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On handling the layered structure of the skull in transcranial direct current stimulation models

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***Abstract*— In a tDCS model study, the accuracy of isotropic and anisotropic single-layer approximations to the actual three-layered skull is evaluated. For both approximation models, the average difference in brain current density with respect to the layered skull model are shown to be small. We conclude that both approximations can be used to accurately compute the current density in the brain, provided that the radial conductivity in the model matches the effective radial conductivity of the three-layered skull.**

I. INTRODUCTION

Over the last two decades researchers' interest in transcranial direct current stimulation (tDCS) has grown considerably. It's ability to non-invasively and painlessly induce polarity dependent cortical excitability modulations, while being safe, mobile and relatively cheap, makes tDCS a promising neurostimulation technique. Transcranial DC stimulation has been shown to improve brain function in patients with neurological diseases like chronic pain [1], Parkinson's disease [2], depression [3] and epilepsy [4] and the scope of applications continues to grow.

Since the weak tDCS current ($\leq$ 2 mA) is sent through the head via two large planar electrodes, the technique suffers from an inherent low focality. Different electrodes and configurations are being investigated in an attempt to increase the focality and thereby the effects of tDCS. Particularly useful in these investigations are volume conduction models that simulate the current flow in the brain due to tDCS. Growing computational capabilities continuously allow more detail in these models.

In tDCS the relatively poorly conducting skull poses a substantial barrier to the current. Miranda et al [5] showed that in a simulation of tDCS with a spherical model a considerable amount of the injected current did not reach the brain compartment. The low skull conductivity also causes the injected current to spread, reducing its focality. This suggests that modeling the human skull accurately is an important step in improving tDCS models.

A large part of the human cranial bone consists of two layers of compact tissue (compacta) enclosing one layer of cancellate bone (spongiosa), the latter being more conductive. This layered structure causes the skull to be less conductive in the radial than the tangential direction. In tDCS modeling, these properties have either been disregarded by modeling the skull as an isotropic compartment [6] or incorporated by approximating the skull as an anisotropic layer [7].

It has been shown in tDCS modeling that including tissue anisotropy may have significant consequences on the results. [7]. One would expect a model that is even closer to the actual anatomy, i.e. with three separate skull layers, to further improve the accuracy of tDCS models. This approach has been shown to improve current density estimations in transcranial electrical stimulation modeling [8] and EEG source localization estimations [9]. On the other hand, in tDCS the current crosses the skull predominantly in the radial direction, which might imply that the tangential conductive properties are of minor importance, and hence the skull might be modeled adequately by a single anisotropic, or even isotropic, layer.

In this study we compare layered, anisotropic and isotropic skull models for tDCS. As we aim to focus on the difference in brain current density predicted by these different descriptions of the skull we have chosen to use a concentric spherical volume conduction model with compartments representing skin, skull and brain, rather than a completely realistic head model. However, the methods used can be applied to realistic head models as well. In the reference model the skull is represented by three isotropic layers (*gold standard*). In addition, we model anisotropic and isotropic single-layer approximations to the skull's structure and compare the results of all modeling approaches.

II. METHODS

A. Geometry

We used the geometry of the spherical head model introduced by Rush and Driscoll [10] as the basis for three models, of which only the conductive properties of the skull compartment were different. The head model consisted of three concentric spheres with radii of 80, 85 and 92 mm representing brain, skull and skin, respectively. The tDCS electrodes were modeled as square patches with a surface area of 16 cm^2 and a thickness of 4 mm. Two such electrodes were placed 180 degrees apart on the outer sphere and were given the conductivity of saline (1.4 S/m); for brain and skin we chose 0.333 and 0.435 S/m, respectively [11]. We used COMSOL Multiphysics 3.5a (COMSOL AB, Stockholm, Sweden) with MATLAB R2009a (The Mathworks, Natick, MA) to create and mesh the described geometry, yielding a mesh of 507,475 nodes and 3,017,768 4-node tetrahedrons.

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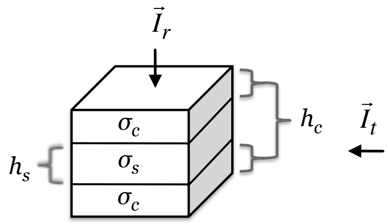

Fig. 1 Schematic approximation of a piece of human skull as a block consisting of three layers with each its own conductivity σ and height h. The subscripts c, s represent the compact and spongy layers, respectively.

B. Skull models

1) Reference model: In order to match the real skull properties as closely as possible, we divided the 5 mm thick skull layer into three layers representing the lower compacta, spongiosa and upper compacta. Akhtari et al. [12] measured thicknesses and conductivities of the layers of live human skull. We used averages of the thicknesses they reported to scale the three skull layers in our model, resulting in 1.2, 2.3 and 1.5 mm thickness from outmost to innermost layer, and adopted the average compacta (7.0 mS/m) and spongiosa (25 mS/m) conductivities.

2) Anisotropic model: We approximated the three isotropic skull layers in the reference model by a single anisotropic layer. Each element belonging to the skull compartment was, based on its orientation, given its own anisotropic conductivity tensor, the radial and tangential components of which are the same for all elements.

An obvious choice for the radial and tangential conductivities of a single-layer anisotropic skull model that should represent the actual three-layered skull, are those that are equivalent for uniform currents in radial and tangential direction. In order to determine these values, consider a rectangular piece of three-layered skull as an isolated block. This block, schematized in Fig. 1, consists of three isotropic layers with σ_i the conductivities of the layers and h_i the heights for $i = c, s$ (c for compacta, s for spongiosa). If we now imagine a uniform current flowing through this conductor in either the radial or tangential direction ($\vec{I}_r$ and $\vec{I}_t$ in Fig. 1), we can calculate the equivalent conductivities for the block as a whole in both situations:

$$\frac{1}{\sigma_r} = \frac{\lambda_c}{\sigma_c} + \frac{\lambda_s}{\sigma_s} \text{ and}$$
$$\sigma_t = \lambda_c \sigma_c + \lambda_s \sigma_s, \tag{1}$$

where $\lambda_i = h_i/(h_c + h_s)$. For the values of σ_c and σ_s in the reference model we find $\sigma_r = 10.5$ mS/m and $\sigma_t = 15.3$ mS/m. We will term this pair of values the *equivalent* anisotropic conductivities.

Although these values are truly equivalent for uniform radial or tangential current density, in general they are not, and the current densities computed from the reference and the anisotropic model will differ. In order to verify whether these values are at least optimal if not equivalent, we have performed the comparison for a grid of (σ_r, σ_t) values around the equivalent values, resulting in the ranges $\sigma_r = \{7 : 14\}$ mS/m and $\sigma_t = \{14 : 21\}$ mS/m.

Combined, σ_r and σ_t serve as a set of eigenvalues from which we construct the diagonal tensor $\mathbf{D} = \text{diag}(\sigma_r, \sigma_t, \sigma_t)$. For each tetrahedral skull element we determine the normal direction at its centre of mass and rotate $\mathbf{D}$ such that its radial component is directed along this normal, providing a correctly directed anisotropy for each element.

3) Isotropic model: Another common method to model the skull is as one isotropic layer. For the conductivity value of this layer it is common to use a measure of bulk skull conductivity, such as the volume constraint [13]:

$$\frac{4}{3}\pi\sigma_b^3 = \frac{4}{3}\pi\sigma_r\sigma_t^2. \tag{2}$$

Inserting the appropriate properties of our reference model via (1) into this constraint, provides us with a bulk conductivity of $\sigma_{\text{skull}} = \sigma_b = 13.5$ mS/m.

On the other hand, one expects the current from the tDCS electrodes to cross the skull mainly radially, with little current flowing tangentially through the skull. According to this line of reasoning the radial conductivity computed for the anisotropic model, 10.5 mS/m, would be a more appropriate value for the conductivity of the homogeneous skull model.

We solved the isotropic model for a range of conductivity values $\sigma_{\text{skull}} = \{1 : 20\}$ mS/m, which includes both values mentioned above.

C. Computations

Modeling tDCS entails estimating the potential distribution inside the head as a result of potentials applied on the electrodes at the scalp. This bioelectric problem can be described by the quasi-static Maxwell equations, which lead to Laplace's equation $\vec{\nabla} \cdot \boldsymbol{\sigma} \vec{\nabla} \Phi = 0$, with $\boldsymbol{\sigma}$ and Φ the electric conductivity and potential, respectively.

We used SCIRun 4.0 (Scientific Computing and Imaging Institute, Salt Lake City, UT) to solve this equation on a finite element mesh with Neumann boundary conditions, $\boldsymbol{\sigma} \vec{\nabla} \Phi \cdot \vec{n} = 0$, at the skin surface and Dirichlet boundary conditions, $\Phi = \Phi_0$, at the surfaces of the electrodes. The potentials applied to the electrodes were chosen such that the total current flowing between them was 1 mA.

D. Analysis

The effectiveness of transcranial direct current stimulation is believed to be related to the current density in the target brain area [14]. We used $\vec{J} = -\boldsymbol{\sigma} \vec{\nabla} \Phi$ to calculate the current density in each element. For each model we gathered the values of $|\vec{J}|$ for all m elements of the brain compartment into an array $\mathbf{J}$ and compared the results of each approximation model ($\mathbf{J}$) to those of the reference model ($\hat{\mathbf{J}}$) using the relative difference measure [15]:

$$\text{RDM} = \sqrt{\sum_{k=1}^{m} \left(\frac{\hat{J}_k}{\|\hat{\mathbf{J}}\|} - \frac{J_k}{\|\mathbf{J}\|} \right)^2}. \tag{3}$$

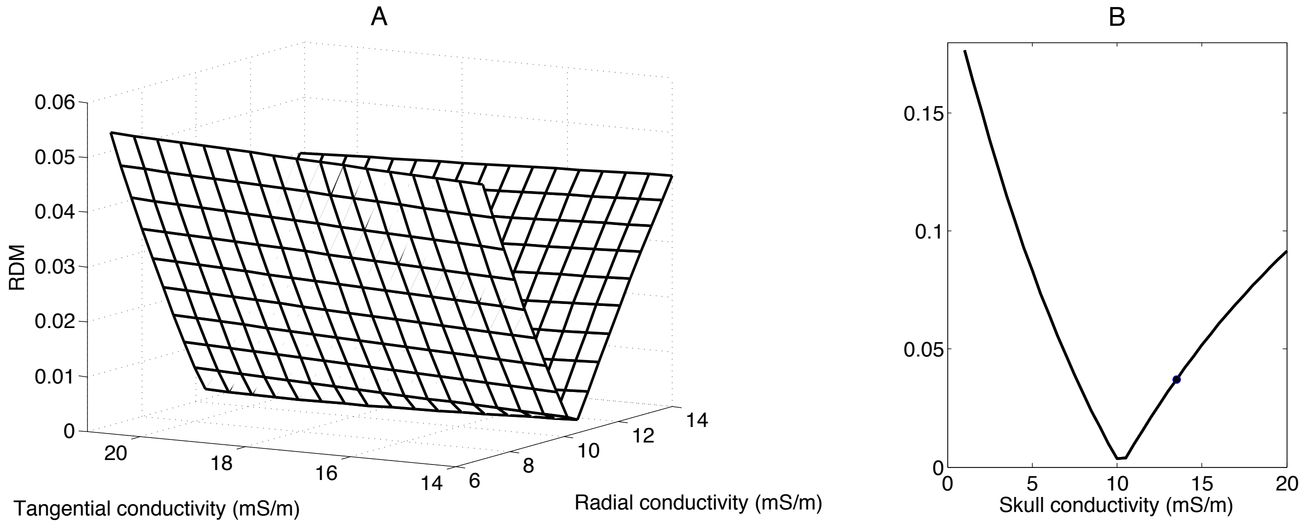

Fig. 2 RDM differences between current densities in the brain compartment of the reference model and in the approximation models. The reference model, with conductivities equivalent to $\sigma_r = 10.5$ mS/m and $\sigma_t = 15.3$ mS/m, was compared with A) the anisotropic model for a grid of pairs $\{\sigma_r,\sigma_t\}$ and B) the isotropic model for a range of isotropic conductivity values. The dot in B) indicates the result for $\sigma_{\text{skull}} = \sigma_b$.

III. RESULTS

We simulated tDCS in a spherical head model and compared two skull approximation models to the realistic model. Fig. 2 presents the RDM of the brain compartment's current densities in the reference and in the anisotropic model for each combination (σ_r,σ_t). It shows a large influence of σ_r on the error and almost no influence of σ_t. The plot has a minimum RDM of 0.0013 for σ_r = 10.5 mS/m. This corresponds to the radial conductivity value computed using (1) to calculate the equivalent conductivities of the isotropic three-layered skull in the reference model.

Fig. 2 displays RDM differences between brain current densities in the reference model and in the isotropic single-layer model. It can be seen easily in this plot that the bulk skull conductivity as calculated via (2), indicated in the plot with a dot, is not the optimal value for approximating the skull. The plot has a minimum RDM of 0.0037 at σ_{skull}=10.5 mS/m, which is exactly the value of the equivalent radial conductivity σ_r in the reference model. Overall, the results show that, independent of the modeling approach, σ_r is by far the dominant factor in determining the conductive properties of the skull and its value should be equal to the equivalent radial conductivity of the reference model. When modeling with these optimal values, the deviation from the ideal model is similar and small for both methods.

The RDM provides a measure for the *average* difference in the brain compartment between the current densities computed for the different models. Fig. 3 shows the *distribution* of the current density on a plane through the center of the A) reference model, B) anisotropic and C) isotropic single-layer models. For the compacta and spongiosa conductivities measured by Akhtari et al., which were used in the analysis above and correspond to a conductivity ratio $\sigma_t/\sigma_r = 1.46$, the differences between the reference model and the optimal single-layer models are too small to be distinguishable in a current density plot. In order to demonstrate the different nature of the current densities predicted by the three skull models, we used for Fig. 3 the optimal models that correspond to the conductivity ratio 10. The plot shows that even for this higher conductivity ratio the distributions in the brain compartment are almost identical for all three models, but differ distinctively in the skull compartment. The different modeling approaches are easily recognized in these plots. The reference model has a highly conductive spongiosa layer in the middle of the skull compartment, through which a significant amount of current is shunted. In the models with one skull layer, the anisotropic model conducts better in the tangential direction than the isotropic model does and therefore more current flows axially along the superficial part of the skull. Close to the brain compartment, this advantage is overruled by the much higher brain conductivity and less current flows via the skull. The color scale in this plot was optimized for the skull, hence the differences in skin current density are not visible. In this compartment the current densities were quite different as well, so the different skull modeling approaches lead to large discrepancies in the skin and skull, but almost no difference in the brain compartment.

IV. DISCUSSION

In this study we investigated different representations of the human skull in a spherical head model for the application of transcranial direct current stimulation.

We found that approximating the skull by one layer results in distorted current densities in the skin and skull layers, but in the brain compartment there is little difference between the models. The minimum errors in the brain compartment for both approximations are small and both can be used to model the skull well. However, if one wishes to study current densities caused by tDCS in the scalp, for example to examine concurrent scalp muscle stimulation, these approximation models should not be used.

Our results show that the radial conductivity of the skull

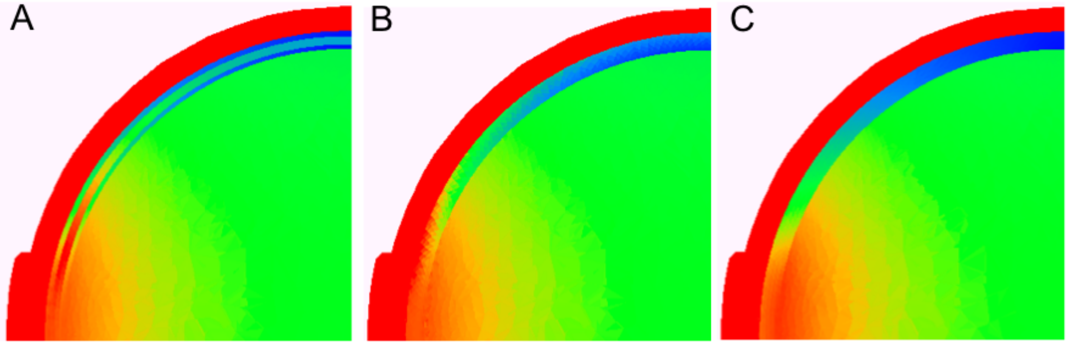

Fig. 3 Current density (a.u.) on a plane through the center of the A) reference, B) anisotropic and C) isotropic single-layer models with conductivity values equivalent to an anisotropy ratio of 10.

determines most of its conductive properties in tDCS. This dominant role of the radial conductivity of the skull was also found in EEG source localization studies [16]. When modeling transcranial direct current stimulation, the choice of the value for the radial conductivity seems crucial. With optimal values, both approximations performed well and one could conclude that modeling the skull realistically is unnecessary. However, for increasing conductivity ratios we observed large deviations from the ideal model. This result should always be taken into account when comparing skull modeling approaches for tDCS simulations and possibly also for other stimulation modalities.

In this study we used a spherical approximation to a human head. Several studies concluded that improper modeling of the skull's thickness [17], curvature [18] or inhomogeneity [16] can lead to large errors in modeling results. Furthermore, the conductivity of the skull is dependent on the relative amounts of spongy and cancellate bone, which is not constant throughout the skull. Tang et al. [19] indicated that the proportion of spongy tissue in the skull highly correlates with its radial conductivity, which as we showed accounts for the largest part of the anisotropic properties of the skull. We are planning future research that will include a realistic head model in which the three skull layers are segmented separately and highly accurately.

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REFERENCES

[1] Fregni F, Boggio PS, Lima MC, Ferreira MJ, Wagner T, Rigonatti SP, Castro AW, Souza DR, Riberto M, Freedman SD, Nitsche MA, and Pascual-Leone A. A sham-controlled, phase ii trial of transcranial direct current stimulation for the treatment of central pain in traumatic spinal cord injury. *Pain*, 122(1):197–209, 2006.

[2] Fregni F, Boggio PS, Santos MC, Lima M, Vieira AL, Rigonatti SP, Silva MT, Barbosa ER, Nitsche MA, and Pascual-Leone A. Noninvasive cortical stimulation with transcranial direct current stimulation in parkinson's disease. *Movement Disorders*, 21(10):1693–1702, 2006.

[3] Fregni F, Boggio PS, Nitsche MA, Rigonatti SP, and Pascual-Leone A. Cognitive effects of repeated sessions of transcranial direct current stimulation in patients with depression. *Depressio and Anxiety*, 23(8):482–484, 2006.

[4] Fregni F, Thome-Souza S, Nitsche MA, Freedman SD, Valente KD, , and Pascual-Leone A. A controlled clinical trial of cathodal dc polarization in patients with refractory epilepsy. *Epilepsia*, 47(2):335–342, 2006.

[5] Miranda PC, Lomarev M, and Hallett M. Modeling the current distribution during transcranial direct current stimulation. *Clinical Neurophysiology*, 117(7):1623–1629, 2006.

[6] Sadleir RJ, Vannorsdall TD, Schretlen DJ, and Gordon B. Transcranial direct current stimulation (tdcs) in a realistic head model. *NeuroImage*, 51(4):1310–1318, 2010.

[7] Suh HS, Kim SH, Lee WH, and Kim TS. Realistic simulation of transcranial direct current stimulation via 3-d high-resolution finite element analysis: Effect of tissue anisotropy. *Conf Proc IEEE Eng Med Biol Soc.*, pages 638–641, 2009.

[8] Holdefer RN, Sadleir R, and Russell MJ. Predicted current densities in the brain during transcranial electrical stimulation. *Clinical Neurophysiologyy*, 117(6):1388–1397, 2006.

[9] Pohlmeier R, Buchner H, Knoll G, Rienaecker A, Beckmann R, and Pesch J. The influence of skull - conductivity misspecification on inverse source localization in realistically shaped finite element head models. *Brain Topography*, 9(3):157–162, 1997.

[10] Rush S and Driscoll DA. Current distribution in the brain from surface electrodes. *Anesthesia and Analgesia*, 47(6):717–723, 1968.

[11] Haueisen J, Ramon C, Eiselt M, Brauer H, and Nowak H. Influence of tissue resistivities on neuromagnetic fields and electric potentials studied with a finite element model of the head. *IEEE Transactions on Biomedical Engineering*, 44(8):727–735, 1997.

[12] Akhtari M, Bryant HC, Mamelak AN, Flynn ER, Heller L, Shih JJ, Mandelkern M, Matlachov A, Ranken DM, Best ED, DiMauro MA, Lee RR, and Sutherling WW. Conductivities of three-layer live human skull. *Brain Topography*, 14(3):151–167, 2002.

[13] Wolters CH. *Influence of Tissue Conductivity Inhomogeneity and Anisotropy on EEG/MEG based Source Localization in the Human Brain*. PhD thesis, MPI of Cognitive Neuroscience Leipzig, 2003.

[14] Nitsche MA and Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *Journal of Physiology*, 527(3):633–639, 2000.

[15] Meijs JWH, Weier OW, Peters MJ, and van Oosterom A. On the numerical accuracy of the boundary element method. *IEEE Transactions on Biomedical Engineering*, 36(10):1038–1049, 1989.

[16] Dannhauer M, Lanfer B, Wolters CH, and Knoesche TR. Modeling of the human skull in eeg source analysis. *Human Brain Mapping*, 2010.

[17] Cuffin BN. Effects of local variations in skull and scalp thickness on eeg's and meg's. *IEEE Transactions on Biomedical Engineering*, 40(1):42–48, 1993.

[18] Wagner T, Fregni F, Fecteau S, Grodzinsky A, Zahn M, and Pascual-Leone A. Transcranial direct current stimulation: A computer-based human model study. *NeuroImage*, 35(3):1113–1124, 2007.

[19] Tang C, You F, Cheng G, Gao D, Fu F, Yang G, and Dong X. Correlation between structure and resistivity variations of the live human skull. *IEEE Transactions on Biomedical Engineering*, 55(9):2286–2292, 2008.