Effects of Spike Averaging on EEG, MEG and Combined EEG/MEG Source Analysis of Epileptic Activity

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Introduction

Determining the location and the extent of the epileptogenic tissue is of great importance for a successful surgery and seizure freedom. In most source localization studies either each interictal spike was localized separately or all spikes were first averaged (grand-average) and then localized. The former might give an estimate on the size of the irritative zone while the latter benefits from improved signal-to-noise-ratio (SNR). Many papers suggested the size of the irritative zone as an indicator of the focality and the chance of seizure freedom after surgery (Oishi et al., 2006). In this study, we chose a compromise between those by using sub-averages and compared its performance with single and grand-averaged spikes. Moreover we investigated if combined EEG/MEG (EMEG) has advantages compared to single modality EEG or MEG localizations.

Noninvasive EEG-MEG measurements

A patient suffering from pharmaco-resistant focal epilepsy has been measured with simultaneous EEG (80 Electrodes) and MEG (275 gradiometers).

Somatosensory Evoked Potentials (SEP) and Fields (SEF): Electrical stimulation of the medianus nerve with randomized inter-stimulus interval (ISI) 350 - 450 ms for 7 minutes.

Spontaneous measurements: The patient was advised to relax and was measured for 24 minutes.

Stereo-EEG measurements

Measurements from 14 intracerebral depth electrodes with in total 167 contacts have been used. 24 leads from 5 different electrodes and 8 leads from 2 electrodes were active during temporal interictal spikes and seizure onset, respectively. sEEG results were accepted as the ground truth and used to assess the accuracies of other methods. The convex hull determined from sEEG interictal spikes is shown in Fig.1 with green dots.

MRI measurements

T1-weighted (T1w-), T2-weighted (T2w-) and diffusion-tensor (DT-) MRI scans were acquired on a 3T scanner. T1w- and T2w- MRIs had 1.17 mm and DT-MRI had 1.875 mm edge length for the measured cubic voxels. The total acquisition time required for these three scans was 27 minutes (approximately 9 minutes each).

Spike detection

BESA Research has been used to mark epileptic spikes. First, 10 clear left temporal epileptic spikes were selected and averaged using temporal source montage. Then, the averaged signal was used in template search to find spike candidates. After visual inspection 200 left temporal spikes have been selected for further analysis.

Head model and source space construction

- T1w- and T2w- MRIs were used to segment skin, skull compacta, skull spongiosa, cerebrospinal fluid, gray and white matter. A pipeline that includes FSL, Freesurfer and CURRY has been used for segmentation. DT-MRI has been used to model white matter anisotropy (Fig. 1).
- The SEP-SEF data has been used in an iterative fashion to calibrate patient specific skull compacta and spongiosa conductivities.
- We constructed a 2 mm source space, constrained inside the gray matter, with a custom written Matlab code. It was ensured that all source space points were sufficiently away from other tissues, thus satisfies the Venant condition.
- A geometrically adapted hexahedral mesh with 1 mm resolution was constructed with Vgrid, and SimBio software was used for calculating the EEG and MEG leadfield matrices from the FE mesh.

Subaveraging procedure

Ten subaverages starting from 5 (Av5) as multiples of 5 until 50 (Av50) spikes were constructed with random drawing using Matlab. Each subaverage group consists of 200 subaveraged signals. It was insured that none of the spikes appear twice in the same average.

Source reconstruction

The source space, and the leadfield matrices calculated with SimBio were imported to CURRY 7, and moving dipole scans for EEG, MEG and EMEG were calculated from -33 to 0 ms (EEG peak).

Results

- Localizations obtained with varying subaverages differed considerably from each other and most accurate results were obtained from sub-averages of 10 (Table 1).
- EMEG localizations were closer to the centers of the irritative and seizure-onset zones than EEG and MEG alone (Fig. 2).
- The localization error at the spike onset was 4 mm and increased up to 25 mm at the spike peak (Fig. 2).
- The scatter size was highly correlated to SNR (the closer to the spike peak (0ms), the higher the SNR) (Fig.3).

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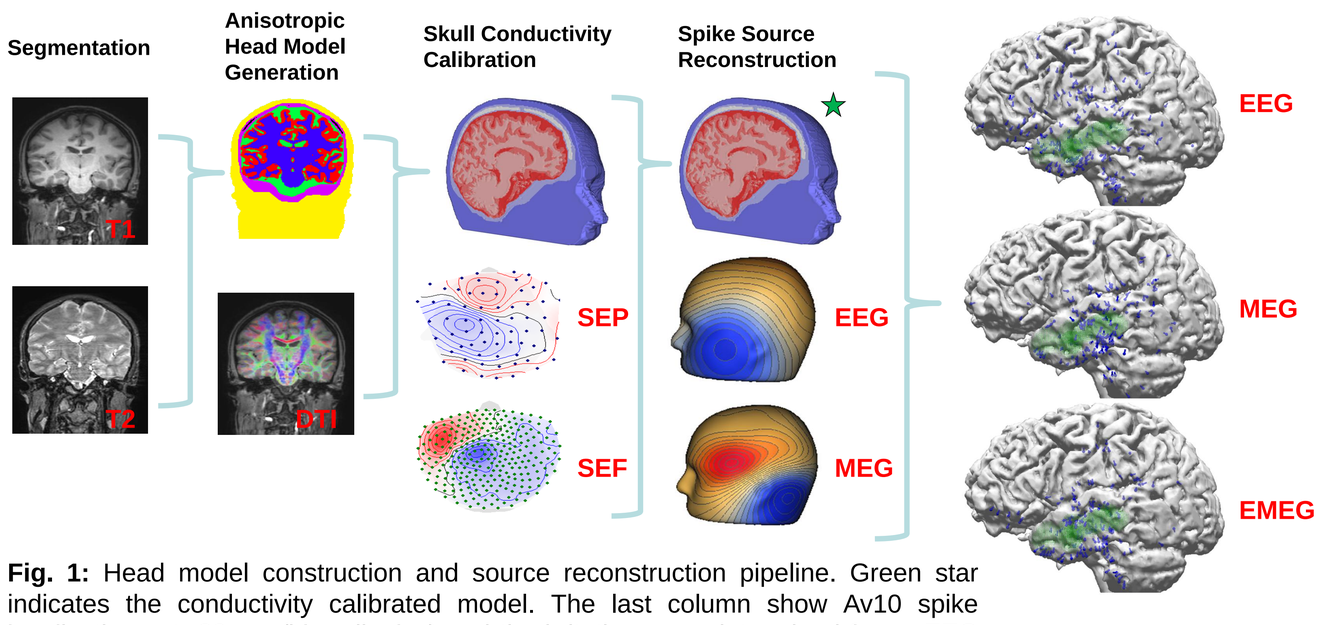

Fig. 1: Head model construction and source reconstruction pipeline. Green star indicates the conductivity calibrated model. The last column show Av10 spike localizations at -30 ms (blue dipoles) and the irritative zone determined from sEEG (green dots).

	EEG	MEG	EMEG
Single spikes	23 / 34	28 / 33	29 / 36
Av10	17 / 27	16 / 15	6 / 15
Grand-average	34 / 38	28 / 22	14 / 18

Table 1: The distances (in mm) of EEG, MEG, EMEG; single spike, Av10 and grand-average localizations to the center of the irritative zone / seizure onset zone. The localizations are given for -33 ms.

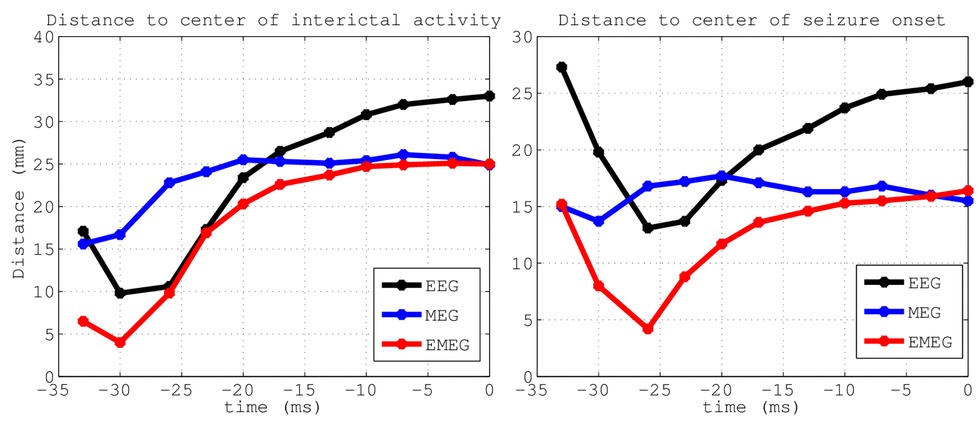

Fig. 2: The distances of EEG, MEG and EMEG localizations to the center of the irritative zone (left) and seizure onset zone (right).

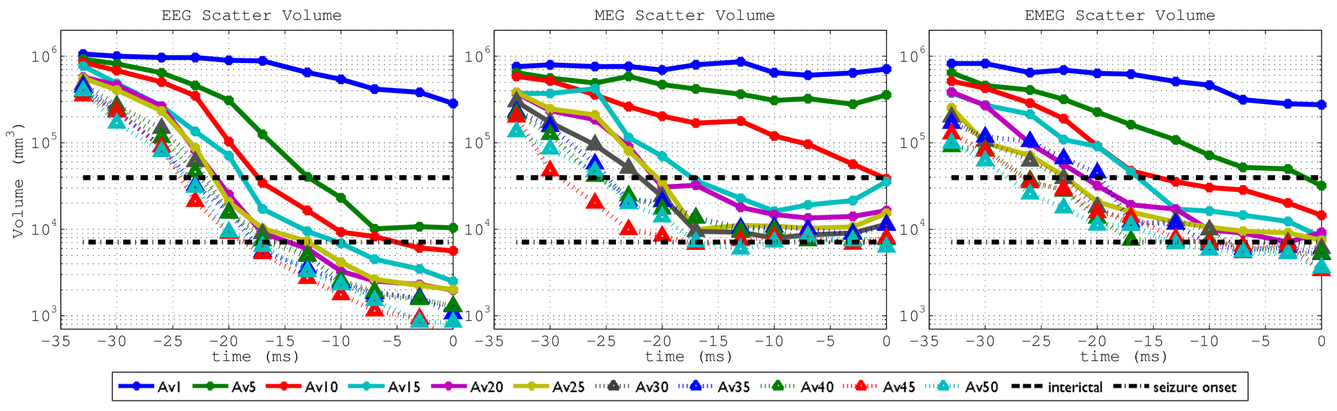

Fig. 3: The plot of scatter volume (mm^3) versus time for different subaverages. Each color/symbol represents a different subaverage and Av1 indicates single spike localizations. Black dotted lines indicate the volumes determined from the active sEEG leads during interictal spikes and seizure onset.

Conclusions

- Combined EEG/MEG source analysis can increase accuracy and confidence of localizations.
- Using spike onset instead of peak could help avoiding mislocalizations due to propagation.
- The SNRs of single spikes at the onset are not always sufficient for reliable localizations and therefore, averaging should be performed.
- Sub-averaging might achieve accuracies that neither single nor grand-averaged spike localizations can achieve.
- The size of the dipole scatter depends highly on SNR; thus, one should be very careful interpreting this.

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