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Comparison of spherical and realistically shaped boundary element head models for transcranial magnetic stimulation navigation

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HIGHLIGHTS

- Volume conductor models influence TMS electric field estimates.
- Present TMS navigation systems use computationally simple spherical conductor models.
- Anatomically realistic boundary-element models can improve TMS targeting especially at prefrontal and temporal regions.

ABSTRACT

Objective: MRI-guided real-time transcranial magnetic stimulation (TMS) navigators that apply electromagnetic modeling have improved the utility of TMS. However, their accuracy and speed depends on the assumed volume conductor geometry. Spherical models found in present navigators are computationally fast but may be inaccurate in some areas. Realistically shaped boundary-element models (BEMs) could increase accuracy at a moderate computational cost, but it is unknown which model features have the largest influence on accuracy. Thus, we compared different types of spherical models and BEMs.
Methods: Globally and locally fitted spherical models and different BEMs with either one or three compartments and with different skull-to-brain conductivity ratios (1/1–1/80) were compared against a reference BEM.
Results: The one-compartment BEM at inner skull surface was almost as accurate as the reference BEM. Skull/brain conductivity ratio in the range 1/10–1/80 had only a minor influence. BEMs were superior to spherical models especially in frontal and temporal areas (up to 20 mm localization and 40% intensity improvement); in motor cortex all models provided similar results.
Conclusions: One-compartment BEMs offer a good balance between accuracy and computational cost.
Significance: Realistically shaped BEMs may increase TMS navigation accuracy in several brain areas, such as in prefrontal regions often targeted in clinical applications.

1. Introduction

The motivation to improve electromagnetic modeling of transcranial magnetic stimulation (TMS) stems from the need for accurate yet practical methods for quantifying and navigating TMS. In TMS (Barker et al., 1985) a current pulse is applied to a coil located on the subject's scalp, which generates a magnetic field (B field). The time-varying B field induces an electric field (E field) that alters the transmembrane voltage of neurons to the extent of triggering action potentials (see, e.g., Ilmoniemi et al., 1999). The intensity, spatial distribution, and maxima of the E-field depend on (i) the TMS coil geometry (for example, a small figure-of-eight TMS coil produces a reasonably focal E field) and (ii) the head shape and conductivity properties. Without sufficiently accurate physical models of the head ("volume conductor models"), navigated TMS systems may falsely guide the stimulation to a sub-optimal location and/or intensity. The accuracy that is needed or that could

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be achieved with navigated TMS is presently not well characterized. However, even a subtle difference in coil location, orientation, or stimulus amplitude may determine, for instance, which finger is stimulated, or whether a given experimental effect is present or absent (see, e.g., Lisanby et al., 2000; Pascual-Leone et al., 2000; Sack et al., 2009). Therapeutic effects of TMS might also depend on navigation accuracy, as suggested by TMS and epidural cortical stimulation studies in depression (Herbsman et al., 2009; Kopell et al., 2011).

The TMS-induced E field is determined by the Maxwell–Faraday law of induction $\nabla \times \vec{E} = -\partial \vec{B}/\partial t$, from which it follows that the *total E field* has the general form $\vec{E} = -\partial \vec{A}/\partial t - \nabla \varphi$. The first term involving the vector potential $\vec{A}$ corresponds to the *primary field* induced by the current in the coil, whereas the second term involving the scalar potential φ is determined by the boundary conditions of the volume conduction problem and is called the *secondary field*. The total E field drives passive ohmic currents in the volume conductor $\vec{J} = \sigma \vec{E}$, and if it is tentatively assumed that the head is a homogeneous passive volume conductor with conductivity σ immersed in a non-conducting medium (air), then it follows by charge conservation that charge must accumulate on the conductivity boundary to render the current into the non-conducting medium equal to zero. This surface charge is responsible for generating the secondary E field $-\nabla \varphi$.

The charge accumulation has been computationally determined for a semi-infinite space in (Tofts, 1990), and an appropriate measurement using a dipole probe was described in (Tofts and Branston, 1991). Other groups have presented techniques for calculating and measuring the E field for specific geometries, such as a sphere, further demonstrating that the conductivity boundaries substantially influence the total E field induced by TMS (Cohen and Cuffin, 1991; Durand et al., 1992; Roth et al., 1990; Yunokuchi and Cohen, 1991). An important theoretical connection, based on the principle of reciprocity (Plonsey, 1972), between magnetoencephalography (MEG) and TMS was utilized by (Heller and van Hulsteyn, 1992): the TMS E field can be obtained directly by applying computational methods employed in MEG forward modeling. Perhaps the most drastic effect of the secondary E field for a spherically symmetric volume conductor was immediately re-derived: independent of the TMS coil position, orientation, and shape, the radial component of the total E field is zero inside the volume conductor. This reflects the well-known fact that radial primary currents in a spherically symmetric volume conductor do not produce external magnetic fields (Baule and McFee, 1965; Grynszpan and Geselowitz, 1973). This theoretical prediction has also been experimentally confirmed (Cohen and Cuffin, 1991; Yunokuchi and Cohen, 1991).

The charge accumulation, giving rise to the secondary fields, potentially occurs on all locations of the volume conductor where the conductivity changes. Thus, both inhomogeneity and anisotropy of tissue conductivity may have an effect on the E field (Miranda et al., 2003) except in special cases (Ilmoniemi, 1995). With increasing computational power, development of numerical methods, imaging technologies, and image processing algorithms, several groups have tackled the problem of calculating the effects of tissue conductivity on the TMS E field in an anatomically realistic head model, typically obtained from magnetic resonance imaging (MRI) data. The tissue types that have different conductivities include (but are not limited to), skin, skull, cerebro-spinal fluid (CSF), gray matter, and white matter. The effects of tissue heterogeneity on TMS-induced E fields have been studied using the Boundary Element Method (BEM) (Salinas et al., 2009), the Finite Element Method (FEM) (Chen and Mogul, 2009; Thielscher et al., 2011; Wagner et al., 2004), and the Finite Difference Method (FDM) (Toschi et al., 2008). The effects of the conductivity anisotropy in white matter have been studied with FEM (De Lucia et al., 2007; Opitz et al., 2011) utilizing diffusion tensor imaging (DTI) to estimate the conductivity tensor (Tuch et al., 2001). The effects of tissue heterogeneity and anisotropy have varied across studies, partially due to the assumed conductivity values and methods used (Gabriel et al., 2009). However, it is clear that anatomically realistic modeling of the TMS-induced E fields is useful.

All currently existing on-line TMS navigation devices estimate the induced E fields using spherical conductor models, and may display the results overlaid with the individual anatomical MRI to assist in positioning the coil (Hannula et al., 2005; Ruohonen and Karhu, 2010). Increasing the realism and detail of the conductor model has the potential to increase targeting and dosing accuracy, but it comes at a significant computational cost: the most complex models are presently incompatible with real-time TMS navigation. The ideal level of conductor model complexity depends also on whether on-line instantaneous results are required for navigation during the experiment, or if more accurate but slower off-line computations are desired (e.g., for planning of post-stroke therapy sessions in the presence of tissue pathology). Moreover, highly refined conductor models employing FEM with anisotropic tissue conductivities typically require significant imaging resources in the form of several types of MRI scans and/or high-resolution computer tomography (CT), and even then building the model may take a significant amount of manual work and expertise for each subject/patient (Windhoff et al., 2013) which may partially explain why such models have not been used in large-scale studies.

It is therefore useful to examine where the computational and imaging resources should be placed to provide the largest gains in targeting and dosing accuracy. In this article, we present a computationally efficient and robust BEM approach for anatomically realistic modeling of the E fields, based on a three-compartment model of the head. BEM models are presently routinely used in MEG studies, and thus can be adapted to TMS as well. In the present study, we systematically quantified the effect of volume conductor shape (realistic vs. spherical) and the choice of skull conductivity value on TMS-induced E fields at different locations on the surface of the brain; we are not aware of prior studies with this focus. We varied the realism of the conductor model shape (globally or locally fitted spherical, or realistically shaped), number of BEM layers (one or three), and the skull-to-brain conductivity ratio. The presented methods and results are practical in the sense that they can be readily applied to off-line computations to improve their precision but could also be developed to accommodate on-line navigation. The most complex volume conductor models, which incorporate tissue anisotropies using FEMs, are currently clearly incompatible with (near) real-time applications. Moreover, the work required to construct FEMs (see, e.g., Windhoff et al., 2013) hamper their applicability to large-scale empirical studies even for off-line applications. Consequently, FEMs are not included in the present comparisons (see also Section 4).

2. Methods

2.1. Computational methods

According to the electromagnetic reciprocity principle (Heller and van Hulsteyn, 1992; Plonsey, 1972), the quasi-static E field induced by current $I(t)$ in a coil satisfies the following relationship:

$$\vec{Q}(\mathbf{r}_q) \cdot \vec{E}(\mathbf{r}_q, t) = -\frac{\mathrm{d}I(t)}{\mathrm{d}t} \sum_i \int_{C_i} \vec{B}(\mathbf{r}) \cdot \mathrm{d}\vec{S}_i(\mathbf{r}), \tag{1}$$

where $\vec{B}(\mathbf{r})$ is the magnetic field at location $\mathbf{r}$ due to a current dipole $\vec{Q}(\mathbf{r}_q)$ located at $\mathbf{r}_q$ inside the volume conductor, and $\mathrm{d}\vec{S}_i(\mathbf{r})$ is the differential area element of the surface which is bound by the coil winding C_i. Using Eq. (1), the E field can be calculated at an arbitrary