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The Influence of Conductivity Changes in Boundary Element Compartments on the Forward and Inverse Problem in Electroencephalography and Magnetoencephalography

Der Einfluß der Änderung der Schalenleitfähigkeit bei Randelementemodellen auf die Vorwärtsrechnung und das inverse Problem in Elektroenzephalographie und Magnetoenzephalographie

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Key words: Conductivity – boundary element method – BEM – EEG – MEG

Source localization based on magnetoencephalographic and electroencephalographic data requires knowledge of the conductivitiy values of the head. The aim of this paper is to examine the influence of compartment conductivity changes on the neuromagnetic field and the electric scalp potential for the widely used three compartment boundary element models. Both the analysis of measurement data and the simulations with dipoles distributed in the brain produced two significant results. First, we found the electric potentials to be approximately one order of magnitude more sensitive to conductivity changes than the magnetic fields. This was valid for the field and potential topology (and hence dipole localization), and for the amplitude (and hence dipole strength). Second, changes in brain compartment conductivity yield the lowest change in the electric potentials topology (and hence dipole localization), but a very strong change in the amplitude (and hence in the dipole strength). We conclude that for the magnetic fields the influence of compartment conductivity changes is not important in terms of dipole localization and strength estimation. For the electric potentials however, both dipole localization and strength estimation are significantly influenced by the compartment conductivity.

Schlüsselwörter: Leitfähigkeit, Boundary Element-Methode, BEM, EEG, MEG

Die Gewebeleitfähigkeitswerte des Kopfes sind für Quellenlokalisationen, basierend auf magnetoenzephalographischen und elektroenzephalographischen Daten, erforderlich. Das Ziel dieser Arbeit besteht darin, den Einfluß von Leitfähigkeitsänderungen auf das neuromagnetische Feld und die elektrische Potentialverteilung auf der Kopfoberfläche für die weitverbreiteten 3-Schalen-Randelementemodelle zu untersuchen. Sowohl die Analyse von Meßdaten als auch die Simulationen mit im Gehirn verteilten Einzeldipolen führten zu zwei wesentlichen Ergebnissen. Erstens war die Empfindlichkeit gegenüber Leitfähigkeitsänderungen beim elektrischen Potential ungefähr eine Größenordnung höher als beim magnetischen Feld. Dies galt sowohl für die Topologie (und damit für die Dipollokalisation) als auch für die Amplitude (und damit für die Dipolstärke). Zweitens zeigten Leitfähigkeitsänderungen der innersten Schale (Gehirn) die geringsten Änderungen in der Topologie des elektrischen Potentials (und damit in der Dipollokalisation), aber dabei eine sehr starke Änderung in der Amplitude (und damit in der Dipolstärke). Es kann geschlußfolgert werden, daß der Einfluß der Leitfähigkeitsänderung auf die Dipollokalisation und die Bestimmung der Dipolstärke aus dem magnetischen Feld vernachlässigt werden kann. Die Berechnung von Dipolort und -stärke aus dem elektrischen Potential ist jedoch signifikant von der Leitfähigkeit der Schalen abhängig.

1 Introduction

The *in vivo* conductivity values of the different tissues of the human head are needed for forward and inverse modeling in magnetoencephalography (MEG) and electroencephalography (EEG). We have previously examined the influence of tissue resistivity changes on magnetic fields and electric potentials using a high resolution inhomogeneous finite element method (FEM) model [10]. This paper extends this work to a three compartment homogeneous boundary element method (BEM) model. While FEM models still require large computational resources, BEM models are already widely available on PCs or workstations and are included in commercial software packages like CURRY (NeuroScan, Sterling, VA, USA) or ASA (ANT b.v., Hengelo, The Netherlands).

For a number of paradigms in clinical and basic research it is useful to analyze amplitude variations of MEG data (see e.g. [7]). One serious problem when applying conventional EEG amplitude analysis to MEG as well, is the varying distance between the source of the magnetic field and the pickup coils for successive measurement sessions. It is hardly possible to readjust a MEG system to exactly the same position with respect to the human head and the sources within it. The recorded magnetic field strength strongly depends on the distance to the source. Thus, it is erroneous to compare magnetic field amplitudes after a readjustment of the MEG device. Alternative methods are the direct comparison of the underlying source strength and the transformation of the MEG signals to standard sensor locations using multipole expansions [4] or minimum norm estimates [14]. However, our previous study [10], which employed an inhomogeneous FEM model, showed the strong influence of conductivity changes in the vicinity of the source on the magnetic field and thus on the estimated dipole strength. Additionally, a systematic investigation of conductivity changes using BEM models and simplified geometries for certain brain inhomogeneities also found significant effects on the magnitude of magnetic fields and electric potentials [12]. There are also studies which show that even within simple spherical volume conductors inhomogeneities close to sources can significantly affect MEG and EEG [18, 19]. Therefore, one of the aims of this study was to quantify this influence in a homogeneous three compartment BEM model.

Some studies have investigated the influence of the ratio of conductivities on source localization with the help of spherical models (see e.g. [2, 5, 17]) and with compartmental BEM models (see e.g. [11]). However, these studies do not consider the influence on the source strength. Also, these studies only use relative conductivity values (compartment ratios), since separate MEG and separate EEG modelings with compartmental models (BEM or spheres) do not need absolute conductivity values. For combined MEG/EEG analysis absolute conductivity values are advantageously. A recent study demonstrated that in the past modelers have used cerebrospinal fluid conductivity values that are 44 % lower than the actual values [3]. Although we do not employ a separate compartment for cerebrospinal fluid it is included in our innermost compartment. Thus, our paper gives a first estimate of the errors to be expected due to this wrong conductivity values used in the past.

The aim of this paper is to investigate the influence of conductivity changes in a three compartment BEM model for dipolar sources in different areas and depths of the brain. Additionally, it provides information about the common and differential behaviour of the influence of tissue conductivity changes for FEM and BEM models. We analyze source localizations based on somatosensory evoked potentials (SEPs) and fields (SEFs) and dipole simulations in order to assess the conductivity influence on the forward and inverse problem of EEG and MEG.

2 Methods

2.1 Somatosensory evoked potentials and magnetic field

We stimulated the right median nerve of a healthy right-handed volunteer according to the IFCN recommendations [15] (0.2 ms square wave, 1000 trials, 1 Hz stimulus frequency, stimulus strength sensor + motor threshold). MEG was recorded simultaneously with EEG using a 31 channel biomagnetometer (Philips, Hamburg, Germany) above the contralateral somatosensory cortex. EEG was recorded with the help of 28 electrodes in the same area (2 cm electrode distance, Cz, C3, P3, Cp3 included, Fz additionally). The impedance was 2.4 ± 0.5 kΩ (mean ± standard deviation). Reference electrodes were attached to both mastoids (connected via a 100 kΩ decoupling resistor). Both MEG and EEG data were amplified with Synamp devices (Neuroscan Inc., Herdon, USA) and 20 Hz to 300 Hz bandpass filtered. Common average reference was used for source localization from EEG data. Signal to noise ratio was 16.7 for magnetic data and 7.7 for electric data. Written informed consent was obtained.

A three compartment BEM model (linear potential approximation, isolated potential approach [6]) was constructed out of a T1 weighted MRI data set of the head (256 slices with 1 mm thickness). Three compartments were segmented out of this data set (outer scalp boundary, outer skull boundary and outer brain boundary). The outer brain boundary was flattened and dilated by 2 mm in order to represent the inner skull boundary. All three boundaries were thinned, and triangulated with the side length of the triangles of 7 mm. The model included 6292 uniform triangles and took 158 MByte and 12 hours CPU time on an Ultra Sparc One for BEM initialization. A homogeneous conductivity of 0.33, 0.0042 and 0.33 S/m (scalp, skull, brain) [17] was assumed for all three compartments for the reference model. In order to assess the influence of conductivity changes, the conductivity of each compartment was varied by ±10 %, ±25 % and ±50 % while the remaining two compartments were kept at mean value. The coordinate system transformation between MRI and MEG/EEG coordinates was performed with the help of 4 anatomical landmarks (nasion, left/right ear, Cz).

Source localization was compared for EEG data and MEG data analysis. Since quasispherical correction is often used in MEG based source localizations we additionally compared MEG source localization with and without quasispherical correction. Quasispherical correction describes the use of dipoles with tangential directions only. The reason for this correction is that MEG is 6 to 10 times more sensitive to tangential dipoles than to radial dipoles [9, 13]. The center of projection for the quasispherical correction was the center of a sphere fitted into the brain compartment.

All source localizations were carried out with the help of the software CURRY (NeuroScan, Sterling, VA, USA).

2.2 Simulations

For the simulations we varied the conductivity of each compartment as pointed out in the previous section.

The dipole depth (distance from the innermost compartment) was 1 mm, 2 mm, 5 mm, 10 mm, 20 mm, 30 mm, 40 mm and 50 mm for each brain area. We considered tangential dipoles in the frontal, temporal, parietal and occipital area of the brain. For all dipoles at a depth of 1 mm we ensured that for all BEM discretizations the dipole is within the innermost compartment. Fig. 1 shows different brain areas and dipole depth together with the innermost compartment of the BEM model. The coordinate system used for both simulations and source localizations is also indicated in Fig. 1. It relates to the MRI data set, and the zero point is at the bottom front of the first sagittal slice. The x coordinate goes from right to left, the y coordinate from frontal to occipital, and the z coordinate from inferior to superior.

128 electrodes were used according to the international 10–20 system for the simulation of the electric potential distribution (common average reference). The same sensor configuration as for the somatosensory evoked fields with 31 channels was employed for the simulation of the magnetic fields. For each brain area the sensor system was centrally positioned above the dipole positions and the zero line was in the middle of the sensor array. The sensors were located at the same distance to the scalp as for the measurements above. We calculated the fields and potentials for each single dipole in each brain region and for each conductivity profile. Then, we compared the reference model for each dipole to all other models.

In order to assess changes in both the amplitude and the topography of the calculated fields and potentials we calculated the correlation coefficient and the deviation of scaling (amplitude) between the reference model (mean value of compartment conductivities) and the different conductivity and discretization variations [8]. We defined the deviation of scaling for electric potentials (*DSE*) according to:

$$DSE = \left| \frac{\sum_{i=1}^{M} \left|\varphi_i^{ref}\right| - \sum_{i=1}^{M} \left|\varphi_i^{test}\right|}{\sum_{i=1}^{M} \left|\varphi_i^{ref}\right|} \right| \quad (1)$$

where summation is over all electrodes i with $M = 128$. φ^{ref} depicts the potentials computed with the reference model, and φ^{test} depicts the potentials to be compared. Similarly, we defined the deviation of scaling for magnetic fields (*DSM*). All dipole simulations were performed with the help of the software CURRY (NeuroScan, Sterling, VA, USA) and all other computations with PV-Wave (Visual Numerics, Boulder, CO, USA).

3 Results

3.1 Somatosensory evoked potentials and magnetic field

Dipole localizations were performed at the time instant of the maximum of the first cortical activity (N20m) in the magnetic field. It is assumed that a single current dipole is sufficient to explain the cortical activity at that instant in time [1] and that the activity is located in Brodmann area 3b. The principal component analysis over 5 ms after onset of the N20 confirmed the above statement with 93 % for the first component for MEG data. The dipole localization results were projected onto the MRI data set. We found a localization in area 3b for MEG data. The localization result based on EEG data was shifted by 5 mm into the direction area 1 when compared to the MEG localization. This difference can be explained by the activity beginning in area 1.

Source localization and dipole strength differences between the reference model and the models with the conductivity changes given above are shown in Fig. 2. The localization difference is the absolute distance in space and the dipole strength difference is given in % of the dipole strength computed with the reference model. For both the localization difference and the strength difference we observe that EEG is approximately one order of magnitude more sensitive to conductivity changes than MEG. While for MEG the maximum localization distance is 0.35 mm, for EEG this distance is 3.2 mm. The maximum strength difference

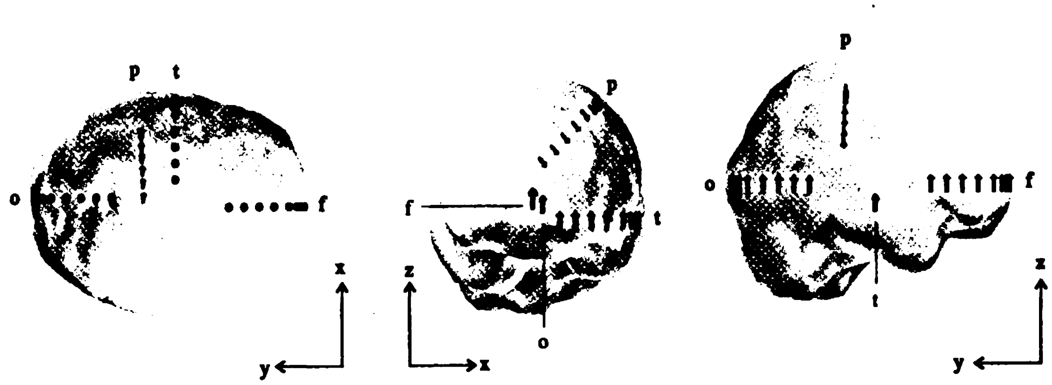

Figure 1. Innermost compartment of the BEM model, coordinate system and dipoles used. The brain areas are marked with letters (f – frontal; t – temporal; p – parietal; o – occipital). Each arrow represents one dipole.

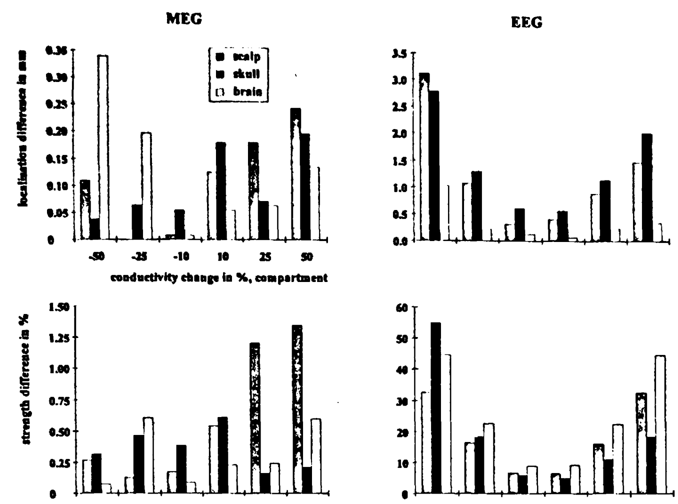

Figure 2. Dipole localization difference (top row) and dipole strength difference (bottom row) from the somatosensory evoked magnetic field (MEG, left column) and electric potentials (EEG, right column) at the time instant of the first cortical answer (N20). The localization difference is the absolute distance in space between the localization based on the reference model and the models with the conductivity changes depicted. The dipole strength difference is given in % of the dipole strength computed with the reference model.

is 1.4 % for MEG and 55 % for EEG. Only the values for MEG without quasispherical correction are presented in Fig. 2. The values for MEG with quasispherical correction are even smaller for both localization difference and strength difference. The maximum localization difference is 0.14 mm and the maximum strength difference is 0.6 %.

For EEG the conductivity change of the brain compartment yields the lowest localization difference, while at the same time it yields very high dipole strength differences. For MEG we do not observe a systematic difference between the compartments. Also, EEG shows a clear dependency on the absolute conductivity change. The higher the percentage of conductivity change the higher the localization and strength differences. MEG exhibits no similar systematic trend for all compartments.

3.2 *Simulations*

Fig. 3 shows the correlation coefficients and *DSM*/*DSE* values for all simulated dipoles in all brain areas and depths for the 7 mm BEM model. The most striking result in this figure is that both the amplitude and the topology of electric potentials are approximately one order of magnitude more sensitive to conductivity changes than the magnetic fields. While the mean correlation coefficients for the magnetic fields are always above 0.9996, the ones for the electric potentials are only above 0.995. The mean values for *DSM* are below 4.1 % while the mean values for *DSE* are in two cases even higher than 40 %.

For the electric potentials, the brain compartment exhibits the highest *DSE* values, while at the same time it also shows the highest correlation coefficient when compared to the other two compartments. That means conductivity changes in the brain compartment yield strong amplitude changes but weak topology changes in the EEG. The skull and scalp compartment

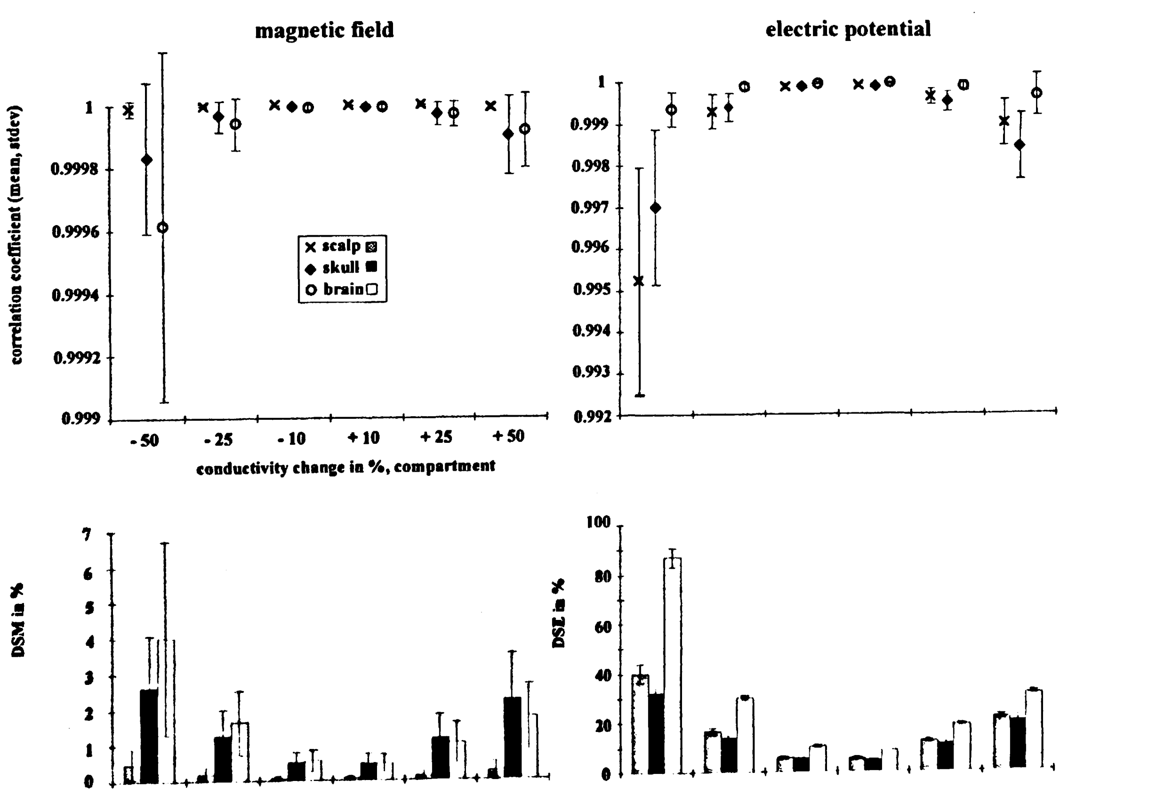

Figure 3. Correlation coefficients (top row) and *DSM*/*DSE* values (bottom row) for magnetic fields (left column) and eletric potentials (right column). The average is over all dipoles in all brain areas and depths. The BEM discretization is 7 mm.

show aproximately the same *DSE* values, with slightly higher values for the scalp compartment. Also, the correlation coefficients for skull and scalp compartment are similar for the electric potentials.

For the magnetic fields, the scalp compartment shows the lowest sensitivity to conductivity changes. The mean *DSM* values are below 1 % and correlation coefficients are above 0.9999. The other two compartments (skull and brain) are similar to each other *(DSM* and correlation coefficient).

The standard deviation given in Fig. 3 represents the influence of different brain regions and depths.

The standard deviation increases in a nonlinear manner with increasing or decreasing conductivity changes. The 32 values on which the average in Fig. 3 is based are not gaussian-distributed. Also, the probability distributions are not parallel to each other; they even cut each other. Therefore, we do not attempt statistical mean value analysis of the data.

Fig. 4 demonstrates the nonlinear influence of the dipole depth on the changes in the magnetic field and electric potential caused by conductivity changes. The trends are very similar for all levels of conductivity changes (±50%, ±25%, ±10%); only the absolute values differ. Thus, only the –50% changes are shown in Fig. 4. Also, regional differences are not very high and thus only two regions of the brain with th are shown.

Electric potentials and magnetic fields show different trends with increasing dipole depth. While the electric potentials are less influenced by conductivity changes for deeper dipoles (higher correlation, lower *DSE*), the magnetic field for deeper dipoles is more influenced (lower correlation, higher *DSM*). However, *DSM* values tend to oscillate for temporal and frontal brain areas. Magnetic correlation coefficients oscillate only for the frontal region (solid lines in Fig. 4); dipoles in the temporal and occipital regions behave like the

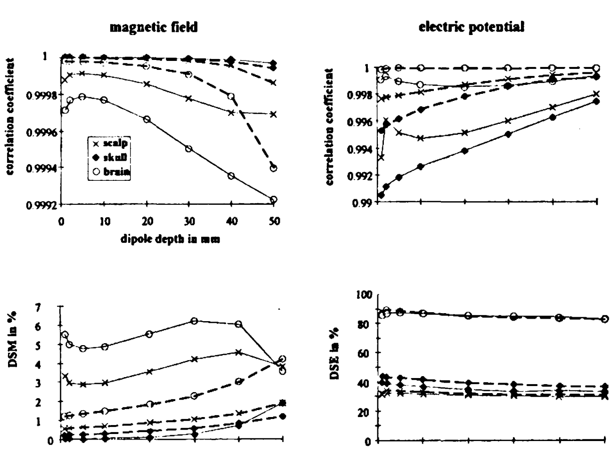

Figure 4. Correlation coefficients (top row) and *DSM/DSE* values (bottom row) for magnetic fields (left column) and electric potentials (right column) over dipole depth in frontal and parietal brain areas. Dipoles in the frontal area are connected by solid lines and dipoles in the parietal area are connected by dashed lines. The BEM discretization is 7 mm and the conductivity change –50 %.

parietal dipoles (dashed lines in Fig. 4). The influence described for magnetic field correlation is reversed for the skull and brain compartment when using a whole head MEG system for simulations (see discussion section). The regional differences can be due to the different thickness profile of the skull and scalp compartments as well as due to the local geometry, especially at the base of the skull (temporal, frontal) in the area of the sources. Some results in Fig. 4 tend to diverge for the most superficial dipole. This could be caused by the discretization error of the BEM model, as discussed below.

4 Discussion

Both the analysis of measurement data and the simulations with dipoles distributed in the brain showed two major results. First, we found the EEG to be approximately one order of magnitude more sensitive to conductivity changes than the MEG. This is valid for the topology (and hence dipole localization) and the amplitude (and hence dipole strength). Based on the mathematical formulation of the BEM, the higher sensitivity to conductivity changes is in principle expected. However, here we first quantify this influence. Second, changes in the brain compartment conductivity yield the lowest change in the electric potentials topology (and hence dipole localization), but a very strong change in the amplitude (and hence in the dipole strength).

The localization results for MEG and EEG in Fig. 2 showed systematic trends for EEG but not for MEG. MEG with quasispherical correction also shows no systematic behavior for the conductivity changes, but has a lower level of dipole localization and strength changes. The lower level of changes is expected, since MEG with quasispherical correction yields a generally higher stability of the inverse solution [8]. We found this higher stability in more than 200 SEF/SEP studies performed during the last two years.

The position of the dipole localized from the SEF measurements is approximately 16 mm below the surface of the innermost compartment. Therefore, one can compare the localization results based on the conductivity variations with the simulation results obtained for the dipole at 10 mm depth in the parietal brain region. This comparison gives an estimate of the relation between the value of the correlation coefficient and the localization error to be expected. Fig. 5 shows a correlation plot for the results of the measured data and the simulated data for EEG. For MEG data no correlation was observed. Also, the truncation of the correlation coefficient of the simulation-based data after 7 significant digits did not provide enough information for smaller conductivity variations (±10 % and ±25 %) for the MEG data.

Although we found no clear linear correlation between the measurement-based results and the simula-

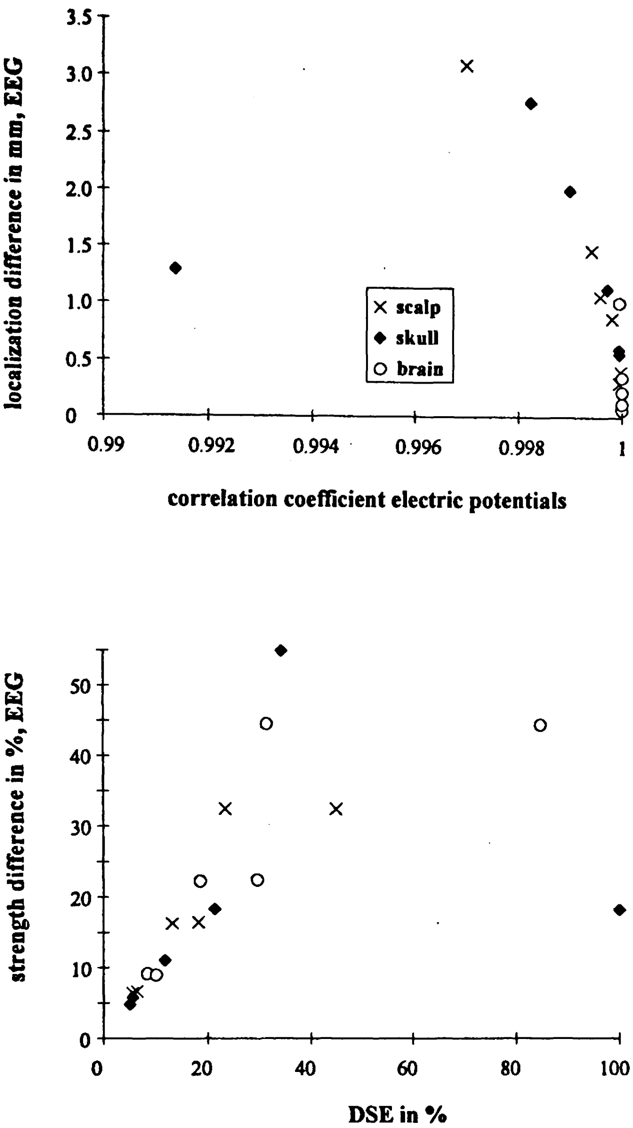

Figure 5. Correlation plot of source localizations and simulations for electric potentials. The localization difference for the SEP measurements is correlated to the corresponding correlation coefficients for the parietal dipole 10 mm below the surface (top) and accordingly the strength difference to the DSE values (bottom).

tionbased results in Fig. 5, two conclusions are likely. First, the larger the *DSE* values are the larger is the instability of a dipole strength computation. This can be observed in the plot *DSE* over strength difference as a divergence for larger values. Second, in order to reach a localization error below 1 mm the correlation between the potential distributions has to be above 0.999. A correlation of 0.996 might suffice for 2–3 mm localization error. However, there are important limitations to this comparison. It is applied to only one dipole position and based on only one set of measurements. Therefore, it can only serve as a first estimate of the relation between the correlation coefficient and the localization error to be expected. More research is necessary to further reveal this relation.

Roth et al. [16] found a localization error of up to 3.1 mm due to parameter variations including a 20 % conductivity variation. However, it is not clear whether the localization error results from the conductivity variation or from scalp and skull thickness variations.

Ary et al. [2] investigated the error caused by different conductivity ratios (skull/scalp: 1/66, 1/80 and 1/100; with equal conductivity for brain and scalp) in a model consisting of three concentric spheres. They found that the maximum variation of the source location introduced by these different conductivity ratios is ±2 % of the outside radius of the scalp.

Cuffin [5] investigated the effects of conductivity changes in a small eccentric sphere (bubble) within a 3 layer concentric spherical model. He found only a small influence on the general spatial patterns of the magnetic field and the electric potentials but a significant influence on the field and potential amplitudes. Also, the effects on the field amplitudes were found to be only somewhat smaller than on the potential amplitudes. In contrast to the paper by Cuffin we varied in this paper the conductivity of the compartments and observed different effects. However, the results obtained by Cuffin are in good agreement with our previous study [10] as discussed below.

Homma et al. [11] recorded electric potentials due to subdural stimulation in two epileptic patients with the help of 21 electrodes according to the international 10–20 system. For source reconstruction they varied the conductivity ratios of the three compartment BEM model between 1/1/1 and 1/120/1 (scalp/skull/brain) and found that a ratio of 1/80/1 was best suited for source localization. However, the use of only 21 electrodes can yield a serious undersampling of the potential distribution and hence unstable localization results. Also, it has been shown that dipole positions close to the skull boundary can lead to unstable dipole localizations due to the numerical inaccuracies of the BEM (see e.g. [8]). This instability can also produce the wide range of localization errors for the four stimulations in two patients. For the reasons given above it is difficult to compare our results with the results obtained in these studies.

Based on a BEM model using simple geometries, a paper by Huang et al. [12] suggested that the magnetic field should be less affected by conductivity changes, as compared to the surface potentials. In our study we found the magnetic field to be one order of magnitude less sensitive to conductivity changes than electric potentials which thus confirms and quantifies the results of the above study.

In a previous study [10] we used an inhomogeneous FEM model and quantified the influence of conductivity changes on the magnetic field and the electric potentials. The results of this previous study cannot be directly compared with the results in this paper since conductivity changes in an inhomogeneous model cannot be compared with the conductivity changes in a homogeneous compartmental model. For the sake of completeness we summarize in the following the differences found between the inhomogeneous model in the previous study and the homogeneous compartmental model in this study. First, we observed a strong influence of conductivity changes in the vicinity of the source on the magnetic field amplitude (*DSM*) with the inhomogeneous model, but only a weak influence with the homogeneous compartmental model. This is to be expected, since conductivity changes in the inhomogeneous model affect the local conductivity profile around the source, while for the homogeneous compartmental model only the conductivity level and not the local conductivity profile is changed. Second, for the inhomogeneous model the changes in the electric potentials and magnetic fields were in the same order of magnitude (*DSM/DSE* and correlation coefficients) while for the homogeneous compartmental model fields and potentials were distinguished by one order of magnitude. In general, inhomogeneous models provide a more detailed approximation of the real human head than homogeneous compartmental models.

All MEG source localizations and simulations in this paper are based on the 31 channel Philips biomagnetometer. This gives us the opportunity to directly assess the influence factors for our MEG system. However, other laboratories use other MEG systems with other properties. In order to crossvalidate the results obtained in this study we repeated a set of simulations with a different MEG system. We chose the layout of a 148 channel whole head magnetometer system by BTi (San Diego, USA) for this purpose. In the comparison with the results for the 31 and 148 channel system we found, as expected, similarities for all results presented above, since we considered noise-free simulations only. But we also found one systematic difference: while for the 31 channels the correlation coefficient for magnetic fields decreased with increasing dipole depth in the case of brain and skull compartments, for the 148 channels these correlation coefficients increased (see also results section). This is probably explained by the different coverage of the two systems, since for deeper dipoles the 31 channel system did not cover the minimum and the maximum of the magnetic field distribution.

A recent study [8] investigated the influence of boundary element discretization on the neuromagnetic forward and inverse problem. They found, that in order to obtain acceptable localization errors the ratio of dipole distance to the surface and triangle side length must not be less than 0.5. Also, the overall triangle side length must be less than 10 mm. In this paper the BEM resolution used for all calculations was 7 mm, thus fulfilling the second above requirement for all dipole positions. The first requirement is not fullfilled for the very superficial dipoles. For these superficial dipoles one can expect a numerical error introduced by the BEM model due to the discretization of 7 mm. Therefore, results based on dipole positions at a depth of 1 mm and 2 mm need to be interpreted with caution. This fact can explain the deviations from the curves in Fig. 4 for the very superficial dipoles.

Additionally, in order to verify our results and the accuracy of the BEM model, we computed all results in this paper also with a BEM model with a triangle side length of 8 mm (4939 boundary elements). We found a difference between these two models of less than 0.118 % for the *DSE* values and 0.005 % for the *DSM* values for all dipoles. The difference in correlation coefficients of the electric potentials were less than 0.00023 and the difference in correlation coefficients of the magnetic fields were less than 0.00029 for the dipoles deeper than 5 mm. The superficial dipoles (1 mm and 2 mm below the surface) showed a larger maximum difference in the correlation coefficients of 0.014 for the electric potentials and 0.00036 for the magnetic fields.

All results presented in this paper are restricted to the assumption of one dipolar source. For multiple sources (e.g. 2 or 3 dipoles) we would expect that the conductivity changes will not have less effect on the magnetic field and electric potential. Also, we do not expect that the principle result of this study, namely that EEG is much more sensitive to conductivity changes in the homogeneous compartmental BEM model than MEG, will change for multiple dipoles.

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897

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