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Interindividual variability of skull conductivity: an EEG-MEG analysis.

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Abstract. Source localizations based on EEG and MEG show different accuracies. One of the major differences between EEG and MEG localization is that the former depends on electrical tissue conductivities. It is hypothesized that an incorrect assumption of the skull conductivity value is a major contributor to EEG inaccuracy. In a simulation study, it is shown that assuming single skull conductivity for a population of subjects that show a realistic inter-individual variability for this value EEG localization inaccuracy is mainly in the direction between source and skull. This is confirmed by a re-analysis of EEG-MEG data obtained from a group of epilepsy patients. In the direction parallel to the skull EEG and MEG accuracy are comparable. For source localization, the EEG can be as accurate as MEG can, if individual conductivity values are supplied.

Keywords: EEG;modeling;dipole;skull;conductivity.

1. Introduction

Since the introduction of the equivalent current dipole inside a set of concentric spheres as a tool for performing EEG source localization, attempts have been made to determine the electrical conductivity of the human skull. This has resulted in a large number of papers and a corresponding large number of different values for the conductivity. This variability is in part caused by different approaches chosen in these various studies. Data was obtained from *post-mortem* skull soaked in a saline solution, freshly excised skull or *in vivo* skull [Wendel and Malmivuo, 2006]. Measurement methods include four point methods [Oostendorp *et al.*, 2000], model-based impedance estimation [Hoekema *et al.*, 2003], analysis of simultaneous EEG-MEG evoked response data [Gonçalves *et al.*, 2003] and simultaneous intracranial- and surface EEG [Zhang *et al.*, 2006]. Summarizing al these studies, when expressed as a skull to skin conductivity ratio, values ranging from 1/5 to 1/100 have been reported [Wendel and Malmivuo, 2006]. This raises questions about the validity of results obtained using EEG source localization procedures based on an assumed `realistic' skull conductivity value. It is well known that errors resulting from assuming a wrong conductivity value can be substantial [Huiskamp *et al.*, 1999]. This has been a major reason for using (expensive) MEG for source localization. MEG is fundamentally insensitive to the exact value of skull conductivity.

Instead of a quest for the 'true' value of skull conductivity, if may make more sense to consider individual skull conductivity in EEG source localization procedures. Some of the studies mentioned above indeed have demonstrated inter-individual variability [Hoekema *et al.*, 2003, Gonçalves *et al.*, 2003]. Substantial inter-individual variability as the greatest contributor to the observed range of conductivity values reported in the literature would have an impact on the prospect of source localization on basis of EEG that is as accurate as MEG is. In this paper, this issue is addressed by comparing EEG and MEG simulation data for various assumed conductivity ratios to real data measured in a group of epilepsy patients with well-defined lesions that can be assumed to cause focal interictal activity. For MEG there should be no influence of skull conductivity on source localization variability. The extend to which this does not hold for EEG is investigated in this study. If a substantial part of EEG localization variability can be attributed to inter-individual variability in skull conductivity, proper EEG source localization should be accompanied by an estimation of this skull property [Ferree *et al.*, 2000].

2. Material and Methods

2.1. Simulations

A boundary element model was constructed based on a 3DT1 MRI of one of the patients of a previous study [Jansen *et al.*, 2006]. The model consisted of a skin and an inner- and outer skull compartment, each consisting of approximately 1500 vertices. Electrode positions in 85 electrodes and 151 MEG gradiometers as co-registered to the 3DT1 for that patient were used. Conductivity values of 0.33 $S.m^{-1}$ were used for the skin and the brain (=inner skull) compartments. For the skull a conductivity ratios with respect to this value of 1/5, 1/10, 1/20, 1/40 1/60 1/80 and 1/100 were used, covering the ranges reported in the literature. For MEG only the brain compartment was considered. The forward problem was solved using methods as described in [Oostendorp and van Oosterom*,* 1989] and [Oostendorp and van Oosterom*,* 1991]. In total, a set of 99 EEG-MEG simulations was performed, for each simulation a conductivity ratio was randomly selected from the above list, and randomly a location was selected from the cortical segmentation available from the same 3DT1 set. Only cortical points were chosen that had a distance to the center of the head greater than 4.2 cm. At these locations, a current dipole with unit strength and random orientation was assumed. Uncorrelated noise was added to the simulated EEG and MEG, amounting to a relative difference with the noiseless signal of 20%. For each simulated EEG and MEG a single dipole estimation was performed, with the original cortical location used as a seed, in the volume conductor model with a conductivity ratio of 1/20 [Zhang *et al*., 2006].

2.2. Real data

Real data was obtained from a study on EEG and MEG measurements of interictal spikes in a group of 19 patients that had epilepsy related to tuberous sclerosis (TSC) [Jansen *et al.,* 2006]. These patients show multiple focal lesions in the brain that are believed to be the cause of focal interictal activity arising from the same region. EEG and MEG data acquired simultaneously using 32 or 64 electrodes and 151 MEG sensors were available in all cases, but the EEG was used in only five cases. In the remaining 14 cases a higher quality 85 channel EEG measured separately was used. Spikes were identified in each modality separately, by three observers, and only consensus spikes from sets that showed a high inter-observer agreement (Cohen's kappa value >0.4) were used for subsequent processing. For the 85 channel recordings, EEG data measured simultaneous with MEG was used to make sure that EEG and MEG spikes could be attributed to the same source. Spikes were spatio-temporally clustered and averaged [Van 't Ent *et al.*, 2003]. Source localization of averaged spikes in EEG and MEG was performed using an implementation of the MUSIC algorithm [Mosher *et al.*, 1992] in CURRYv3.0 software in a realistic volume conductor model. The conductivity ratio used was again 1/20.

2.3. Analysis

For each modality (EEG/MEG) and for each of the estimated dipole locations in the simulation the distance in x, y and z-direction to the original location was computed (+x direction from right to left ear, +y from nasion to inion, +z upwards). Also, for each original location a rotation was defined such that a vector pointing from the origin (at the center of gravity of the brain compartment) to that location was in the +z direction (fig. 1). For each of the selected cortical point this resulted in the skull surface always being upwards (+z') and the center of the head downwards. In this coordinate system again distances dx', dy' and dz' between the original and estimated position were computed. Scatter plots of dx, dy, dz, and dx', dy', dz' were made and compared, and for the whole set the average distances from the original location and standard deviations were computed.

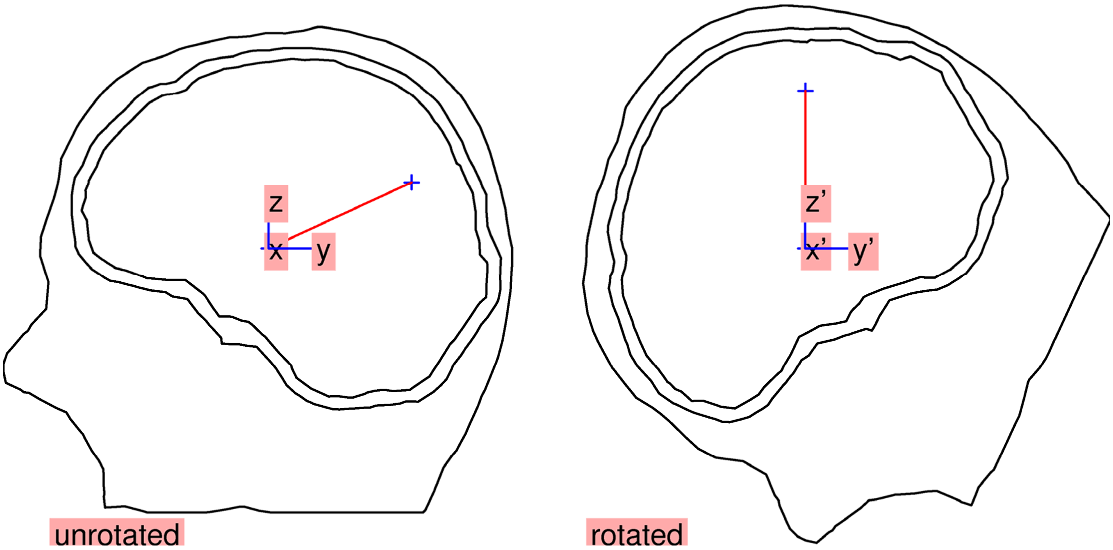

Figure 1. *Demonstration of the rotation to "skull-upward" . Assumed source location is indicated by the blue "+" symbol. x and x' axes are pointing outwards.*

For the real data, the distance from the maximum of the MUSIC metric to the nearest lesion was computed [Jansen *et al.,* 2006]. As in the simulation study, a new coordinate system x', y', z' was set up in which the skull was always upwards from the lesion and the center of the head downwards, and distances were recomputed. Scatter plots for dx, dy, dz, and dx', dy', dz' were made and compared, and for the whole group average distances from the lesion and standard deviations were computed.

3. Results

3.1. Simulations

In fig. 2 the geometry of the volume conductor model and the location of the 99 dipoles chosen randomly from the cortex segmentation are shown.

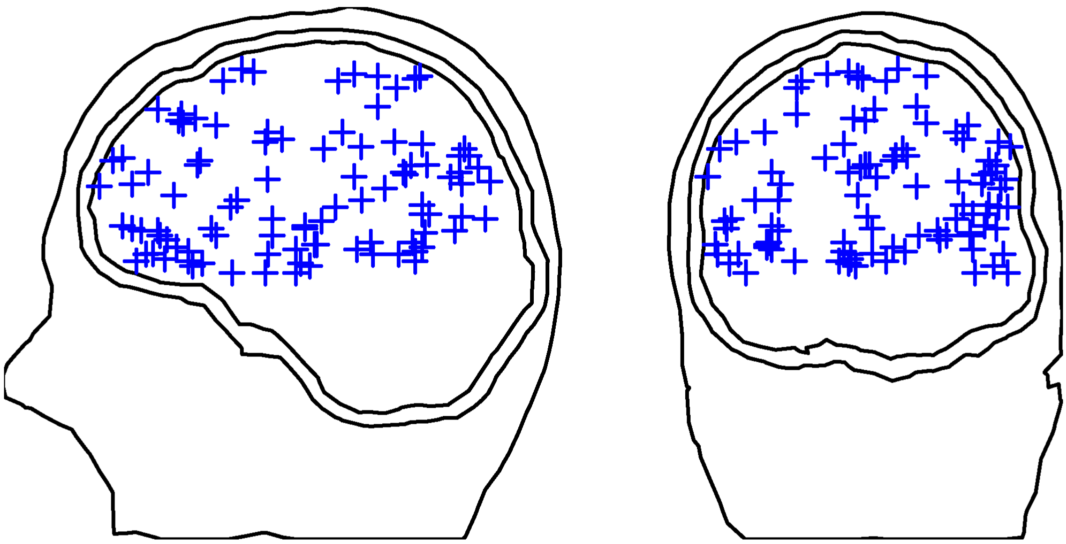

Figure 2. *Volume conductor model and set of 99 source locations used in the simulation study,*

A simulated EEG potential and MEG field distribution after addition of 20% noise is shown in fig. 3.

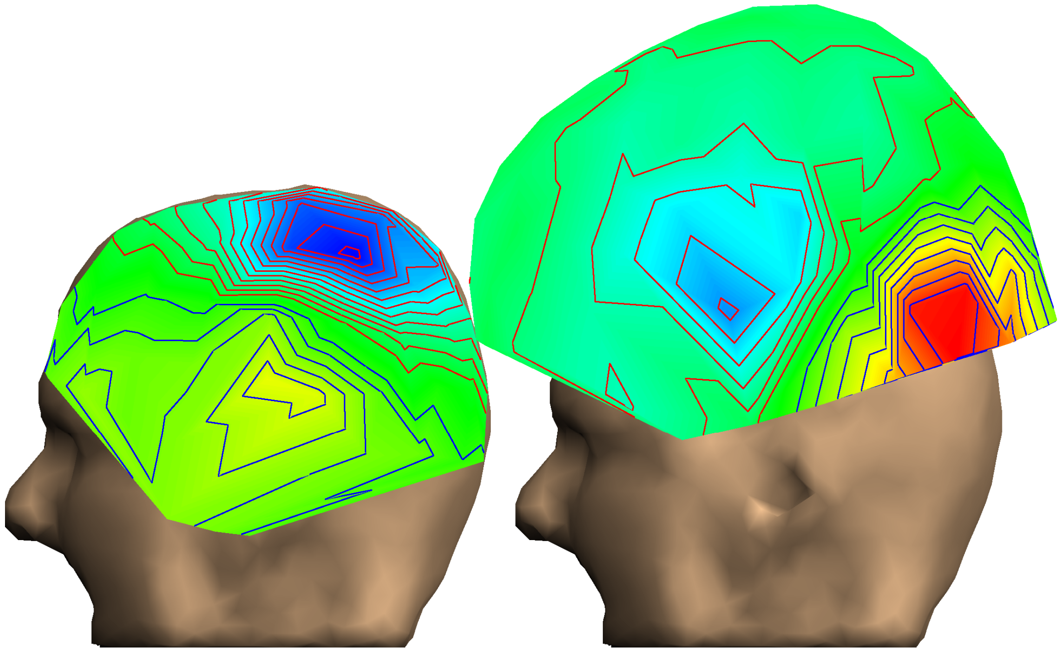

Figure 3. *Simulated EEG and MEG of same source with 20% noise added in 85 electrode cap (left) and 151 channel MEG helmet (right).*

For the 99 simulations, each based on a randomly chosen position, orientation and conductivity ratio, the scatter of the estimated source locations using the conductivity ratio of 1/20 is shown in fig. 4.

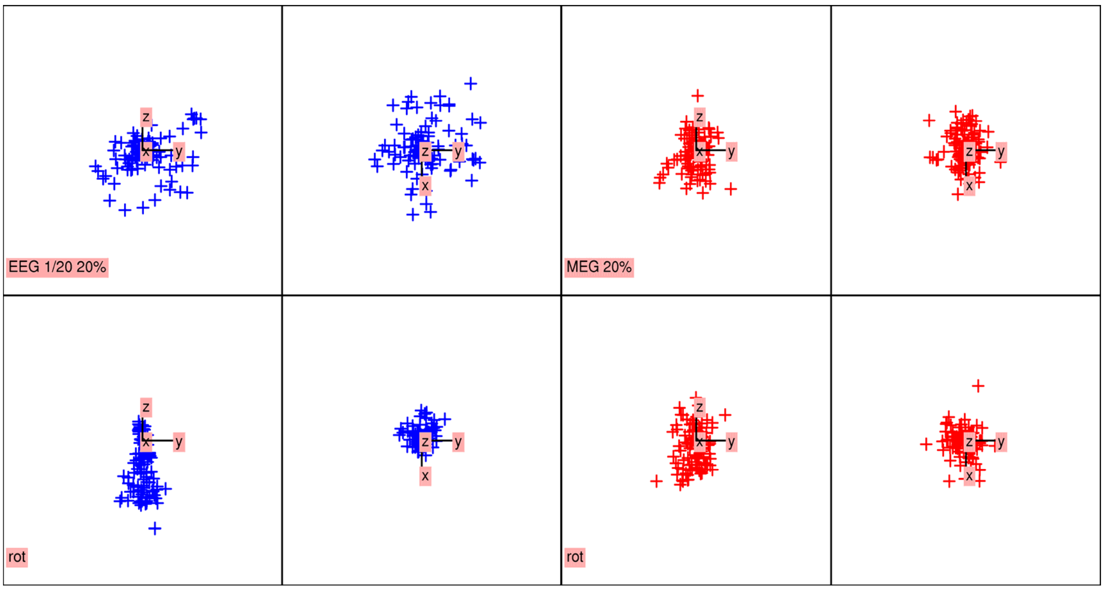

Figure 4. *Scatter of estimated dipole location for simulations. Left four panels in blue show EEG results, in right panels in red MEG results are shown. Upper four panels are for the original coordinate system xyz, lower four panels for rotated system x'y'z' , with skull surface in the +z' direction. Within each set of four panels of identical color the right panel shows a left lateral view, the right panel a top view. Length of indicated axes is 2.5 mm.*

EEG results are shown in the left four panels in blue, MEG results in the right panels in red. The upper four panels show the results in the original, unrotated coordinate system, the lower four panels show the same results in the rotated system x'y'z', where the skull surface is in the +z' direction. A left lateral and top view is shown for each situation. Note that in the unrotated coordinate system the scatter is isotropic, and is larger for EEG than for MEG. In the rotated x'y'z' system with the skull surface upwards scatter for the EEG is mainly in the -z' direction, whereas scatter in the other directions is smaller, and comparable to the scatter for MEG. Also, note that for MEG the rotation of the coordinate system has no effect. Average distances and standard deviations are given in table 1.

3.2. Real data

The scatter-plots for the real data from the group of epilepsy patients are shown in fig. 5. The layout is as in fig. 4. Note that results for the real data also show a reduction of scatter for EEG in the directions parallel to the skull surface, and that for the assumed conductivity ratio of 1/20 the scatter is mainly in the -z' direction. Scatter for the MEG results are isotropic for both the unrotated and rotated coordinate system. Average distances and standard deviations are given in table 1.

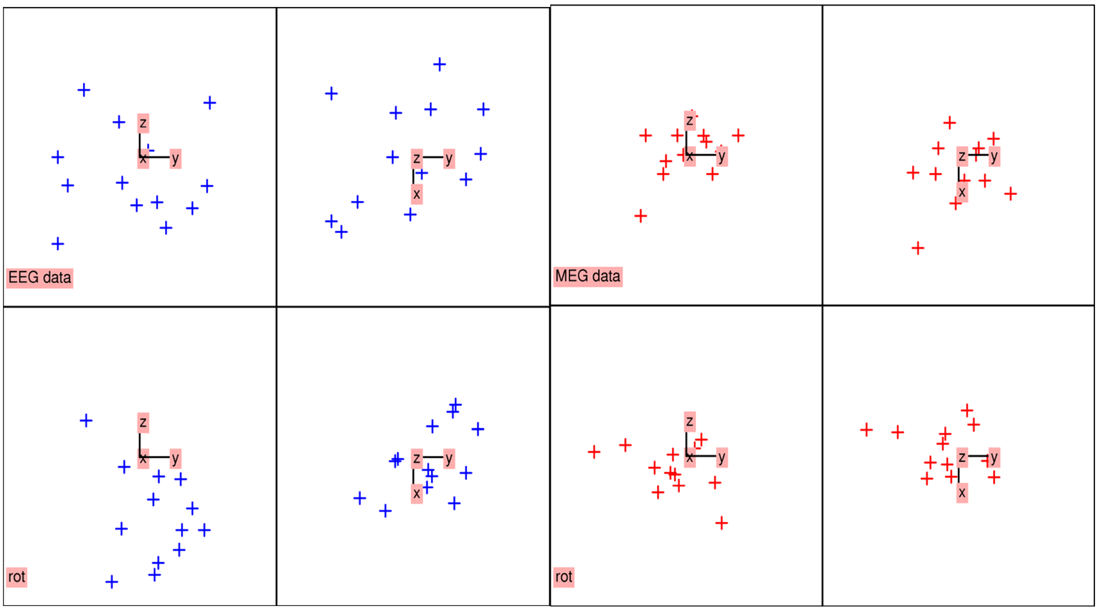

Figure 5. *Scatter of estimated dipole location for real data of group of epilepsy patients. For further explanation of legend see fig. 4..*

***Table 1**.Mean distances and standard deviations (STD) in mm for simulated and real data EEG and MEG for unrotated and rotated coordinate system.*

Simulation	***x** mean/STD*	***y** mean/STD*	***z** mean/STD*
EEG	4.9 / 4.9	5.0 / 4.8	3.9 / 3.9
MEG	3.9 / 3.0	2.7 / 2.5	3.9 / 3.2
EEG rotated	1.9 / 1.9	1.6 / 1.5	8.7 / 6.2
MEG rotated	2.7 / 2.9	2.6 / 2.2	5.0 / 3.4
Real data	***x** mean/STD*	***y** mean/STD*	***z** mean/STD*
EEG	12.5 / 7.5	13.6 / 8.6	11.8 / 6.7
MEG	7.7 / 6.7	7.6 / 4.6	5.5 / 4.4
EEG rotated	8.2 / 4.8	10.0 / 5.1	18.2 / 10.3
MEG rotated	5.7 / 3.0	9.0 / 7.4	5.8 / 4.8

4. Discussion

Although it has been demonstrated earlier that the skull conductivity ratio influences mainly the depth of an estimated dipole in EEG source localization, this study shows that from a proper analysis of this effect in a population study, inter-individual variability emerges as a major contributor to EEG inaccuracy. Assuming realistic noise levels in simulation and comparing the results for real data it is shown that without this variability EEG can be as accurate as MEG can. Scatter of results in directions parallel to the skull surface are comparable. In addition to this, in the (small) population of epilepsy patients, the bias of the scatter of EEG results is along the -z' axis – suggesting that for this group the assumed conductivity ratio of 1/20 is too high. It should be noted that in the patient-group chosen here, tuberous sclerosis epilepsy, it is known that a much use of anti-epileptic drug (*fenytoine*) can cause skull thickening (*osteomalacia*).

Other modeling errors are known to cause an inaccuracy in dipole localization, *e.g.* using spherical volume conductor models or generic realistic models. In this study, individual realistic geometry was used in all cases. Another source of error may be the incorrectness of the dipole assumption. Modeling a distributed source as a single dipole can cause a localization error that has a depth bias. Such an effect, however, depends on the orientation and curvature of the source and there is no reason for assuming that these would be similar throughout the patient group. In addition, this effect should be observable in the MEG as well.

This study did not address the issue of *intra*-individual variability of skull conductivity. In fact, the range of different conductivity values reported in the literature might reflect the range of conductivity values for the different parts of the skull that were measured in these various studies: the constituents of skull bone (calceous v.s. spongeous bone) differ in, *e.g.*, the temporal and occipital area. The analysis of this would require a volume conductor model that is based on more accurate individual anatomical data (based on CT rather than MRI) and a much larger study population.

5. Conclusions

This study shows that inter-individual variability of skull conductivity can explain much of the inaccuracy that is observed in EEG source localization. This inaccuracy is biased in depth. If individual skull conductivity values are known and used in a realistic volume conductor model for dipole localization, the inaccuracy will be more isotropic, and can be as small as is the case with MEG source localization.

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