Influence of Brain-Scalp Distance on Focality of the Quadruple Butterfly Coil for Transcranial Magnetic Stimulation

Oluwaponmile F. Afuwape[1,2], Joseph Boldrey[1], Priyam Rastogi[1], Sarah A. Bentil[2], and David C. Jiles[1], *Life Fellow, IEEE*

[1]Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011, USA
[2]Department of Mechanical Engineering, Iowa State University, Ames, IA 50011, USA

Transcranial Magnetic Stimulation (TMS) is a neuromodulation technique that non-invasively depolarizes neurons in the brain. During TMS, a pulse (or multiple pulses) of a time-varying magnetic field (H) is delivered to the brain using specialized coils. The Quadruple Butterfly Coil (QBC) is a novel coil design that shows increased focality of the induced electric field over that of the standard figure-of-eight (FoE) coil. Using 50 different head models created from MRI scans of healthy individuals, our research investigated the role that brain-scalp distance (BSD) plays in the brain's response to the magnetic fields generated by the QBC and FoE. The variability of BSD is an inherent characteristic in the human population. As the BSD increases, so does the distance between the brain and TMS coil. Therefore, the anatomical variation of BSD is an independent variable that may play a significant role in the intensity of the induced electric field produced in the brain. Our results show no significant difference of the QBC's focality to that of the FoE with respect to BSD.

***Index Terms* — Biomedical, Brain, Non-Invasive, TMS.**

I. Introduction

Transcranial Magnetic Stimulation (TMS) is a neuromodulation technique which is capable of non-invasively activating neurons in the brain. During TMS, a pulse (or multiple pulses) of a time-varying magnetic field (H) is delivered to the brain. The magnetic field induces an electric field (E) in the brain which, at sufficient levels, causes neurons to depolarize [1]. The U.S. Federal Drug Administration (FDA) approved TMS for treating major depressive disorder (MDD) in 2008, certain types of migraine headaches in 2013, and obsessive compulsive disorder (OCD) in 2018 [2]. Among other indications, TMS is being considered as viable therapy for post-traumatic stress disorder (PTSD) [3] as well as Parkinson's Disease (PD) [4]. In the future, TMS may become an alternative to deep brain stimulation (DBS). An inherent risk in DBS arises from neurosurgical implantation of stimulation electrodes into the brain. The risk involved with neurosurgery has brought TMS into consideration as a viable alternative to DBS for treatment of essential tremor, dystonia, PD, and a wider range of clinical depression [5].

One of the challenges in the development of TMS therapy is the ability to deliver a focused magnetic field to a specific targeted region in the brain. In the process of delivering a sufficiently strong H field to the targeted region, surrounding areas of the brain can be stimulated unnecessarily. Stimulating non-target areas can result in side effects ranging from mild discomfort such as tingling sensations in the scalp, headaches, neck pain, and tooth pain to more adverse side effects such as fainting, and seizures [6]. The figure-of-eight (FoE) TMS coil was developed in 1988 by Ueno et al. [7] and has become the most commonly used coil for TMS therapy and research [6]. The Quadruple Butterfly Coil (QBC) is a novel design TMS coil developed by Rastogi [8] that significantly increases the focality of the magnetic field compared to the FoE coil. The QBC generates a sufficiently high E field intensity in order to trigger neuronal depolarization, while stimulating a significantly lower total brain volume than the FoE coil. The reduction of brain volume (defined as the total volume of grey matter and white matter) exposed to high E field intensities is by 11% when comparing the QBC with the FoE coil. Focality is measured using the V-Half metric (the volume of the brain exposed to at least one-half of the maximum induced electric field intensity (E_{MAX}) in the brain).

Multiple studies have shown a direct correlation between the brain-scalp distance (BSD) and the brain's response to the magnetic pulse generated during TMS [9], [10]. One study showed that a 3% increase in TMS output is necessary to elicit the same response for every millimeter increase in distance between the coil and the target within the brain [11]. If the stimulator output is increased to adjust for the increased BSD, there will be an increase in the H field passing through the tissue to reach the target site. This might result in a larger total volume of tissue unnecessarily receiving stimulation. This, in turn, increases the possibility of stimulating non-target areas which will increase the occurrences of side effects, and reduce focality [11]. The need for increased H field strength along with the reduced focality as the BSD increases can significantly reduce the efficacy of TMS therapy as well as increasing patient discomfort.

The goal of our research is to investigate the effects of the BSD on the performance of the QBC in comparison to that of the FoE.

Manuscript received May 8, 2020; revised August 2, 2020. Oluwaponmile F. Afuwape and Joseph Boldrey are co-first authors. Corresponding author: Joseph Boldrey (e-mail: joeb@iastate.edu).

II. Computer Simulations

The QBC was modeled, and finite element (FE) simulations were run, using Sim4Life software [12] on head models derived from Magnetic Resonance Imaging (MRI) scans of 50 healthy subjects. The Sim4Life software is a low frequency magneto-quasi-static solver that uses the FE method to compute the magnetic field and induced electric field within the head models. The QBC coil configuration, shown in Fig. 1, consists of two coil groups: a large set of coils and a small set of coils. The large coils have the same dimension as the FoE coil (a diameter of 95 mm) and the small coils have dimension of 40% the size of the large coils. These two sets of coils have the same number of turns (9 on both sides of each set which makes for 36 turns in total) and make a right angle with one another.

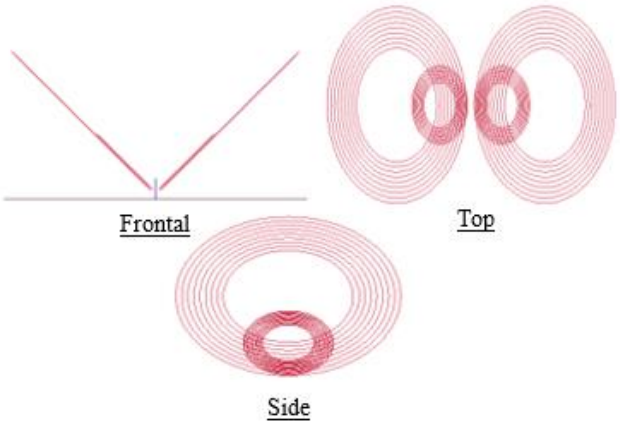

Fig. 1. Three different views of the Quadruple Butterfly Coil.

The QBC was placed at a distance of 5 mm from the vertex of each head model. This distance accounted for the insulation of the QBC, as seen in Fig. 2. The coil was pulsed at a frequency of 2.5 kHz and a current with an amplitude of 5 kA. A total of 50 simulations were run with the coil.

The BSD is obtained in the Sim4Life software using the integrated measuring tool. This distance is taken as the vertical distance from the vertex (origin 0,0,0) to the highest point on the grey matter. However, due to the uniqueness of each head model and the gyri on the right and left hemisphere, the grey matter may not always be on the same level. Fig. 2 shows the FE simulation setup in the Sim4Life software, with the grey matter in place. The vertical distance from the vertex is then measured perpendicularly to the connecting line of the brain lobes and taken as the BSD. The connecting line was established by selecting the highest point (peak) of each lobe and connecting them with a straight line.

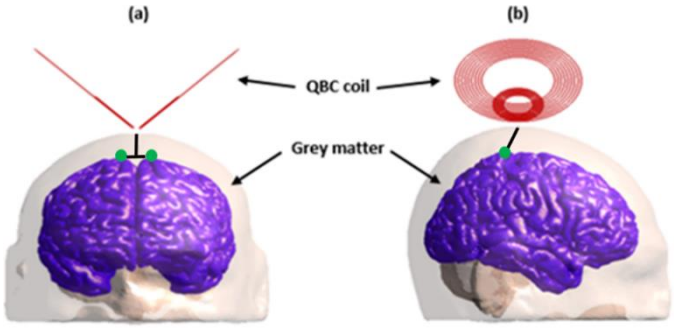

Fig. 2. Representative images of the FE simulation model in the Sim4Life software. Frontal view (a) and right hemisphere view (b) of the head model, Quadruple Butterfly Coil and grey matter.

The green dots (enlarged for clarity), in Fig. 2, are the peaks of each hemisphere of the grey matter. The straight lines (enlarged for clarity) in the same figure represent the vertical distance drawn perpendicularly downward from the vertex, and the line connecting each lobe. The 50 MRI scans of healthy subjects with ages ranging from 25-35 years were sourced from the Human Connectome Project Model Library [13] and developed using the SimNIBS pipeline by Lee et al. [14]. Each head model had seven different anatomical structures which included the skin (sn), skull (sk), cerebrospinal fluid (csf), grey matter (gm), white matter (wm), cerebellum (cb), and ventricles (vc), as shown in Fig 3.

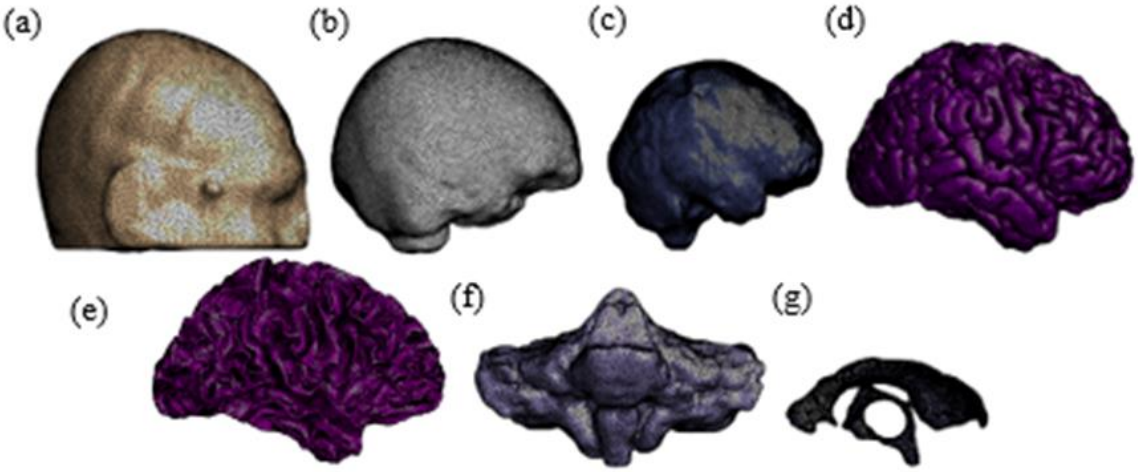

Fig. 3. The seven different anatomic variations (with the edges of their voxel shown) are (a) skin (sn), (b) skull (sk), (c) cerebrospinal fluid (csf), (d) grey matter (gm), (e) white matter (wm), (f) cerebellum (cb), and (g) ventricles (vc)

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/TMAG.2020.3017565, IEEE Transactions on Magnetics

The electrical properties of the anatomical structures, used in the FE simulations, were sourced from the Information Technologies in Society (IT'IS) foundation database [15] and are defined in Table I. The computed E_{MAX} (i.e. maximum induced electric field) values were extracted and exported to MATLAB [16] for post processing and interpretation.

TABLE I
ELECTRICAL PROPERTIES OF ANATOMICAL STRUCTURES AT A FREQUENCY OF 2.5 KHZ

Structure Name	Relative Permittivity	Electrical Conductivity (S/m)
Skin (sn)	1140	0.0002
Skull (sk)	1440	0.0203
Cerebrospinal fluid (csf)	109	2
Grey matter (gm)	78100	0.104
White matter (wm)	34300	0.0645
Cerebellum (cb)	78400	0.124
Ventricles (vc)	102	2

III. Analysis

The E_{MAX} was extracted from the FE simulations for each of the 50 head models. Fig. 4 shows the color map of the induced electric field on the skin and the grey matter, respectively, of one of the head models. A maximum induced value of 210 V/m was observed on the skin while a maximum value of 101 V/m was observed on the grey matter.

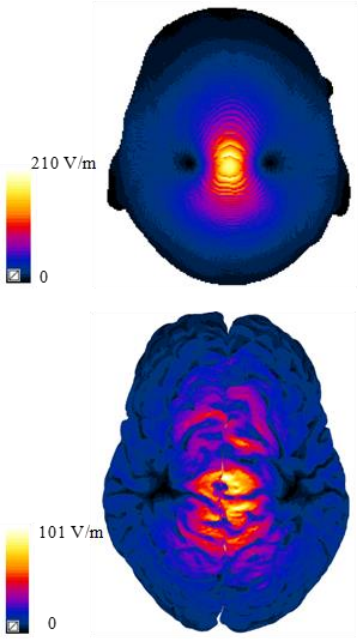

Fig. 4. Induced electric field in skin (top) and grey matter (bottom) from one of the head models.

A box plot showing the characteristic distribution of the E_{MAX} values, across the 50 head models on the basis of the minimum, maximum, median, first quartile, and third quartile, is presented in Fig. 5.

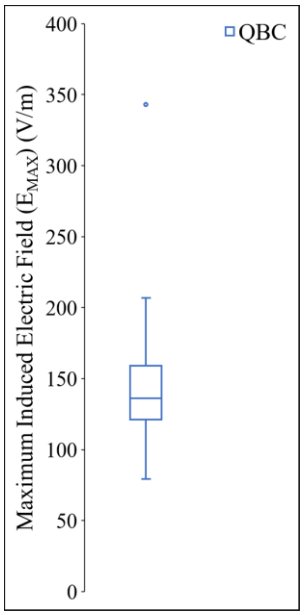

Fig. 5. Box plot shows the distribution of the maximum induced electric field, for the 50 head models.

The maximum and minimum values of E_{MAX}, among the 50 head models, was calculated as 343 V/m and 79 V/m respectively. The average E_{MAX} and standard deviation value, across the 50 head models, was calculated as 144 V/m and 41 V/m respectively.

A graph showing the variation of E_{MAX} with the BSD for both the QBC and FoE coil is presented in Fig. 6. Our results show that the E_{MAX} generated by both the QBC and FoE coil decreases as the BSD increases, with an R-squared value of 0.4293 for the QBC and an R-squared value of 0.4141 for the FoE coil. These results agree with the conclusions of Lee et al. [16] that used a FoE coil on the same set of 50 head models and also used the same FE simulation parameters as our study.

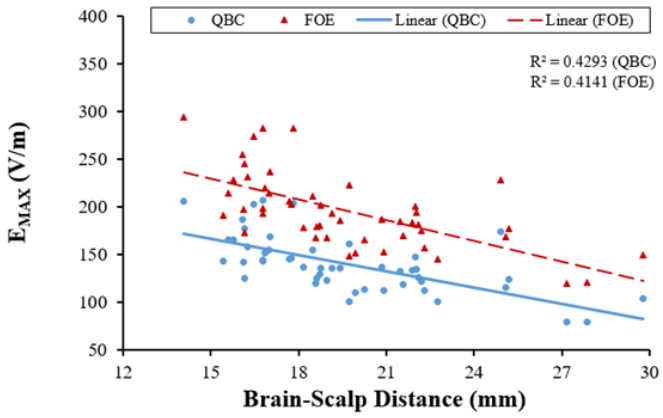

Fig. 6. Comparison between the maximum induced electric field (E_{MAX}) versus brain-scalp distance for 50 head models, using the Quadruple Butterfly Coil and Figure-of-Eight Coil.

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/TMAG.2020.3017565, IEEE Transactions on Magnetics

A graph showing the variation of V-Half versus the BSD for both the QBC and FoE coil is presented in Fig. 7. Our results show that the V-Half stimulated by the QBC and FoE coil shows no significant statistical correlation with the increasing BSD. The R-squared values are 0.0899 for the QBC and 0.0351 for the FoE coil. These results are also in good agreement with the conclusions of Lee et al. [16] that used a FoE coil on the same set of 50 head models with the same FE simulation parameters as our study.

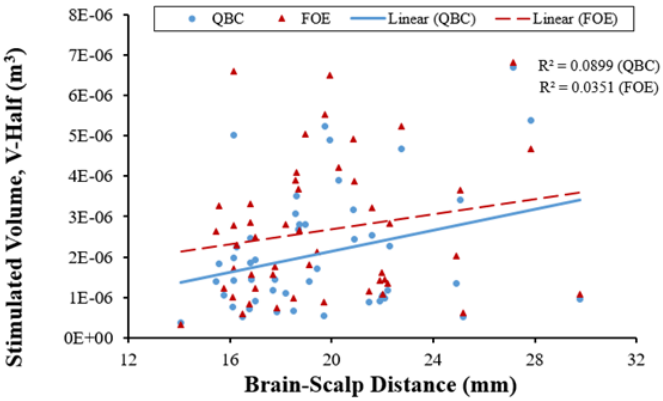

Fig. 7. Stimulated Volume versus brain-scalp distance for 50 head models using the Quadruple Butterfly Coil.

IV. Conclusion

The variability of BSD plays a role in the brain's response to TMS. With our study, we conclude that the E_{MAX} in the brain induced by the QBC decreases with BSD. This confirms that, without regards to the coil configuration, the BSD has a significant effect on E_{MAX}. However, there is no significant correlation between BSD and the V-Half (the metric for focality).

We used MRI scans of healthy subjects ranging in age from 25-35 years in our study. To further investigate the role of BSD in TMS, we intend to conduct further simulations using MRI scans from unhealthy adults and older generational cohorts, since BSD has been found to increase with age [16].

Acknowledgment

We thank Erik Lee and Dr. Ravi Hadimani for their support and contributions to the research. This work was supported in part by the Galloway Foundation, and the Stanley Chair in Interdisciplinary Engineering at Iowa State University.

References

[1] C. Miniussi, W. Paulus, P. Rossini, (2013). "Transcranial Brain Stimulation". Boca Raton: CRC Press, https://doi.org/10.1201/b14174.

[2] "FDA permits marketing of transcranial magnetic stimulation for treatment of obsessive compulsive disorder | FDA." [Online]. Available: https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-transcranial-magnetic-stimulation-treatment-obsessive-compulsive-disorder. [Accessed: 04-May-2020].

[3] R. J. Koek, J. Roach, N. Athanasiou, M. van 't Wout-Frank, and N. S. Philip, "Neuromodulatory treatments for post-traumatic stress disorder (PTSD)," Prog. Neuro-Psychopharmacology Biol. Psychiatry, vol. 92, no. December 2018, pp. 148–160, 2019, doi: 10.1016/j.pnpbp.2019.01.004.

[4] D. H. Benninger and M. Hallett, "Non-invasive brain stimulation for Parkinson's disease: Current concepts and outlook 2015," NeuroRehabilitation, vol. 37, no. 1, pp. 11–24, Aug. 2015, doi: 10.3233/NRE-151237.

[5] M. D. Fox et al., "Resting-state networks link invasive and noninvasive brain stimulation across diverse psychiatric and neurological diseases," Proc. Natl. Acad. Sci., vol. 111, no. 41, pp. E4367–E4375, Oct. 2014, doi: 10.1073/pnas.1405003111.

[6] S. Rossi et al., "Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research," Clin. Neurophysiol., vol. 120, no. 12, pp. 2008–2039, 2009.

[7] S. Ueno, T. Tashiro, and K. Harada, "Localized stimulation of neural tissues in the brain by means of a paired configuration of time-varying magnetic fields," J. Appl. Phys., vol. 64, no. 10, p. 5862, 1988.

[8] P. Rastogi, "Novel coil designs for different neurological disorders in transcranial magnetic stimulation," PhD Thesis, Iowa State University, Ames, IA, USA, 2019. Available: https://lib.dr.iastate.edu/etd/17547

[9] M. G. Stokes et al., "Biophysical determinants of transcranial magnetic stimulation: Effects of excitability and depth of targeted area," J. Neurophysiol., vol. 109, no. 2, pp. 437–444, 2013.

[10] K. A. McConnell et al., "The transcranial magnetic stimulation motor threshold depends on the distance from coil to underlying cortex: A replication in healthy adults comparing two methods of assessing the distance to cortex," Biol. Psychiatry, vol. 49, no. 5, pp. 454–459, 2001.

[11] M. G. Stokes et al., "Simple metric for scaling motor threshold based on scalp-cortex distance: Application to studies using transcranial magnetic stimulation," J. Neurophysiol., vol. 94, no. 6, pp. 4520–4527, Dec. 2005, doi: 10.1152/jn.00067.2005.

[12] E. Neufeld, M. C. Gosselin, D. Sczcerba, M. Zefferer, and N. Kuster, "Sim4Life: A Medical Image Data Based Multiphysics"

[13] D. C. V. Essen *et al.*, "The Human Connectome Project: A data acquisition perspective," *NeuroImage*, vol. 62, no. 4, pp. 2222–2231, 2012, doi: https://doi.org/10.1016/j.neuroimage.2012.02.018.

[14] E. G. Lee et al., "Investigational Effect of Brain-Scalp Distance on the Efficacy of Transcranial Magnetic Stimulation Treatment in Depression," IEEE Trans. Magn., vol. 52, no. 7, pp. 1–4, 2016.

[15] P. Hasgall *et al.*, "'IT'IS Database for thermal and electromagnetic parameters of biological tissues,' Version 4.0, May 15, 2018, DOI: 10.13099/VIP21000-04-0. itis.swiss/database."

[16] "MATLAB and Statistics Toolbox Release 2019a, The MathWorks, Inc., Natick, Massachusetts, United States.".