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Head model and electrical source imaging: A study of 38 epileptic patients

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ABSTRACT

Electrical source imaging (ESI) aims at reconstructing the electrical brain activity from scalp EEG. When applied to interictal epileptiform discharges (IEDs), this technique is of great use for identifying the irritative zone in focal epilepsies. Inaccuracies in the modeling of electro-magnetic field propagation in the head (forward model) may strongly influence ESI and lead to mislocalization of IED generators. However, a systematic study on the influence of the selected head model on the localization precision of IED in a large number of patients with known focus localization has not yet been performed.

We here present such a performance evaluation of different head models in a dataset of 38 epileptic patients who have undergone high-density scalp EEG, intracranial EEG and, for the majority, subsequent surgery. We compared ESI accuracy resulting from three head models: a Locally Spherical Model with Anatomical Constraints (LSMAC), a Boundary Element Model (BEM) and a Finite Element Model (FEM). All of them were computed from the individual MRI of the patient and ESI was performed on averaged IED.

We found that all head models provided very similar source locations. In patients having a positive post-operative outcome, at least 74% of the source maxima were within the resection. The median distance from the source maximum to the nearest intracranial electrode showing IED was 13.2, 15.6 and 15.6 mm for LSMAC, BEM and FEM, respectively. The study demonstrates that in clinical applications, the use of highly sophisticated and difficult to implement head models is not a crucial factor for an accurate ESI.

1. Introduction

In pharmacoresistant focal epilepsy the surgical resection of the epileptogenic area is a therapy of choice for reducing the frequency of seizures. During the presurgical evaluation, the precise identification of the epileptogenic zone is crucial in order to guide the removal of the epileptic foci and spare as much as possible the functionally relevant areas of the cortex. Several techniques are considered together to get a trustworthy estimation of the epileptogenic areas. Among them, electrophysiological investigations are particularly suited as they directly measure the neuroelectrical alterations that are the hallmark of epileptic activity. Compared to intracranial recordings, scalp electrical potentials are easy to acquire but they measure remote effects of electrical currents generated within the brain. As such, they do not allow a precise localization of the origin of electrophysiological abnormalities. The electrical source imaging (ESI) attempts to overcome this drawback by reconstructing the activity in the brain from a map of scalp potentials. Reviews (Kaiboriboon et al., 2012; Plummer et al., 2008) recently confirmed that ESI is a valuable tool for estimating the source of interictal epileptic discharges (IEDs) and clinical validation studies showed that these generators are reliable estimates of the seizure onset zone (Coutin-Churchman et al., 2012; Megevand et al., 2014) and the epileptogenic zone (Brodbeck et al., 2011).

ESI involves two steps. The first one, called resolution of the forward problem, consists in modeling how electrical currents generated in the brain propagate to the scalp electrodes, where their consequences are actually recorded. The second step, called resolution of the inverse problem, consists in inverting the forward model in order to get brain activity from scalp potential. The resolution of the forward problem

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highly depends on the head model (head geometry and tissue conductivity) and is eventually achieved by solving the Maxwell's equations accordingly, producing the forward operator called the leadfield matrix. Regardless of the ability of a method to invert the leadfield matrix, an inaccurate leadfield model will produce a bad inverse solution, and consequently will lead to an inaccurate ESI. More than thirty years ago, when the EEG inverse problem was first considered, the head model was a single semi-sphere with homogenous and isotropic electrical conductivity. Since then, head models have been greatly improved (Grech et al., 2008) and they can now account for multiple types of tissue and anisotropic conductivities. Most important in the context of presurgical evaluation is the use of realistic head models based on the individual MRI of the patient. The most commonly used realistic models are the Boundary Element Models (BEM) and the Finite Element Models (FEM). The superiority of BEM and FEM over 3-shell spherical head models has been proved using simulated data (Akalin Acar and Makeig, 2013; Fuchs et al., 2007) as well as small group of patients (Guggisberg et al., 2011; Wang et al., 2011). The downside of these sophisticated head models is an increased computational load. The Locally Spherical Model with Anatomical Constraints (LSMAC) (Brunet et al., 2011) tries to compensate this computational cost by using analytical equations while keeping the realistic aspect of the head geometry. In this model the leadfield is calculated iteratively using a spherical model with a different radius for each electrode. It is an improved version of the SMAC model (Spinelli et al., 2000) and has been successfully applied in recent experimental studies (Avanzini et al., 2013; Becker et al., 2013; Berchio et al., 2014) but, to our knowledge, has not been validated in patients with known focus localization and has not been compared to the well-established BEM and FEM. Besides, BEM and FEM themselves have not been evaluated on a large set of real data. We here present such a validation and comparison study on data of 38 epileptic patients in whom the irritative zone was known from intracranial recordings and in the majority of whom the epileptogenic area was surgically removed, allowing comparison of the ESI source maximum with the intracranial electrode positions and the resected zone.

2. Material and methods

2.1. Patients

The patient dataset (Megevand et al., 2014) included $n = 38$ patients (age at evaluation 24 ± 12 years, range 3–51 years, 21 male, 17 female) matching following inclusion criteria: i) they suffered from drug resistant partial epilepsy, ii) they had high-density scalp EEG (128 or 256 channels) showing interictal spikes, iii) they underwent intracranial EEG showing interictal spikes. 32 of them also had a surgical resection of supposed epileptic areas of the brain. The retrospective study presented here is part of a larger neuroimaging program in epilepsy approved by the local ethics committee.

2.2. Scalp EEG

Fourteen patients were recorded using the 128-electrode Geodesic Sensor Net and 24 using the 256 electrode Geodesic Sensor Net. Electrode impedances were kept below 20 kΩ (Ferree et al., 2001) and signal was 0.1–100 Hz band-pass filtered. We recorded at least 30 minutes of continuous EEG at 256–1000 Hz sampling frequency. Peaks of 20–50 interictal spikes with similar scalp distribution were marked by expert neurologists (SV, MS) and averaged within a window of 1s centered on the marked peaks. For further analysis, electrodes on the cheek and the neck were systematically removed from the EEG because they were too noisy and artifact-laden. If other channels exhibited strong and repetitive artifacts, they were also removed and the corresponding signal rebuilt by interpolating neighboring electrodes using a spherical spline. Hence, 204 electrodes from the 256-electrode recordings were used for the analysis, and 125 were kept from the 128-electrode cap.

2.3. Irritative zone

The estimation of the irritative zone (IZ) was based on intracranial EEG recordings. Thirteen patients were implanted with only subdural grids and strips, 12 patients had only depth electrodes, and 13 had both subdural and depth electrodes. Positions of intracranial electrodes were calculated using the post-implantation imaging (CT for 36 patients and MRI for 2 patients) and coregistered with solution points of ESI. Interictal recordings were reviewed by board certified EEG experts (MS, SV). Contacts showing interictal spikes formed the irritative zone. Contacts involved only in the propagation of interictal spikes were not included in the IZ. In IZ the electrode showing in average the highest peak amplitude was considered as the centroid of IZ. The location of this electrode will be denoted by max-IZ in the following.

2.4. Surgery

Surgical resection of the supposed epileptogenic area of the brain was performed on 32 patients. Post-operative follow-up of at least one year allowed neurologists to determine outcome of surgery. 15 patients had an Engel class I outcome (seizure free), 8 had Engel class II (decrease of seizure frequency of more than 80%), 7 had Engel class III (decrease of seizure frequency 50–80%) and 2 had Engel class IV (no change). Engel class I and II were considered as positive outcome while Engel class III and IV were considered as negative outcome. All operated patients had post-operative MRI acquired at 1.5 or 3 Tesla with T1 weighting. We used these images to precisely determine the resected areas and coregistered them with the solution points used in the ESI.

2.5. Inverse solution

We used the inverse method LORETA (Pascual-Marqui et al., 1994) implemented in Cartool (Brunet et al., 2011). This method basically provides a pseudo-inverse matrix of the leadfield matrix using a least square Tikhonov-regularized solution under a smoothness constraint. The pseudo-inverse applied on the peak of averaged spikes gave us an estimation of the underlying brain activity. More precisely, strength of dipoles associated with each solution point was obtained. While several studies suggested that source localization at the peak of the spikes may be contaminated by spike propagations (Alarcon et al., 1994; Lantz et al., 2003a; Ray et al., 2007), we wanted to ensure that the SNR was sufficiently high for all patients, which was not the case when performing the ESI at the half of the rising-phase. The source of surface spikes is known to be spatially extended (Tao et al., 2005). As LORETA is not able to determine the extension, we took into account only the solution point with maximal source strength. This point will be denoted ESI-max in the following.

2.6. Leadfield matrix and head models

The leadfield matrix is a linear operator that transforms current generated at solution points in the brain into scalp potentials. It depends on i) the position of the solution points, ii) the position of the scalp electrodes, and iii) the volume conductor model.

We constrained the solution points in the gray matter using the individual pre-implantation T1 MRI and placed them on a regular grid of 6 mm resolution (yielding 3000 to 5000 solution points). Scalp electrodes were coregistered with the individual T1 pre-implantation MRI performing a 9-parameter transformation of a template cap[1] such that T9, T10 and Cz were placed according to the 10–20 system. Electrodes of the transformed template cap were then projected onto the head surface. Solution point generation and electrode coregistration

[1] Available at https://sites.google.com/site/cartoolcommunity/files.