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Comparison of Coil Designs for Transcranial Magnetic Stimulation of a Pig Model

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Abstract—
Transcranial Magnetic Stimulation (TMS) is a modulation tool that is non-invasive and used to treat neuropsychiatric disorders. Over the last decade, TMS has been approved by the United States Food and Drug Administration (FDA) for the treatment of Major Depressive Disorders (MDD) and Obsessive-Compulsive Disorder (OCD). TMS is based on Faraday's law of electromagnetic induction, involving the generation of time-varying magnetic fields from electromagnetic coils when intense pulses of current flow through the coils. This transient magnetic field, in turn, induces an electric field within the brain, which results in excitation or inhibition of the brain's neurons. Several coil designs have been proposed for achieving targeted stimulation at great depth within the brain. With the advancement in TMS technology, there is a need for preclinical studies and testing of proposed coil designs. Using animal models to conduct these preclinical studies becomes of utmost importance, especially since a successful animal trial precedes a human clinical trial. In this research, the authors model six different coil designs for an anatomically heterogeneous adult pig model. The magnetic field intensity, H (A/m), and electric field intensity, E (V/m), were calculated and compared for each coil configuration. The maximum induced electric field in the scalp and brain (grey matter) were compared for all the different coil configurations. The electric field distribution as a function of depth within the brain was also compared for the different coil configurations.

***Clinical Relevance*—**
This study will be beneficial to TMS coil designers and researchers to treat neuropsychiatric disorders and in the preclinical development of TMS coils. Results from studies with pig models are easy to compare with that of humans, and this will help to guide our understanding of the mechanism of TMS.

I. Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive medical tool that utilizes electromagnetic coils to polarize or depolarize the brain's neurons to research and treat neuropsychiatric disorders [1]. TMS was first developed in the 1980s and has since been used as an approved treatment for Major Depressive Disorder (MDD) and Obsessive-Compulsive Disorder (OCD) [2]. TMS functions on the principle of electromagnetic induction, where time-varying magnetic fields generated from TMS coils induce electric fields in the brain's neurons. This electric field causes excitation or inhibition required for altering the electric potential within the brain's neurons.

Coil designs for animals have been essential in recent times for the advancement of TMS studies. This is because animal studies, especially during the preclinical development of TMS coils, are necessary for testing the effectiveness and assessing the safety of the TMS coil designs and protocols.

Pigs are considered translational research models because of their similarities in anatomy and physiology to the human models [3]. They have been used to model certain neurological and psychiatric disorders such as anxiety disorders, schizophrenia, Alzheimer's disease, stroke, traumatic brain injury, and Parkinson's disease [4]. Pigs have also been considered possible tissue donors for humans with neurodegenerative diseases because of their similar brain developmental stages with humans [4]. This similarity in brain developmental stages also makes them potential models for brain research involving pediatric subjects. In addition to this, the pig brain has been successfully mapped and has been used to record motor evoked potential (MEP), confirming its proven potential in neuroscience research [5]. Also, for ethical reasons, they are considered a significant biomedical research model [4]. The ready availability of the pig model for experiments due to agricultural production also helps in advancing neuroscience research [6].

The pig's gray and white matter more closely resembles that of humans than rats or mice. Both pigs and humans have gyrencephalic brains, whereas rats and mice have lissencephalic brains [4]. With this similar cerebral columnar organization in pigs and humans [6], it becomes easy to compare and generalize responses from stimulation of the pig model with humans [7]. The similarities in the hippocampus and subcortical region [6] are also particularly interesting to TMS studies. This is because stimulation at the subcortex and tissues at great depth is necessary for the effectiveness of TMS treatment for certain neuropsychiatric disorders. Table 1 shows the average brain size of different animals that have been used in TMS research and their gyri and sulci structure.

The larger size of the pig brain when compared to that of small animals like rodents have also allowed for the application of techniques such as electroencephalography, positron emission tomography (PET), and magnetic resonance imaging (MRI) to the study of the pig brain [6]. Studies have also shown that similar brain regions are stimulated in both humans and pigs during neuroimaging [6].

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Table 1. TMS Animal Studies, Brain size, and structure

Animal	Average brain size (when fully developed)	Gyri and sulci structure
Mouse	About 0.5 g [6]	Lissencephalic [6]
Rat	About 2 g [6]	Lissencephalic [6]
Cat	About 30 g [6]	Gyrencephalic [6]
Dog	70-130 g (depends on breed) [6]	Gyrencephalic [6]
Pig	80-180 g (depends on breed, body size and length of time of domestication) [4]	Gyrencephalic [6]
Human	1300-1400 g [6]	Gyrencephalic [6]

This research paper models six different TMS coil designs on a high-resolution MRI-derived pig model. The modeled coils are scaled versions of some commercially available and novel coil designs for the human models.

II. Method

A. Finite Element Analysis Model

The animal model used in this analysis was the adult domesticated male pig model (Fig. 1) developed by Information Technologies in Society (IT'IS) Foundation database as a part of their Virtual Zoo Project [8]. The pig model is 977 mm long (excluding the tail), weighs 35 kg, and comprises 103 different tissue layers [8]. The electrical conductivity and electrical permittivity values of the various tissues were obtained from the IT'IS database and assigned based on the operational frequency [8]. Simulations were conducted using Sim4Life, a low-frequency finite element software for quasistatic electromagnetic analysis. The six different coils were modeled and supplied with a current of amplitude 5000 A at an operational frequency of 2500 Hz. The coils were modeled to deliver 100% power output. Results from these simulations are comparable to the outputs from a conventional clinical TMS stimulator. Also, the modeled coils are scaled versions of the conventional human TMS coils, and this is because the ratio of brain to coil size has a significant impact on the effectiveness of the TMS coil [9]. The coils were positioned in an orientation parallel to the plane of the pig's head and at a 5 mm distance from the center of the pig's scalp. The center of the pig's scalp is considered the origin (0,0,0) in the analysis, and the 5 mm distance accounted for the coil's insulation. The six different modeled coils (shown in Fig. 2) are the: a) circular coil, b) figure-of-eight (FOE) coil, c) Helmholtz coil, d) V coil, e) Animal Halo coil, and f) Quadruple Butterfly coil (QBC). The coil designs were taken from the work of [10] and [11]. The circular coil (Fig. 2a) has an outer radius of 45 mm, an inner radius of 20 mm, and 12 turns. The FOE coil (Fig. 2b) has two sets of windings placed side by side (oriented on the *xy*-plane) with

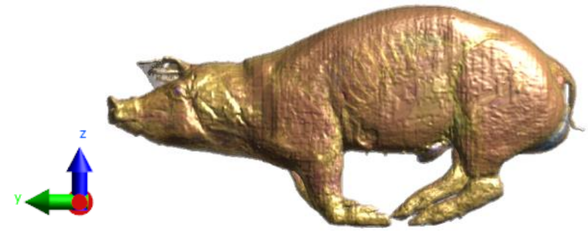

Fig. 1: Heterogeneous Adult Pig Model (the triad shows the different axes with the red arrow aligning with the *x*-axis).

a 5 mm spacing. Each set has an outer radius of 47.5 mm, an inner radius of 27.5 mm, and 9 turns each. The Helmholtz coil (Fig. 2c) has two sets of coils (oriented on the *xz*-plane) with a spacing of 94.91 mm. Each set has an outer radius of 157.05 mm, an inner radius of 106.82 mm, and 5 turns of coils. The V coil (Fig. 2d) has two sets of coils inclined at 45° to each other, and each set with 15 turns, an outer radius of 34.99 mm and an inner radius of 11.21 mm. The Animal Halo coil (Fig. 2e) has two sets of coils, with one set parallel to the plane of the pig scalp and having an inner radius of 97.95 mm and an outer radius of 147.41 mm. The other set of coils is oriented perpendicularly to the first set and positioned around the pig's neck. This set has an inner radius of 91.14 mm and an outer radius of 166.36 mm. Each set has 10 turns of coils. The QBC (Fig. 2f) has a large and small group of coils, with each group containing two sets of coils, and each set inclined at 45° to each other. The small coils (shown in red in Fig. 2f) have an inner radius of 8.25 mm and an outer radius of 14.25 mm. The large coils (shown in blue in Fig. 2f) have inner diameters of 20.625 mm and an outer radius of 35.625 mm.

III. Results And Discussion

A. Magnetic Field Intensity profile

The magnetic field intensity, H (A/m), for all the coils were calculated. The magnetic field distribution with distance along the coronal (*xz*-) and sagittal (*yz*-) plane is presented in Fig. 3. The six coils exhibited different magnetic field profiles, which is explainable since they all have different configurations. The QBC generated the highest magnetic field intensities amongst all six coils. The magnetic field distribution for the V coil, and QBC (Fig. 3d and f) were observed as having a similar profile on both the *xz*- and *yz*-planes. At the origin, we also observed that the circular coil (Fig. 3a) and FOE coil (Fig. 3b) exhibited a similar profile with a trough-like profile at the center of each set of coils. In comparison with the FOE coil, the circular coil generated a higher magnetic field intensity. For comparisons between the *xz*-plane and *yz*-plane, the Helmholtz coil and the Animal Halo coil exhibited their maximum magnetic field intensities on the *yz*-plane (shown in Fig. 3c and e). This is explainable since the orientation of both coils aligns with the *yz*-plane the most. All the other coils had their maximum intensities along the *xz*-plane.

B. Electric Field Intensity profile

i. Electric Field Intensity with Depth

The electric field intensity, E (V/m), for all the coils were calculated. The distribution for the different coil configurations is presented in Fig. 4. It was observed that each

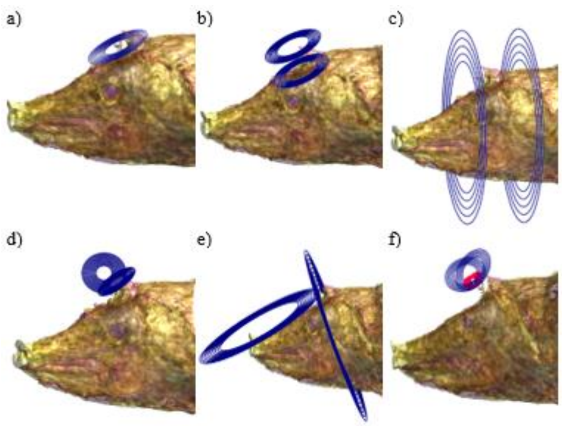

Fig. 2: Six (6) different coil configuration for studying the effect of TMS on Pig Model a) circular coil, b) FOE coil, c) Helmholtz coil, d) V coil, e) Animal Halo coil, and f) QBC (small group of coils shown in red).

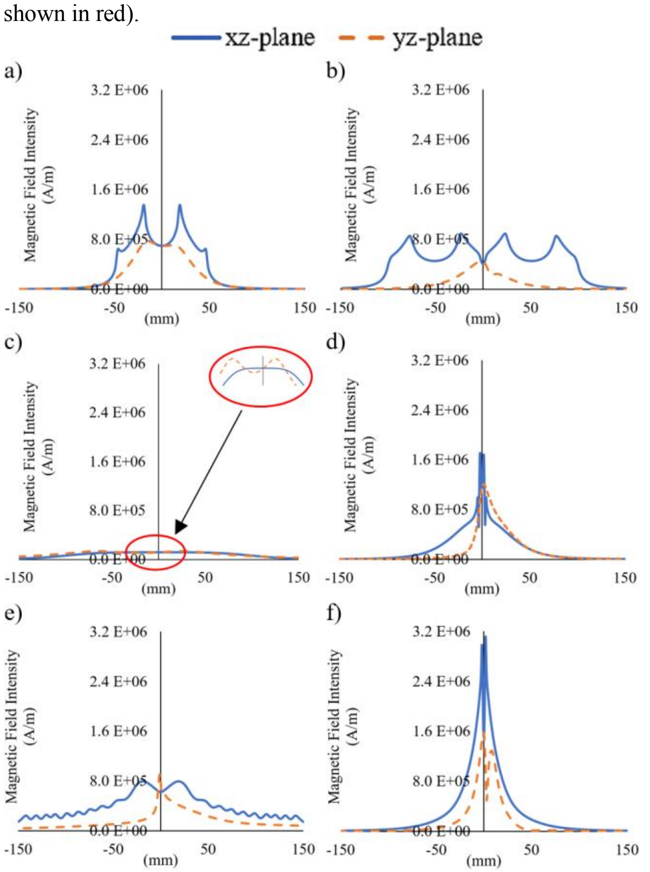

Fig. 3: Magnetic field intensity, H (A/m) distribution along the coronal (*xz-*) and sagittal (*yz-*) plane for six different coil configurations a) circular coil, b) FOE coil, c) Helmholtz coil (inset presented to show the profile at the origin), d) V coil, e) Animal Halo coil, and f) QBC.

coil exhibited unique electric field distribution, and this was because they generated varying magnetic field intensities. A decrease in the electric field intensity with depth was also observed with all the coils. For the Helmholtz coil, a spike in the distribution was observed at about 150 mm depth. This is due to the coil's configuration and orientation since the 150 mm depth is where the outer radius of the coil lies. This is beneficial, especially when deep TMS is desired. The FOE coil (Fig. 4b) induced the highest electric field intensity, followed by the Helmholtz coil (Fig. 4c) and QBC (Fig. 4f), which both induced about the same range of maximum induced electric field intensity of 130 V/m. The attenuation rate of the QBC is also observed to be faster than the Helmholtz coil. The circular (Fig. 4a) and Animal Halo coil (Fig. 4e) induced the same range of electric field intensity of about 80 V/m. The V coil induced the least electric field intensity (Fig. 4d) of about 10 V/m magnitude.

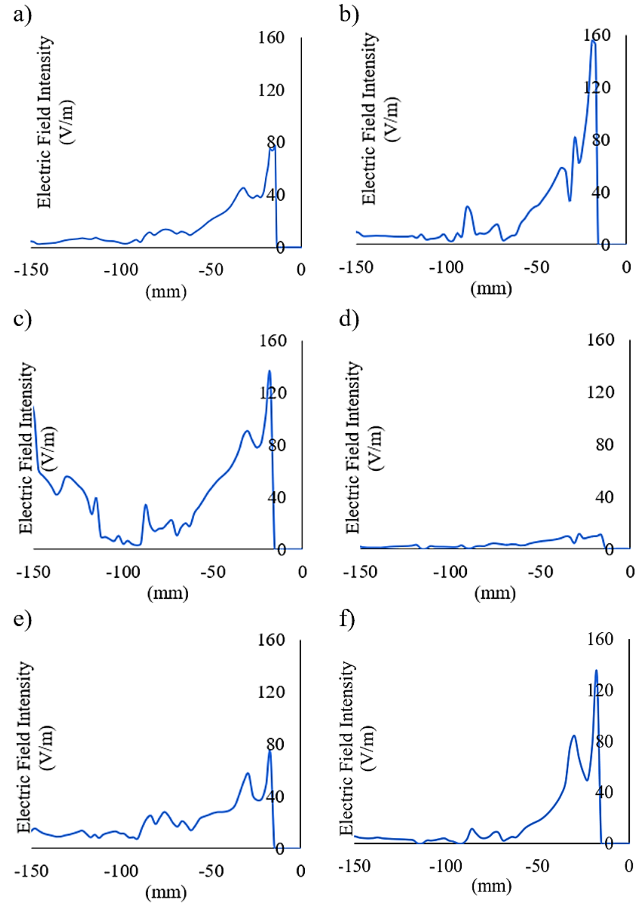

Fig. 4: Electric field intensity, E (V/m) distribution with depth for six different coil configurations a) circular coil, b) FOE coil, c) Helmholtz coil, d) V coil, e) Animal Halo coil, and f) QBC.

ii. Electric Field Intensity on Scalp

The electric field intensity distribution on the scalp for the different coil configurations is shown in Fig. 5. The induced electric field intensity has been normalized to 150 V/m for all six coils for easy comparison. It is observed that each coil exhibits different electric field distribution. The distribution of the induced electric field is presented from the head towards the neck. The entire animal model was not presented since no spread was observed in that region. The Helmholtz coil (Fig. 5c) and the Animal Halo coil (Fig. 5e) stimulated large areas of the pig scalp, leading to the overstimulation of the pig scalp and other non-target areas. The V coil and QBC (Fig. 5d and f) stimulated specific scalp regions; hence, they could be considered focal coils. The circular coil (Fig. 5a) and FOE coil (Fig. 5b) also stimulated some non-target areas but with lesser spread than the Helmholtz and Animal Halo coil.

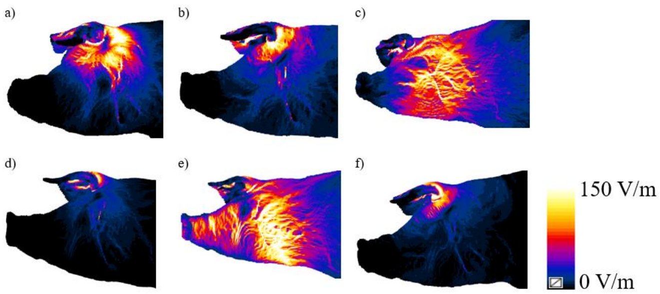

Fig. 5. Electric field intensity, E (V/m) distribution on the pig's scalp for the six coil configurations a) circular coil, b) FOE coil, c) Helmholtz coil, d) V coil, e) Animal Halo coil, and f) QBC.

iii. Electric Field Intensity on the brain (grey matter)

The electric field distribution on the grey matter for the different coil configurations is presented in Fig. 6. The induced electric field intensity has been normalized to 100 V/m for all six coils for easy comparison. It was observed that the Helmholtz coil (Fig. 6c) stimulated the whole surface area of the grey matter. This is beneficial since stimulation at great depth is required to treat disorders such as Parkinson's disease. There is also an unnecessary stimulation of non-target areas observed with the Helmholtz coil. A very low or no stimulation (of 10 V/m) was observed from the V coil (Fig. 6d). This confirms that the V coil cannot be considered for deep TMS. The circular coil (Fig. 6a), FOE coil (Fig. 6b), and QBC (Fig. 6f), when compared to the Helmholtz coil, stimulate a lesser region of non-target areas. Fig. 7 presents slice views along the coronal (*xz*-) plane of all the six coil configurations to check for overstimulation from the coils. The Helmholtz coil (Fig. 7c) and Animal Halo coil (Fig. 7e) exhibits stimulation beyond 100 mm. Both coils can be considered coils for deep TMS; however, they also exhibit stimulation of some non-target areas. The circular coil (Fig. 7a), FOE coil (Fig. 7b), and QBC (Fig. 7f) exhibit superficial stimulation, although highly localized at the target areas. Fig. 7d confirms that the V coil delivers low stimulation, hence cannot be considered a coil for deep TMS.

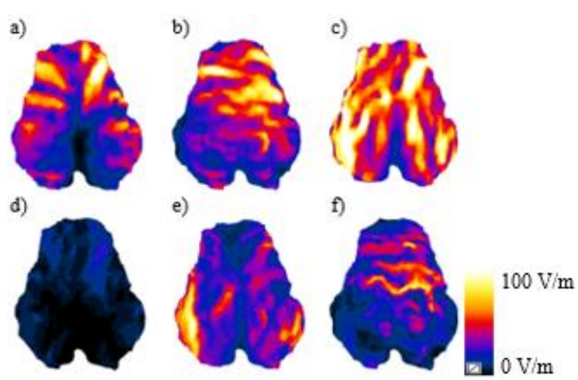

Fig. 6. Electric field intensity, E (V/m) distribution on the pig's brain (grey matter) for the six coil configurations a) circular coil, b) FOE coil, c) Helmholtz coil, d) V coil, e) Animal Halo coil, and f) QBC.

IV. Conclusion

TMS studies have been conducted on an anatomically heterogeneous adult pig model. The authors modeled six different coil configurations. The magnetic field and electric field intensities were compared, and varying coil configurations on TMS responses were analyzed. The Helmholtz and Animal Halo coils are considered coils for deep TMS, while the circular coil, FOE coil, and QBC are considered superficial coils for localized stimulation. This study will be beneficial to TMS researchers in treating neuropsychiatric disorders and in the preclinical development of TMS coils.

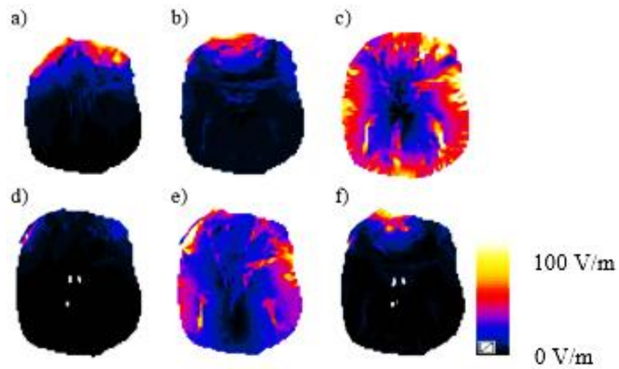

Fig. 7. Slice view along coronal *(xz-)* plane showing the electric field intensity, E (V/m) distribution on the pig's brain (grey matter) for the six coil configurations a) circular coil, b) FOE coil, c) Helmholtz coil, d) V coil, e) Animal Halo coil, and f) QBC.

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