are used, the forward ESI problem should be solved numerically. Here, we used an accurate Boundary Element Method (BEM) implementation by Akalin-Acar and Gencer [3] that allows the use of intersecting tissue boundaries (eyes, holes in the skull etc.) and can also handle models with multiple compartments inside the skull [4].

Another factor that affects the epilepsy source localization is the identification and isolation of epilepsy related sources from the EEG background signal. Ebersole and Hawes-Ebersole have shown that much of the epileptic spike activity recorded by subdural electrodes is not visible on the scalp [5]. Several researchers investigated the size of the area that must be synchronously active for the spikes to be visible on the scalp EEG recordings. While smaller cortical areas create signals that can be measured from the scalp, the amplitude may not be high enough to be recognizable as a spike in the background EEG activity, including the activities of other brain sources, muscle and eye movements and even the heart. In this study, we use Infomax Independent Component Analysis (ICA) developed by Makeig *et al* [6] for removing eye and muscle activity artifacts and also to identify and separate functionally independent components. So far only a few studies have applied ICA to EEG data recorded from epilepsy patients. Several papers have demonstrated that ICA may aid detection of epileptic seizure activity [7], [8]. For example, in an analysis of twenty four EEG seizures from medial temporal lobe epilepsy patients, successful lateralization of spikes increased from 75% to 96% after applying ICA [9].

ICA is applied to simultaneously recorded 78 channel intracranial and 29 channel scalp EEG. Source localization is performed using only scalp EEG, only intracranial EEG and both. Using this data, relationships between noninvasive and invasive human electrical brain data are investigated. Below, in the next section, methods for generation of realistic head models are explained and the results of the model generated for this study are given. In the third section, the ICA and source localization are explained.

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II. Head Modeling of the Epilepsy Patient

Some patients who will undergo epilepsy surgery first undergo a pre-surgical procedure in which a part of their skull is removed and areas around the suspected epileptogenic zone are recorded and stimulated to determine whether the seizure generating region is localized and suitable for operation, e.g. not within or too close to eloquent cortex. Before this pre-surgical procedure, magnetic resonance (MR) images are acquired. After the surgery, to locate the intracranial electrodes CT images of the head are acquired. To generate an electrical forward head model, first the MR and CT images of the patient are co-registered. The skull, intracranial electrodes, and the plastic sheet where the subdural electrodes are located are segmented from the CT images. The brain and the scalp are segmented from the MR images using Otsu thresholding, region growing, morphological operations, masking, and curvature anisotropic filtering [10]. A mesh generation algorithm, described in [3], is used to convert the segmented volumes into mathematical representation. The mesh generation algorithm uses triangulation, coarsening, smoothing, and topological correction steps. The flowchart for obtaining a model is shown in Figure 1.

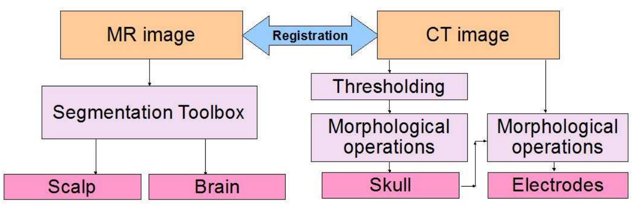


Fig. 1. MR and CT registration algorithm.

For this study, a realistic head model was generated for a patient having a porencephalic cyst in the fronto-parietal brain. A pre-surgical T1-weighted MRI was recorded with a resolution of 256 slices in axial, 256 slices in sagittal and 120 slices in coronal direction and a voxel-size of $0.86\times1.6\times0.86$ mm. A post-surgical CT was taken with a resolution of 68 slices in axial, 512 in sagittal and 635 in coronal and a voxel-size of $0.49\times0.49\times2.65$ mm. The CT and MR images are registered using methods in the ITK Toolbox (www.itk.org). The registered dataset was segmented into scalp, skull, cerebrospinal fluid (CSF), brain, plastic sheet, and intracranial electrodes. Figure 2 shows the BEM meshes for the skull, plastic sheet, and the scalp. Here, the CSF is not modeled for simplicity. The resulting model is used in forward/inverse problem (FP/IP) calculations to localize independent sources of simultaneously recorded iEEG and sEEG data.

III. Simulation Studies on the Accuracy of Forward Modeling

A series of simulations were produced to study the effects of head modeling on the forward problem calculations. The FP solutions on the scalp surface for the model shown in the previous section were compared with the solutions for the following models with 7813 dipole locations, each oriented

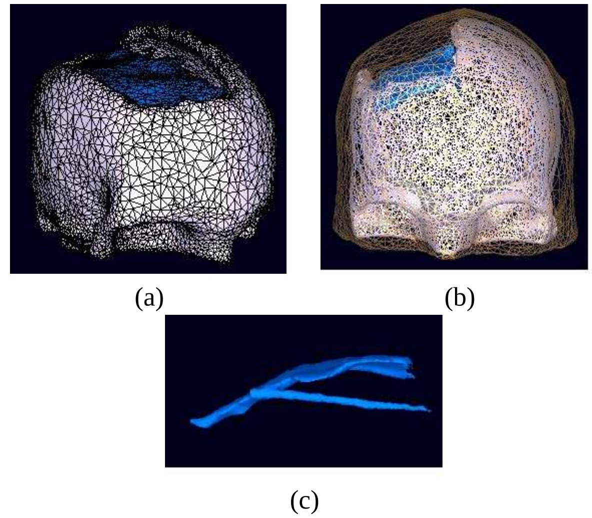


Fig. 2. BEM model of the scalp, skull and the plastic sheet, represented by 10000, 30000, and 7000 faces, respectively. (a) Skull and electrode sheet faces, (b) scalp, skull and sheet faces, (c) plastic sheet model of the plastic grid and strip electrode matrices.

in 3 different orthogonal directions: 1. The same model without the sheet, 2. A four-layer head model with closed skull, and 3. A three-layer head model with closed skull. Differences between the potential field topographies using the three models differed between 20-70%, the differences increasing as the dipoles approached the skull opening.

To determine whether it may be possible to use a single-layer brain model for intracranial EEG studies, the FP solutions on the brain surface of the four-layer head model were compared with the potentials obtained using a single-layer brain surface. The topographic difference between the two models was 13-40%. These results showed that it is crucial to use an accurate head model for correct source localization. Because of space limitations here, these results will be reported more completely elsewhere.

IV. ICA and Source Localization

This section describes the Independent Component Analysis of the iEEG and sEEG recordings. Dipoles are fitted to selected components using the realistic BEM head model. The ICA decomposition and source localization are described in the following sections.

A. *Independent Component Analysis*

Infomax Independent Component Analysis (ICA) has proven to be an effective method for removing eye and muscle activity artifacts from scalp EEG data, thus increasing the potential signal-to-noise ratio of subsequent analyses [6]. ICA can also identify and separate functionally independent components, which for normal scalp EEG prove to be most often associated with scalp maps matching the projection of a single equivalent current dipole.

In this work, sixteen minutes of simultaneously acquired 78 iEEG data from subdural electrodes (Figure 3) and 29 sEEG data from scalp electrodes from an epilepsy patient during drowsy resting were decomposed by extended infomax ICA ([6]) into 107 maximally independent component (IC) processes. ICA decomposition returned a vector of weights giving the relative strength and polarity of the projection of each IC source process to each of the electrodes, and an activation time series giving the time course of activity of each IC process during the data time period. Figure 4 shows maps of the projection patterns of two IC processes to the scalp in (a) and (b), and to the subdural electrode grids in (c) and (d). Figure 4 (e) and (f) show the projection patterns of the IC processes projected onto a detailed model of the patient's cortex derived from the patient MR head image by using Freesurfer (http://surfer.nmr.mgh.harvard.edu/). These two components were chosen because they represent orthogonal activity patterns. The IC shown in Figure 4 (a), (c) and (e) projects to a small number of adjacent electrodes all with the same polarity, representing a gyral source. The IC on Figure 4 (b), (d) and (f), on the other hand, is a sulcal source, projecting to two separate pools of adjacent electrodes with opposite polarities. The results of ICA decomposition ap-

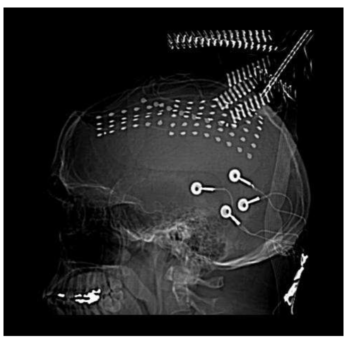


Fig. 3. CT image of the implanted grid electrodes. The two grids (6×8, 4×6) and one medial strip (1×8) implanted in the patient for monitoring.

plied to these and similar data force a reinterpretation of the nature of iEEG signals. In both clinical and research practice, it is nearly universally assumed that proximal signal sources must dominate signals received by electrodes placed on or in the brain surface, despite the potential influences of volume-conducted potentials from all parts of the brain on each electrode. That is, it is currently assumed that each iEEG channel signal may be considered to be a locally generated signal independent of other more distal source activities. ICA decomposition, by removing or minimizing the presence of volume conducted signal summation at the electrodes, demonstrates that each recorded iEEG signal is in fact the sum of a number of more proximal and more distal source processes. For cortical grid electrodes, the percent variance accounted for by any single (and, typically, proximal) IC source ranges in our experience between about 20% and 80%. The two IC sources above account for at most 47% (left) and 22% (right) of channel variance at their maximally projecting channel.

B. Inverse Problem Solutions

To localize the sources of the ICs single dipoles were fitted to selected ICA components. For this purpose, a three-

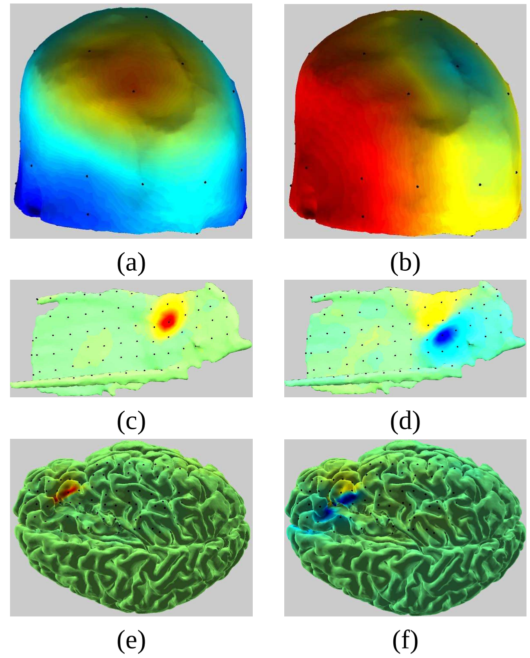


Fig. 4. Potential maps of two IC processes projected on the scalp electrodes (a) and (b), on the intracranial electrodes (c) and (d), and on the brain (e) and (f). Red color of potentials represents positive values and the blue color represents negative values. Multiplying these maps by the (two-sided) IC time courses gives the activity at each channel associated with the IC source.

dimensional dipole grid was constructed with a set of three orthogonal dipoles at each point. The grid contained 12,061 points with 5-mm spacing, for a total of 36,183 dipoles. This grid is illustrated in Figure 5. The lead field for each of the dipoles was constructed using the BEM solver.

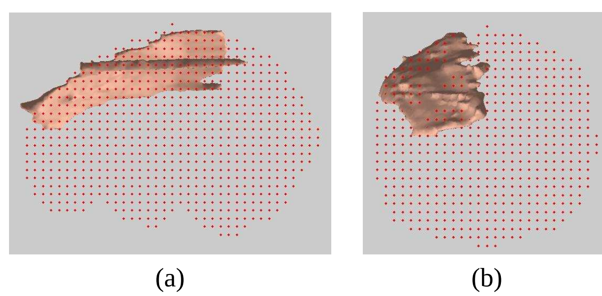
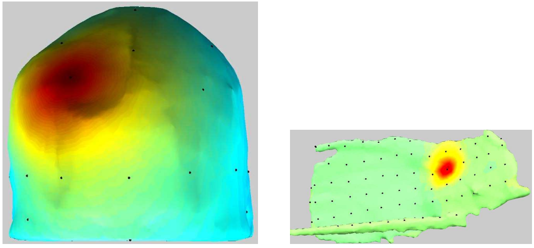


Fig. 5. Grid of dipoles located in the brain region with 0.5 mm spacing is shown with the plastic sheet model. (a) A view from right side of the brain, (b) a view from the front.

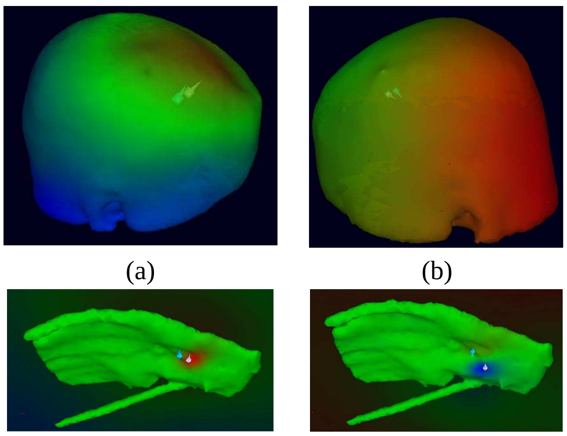
Next, field error at each grid point was calculated, and 20 grid points with lowest field error values were selected. A local search was initiated from each of these points, and the resulting dipole with minimum error was accepted as the dipole fit. By starting the local search from multiple points, the possibility of converging to a local minimum is reduced. This method was first validated using simulated data obtained from FP solutions, and was then applied to independent component maps extracted from subject recordings. The scalp and grid projections of one of the simulated dipoles is shown in Figure 6.

For each IC, the source localization was performed three



(a) (b)

Fig. 6. Forward projection of the field distribution of a simulated single dipole source (a) on the scalp EEG, and (b) on intracranial iEEG grids.



(a) (b) (c) (d)

Fig. 7. Inverse problem results of the two components shown in Figure 4. The blue dipole is estimated from scalp potentials and the white dipole from subdural electrodes. (a) and (c) are the source estimates for the IC representing a radial source on the scalp and sheet, respectively. (b) and (d) are the source estimates for the IC representing a tangential source on the scalp and sheet, respectively. The distances between the source estimates using sEEG and iEEG are 10.5 mm and 13.5 mm for the radial and tangential sources, respectively.

times, first using only the sEEG data. Second, we localized the same source using the iEEG map only. Finally, we localized the same component using both the sEEG and iEEG maps. The dipole source estimated for the component (shown in the left of Figure 7) is radially oriented, while the dipole for the component on the right is tangentially oriented. In particular, the tangentially oriented (sulcal) source on the right in Figure 7 does not dominate any iEEG channel signal. ICA-built spatial filters for independent signal sources, provide an opportunity to dissociate iEEG signal sources from the exact locations of the recording electrodes, and to use iEEG data to find and image off-gridnormal and pathological iEEG signal sources.

The source locations estimated using the joint sEEG and iEEG map are very similar to sources estimated from iEEG only. When sEEG data is used for estimation, there is a difference of 10.5 mm for the radially oriented dipoles, and 13.5 mm for the tangentially oriented dipoles compared with the sources estimated from the iEEG data. One of the reason for the difference between these results may be the low spatial sampling of scalp data. It is shown that the localization precision of epileptic sources drastically increses when the number of electrodes are increased from 31 to 63 [11]. Another factor may be related to registration of the scalp electrodes to the model. Since the electrode positions were not digitized during data acquisition, the positions in the model had to be estimated which may have caused additional errors in localization. Finally this model, does not contain the CSF layer. Although this is a thin layer, it may have affected the source localization results.

V. CONCLUSIONS AND FUTURE WORK

Here, we analyzed simultaneously acquired multi-scale EEG recordings using ICA and numerical forward and inverse solution methods and presented preliminary results exploring the relationship between noninvasive and invasive source localization of electrical brain activity. This research is expected to provide valuable insights into the dynamics of epilepsy and the electrophysiology of the human brain.

The next step is to analyze the seizure data using this model. We will investigate state transitions of ictal and interictal EEG data by applying multiple mixture ICA algorithms [12]. This will also provide information about the ability of ICA to isolate seizure components. Time-delayed (neurally propagated) phenomena captured at two or more spatial scales in concurrent surface and intracranial recordings will be investigated.

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