Focused and Deep Brain Magnetic Stimulation Using New Coil Design in Mice

S. D. March, S. McAtee, M. Senter, K. Spoth, D. R. Stiner, L. J. Crowther, R. L. Hadimani, and D. C. Jiles, *Fellow, IEEE*

***Abstract*— Deep brain transcranial magnetic stimulation (TMS) offers promising treatment for neurological disorders that originate from deeper regions of the brain, such as Parkinson's disease. Coils designed for the human head need significant redesigning to stimulate selective regions of the mouse brain for advanced TMS therapy analysis. We report a focused and deep brain TMS coil for mice that is based on a two coil configuration similar to the "Halo coil". A heterogeneous MRI derived head model of mouse was used to obtain an electric field of about 150 V/m in selective deeper regions of the brain. Focality of stimulation was quantified using the ratio of half value volume to half value of depth of electric field. A fabricated prototype of the final coil design was fabricated and characterized to compare simulated and physical magnetic field profiles.**

I. Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive medical technique used to induce neuron excitation and increase brain plasticity [1]. Focused and deep brain TMS therapy on select regions of the brain promises a method of mitigating neurological disorders such as Parkinson's disease or Post-traumatic Stress Disorder [2]. Although non-invasive, TMS procedures are often limited by non-focal stimulation of brain regions and low overall electric field strength. Recent advancements by Crowther *et al.* [3, 4] utilizing the Halo coil design show promising improvements in deep brain penetration for human designed TMS coils. Further investigation of TMS coil performance and effectiveness is still needed. Medical testing of small animals, such as mice, offers a method for TMS examination.

S.D. March is 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 (email: sdmarch@iastate.edu)

S. McAtee is with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA (email: smcatee@iastate.edu)

M. Senter is with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA (email: mjsenter@iastate.edu)

K. Spoth is with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA (email: kkspoth@iastate.edu)

D. R. Stiner is with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA (email: danstiner@gmail.com)

L.J. Crowther is with the Department of Electrical and Computer Engineering, Iowa State University, Ames, IA 50011 USA (email: crowther@iastate.edu)

R. L. Hadimani is 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 (email: hadimani@iastate.edu)

D. C. Jiles is 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 (email: dcjiles@iastate.edu)

The present study investigates a methodical approach for designing a TMS coil for medical testing for mice on the basis of Halo coil designs. TMS coils that are currently used by other research groups for stimulation of animal brains are scaled down versions of standard TMS coils that are used for stimulation of the human brain [5]. Due to the variation in the physiology of the human and mouse brains, the existing Halo coil configuration was redesigned to obtain electric field values of 150 V/m which is similar to the electric field produced in an MRI derived heterogeneous human head model when stimulated using Halo coil [6]. Focality of stimulation was quantified and optimized using ratio of half value volume to the half value depth of penetration of electric field similar to the work carried out by Deng *et. al* [7]. The final coil design was prototyped and compared to simulated models of the design's performance.

II. Methods

A. Mouse Model

Electric and magnetic field simulations were conducted using a low frequency solver in SEMCAD X finite element analysis software with an already available model of an adult mouse. The model was created from a MRI scan consisting of 50 distinct tissue layers was used for heightened simulation accuracy [8]. Such accuracy is required because various tissue layers within the mouse have distinct electrical and magnetic properties, so different regions of the body will produce different results from a model constructed out of homogeneous material. Work by Crowther *et. al.* [6, 9] on homogeneous verses heterogeneous head modeling shows a dramatic difference in coil performance.

B. s_{half} Focality Analysis

Focality implies a strong, localized electric field. As is often the case, however, electric field profiles spread with

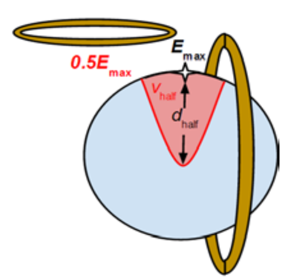

Figure 1. 2-dimensional slice of s_{half} parameters with coils (brown) for a simple spherical head model.

increased penetration depth, thus deep brain stimulation is limited by focality of neuron stimulation, thus it has been difficult to quantify the relationship between electric field strength and penetration depth. Recent work by Deng *et al.* [7] examined 50 coil designs and produced a simple measurement for focality, as described by

$$s_{half} = v_{half} / d_{half} . \qquad (1)$$

where s_{half} is the focality and tangential field spread, v_{half} is the volume of the brain experiencing greater than or equal to half the maximum electric field, and d_{half} is the depth of penetration to which at least half of the electric field maximum reaches. Fig. 1 describes s_{half} for a 2-dimensional slice of a simplified spherical head model. For this study's analysis it is assumed d_{half} occurs directly below the maximum electric field value. Focused electric field profiles produce a narrow v_{half} cone and large d_{half} penetration value. Thus, s_{half} is small for more focused designs. Maximum electric field data collected from simulations using the anatomical mouse model produced s_{half} values for the designs considered in this study, and the values produced were used to optimize later coil design parameters.

s_{half} analysis cannot be the only measure of a good electric field profile, however. As it is defined, s_{half} is simply a ratio of two geometric quantities related to, but not uniquely quantified by, the maximum electric field produced within the brain. Proper coil design analysis must consider the maximum electric field produced, as to allow for comparison between different coil designs with similar s_{half} values.

C. Design Criteria

The coil system developed was designed based on the following constraints: (1) produce focused electric field around 150 V/m inside the brain, (2) magnetic flux at the surface of the coil must have values near 3 T, and (3) coils must support 5000 A current pulses at 2.5 kHz. These design criteria are similar to those used when creating new custom coils for small animal TMS therapy applications.

III. Evolution of Designs

The next section outlines the stepwise process used when developing and improving coil focality and deep brain stimulation performance. Coil designs and their electric field profiles are examined with idealistic coil spacing considerations (Versions 1-3) before examining realistic coil spacing optimization through s_{half} analysis in section IV.

A. Version 1

The first coil design developed is similar to the anatomical placement of the halo model and used as a starting point (Fig. 2). Each coil contains six concentric wire turns. The maximum field values observed are much below the required 150 V/m neuron firing threshold. Also, the electric field is focused toward the front of the brain on the olfactory bulb; this is far from the study's objective of deep brain stimulation. After further experimentation, it was observed that the lower coil did not contribute significantly to the electric field production within the brain.

B. Version 2

The anatomical differences between the human and mouse brain shape and positioning within the skull led to a modification of Version 1, where the coils were rotated 90º (Fig. 3). Again, each coil has six concentric turns. Although the electric field strength is near the required 150 V/m value, the electric field profile is too spread thus not focused. The coil positioned farther back on the mouse's body contributed the most to the field formation due to its close proximity to the brain.

C. Version 3

Version 3 (Fig. 4) combines the upper horizontal coil from the Version 1 and the posterior coil from Version 2. Both coils have 6 turns each. The maximum electric field value exceeds the 150 V/m, and the shape of the electric field profile indicates is a focused coil design. s_{half} value obtained for this design is found to be 114 mm^2.

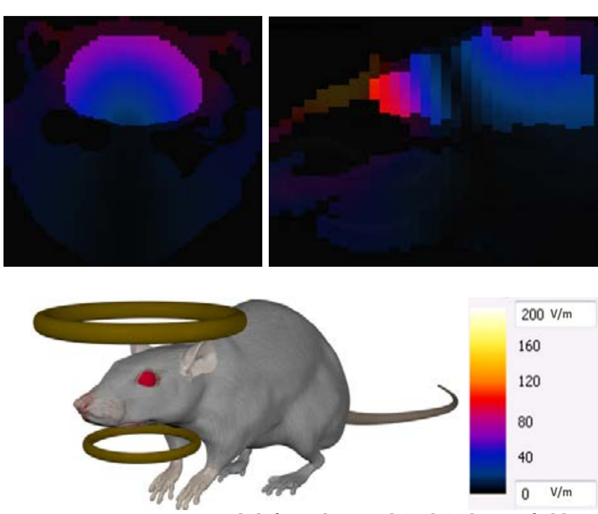

Figure 2. Version 1 coronal (left) and sagittal (right) electric field profiles. Relative anatomical coil poitioning (bottom)

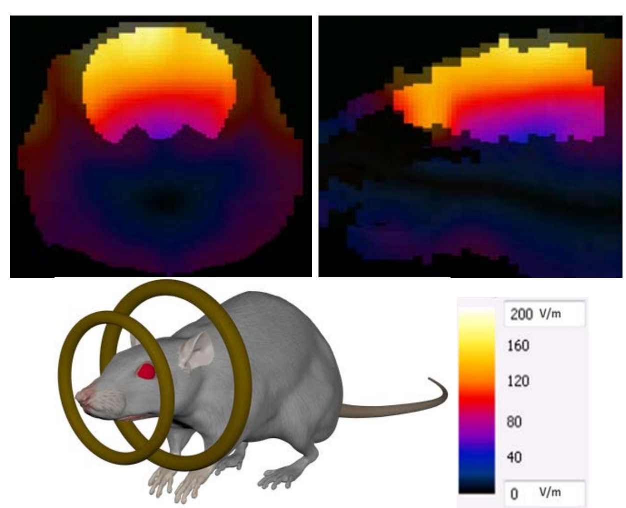

Figure 3. Version 2 coronal (left) and sagittal (right) electric field profiles. Relative anatomical coil poitioning (bottom)

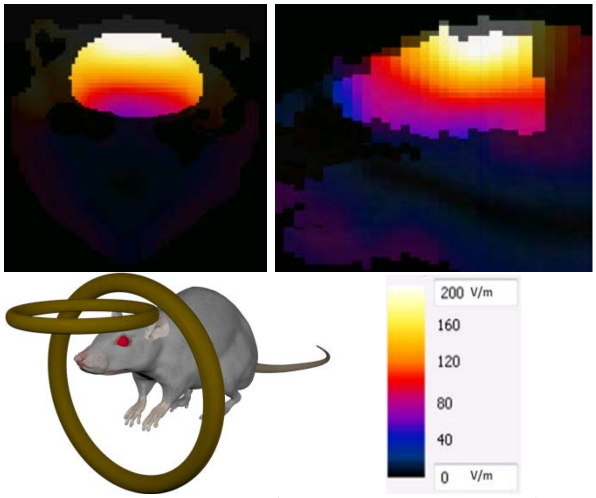

Figure 4. Version 3 coronal (left) and sagittal (right) electric field profiles. Relative anatomical coil poitioning (bottom)

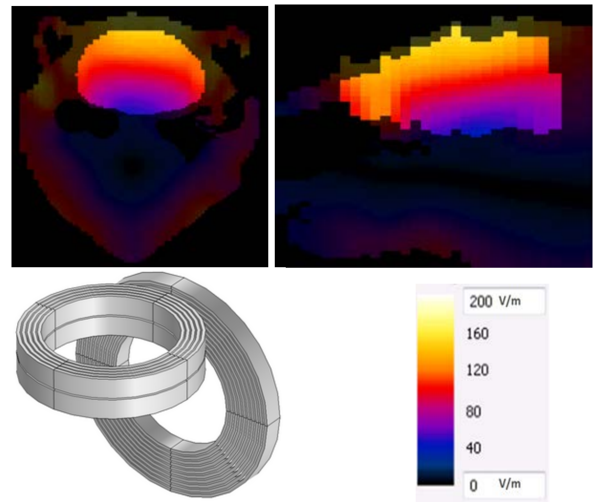

Figure 5. Realistically spaced modification of Version 3 (bottom) with coronal (left) and sagittal (right) electric field profiles.

IV. REALISTIC SPACING INCORPORATION

Idealistic spacing for Versions 1-3 served as a useful tool to generate a model of the electric field profile for different coil designs; however, s_{half} analysis of Version 3 was used to optimize the coil dimensions and spacing under realistic considerations to determine a final design. Coil turns are 0.8 × 5.0 mm in cross section with 1.0 mm spacing between turns, as these are dimensions similar to the commercially available Magstim small animal figure-of-eight coil design. The iterative capabilities of the simulation software allowed for automated generation of test data and s_{half} calculations. Data for the realistically spaced Version 3 (Fig 5) were analyzed for general trends by adjusting the inner radius of each coil and the number of coil turns (Fig 6).

Trends indicate for a particular design, the s_{half} value changes only incrementally (Δs_{half} around 8 mm^2), however, the electric field maximum changes significantly (Δelectric field maximum around 90 V/m). This indicates the importance of analyzing *both* s_{half} and electric field maximum when developing a coil design for deep brain stimulation. For example: our analysis of a standard small animal figure-of-eight design with similar positioning to a mouse's head would produce a low s_{half} value of 115 mm^2, which is very focused when only analyzing s_{half}; however, the design produced an electric field maximum below 100 V/m, which

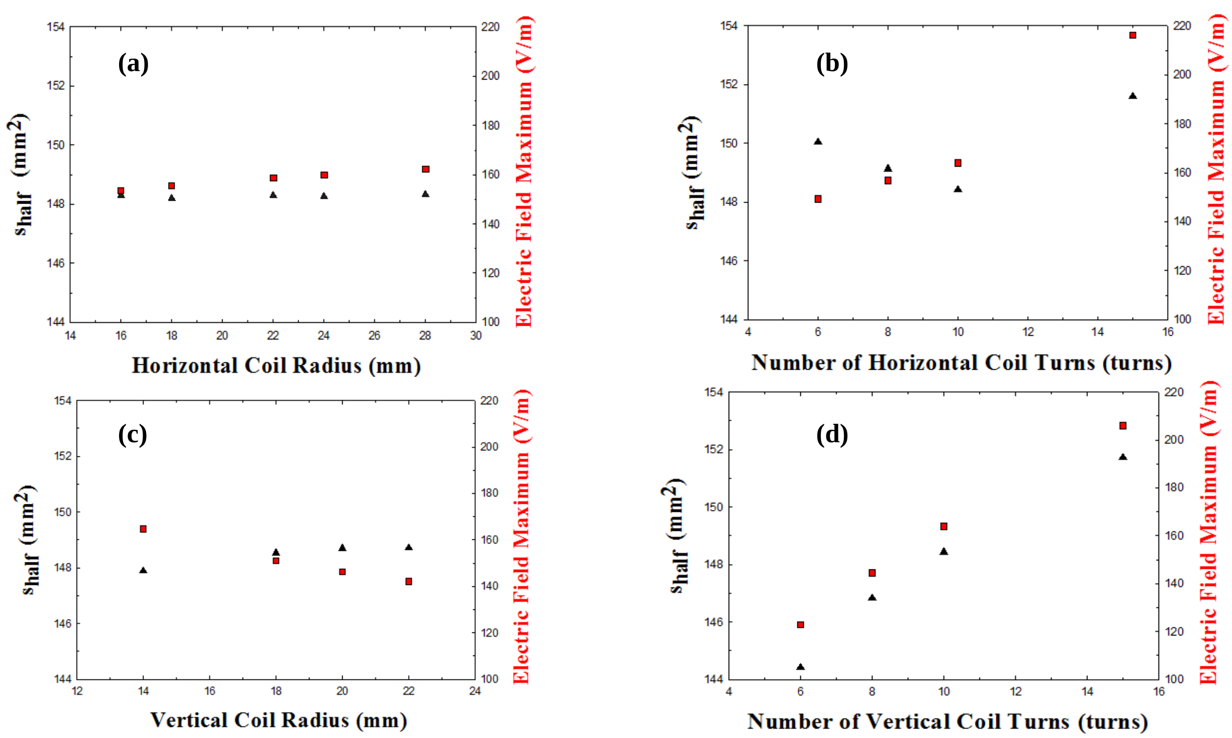

Figure 6. s_{half} and electric field maximums for adjusting coil design parameters. (a) horizontal inner turn radial values and (b) turn values with the vertical coil fixed at 10 turns and an inner radius of 16.0 mm. (c) vertical inner turn radial values and (d) turn values with the horizontal coil fixed at 10 total turns (5 per stack) and inner radius of 20.0 mm

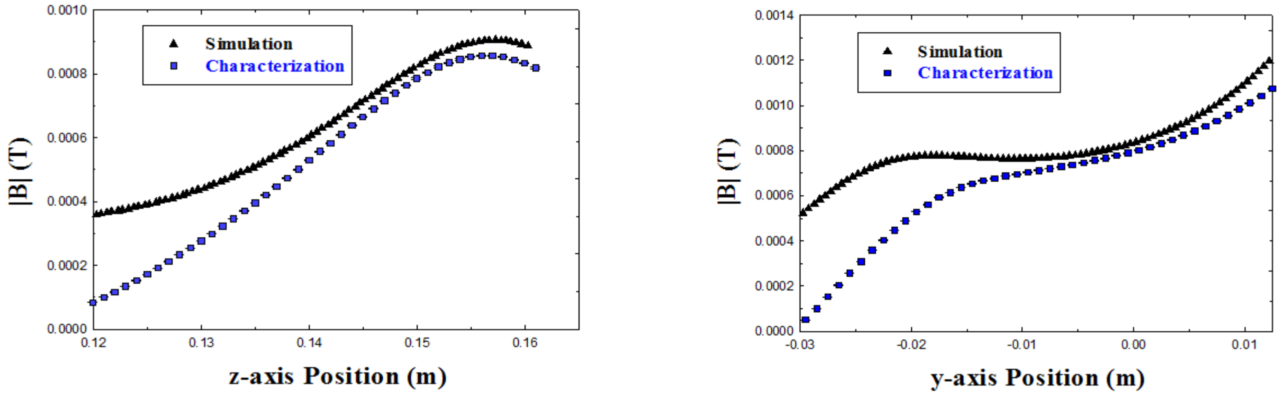

Figure 7. Simulated versus physical coil characterization magnetic field (**B**) profiles along two of the coil's planes. Note, the characterized results are scaled to meet the simulated results to indicate the similarity in the magnetic field trends.

is well below the 150 V/m target value for our design.

For the design shown in Fig 5, 10 horizontal and vertical turns, a larger horizontal coil, and a smaller vertical coil produced the most focused and strongest electric field. For design considerations, the vertical coil inner radius could only be reduced to 19.6 mm to not constrict the mouse's airway, and the maximum horizontal coil inner radius was fixed to 31.6 mm because of fabrication cost considerations. Upon further optimization and coil positioning, this design produced a 165 mm^2 s_{half} value.

V. Fabrication and Measurement of Coil Prototype

The final coil design with realistic spacing was fabricated by Magstim Company LLC, USA. The fabricated coils were supplied with a 3 A constant DC current for practical low-current coil profiling. The corresponding magnetic field was measured using a hall probe and a servo profiling table. Fig. 7 shows the magnetic field (B) profiled using SEMCAD X simulations and the measured values for the fabricated coils produced during coil characterization. The fabricated coils follow the same trend as the simulated coils. The amplitude of the magnetic field is scaled lower for the fabricated coils than the simulated values. This difference may be attributed to slight variations in the positioning of the hall probe, servo table and mismatch of dimensions in the two horizontal coils as they were fabricated in the different sites. The general trend, however, leads to confidence that the electric field produced by the fabricated coils under time-varying conditions is similar to the simulated results.

VI. Conclusion

In order to treat deep brain disorders TMS coils capable of stimulating deeper regions of the brain are essential. Significant research is being carried out in developing deep brain TMS coils for the human brain; however, there are a limited number of reports on the coil designs for animal models, and anatomical differences between humans and mice require modified coil designs to test the effectiveness of TMS therapy. In this paper we have presented several iterations of a TMS coil designs. We have successfully identified a design capable of deep brain stimulation of selected region of the mouse brain. We have calculated the electric field in the mouse brain using an MRI derived heterogonous mouse model, and we have optimized coil performance based on the combination of s_{half} coil focality analysis and electric field profile strength. We have fabricated the coil and measured the field profiles along the axis of the coils which coincide with our simulations. The fabricated coil can be used to stimulate selective regions of the brain of mouse in order to study the neurological disorders originating from deeper regions of the brain, such as Parkinson's disease or Traumatic Brain Injury.

Acknowledgment

This work was supported by the Barbara and James Palmer Endowment and the Carver Charitable Trust at the Department of Electrical and Computer Engineering, Iowa State University.

References

[1] E. M. Wassermann and S. H. Lisanby, "Therapeutic application of repetitive transcranial magnetic stimulation: a review," Clinical Neurophysiology, vol. 112, no. 8, pp. 1367–1377, Aug. 2001.

[2] E. M. Wassermann and T. Zimmermann, "Transcranial magnetic brain stimulation: therapeutic promises and scientific gaps.," *Pharmacology & therapeutics*, vol. 133, no. 1, pp. 98–107, Jan. 2012.

[3] 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, p. 07B314, 2011.

[4] P. I. Williams, P. Marketos, L. J. Crowther, and D. C. Jiles, "New Designs for Deep Brain Transcranial Magnetic Stimulation," *IEEE Transactions on Magnetics*, vol. 48, no. 3, pp. 1171–1178, Mar. 2012.

[5] R. Salvador and P. C. Miranda, "Transcranial magnetic stimulation of small animals: a modeling study of the influence of coil geometry, size and orientation.," *Conference proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, vol. 2009, pp. 674–7, Jan. 2009.

[6] 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, p. 07B325, Mar. 2012.

[7] Zhi-De Deng, Sarah H. Lisanby, Angel V. Peterchev, Electric field depth–focality tradeoff in transcranial magnetic stimulation: Simulation comparison of 50 coil designs, Brain Stimulation, Volume 6, Issue 1, January 2013, Pages 1-13, ISSN 1935-861X, 10.1016/j.brs.2012.02.005.

[8] L. J. Crowther, R. L. Hadimani, A. Kanthasamy, D. C. Jiles, "Transcranial Magnetic Stimulation of Mouse Brain Using High-Resolution Anatomical Models" J.ournal of Applied Physics, submitted, May 2013.

[9] R. L. Hadimani, K. Porzig, L. J. Crowther, H. Brauer, H. Toepfer, D. C. Jiles, "The Effect of Variation of Permittivity and Conductivity on Induced Electric Field in the Brain during Transcranial Magnetic Stimulation" IEEE Trans. Magn, submitted, May 2013.