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Dear Dr. Hallett:

Please find enclosed 3 copies of the manuscript entitled "Effects of Conductivity on Induced E Field" to be considered for publication in the Journal of Clinical Neurophysiology. These models arose from recent collaborative work involving TMS coil design. This paper demonstrates that the induced E fields for various distributions of conductivity in human grey and white matter are nearly invariant. This implies that under normal brain conditions, measurements of the induced magnetic field can be used to directly infer the induced electric field. These calculations and conclusions have important implications for the future use of TMS, especially when combined with brain imaging.

Please address all future correspondence to myself at the above address. I recommend Shoogo Ueno as one of the reviewers.

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Respectfully,

Kent Davey, Ph. D.

Effects of Conductivity on Induced E Field

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Abstract - This document quantifies the effect of changing conductivity within the brain in transcranial magnetic stimulation. Models representative of the brain that demarcate regions of white matter and grey matter add an unnecessary level of complexity to the design and analysis of magnetic stimulators. The induced E field varies little between a precise model with exact placement of white and grey matter from that of its homogeneous counterpart. The E field will increase in grey matter, and decrease in white, but the variation is small. The contour integral of the E field around a closed path is dictated by the flux change through that contour. Extreme examples of white and grey matter distributions are analyzed to show that the induced E fields for these various distributions are nearly invariant.

Background

Magnetic stimulation of the human cranium is now common practice both as a research and a diagnostic tool, and is being increasingly employed in the treatment of depression [1]. In TMS, a time varying magnetic field held near the scalp induces electrical currents in brain. An important question for researchers in this arena is determining exactly where in the brain TMS induces electrical activity, and whether this shifts as a function of differences in conductivity and organization of grey matter, white matter and CSF [2][3][4][5]. A number of effective homogeneous models of the TMS magnetic field have been proposed [6], [7] [8]. Liu and Ueno[9] proposed that when current flow from a lower conductivity region to a higher one, the interface acts as a virtual cathode. An analogy is then drawn to infer the similarities between conventional electric stimulation and magnetic.

This manuscript would support that inference and underscore the fact that at the point that positive ions are driven into a nerve cell, its intracellular potential will rise, and if the rise is sufficient, an action potential results. The nerve cell cannot distinguish whether the rise occurred because of a rapidly changing magnetic field or an imposed electric field. The inner skull boundary condition insures that the normal component of current density is essentially zero on that boundary.

Methods: Several models are tested to determine whether including differences in conductivity between grey and white matter affect the end results. The analyses are performed using numerical boundary element methods [10]. In this technique equivalent surface sources are sought to satisfy Ampere's and Faraday's law in the medium and the boundary conditions on the surface. Both

surface current and surface charge are required on every interface. The induced E field is proportional to frequency; the frequency is held fixed at 5740 Hz in all calculations as are the amp-turns. The brain is represented as a 7.5 cm radius sphere. Due to symmetry only one quarter of both the C core stimulator and the target is modeled.

Results:

Homogeneous Model

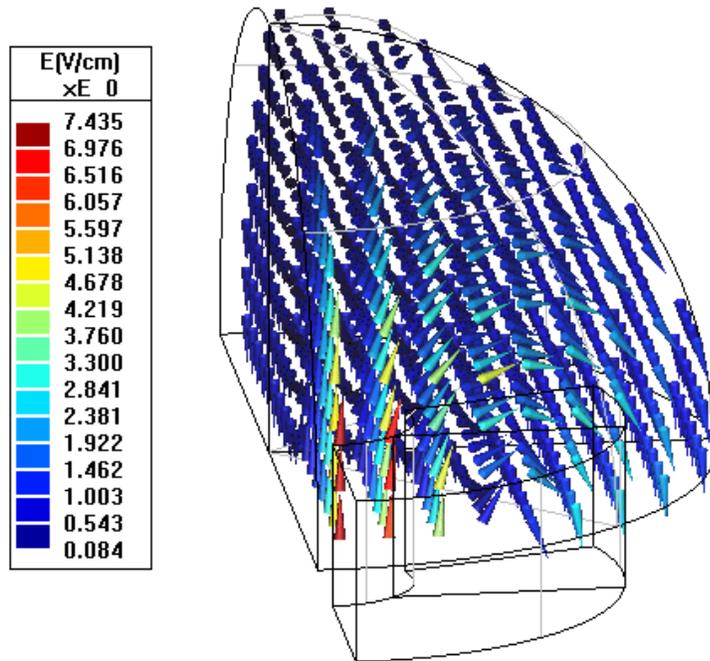
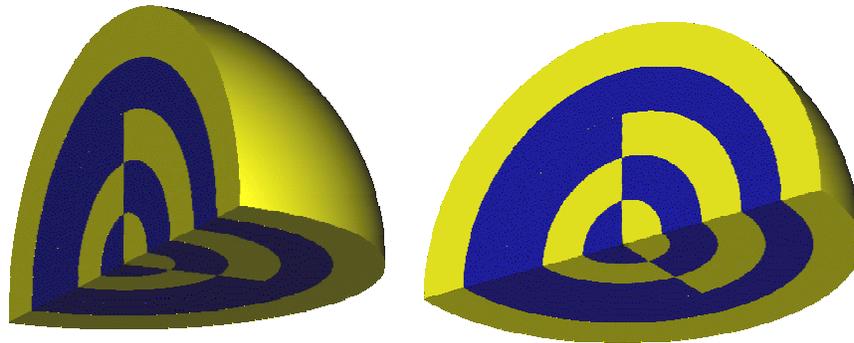


Figure 1 Homogeneous model of the brain with conductivity 0.75 S/m throughout.

Consider first the homogeneous model shown in Figure 1. The brain is depicted as a homogeneous sphere with radius 7.5 cm. The outer surface corresponds to the skull. One quarter of the problem is worked due to symmetry. The arrows depict how the E field curls around the flux face of the magnet. When the conductivity is dropped in half to 0.37 S/m, the resulting E

field differs from Figure 1 by a maximum of 0.17%. This was computed by breaking the 1/4 brain region into 778 sub volumes and computing the E field at the center of those volumes.

Inhomogeneous Model 1 - Concentric spheres



Grey matter = blue
White matter = yellow

Figure 2 Concentric sphere distribution of grey and white matter.

According to [11], the conductivity of white and grey matter is 0.48 S/m and 0.7 S/m respectively. Consider positioning the grey and white matter a number of concentric spherical bands as shown in Figure 2. The band pattern was intentionally altered so that the two 1/8 sections would themselves exhibit a contrast.

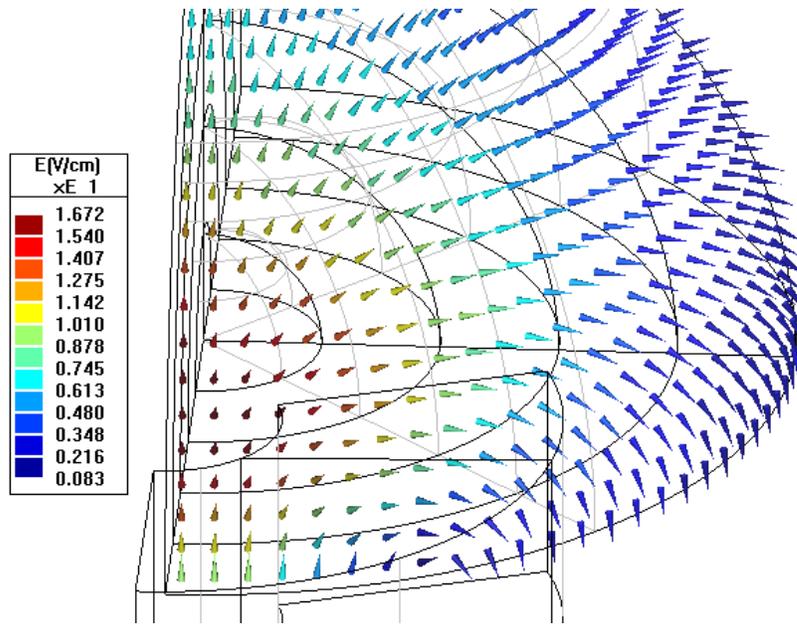


Figure 3 Surface E field plot for the spherical distribution of white and grey matter.

The surface E field obtained from this model is shown in Figure 3. Shown in Figure 4 is a plot of the E field predicted at 3,528 points within the volume of this E Field - Spherical Annuli

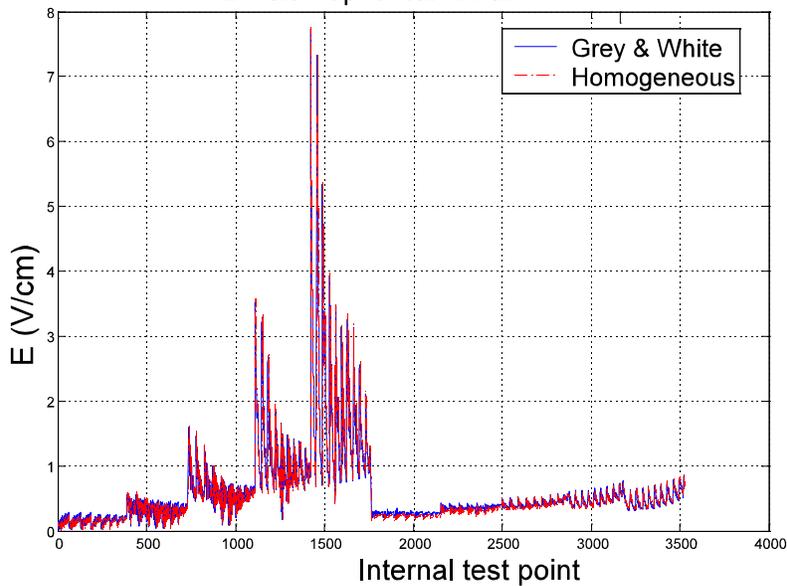


Figure 4 Comparison of homogeneous and inhomogeneous E fields for a spherical annulus model.

model. The mean absolute value of the difference between these two models is 6.8%. Figure 1

does not account for the differences in grey and white matter, while Figure 2 does make such a distinction.

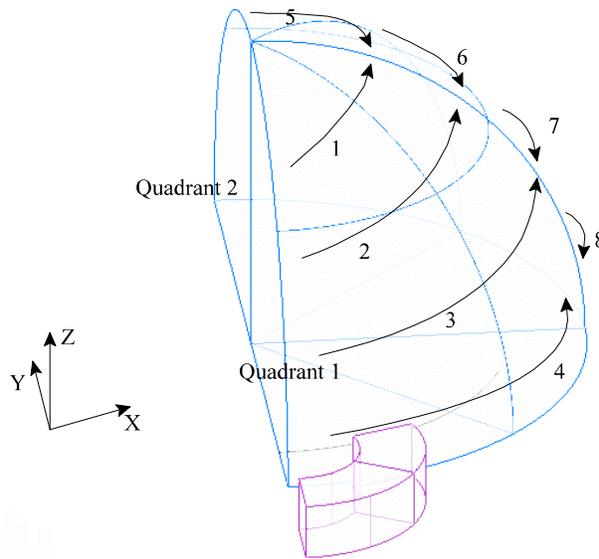
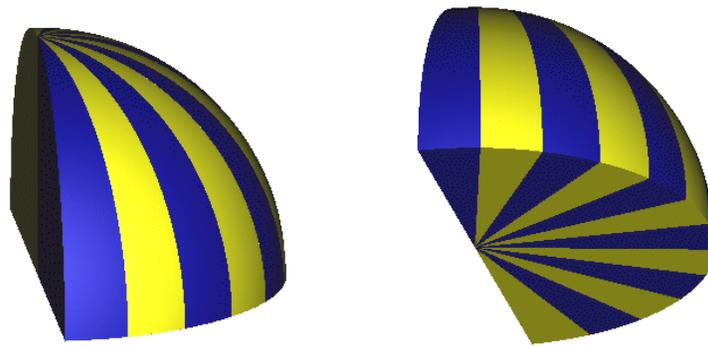


Figure 5 Order of field point comparison within the volume.

Performing a comparison within a volume is challenging, especially if a comprehensive comparison is desired. A simple approach might be to arbitrarily choose a couple of lines within the spherical volume. But the complicated distribution of grey and white matter is critical, allowing for predisposed bias. A better more global approach is obtained by imagining the placement of a test sphere within a cube and then discretizing the cube into 3,528 cubic cells, i.e., by breaking each side into 30 increments. After throwing out all the points that fall outside the sphere, 3,528 cells remain. The E field is computed at the centroid of those cells. Because of symmetry, the field is plotted only in one quarter of the volume. The plot begins in the first quadrant, and then switches to the 2nd quadrant at point 1655. The steps correspond to different z positions. The larger step cluster of points are each associated with a new setting for z, while the smaller step clusters constitute a new setting for y as suggested in Figure 5. The numbered arrows correspond to the order of the planes of points so plotted.

Inhomogeneous Model 2 - Concentric wedges



Grey matter = blue
White matter = yellow

Figure 6 Brain modeled as a series of spherical wedges, alternating white and grey matter.

Shown in Figure 6 is yet another model employing a series of spherical wedges.

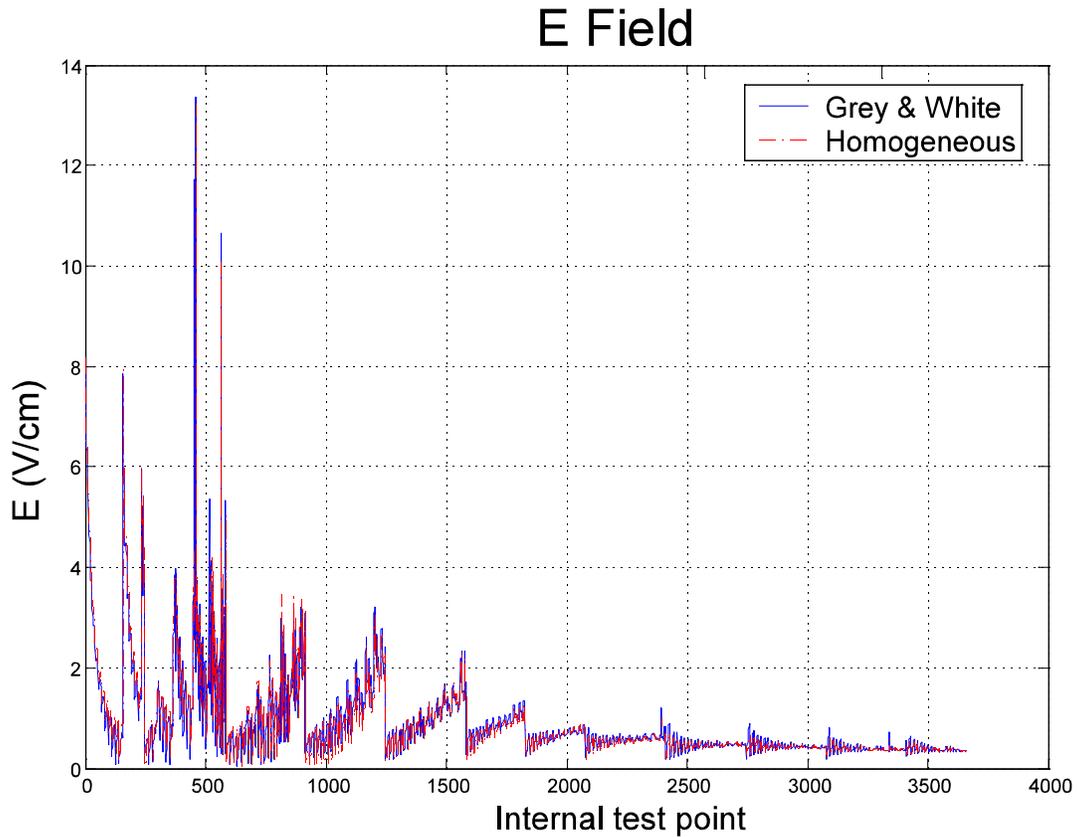


Figure 7 E field comparison between the wedge shaped model, and a homogeneous sphere.

The E field is computed for this model, and compared to that of the homogeneous model in Figure 7. The mean absolute value of the difference between the two E fields is 7.14%, considering a distribution of 3,660 points within the volume.

Inhomogeneous Model 3 - Concentric Wedges with CSF

A final test might suffice to underscore the point being made that paying attention to the distribution of mater in the brain is unwarranted. Baumann [12] has shown that the electrical conductivity of cerebral spinal fluid is 1.45 S/m at room temperature (25 °C) and 1.79 S/m at body temperature (37 °C) across the frequency range 10 to 10 kHz. Using the latter value, consider analyzing another wedge shaped model of the brain, this time with CSF distributed in

equal volume with white and grey matter as suggested in Figure 8. In this extreme case, the volume of CSF is assumed to be equal to that of grey and white matter.

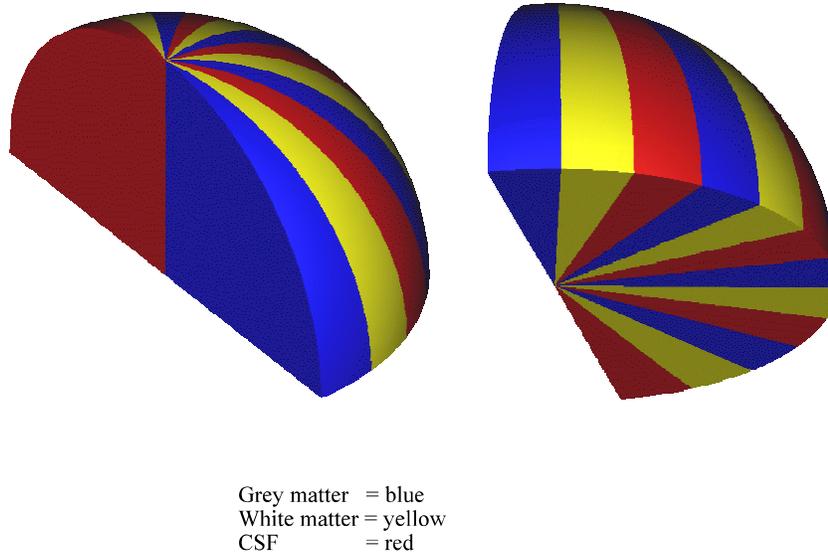


Figure 8 Combination of white, grey and cerebral spinal fluid.

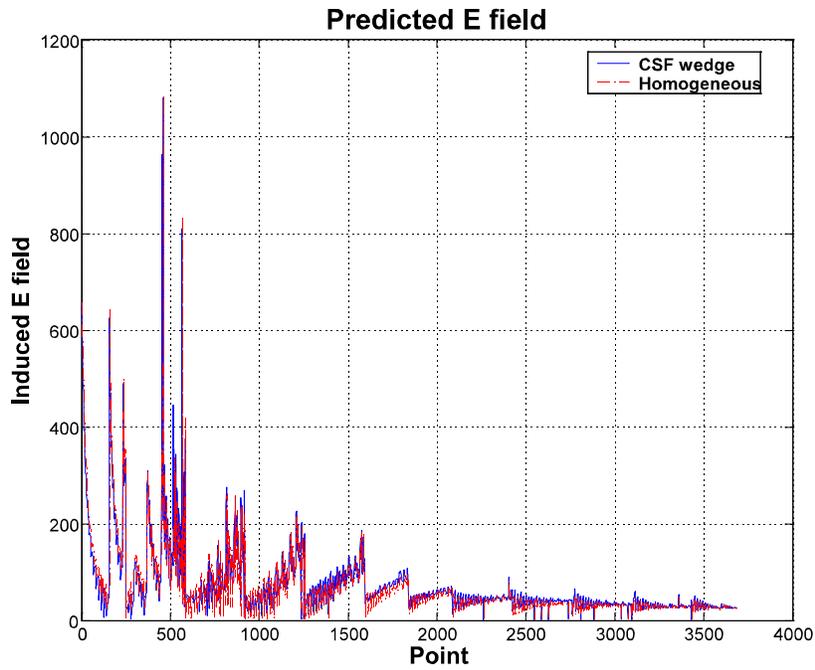


Figure 9 Induced E field predicted with the wedge model interspliced with CSF.

The difference between the E fields, shown in Figure 9, increases to a mean absolute value difference of 15.2% due to the higher conductivity of the cerebral spinal fluid. The fact that such an extreme distribution of the three returns such a small difference supports the claim that efforts to accurately model the brain's composition is unwarranted.

Conclusions

As long as the tissue conductivity differences are small, two homogeneous models will deliver the same induced E field regardless of the conductivity distribution. When the conductivity varies, the total integrated E field around a loop must also remain unchanged. Two models were analyzed containing well defined borders between white and grey matter. Even the wedge model which should exhibit the most pronounced differences, only shows a mean absolute difference of 7.1% from the homogeneous model. The most extreme model would be one in which the white matter, grey matter, and CSF are each treated as an isolated wedge; here the mean of the absolute value of the difference of the E fields is only 15.2%.

Limitations of these models need to be understood in order to properly interpret these findings. Grey matter has an anisotropic conductivity. Although the calculations were performed using isotropic approximations, the invariance of the induced E field suggests that such differences would not affect the conclusions. The complex patterns of human brain involving gyral folding and layering were not modeled. Additionally, other factors will contribute to whether nerve cells are affected by TMS, including myelination and fiber orientation and morphometry relative to the TMS field [13][14].

Acknowledgment

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