2013

A Numerical Dosimetry Study for Pediatric Transcranial Magnetic Stimulation

Lawrence J. Crowther
Iowa State University, crowther@iastate.edu

Ravi L. Hadimani
Iowa State University, hadimani@iastate.edu

David C. Jiles
Iowa State University, dcjiles@iastate.edu

A Numerical Dosimetry Study for Pediatric Transcranial Magnetic Stimulation

Abstract

Transcranial magnetic stimulation (TMS) has been used to study brain function and is being investigated as a possible treatment for a variety of neurological disorders and neuropsychiatric diseases. Most studies implementing TMS utilize adult subjects but the method may also be a beneficial tool in the treatment of pediatric patients. It is known that the structure of pediatric brains differ to those of adults and the use of scaled adult head models for studying exposure to electromagnetic radiation may provide erroneous results. In this study numerical calculations have been performed incorporating high-resolution anatomically realistic human models of varying age to accurately determine how field induced by TMS depends upon the age of the patient. Results show that different protocols should be considered when conducting TMS experiments with pediatric patients to ensure desired neurological effects are achieved in a safe manner.

Disciplines

Electrical and Computer Engineering | Electromagnetics and Photonics

Comments

A Numerical Dosimetry Study for Pediatric Transcranial Magnetic Stimulation

Lawrence J. Crowther, Ravi L. Hadimani, and David C. Jiles, *Fellow, IEEE*

Abstract—**Transcranial magnetic stimulation (TMS) has been used to study brain function and is being investigated as a possible treatment for a variety of neurological disorders and neuropsychiatric diseases. Most studies implementing TMS utilize adult subjects but the method may also be a beneficial tool in the treatment of pediatric patients. It is known that the structure of pediatric brains differ to those of adults and the use of scaled adult head models for studying exposure to electromagnetic radiation may provide erroneous results. In this study numerical calculations have been performed incorporating high-resolution anatomically realistic human models of varying age to accurately determine how field induced by TMS depends upon the age of the patient. Results show that different procedures should be considered when conducting TMS experiments with pediatric patients to ensure desired neurological effects are achieved in a safe manner.**

I. INTRODUCTION

Transcranial magnetic stimulation (TMS) is a painless and non-invasive neuromodulation technique based upon the principles of magnetic induction [1-2]. TMS has been used to study brain function and is being investigated as a possible treatment for numerous brain disorders. The technique already shows good efficacy for the treatment of drug-resistant major depressive disorder [3].

The potential acute adverse effects of TMS are mostly physiological; the possibility of provoking seizures and damaging hearing, both of which can be avoided pursuant to established guidelines [4].

The dosimetry of TMS devices has been calculated with anatomically realistic human head models [5-7] but little work has been performed to calculate induced fields in children at the frequencies associated with TMS devices.

Intricate structural changes occur in the brain during development through infancy and adolescence. Evidence for this includes the findings of a linear increase of white matter occuring whereas an increase of grey matter occurs pre-adolescence followed by a decrease post-adolescence [8]. It has also been observed that the latency of the ipsilateral silent period decreases from an age of 6-7 years old to early adolescence [9], indicating the development of cortical inhibitory neurons and myelination of the corpus callosum.

The electric field induced by TMS therefore depends on the dielectric properties of biological tissue but also upon other age-dependent parameters. The nature of these changes necessitate the study of the brain at different stages of development.

Prior numerical studies of electromagnetic fields in children have utilized scaled adult models, introducing anatomical errors to the simulation due to the non-uniform growth of organs as identified in other studies [10-11].

The present study investigates how the stage of brain development affects the induced electric field in the brain and consequently the regions of the brain that will be stimulated. TMS studies of pediatric brain disorders may gain significant insight from the outcome of this study.

II. METHODS

A. Anatomically realistic human head models

The heterogeneity and anisotropy of electrical conductivity in biological tissues have been shown to have a significant effect upon induced electric field in the brain [7,12]. It is assumed that this will remain true for human brains of different ages. High-resolution anatomically realistic head models of varying ages have been obtained for this study. The models, shown in Fig. 1, were developed as part of the Virtual Family Project [13] and are derived from MRI scans of an adult male and female, aged 34 and 26 years respectively, an 11-year-old female and 6-year-old male. Details of the individual models are provided in Table 1. The resolution of the MRI data is $0.5 \times 0.5 \times 1.0$ mm in the head and $0.9 \times 0.9 \times 2.0$ mm in the trunk and limbs.

In order to observe the effect of tissue heterogeneity an equivalent homogeneous head model has been developed, based on the standard anthropomorphic model (SAM), scaled and oriented to match the dimensions and position of each of the heterogeneous models.

TABLE I. ANATOMICAL MODEL SPECIFICATIONS

Name	Sex	Age [years]	Height [m]	Weight [kg]	BMI [kg/m^3]
Duke	M	34	1.77	72.4	23.1
Ella	F	26	1.63	58.7	22.0

L. J. Crowther is with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50010 USA (phone: 515-294-1097; e-mail: crowther@iastate.edu).

R. L. Hadimani is the with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA and Ames Laboratory, US Department of Energy, Ames, IA 50011 USA (e-mail: hadimani@iastate.edu).

D. C. Jiles is the with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA and Ames Laboratory, US Department of Energy, Ames, IA 50011 USA (e-mail: dcjiles@iastate.edu).

| Billie | F | 11 | 1.47 | 35.4 | 16.5 |
| Thelonious | M | 6 | 1.17 | 19.3 | 14.0 |

Each anatomically realistic body model consists of approximately 80 tissues. Dielectric parameters for these tissues were obtained from the IT'IS tissue database [14]
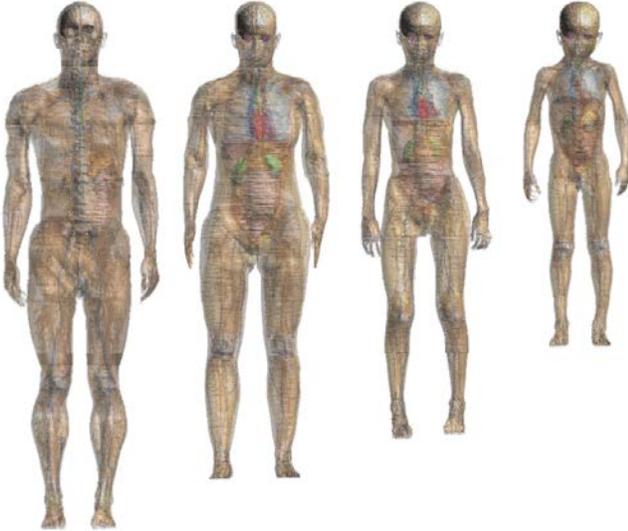

Fig. 1. High-resolution anatomically realistic human body models; male 34-year-old, female 26-year-old, female 11-year-old and male 6-year-old.

which utilizes the work of Gabriel *et al.* [15-17].

The skin component of these models comprises the cellular epidermis and dermis but not the outermost, stratum corneum which contains no excitable nerve endings. Dielectirc properties of major tissues located in the head used in this study are provided in Table 2.

TABLE II. VALUES OF DIELECTRIC PROPERTIES AT 2.5 KHZ

Tissue	Relative Permittivity, ε_r	Electric Conductivity, σ [S/m]
Brain (grey matter)	7.81×10^4	1.04×10^{-1}
Brain (white matter)	3.43×10^4	6.45×10^{-2}
Cerebellum	7.84×10^4	1.24×10^{-1}
Cerebrospinal fluid	1.09×10^2	2.00
Skin	1.14×10^3	2.00×10^{-4}
Skull	1.44×10^3	2.03×10^{-2}

B. Calculation of magnetic and electric field

The magnetic and electric fields were calculated using a method that implements a low frequency solver based on a quasi-static model. This solver assumes zero Neumann boundary conditions and requires current sources (the stimulation coil) to be modeled external to the lossy domain (the biological tissue). The magneto-static vector potential is found via the Biot-Savart law as shown in equation (1).

$$\mathbf{A_0}(\mathbf{r}) = \frac{\mu_0}{4\pi} \int_{\Omega} \frac{\mathbf{J_0}(\mathbf{r'})}{|\mathbf{r} - \mathbf{r'}|} d\mathbf{r'} \qquad (1)$$

The vector potential A is decoupled from the electric field E which is calculated using equation (2).

$$\mathbf{E} = -j\omega\mathbf{A} + \nabla\varphi = \mathbf{E_s} + \mathbf{E_i} \qquad (2)$$

where $\nabla \cdot E_s = 0$ (solenoidal) and $\nabla \times E_i = 0$ (irrotational). The magneto-quasi-static calculation is described by equation (3).

$$\nabla \cdot \sigma\nabla\varphi = j\omega\nabla \cdot (\sigma\mathbf{A_0}) \qquad (3)$$

The simulations assume a sinusoidal magnetic flux density of 2.5 kHz, comparable in frequency to the biphasic pulse produced by commercial TMS systems. 100% stimulator power output was assumed to be to an electric current of 5kA flowing in the copper medium.

C. Magnetic field measurements

A commercially available coil commonly used in the implementation of TMS has been selected for use in this study. The Magstim 2nd Generation Double 70 mm remote control coil has been characterized and modeled for electromagnetic simulations. The coil was determined to have nine windings with inner radius of 32 mm and outer radius of 48 mm. A separation of 1 mm between windings was accounted for to accommodate insulation and air gap.

To validate values obtained from the electromagnetic modeling, magnetic field measurements were conducted and compared to results obtained through simulation. Figure 2 shows the axial component of the calculated magnetic field at a distance of 20 mm, along the length of the TMS coil (x-axis) and also the measured axial magnetic field obtained with a gaussmeter and hall probe. The calculations show good agreement with the measured peak field despite small deviations occurring at the edge of the coil and at the center due to minor simplifications made in modeling the TMS coil.
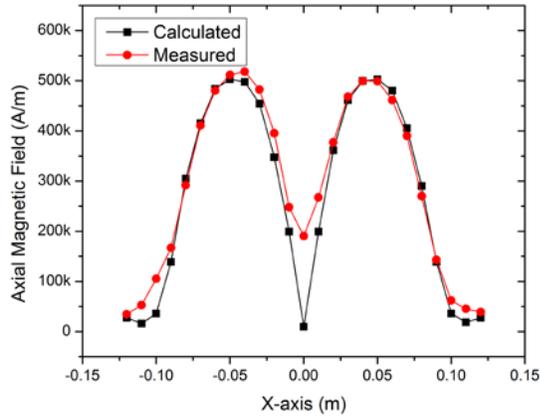
Fig. 2. Measured and calculated axial magnetic field in plane 20 mm from Magstim Double 70 mm remote control coil energized with Magstim 200 stimulator at 100% output.

III. RESULTS AND DISCUSSION

The induced electric field in a central coronal slice of the anatomical head models and corresponding homogeneous head models are shown in Fig. 3. The investigated exposure scenario is of the TMS coil being placed upon the vertex of the head.

DUKE
34-year-old male

Homogeneous 1

ELLA
26-year-old female

Homogeneous 2

BILLIE
11-year-old female

Homogeneous 3

THELONIOUS
6-year-old male
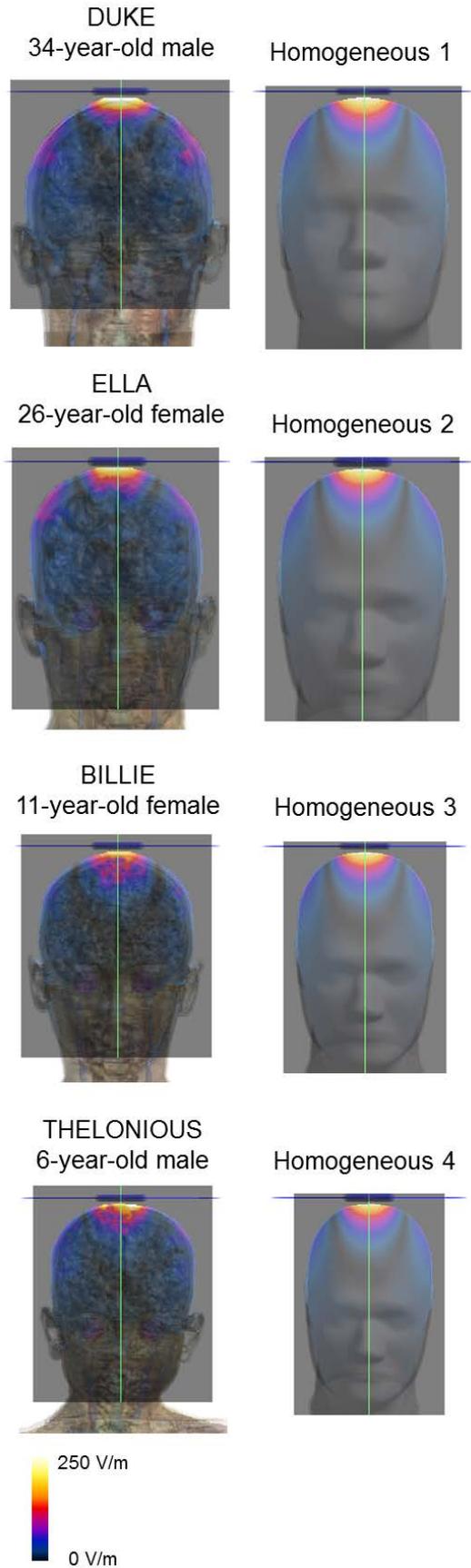
Homogeneous 4

250 V/m

0 V/m

Fig. 3. Calculated induced electric field in coronal slice of heterogeneous human head models and equivalent homogeneous models.

The electric field calculated from the vertex of the head models along the model z-axis (represented in Fig. 3 by vertical lines) for the anatomical head models are shown in Fig. 4. It is observed that the values of electric field in the child models deviate from that of adult models considerably at 20-30 mm, regions where neural tissue is located.
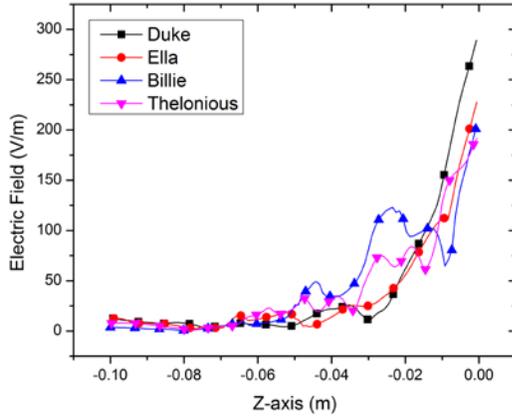

Fig. 4. Induced electric field calculated from vertex of anatomically realistic head models.

The electric field calculated in the homogeneous head models along the model z-axis are shown in Fig. 5. The results show that slightly lower electric field values are found in the child homogeneous head models than in the adult homogeneous head models. This result is consistent with that reported by Weissman *et al.* in studying animal brains which are relatively smaller than those of adult humans [18].
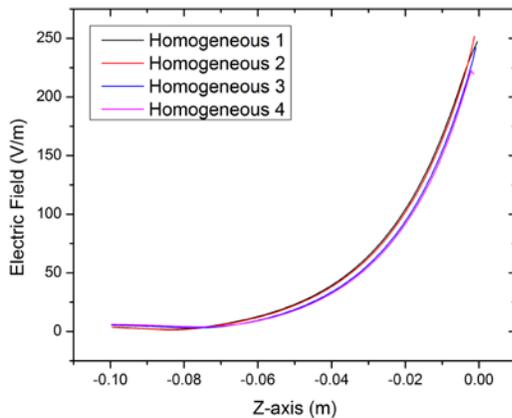

Fig. 5. Induced electric field calculated from vertex of homogeneous head models of different sizes.

To highlight the variation of induced electric field in a heterogeneous head model and how this compares to a corresponding homogeneous head model, Fig. 6 compares the heterogeneous and homogeneous head model results for the adult male. The figure shows that the heterogeneous head model yields higher values than the homogeneous model in the first 10 mm of depth but the inverse is true at greater depths

where grey and white matter are located. This result demonstrates the advantage of using anatomically realistic head models for calculations of human exposure to electromagnetic fields.
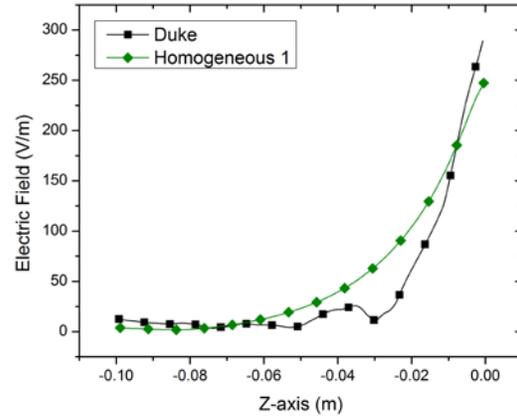

Fig. 6. Induced electric field in anatomically realistic model of adult male and corresponding homogeneous model.

Further numerical studies of pediatric TMS may also consider the potential variation in the dielectric properties with age. It has been demonstrated that the electrical conductivity of bone marrow reduces significantly with age following investigations by Peyman *et al.* [19], although only modest changes in specific absorption rate (SAR) calculations at radio frequencies (significantly higher than the frequencies associated with TMS) were observed.

IV. CONCLUSIONS

This study provides an insight into the effect of brain size upon the electric field induced during TMS using numerical methods and high-resolution anatomical human body models. Electric field calculations have shown that the magnitude of electric field can differ by up to 100 S/m between adult and child head models, as observed in our study at a depth of 25 mm with the 34-year-old and 11-year-old anatomically realistic head models. These results highlight the necessity to consider the structural brain changes that occur during neurodevelopment when conducting TMS for children, adolescents and young adults.

REFERENCES

[1] A. T. Barker and R. Jalinous, "Non-invasive magnetic stimulation of human motor cortex," *Lancet*, vol. 325, no. 8437, pp. 1106–1107, 1985.
[2] P. J. Basser and B. J. Roth, "Stimulation of a myelinated nerve axon by electromagnetic induction," *Medical & Biological Engineering & Computing*, vol. 29, no. 3, pp. 261–268, 1991.

the values of SAR in children when exposed to walkie–talkie devices," *Physics in Medicine and Biology*, vol. 54, no. 2, pp. 227, 2009.

[3] M. S. George, S. H. Lisanby, D. Avery, W. M. McDonald, V. Durkalski, M. Pavlicova, and B. Anderson, "Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial," *Archives of general psychiatry*, vol. 67, no. 5, pp. 507, 2010.

[4] S. Rossi, M. Hallett, P. M. Rossini, and A. Pascual-Leone, "Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research," *Clinical Neurophysiology*, vol. 120, no. 12, pp. 2008-2039, 2009.

[5] M. Lu and S. Ueno, "Dosimetry of typical transcranial magnetic stimulation devices," *Journal of Applied Physics*, vol. 107, no. 9, pp. 09B316-09B316, 2010.

[6] L. J. Crowther, P. Marketos, P. I. Williams, Y. Melikhov, D. C. Jiles, and J. H. Starzewski, "Transcranial magnetic stimulation: Improved coil design for deep brain investigation," *Journal of Applied Physics*, vol. 109, no. 7, pp. 07B314-07B314-3, 2011.

[7] L. J. Crowther, I. C. Nlebedim, and D. C. Jiles, "Developments in deep brain stimulation using time dependent magnetic fields," *Journal of Applied Physics*, vol. 111, no. 7, pp. 07B325-07B325-3, 2012.

[8] J. N. Giedd, J. Blumenthal, N. O. Jeffries, F. X. Castellanos, H. Liu, A. Zijdenbos, T. Paus, A. C. Evans, and J. L. Rapoport, "Brain development during childhood and adolescence: a longitudinal MRI study," *Nature neuroscience*, vol. 2, no. 10, pp. 861-863, 1999.

[9] M. A. Garvey, U. Ziemann, J. J. Bartko, M. B. Denckla, C. A. Barker, and E. M. Wassermann, "Cortical correlates of neuromotor development in healthy children," *Clinical neurophysiology*, vol. 114, no. 9, pp. 1662-1670, 2003.

[10] J. Wiart, A. Hadjem, N. Gadi, I. Bloch, M. F. Wong, A. Pradier, D. Lautru, V. F. Hanna, and C. Dale, "Modeling of RF head exposure in children," *Bioelectromagnetics*, vol. 26, no. S7, pp. S19-S30, 2005.

[11] A. Hadjem, D. Lautru, C. Dale, M. F. Wong, V. F. Hanna, and J. Wiart, "Study of specific absorption rate (SAR) induced in two child head models and in adult heads using mobile phones," *Microwave Theory and Techniques, IEEE Transactions on*, vol. 53, no. 1, pp. 4-11, 2005.

[12] P. C. Miranda, M. Hallett, and P. J. Basser, "The electric field induced in the brain by magnetic stimulation: A 3-D finite-element analysis of the effect of tissue heterogeneity and anisotropy," *IEEE Transactions on Biomedical Engineering*, vol. 50, no. 9, pp. 1074–1085, 2003.

[13] A. Christ, W. Kainz, E. G. Hahn, K. Honegger, M. Zefferer, E. Neufeld, W. Rascher, R. Janka, W. Bautz, J. Chen, B. Kiefer, P. Schmitt, H. P. Hollenbach, J. Shen, M. Oberle, D. Szczerba, A. Kam, J. W. Guag, and N. Kuster, "The virtual family project - development of anatomical whole-body models of two adults and two children," *Physics in Medicine and Biology*, vol. 55, pp. 23–38, 2010.

[14] P. Hasgall, E. Neufeld, M. Gosselin, A. Klingenbock, and N. Kuster, "IT'IS database for thermal and electromagnetic parameters of biological tissues," vol. www.itis.ethz.ch/database, May 20th 2013.

[15] C. Gabriel, A. Peyman, and E. H. Grant, "Electrical conductivity of tissue at frequencies below 1 Mhz," *Physics in Medicine and Biology*, vol. 54, no. 16, pp. 4863–4878, 2009.

[16] S. Gabriel, R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz," *Physics in Medicine and Biology*, vol. 41, no. 11, pp. 2251–2269, 1996.

[17] S. Gabriel, R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues," *Physics in Medicine and Biology*, vol 41, no. 11, pp. 2271–2293, 1996.

[18] J. D. Weissman, C. M. Epstein, and K. R. Davey, "Magnetic Brain Stimulation and Brain Size - Relevance to Animal Studies," *Electroencephalography and Clinical Neurophysiology*, vol. 85, no. 3, pp. 215-219, 1992.

[19] A. Peyman, C. Gabriel, E. H. Grant, G. Vermeeren, and Luc Martens, "Variation of the dielectric properties of tissues with age: the effect on