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Dipole estimation errors in EEG source localization due to not incorporating anisotropic conductivities of white matter in realistic head models

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***Abstract*-The electroencephalogram (EEG) is a useful tool in the diagnosis of epilepsy. EEG source localization can provide neurologists with an estimation of the epileptogenic zone. Many EEG source localization approaches assume head models with isotropic conductivity, while in reality the conductivity of white matter is anisotropic. The conductivity along the nerve bundle is higher than the conductivity perpendicular to the nerve bundle. Using diffusion weighted magnetic resonance images (DW-MRI), we can determine the directions the anisotropic diffusion. Using the latter we can derive the anisotropic conductivity tensor. These anisotropic conductivities can be fused with the realistic head model, derived from MR images. Using a grid of dipoles, placed in white and grey matter regions, we can compare the head model with white matter anisotropy with a head model with isotropic conductivity for the white matter compartment. As quantification measures we used the dipole location and orientation error. Results show that the location error was very small in both white and grey matter regions (< 5 mm). The dipole orientation error had a mean of 3.8 degrees and 6.1 degrees in grey and white matter regions. This would indicate that the systematical error due to not incorporating anisotropic conductivities of white matter is very small.**

I. INTRODUCTION

Electroencephalogram (EEG) dipole source localization has proven to be a valuable tool in the presurgical evaluation of patients suffering from epilepsy [1]. This technique can make an estimate of the active anatomical zone based on the measured EEG.

EEG dipole source localization consists of two subproblems. The forward problem calculates the electrode potentials in a head model, given the source (usually a current dipole). On the other hand, the inverse problem in EEG source localization is solved by finding the dipole which best represents the given potentials at the scalp electrodes. This can be performed iteratively by modifying the dipole parameters, until for a given set of parameters; the associated potentials (found by solving the forward problem) represent best the measured potentials. Besides the current dipole, as a model for active neurons, a volume conductor model is required to perform EEG source localization of the epileptic focus in a head model.

It is known that the conductivity of white matter in the brain is anisotropic, which means that the electrical conductivity of these tissues is direction dependent (see figure 1). In a study with spherical head models, it was shown that neglecting the anisotropic conductivity of white matter had an average error of 4.6 mm (maximum 11.36 mm) area's near the skull and 17.6 mm (maximum 26.1 mm) for area's near the center [2]. However, in this study the anisotropic conductivity was assumed to be in a radial direction this to still be able to use an analytical expression for the forward problem. In reality, the nerve bundles are not oriented along radial direction and must be derived using advanced imaging techniques. The anisotropic conductivities of white matter can be derived from diffusion weighted magnetic resonance images (DW-MRI), which visualizes the direction of self-diffusion of water. Water contains ions, which conduct the electrical activity to the scalp of the head. If water diffuses more easily along one direction, then the conductivity will be bigger along this direction [3, 4].

In this study we investigated the impact of neglecting the anisotropic conductivity of skull and white matter tissues in realistic head models on EEG dipole source localisation. We did this by means of simulations where we compared head models containing white matter anisotropic conducting compartments with isotropic head models.

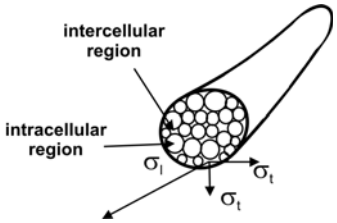


Fig. 1: Anisotropic conductivities in white matter fibres due to different axial and longitudinal constellation of the bundles of axons.

II. METHODS AND MATERIALS

A. Head model

In our study we used a realistic head model that was derived from a segmentation of T1 MR images. The MR images had a resolution of 1 mm×1 mm×1 mm and were obtained by a 3T MR scanner (Siemens Trio, Erlangen, Germany). SPM5 was used to segment the brain compartment in white matter, grey matter and cerebro-spinal fluid (CSF). The skull compartment was constructed by a dilation of the brain compartment and

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was on average 6 mm thick. The scalp compartment was then constructed by performing opening, closing and hole filling operations on the thresholded MR image. The skull, CSF, white matter and grey matter compartment were then pasted on the whole head model. Figure 1 shows an axial, sagittal and coronal plane of the head model. The head model had approximately 4.5 million elements. From the 3D segmented images we extract a grid with the same resolution. This grid is used to solve the forward problem. The conductivity of scalp, skull, CSF and grey matter was chosen to be 0.33 S/m, 0.020 S/m, 1 S/m and 0.33 S/m, respectively. The electrode positions were placed on the head model using a standard 10-20 system with 6 extra temporal electrodes.

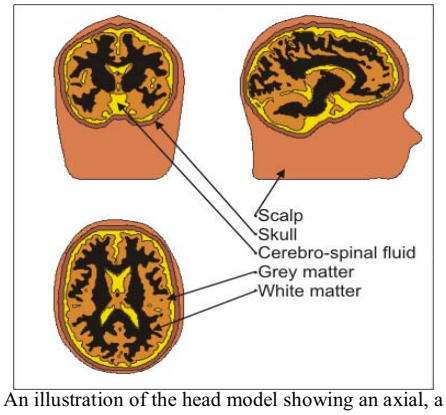


Fig. 2: An illustration of the head model showing an axial, a coronal and a sagittal slice. The different tissue categories are depicted: Scalp, Skull, Cerebro-spinal fluid (CSF), grey matter and white matter.

B. *Incorporation of white matter anisotropic conductivities*

The anisotropic conductivities of the white matter were derived from diffusion weighted imaging (DWI). All images were acquired with a Siemens Trio (Erlangen, Germany) MRI scanner. For the T1 images (256×256×176 matrix of isotropic voxels of 0.9 mm^3) a 3D MP RAGE sequence was used with TE = 1550ms and TR = 2.48ms. The DWI properties are: TR = 10400 ms, TE = 105 ms, 10 b_0 volumes, 60 diffusion sensitizing gradient orientations, b-value = 1000 [s mm^{-2}], 128 x 128 x 60 matrix of isotropic voxels (2.0 mm^3), acquired with a twice refocused spin-echo EPI sequence to reduce eddy current induced image distortion.

The DWIs were realigned and smoothed with a 3D scalar partial-differential-equation filter (or nonlinear anisotropic diffusion filter) [5]. Next, an altered version of the RESTORE method was used to robustly estimate the diffusion tensors [6]: first the original non-smoothed DWIs were used to identify outliers in the data, then these outliers were rejected during the final tensor fitting of the smoothed DWIs. The RESTORE technique corrects for physiological noise such as cardiac pulsation. The T1 volume was coregistered to the average of the 10 b_0 volumes.

From the diffusion weighted images, a diffusion tensor in each voxel of the white and grey matter was calculated. An accurate solution of the forward problem with anisotropic conductivities of white matter requires a fine grid of cubic 1 mm×1 mm×1 mm voxels [7]. The T1 volume and the diffusion tensor images were linearly interpolated to an 1 mm^3 cubic grid. The conductivities in white and grey matter were derived using a linear scaling of the diffusion tensor and the volume constraint [8].

C. *Forward problem*

Solving the forward problem we calculate the potentials at the electrodes. This is done by solving Poisson's equation in the realistic head model:

$$\nabla \cdot \left(\boldsymbol{\sigma}(\mathbf{r}) \cdot V(\mathbf{r})\right) = I\delta(\mathbf{r}-\mathbf{r}_k) - I\delta(\mathbf{r}-\mathbf{r}_l) \quad (1)$$

where $\boldsymbol{\sigma}(\mathbf{r})$ is the place dependent conductivity tensor and $V(\mathbf{r})$ is the potential distribution inside the head model due to a dipole with current source and sink at positions $\mathbf{r}_k$ and $\mathbf{r}_l$.

In spherical head models (1) can be solved using an analytical expression. In realistic inhomogeneous head models numerical methods are needed. In this study we used a finite difference method that can incorporate anisotropic conductivities [7]. Using the head model with the labeled voxels, a cubic computational grid is defined to the vertices at the edges of the voxels. Differentiating (1) in anisotropic media, leads to the following finite difference formulation at each vertex $\mathbf{r}_0$:

$$\sum_{i=1}^{18} A_i V(\mathbf{r}_i) - \left(\sum_{i=1}^{18} A_i\right) V(\mathbf{r}_0) = \mathrm{I}, \quad (2)$$

where $V(\mathbf{r}_i)$ is the potential at vertex $\mathbf{r}_i$ neighbouring to $\mathbf{r}_0$, A_i is a coefficient that is calculated from the conductivity tensors from the voxels. $\mathbf{I}$ represents the current source and sink at $\mathbf{r}_k$ and $\mathbf{r}_l$. In each node we can write an equation according to (2). This results in a system of equations with N unknowns, with N equal to the number of nodes in the head model: $\mathbf{AV}=\mathbf{I}$. In our head model N was equal to 4599754. To solve the system of equations, we used successive over-relaxation to iteratively. Furthermore, reciprocity was used to speed up the forward calculation in the inverse problem.

D. *Inverse Problem*

Solving the inverse problem consists of finding the parameters of the dipole source that best explain the set of measured potentials. We find the optimal dipole position $\mathbf{r}_{opt}$ and components $\mathbf{d}_{opt}$ for the input potentails $\mathbf{V}_{\mathbf{in}} \in \Re^{k\times 1}$ at k scalp electrodes. This is done by minimizing the relative residual energy (RRE):

$$RRE = \frac{\left\|\mathbf{V}_{\mathbf{in}} - \mathbf{V}_{\mathbf{model}}(\mathbf{r},\mathbf{d})\right\|_2^2}{\left\|\mathbf{V}_{\mathbf{in}}\right\|_2^2} + C(\mathbf{r}), \quad (2)$$

where $\mathbf{V}_{\mathbf{model}} \in \Re^{k\times 1}$ are the average referenced potentials obtained from the forward evaluation in the inverse problem.

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$\|\cdot\|$ indicates the L_2-norm. $C(\mathbf{r})$ is zero for dipole positions in the brain compartment (cortical shell, white matter shell and thalamic shell) and is set to a high value elsewhere. This additional term will restrict the solution of the inverse solver to the brain compartment. The Nelder-Mead simplex method is used to find the minimum of the RRE, because of its simplicity and robustness to local minima.

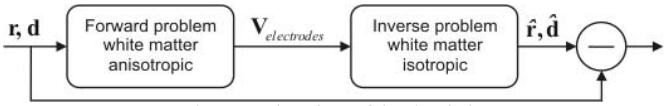


Figure 3: Flowchart of the simulation

E. Simulation set-up

The dipole estimation errors were determined by means of simulations. Three orthogonal planes were chosen in the head model: an axial, coronal and sagittal slice. In each voxel of the white and grey matter of the slices three test dipoles were placed with different orientation: along the X (left-right), Y (front-back) and Z (bottom-top) axis. This resulted in a total of 125463 dipoles. For each test dipole a simulation according to figure 3 was performed.

For each test dipole, the electrode potentials were calculated in a head model with the white matter having anisotropic conductivities by solving one forward calculation. The resulting electrode potentials were then used to solve the inverse problem in a head model where the white matter compartment was isotropic conducting. This resulted in an estimated dipole location and orientation, which we can compare with the test dipole location and orientation.

A flowchart of the simulation is illustrated in figure 3. As quantification measures, we used the dipole location error (DLE) and dipole orientation error (DOE) defined as:

$$DLE = \|\mathbf{r} - \hat{\mathbf{r}}\|, \qquad DOE = \angle(\mathbf{d}, \hat{\mathbf{d}}), \tag{3}$$

with $\mathbf{r}$ and $\hat{\mathbf{r}}$ the location of the test dipole and the estimated dipole, respectively, and $\mathbf{d}$ and $\hat{\mathbf{d}}$ the dipole moments of the test dipole and estimated dipole, respectively.

We also made a distinction between test dipoles placed in grey matter and ones placed in white matter. Although, dipole source are believed to originate only from grey matter regions, investigating the dipole estimation errors in white matter regions may improve the understanding of the influence of white matter anisotropy in EEG source localization.

III. RESULTS

Figure 4 shows the dipole location error as a color code in axial, coronal and sagittal slices of the head model. The rows indicate a different orientation of the test dipole: (a) along X-axis, (b) along Y-axis and (c) along Z-axis. We can see that the error is below 10 mm, both in grey and white matter regions. In figure 5, a histogram of the dipole location error is shown. This shows that most errors in both white and grey matter regions are below 5 mm. More than 80 % of the estimated dipoles have a location error smaller than 2 mm.

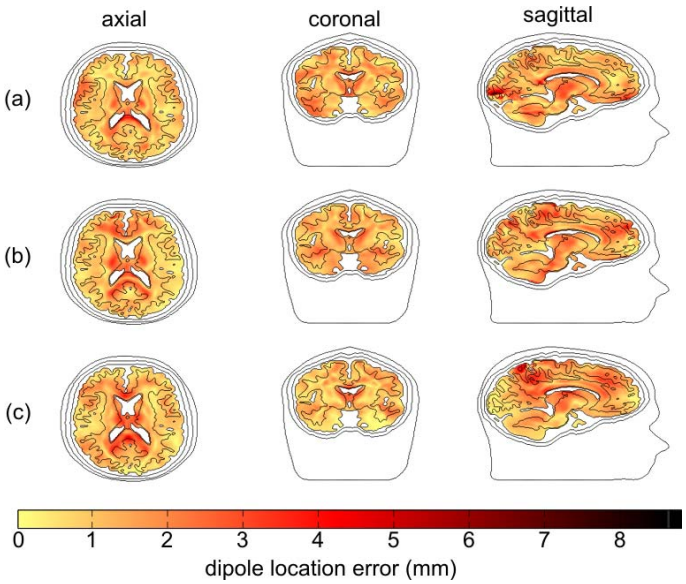


Figure 4: The dipole location error as a color coded map in an axial, a coronal and a sagittal slice of the head model. The colorbar below shows the range of the dipole location error in mm. The rows indicate the different orientations of the test dipole: (a) along X-axis, (b) along Y-axis and (c) along Z-axis.

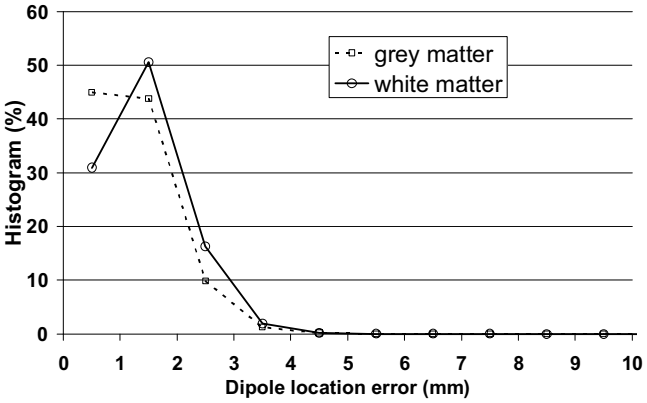


Figure 5: A histogram of the dipole location errors when the test dipoles are situated in grey or white matter. The Y-axis is the relative occurrence expressed in percentage.

The dipole orientation error is depicted in figures 6 and 7. A color coded map of axial, coronal and sagittal slices is shown in figure 6. We can see that arge orientation errors are situated near the center of the brain. In fact, they are situated at places where a large anisotropy was found in the diffusion weighted images. The maximum dipole orientation error had a value of 30 degrees and was situated at the center of the head model. Figure 7 shows a histogram of the dipole orientation errors in grey and white matter regions. In grey matter regions, on

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average 90% of the dipoles showed an orientation error of less than 10 degrees. The average dipole orientation error in grey matter and white matter compartments was 3.8 and 6.1 degrees, respectively.

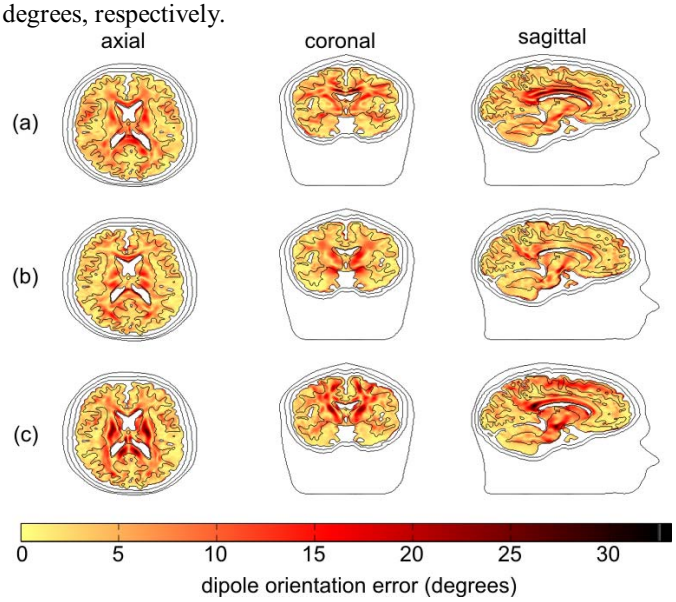


Figure 6: The dipole orientation error (in degrees) as a color coded map in an axial, a coronal and a sagittal slice of the head model. The colorbar below shows the range of the dipole location error in mm. The rows indicate the different orientations of the test dipole: (a) along X-axis, (b) along Y-axis and (c) along Z-axis.

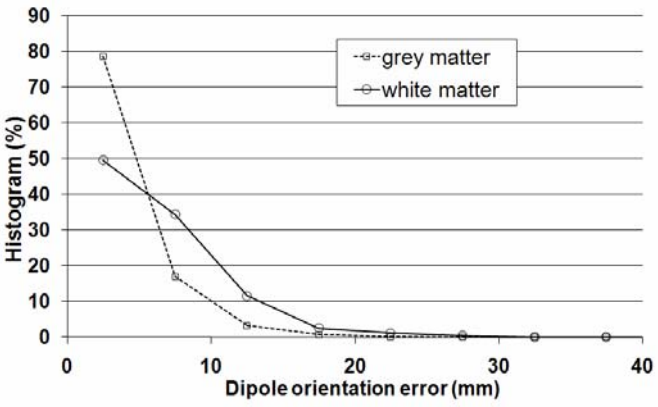


Figure 7: A histogram of the dipole orientation errors (in degrees) when the test dipoles are situated in grey or white matter. The Y-axis is the relative occurrence expressed in percentage

IV. DISCUSSION AND CONCLUSIONS

In this study, we investigated the dipole location and orientation error when the anisotropic conducitivities are not taken into account. Overall we could see that the dipole location error was very small (< 5 mm). Also, the orientation errors were almost always below 10 degrees in both white and grey matter. In results not shown here, it could be seen that the orientation error, due not incorporating anisotropic conductivities of white matter, was largest in regions where a high anisotropy was assumed. These regions were most prominent in the white matter compartment.

A study in spherical head models showed higher values for the mean dipole location error, 4.6 mm in spherical head models in contrast to 1,2 mm in realistic head models. This can be due to the fact that we use a realistic head models, where the nerve bundles are not radially oriented. Moreover, we use a more realistic approach to model the anisotropic conductivity. Instead of appointing one direction to be 9 times larger in conductivity than orthogonal, the conductivity tensor is derived by scaling the diffusion tensor [2].

Overall, we can conclude that the dipole location and orientation errors due to not incorporating the anisotropic conductivities of white matter are very small. Other factors, like the skull conductivity and noise in the EEG, have a larger contribution to the error in the dipole location and orientation estimate.

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