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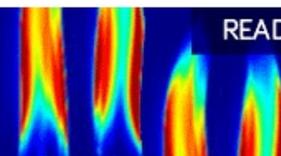
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ABSTRACT

Transcranial Magnetic Stimulation (TMS) is a non-invasive neuromodulation technique for treating neurological and psychiatric disorders. It is a proven technique that is safe and considered very effective when compared to conventional brain surgery or drug therapy. Researchers and clinicians are interested in understanding the distribution of the induced electric field (E-Field) during TMS and determining its effectiveness in treating neurological disorders. TMS studies are primarily focused on enhancing the focality and depth of penetration of the induced electric field in order to increase its effectiveness. Coil orientation has been confirmed to have an effect on the magnitude and direction of the induced E-Field. In this paper, we study the effect of the orientation of the novel Quadruple Butterfly Coil (QBC) on the distribution of the induced E-Field. Finite element analyses were conducted with the orientation of the QBC in steps of 15° over the vertex of two head models and about the transverse (XY –) plane and coronal (XZ –) plane of the head model. The maximum electric field intensity (E-Max) and stimulated volume of the brain (V-Half) were computed and compared to determine the optimal coil orientation.

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I. INTRODUCTION

Transcranial Magnetic Stimulation (TMS) is a non-invasive technique of modulating the neurons of the brain which has been used in research and clinically to treat neurological and psychiatric disorders.^{1,2} 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) using the commercially available Figure-of-Eight coil (in 2008) and the H1 coil (in 2013).³ It was FDA approved for the treatment of migraine headaches in 2013 and obsessive-compulsive disorder in 2018.^{4,5} When compared to other mechanisms of treatment such as deep brain stimulation, TMS is considered safe since it is non-invasive. It is also more effective than drug therapy as it is known to deliver a higher stimulation than antidepressants and with no accompanying side effects.^{6,7}

TMS is based on the principle of Faraday's law of electromagnetic induction. When pulses of current are allowed to flow through

the magnetic coils positioned over the patient's scalp, a time-varying magnetic field is generated. This magnetic field induces an electric field (E-Field) that causes the neurons' activation by modulating the potential in the brain, which results in the polarization or depolarization of the neurons.⁸

In recent years, several coils have been designed to achieve focality and deep penetration of the induced E-field.⁹ Amongst these designs are the circular coil and the Figure-of-Eight Coil (FOE). The FOE coil designed by Ueno *et al.* provides more localized stimulation than the conventional circular coil.^{11,12} The Quadruple Butterfly Coil (QBC) is a novel coil designed by Rastogi *et al.*¹⁰ The QBC consists of large and small sets of coils, with each having two loops. Each set has equal windings inclined at an angle of 45° to the vertical axis.¹³ The large coils have the same dimension as the FOE coil, while the small coils have a 60% reduction in dimension. The QBC exhibits an increased focality with a calculated improvement of 11.6% compared to the FOE coil.

TABLE I. Electrical Properties of the Anatomical Layers (measured at a frequency of 2.5 kHz).

| Tissue name | Electrical conductivity (S/m) | Relative permittivity |
|---------------------------|-------------------------------|-----------------------|
| Cerebellum (cb) | 0.124 | 7.84×10^4 |
| Cerebrospinal fluid (csf) | 2 | 1.09×10^2 |
| Gray matter (gm) | 0.104 | 7.81×10^4 |
| Skin (sn) | 2.0×10^{-4} | 1.14×10^3 |
| Skull (sk) | 2.03×10^{-2} | 1.44×10^3 |
| Ventricles (vc) | 2 | 1.02×10^2 |
| White matter (wm) | 6.45×10^{-2} | 3.43×10^4 |

The modulation of the brain's neurons is dependent on the magnitude and direction of the induced E-Field. Coil geometry, positioning, and orientation affect the E-Field magnitude and direction, and these parameters are required to be optimized to achieve high effectiveness.¹⁴ Coil orientation also plays an important role in producing the required response for neuronal excitation as the coil's orientation relative to the tissue anatomy at the target site influences the intensity of the E-Field. Laakso *et al.* studied the direction of

the E-Field with respect to the anatomy of the cerebral cortex and confirmed that the orientation of the coil affects the induced E-field reaching the crown of the gyri in the target location.¹⁵ Determining the E-Field intensity due to coil orientation is important in assessing the amount of stimulation the neurons receive and which hemisphere of the human brain is preferentially stimulated.^{16,17} Besides the E-Field intensity, the coils' orientation also influences the depth of penetration of the E-Field within the brain. Studying the effect of coil orientation during TMS is useful in reaching target areas and assessing the E-field intensity quantitatively in the event of changes to the protocols during TMS treatment.^{18,19} For clinical applications, determining optimal coil orientation is necessary to achieve maximum E-Field and increased focality. However, clinicians usually neglect this as it results in additional sessions for patients and unnecessary brain stimulation. The computational model study helps to determine in advance the optimal coil orientation, hence eliminating these challenges.

We have studied the effect of the orientation of the QBC on the distribution of the induced E-Field during TMS. Using finite element analysis, the maximum E-Field intensity (E-Max) and stimulated volume of the brain (V-Half) with orientation in steps of 15° about the transverse (XY -) plane and coronal (XZ -) plane over the vertex of two head models were computed and compared to

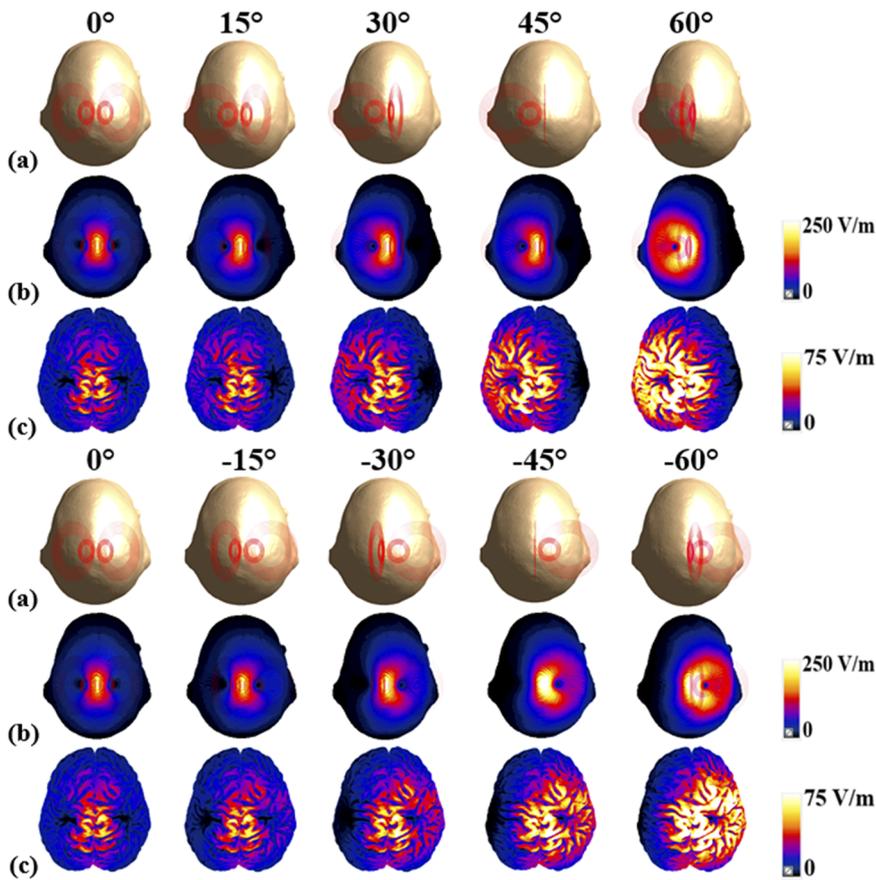


FIG. 1. (a) Coil orientation along the transverse plane of head model 2 (b) Distribution of E-Max on the scalp and (c) Distribution of E-Max on the grey matter. The E-Max have been normalized to a value of 250 V/m on the scalp and 75 V/m on the grey matter for a visual comparison between the various orientations.

determine optimal coil orientation. The V-Half is defined as the volume of the brain exposed to E-Field intensities of at least one-half E-Max.

II. METHOD

Two head models with highly defined anatomical variations were used to determine coil orientation's effect on the induced E-Field.²⁰ Both head models are those of healthy subjects with ages between 26-30 years. These head models were generated from MRI

scans obtained from the Human Connectome Model Library and converted by to 3D-images using the SimNIBS pipeline.^{21,22} The different anatomical layers were the cerebellum (cb), cerebrospinal fluid (csf), gray matter (gm), skin (sn), skull (sk), ventricles (vc) and white matter (wm). The electrical properties (Table I) of the different anatomies of the models were sourced from the Information Technologies in Society (IT²S) foundation database.²³ Simulations were run using a quasi-static, low-frequency electromagnetics field solver, Sim4Life software.²⁴ In the analysis, a current of amplitude 5000 A was allowed to flow through the QBC at an operational frequency

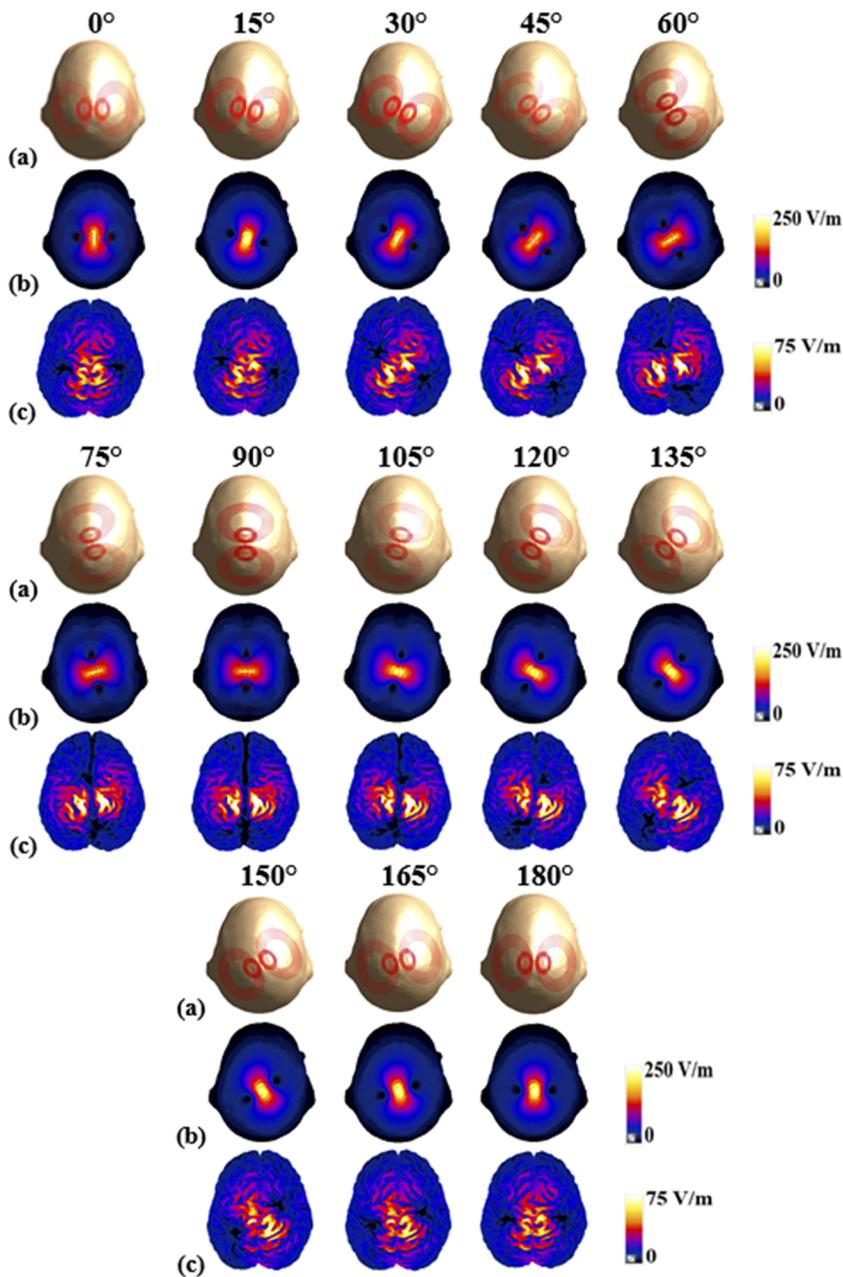


FIG. 2. (a) Coil orientation along the coronal plane of head model 2 (b) Distribution of E-Max on the scalp and (c) Distribution of E-Max on the grey matter. The E-Max have been normalized to a value of 250 V/m on the scalp and 75 V/m on the grey matter for a visual comparison between the various orientations.

of 2.5 kHz, which is comparable to the output from a conventional TMS stimulator.

The QBC orientation was made in steps of 15° over the vertex of the head model in the transverse (XY -) plane and coronal (XZ -) plane. For the transverse plane, a step of 15° within a range of $\pm 60^\circ$ was modeled so that the effect of coil orientation on the induced E-Field over the right and left hemisphere is calculated. Over the coronal plane, a step of 15° was also modeled for a rotation of 180° . A complete 360° rotation was not computed as symmetry was achieved with the coil geometry. Results were exported from Sim4Life for each coil orientation to MATLAB for data processing. The E-Max and V-Half were computed and compared to determine the optimal coil orientation. The optimal orientation is defined as that orientation with a high E-Max and a reduced V-Half so that both increased stimulation and focality is achieved.

III. RESULTS AND DISCUSSION

A visual representation of the coil orientation along the transverse plane of head model 2 is presented in Fig. 1a. The E-Field distribution on the scalp and grey matter is illustrated in Fig. 1b and Fig. 1c respectively. For the orientation with positive angles, that is, 15° to 60° , it was observed that the left hemisphere of the brain was preferentially stimulated, while for the orientation with negative angles, that is, -15° to -60° , it was observed that the right hemisphere of the brain was preferentially stimulated. Another obvious difference with this preferential stimulation is that no symmetry was observed with the E-Field distribution on both hemispheres. This is due to the variations and non-uniformities of the different anatomical layers on both hemispheres. A visual representation of the coil orientation along the coronal plane on head model 2 is presented in Fig. 2a. The E-Field distribution on the scalp and grey matter is illustrated in Fig. 2b and Fig. 2c, respectively.

The effect of orientation on the transverse plane is also compared for both head models based on E-Max and V-Half, as illustrated in the graph shown in Fig. 3a. For the head model 1, the initial

(without any orientation) E-Max and V-Half value were computed as 101.01 V/m and $5.24 \times 10^{-6} \text{ m}^3$ respectively. The highest E-Max occurred at -60° with a value of about 262.69 V/m (160.06 % increase from initial value), while the smallest V-Half occurred at -30° with a value of $2.39 \times 10^{-6} \text{ m}^3$ (54.45 % decrease from the initial value). The V-Half at -60° was $3.38 \times 10^{-6} \text{ m}^3$ (35.59 % decrease), while the E-Max at -30° was 148.05 V/m (46.58 % increase). Both -30° and -60° can be considered as good orientation for the head model 1 since they have a higher E-Max and lower V-Half value than the initial orientation value. However, -60° is considered an optimal orientation as the highest E-Max is achieved with this orientation and about 18.86 % in V-Half difference from -30° . For the head model 2, the initial (without any orientation) E-Max and V-Half value was 125.1 V/m and $5.01 \times 10^{-6} \text{ m}^3$ respectively. The highest E-Max occurred at 60° with a value of about 228.22 V/m (82.44 % increase from initial value), while the smallest V-Half occurred at -15° with a value of $4.81 \times 10^{-6} \text{ m}^3$ (3.99 % decrease from the initial value). The V-Half at 60° was $7.48 \times 10^{-6} \text{ m}^3$ (49.43 % increase), while the E-Max at -15° was 130.28 V/m (4.15 % increase). Although the 60° orientation exhibited an increased V-Half, however, the spread is still minimal. Both -15° and 60° can be considered good orientation for the head model 2 since they exhibited a higher E-Max than the initial value.

The effect of orientation on the coronal plane is also compared for the two head models based on E-Max and V-Half, as illustrated in the graph shown in Fig. 3b. For the head Model 1, the initial (without any orientation) E-Max and V-Half value were computed as 101.01 V/m and $5.24 \times 10^{-6} \text{ m}^3$ respectively. The highest E-Max occurred at 120° with a value of about 132.35 V/m (31.03 % increase from initial value), while the smallest V-Half occurred at 105° with a value of $1.97 \times 10^{-6} \text{ m}^3$ (62.36 % decrease from the initial value). The V-Half at 120° was $2.06 \times 10^{-6} \text{ m}^3$ (60.74% decrease), while the E-Max at 105° was 130.84 V/m (29.54 % increase). Both 105° and 120° can be considered good orientation for the head model 1 since they have a higher E-Max and lower V-Half value than the no orientation value. However, 120° is considered an optimal orientation since the

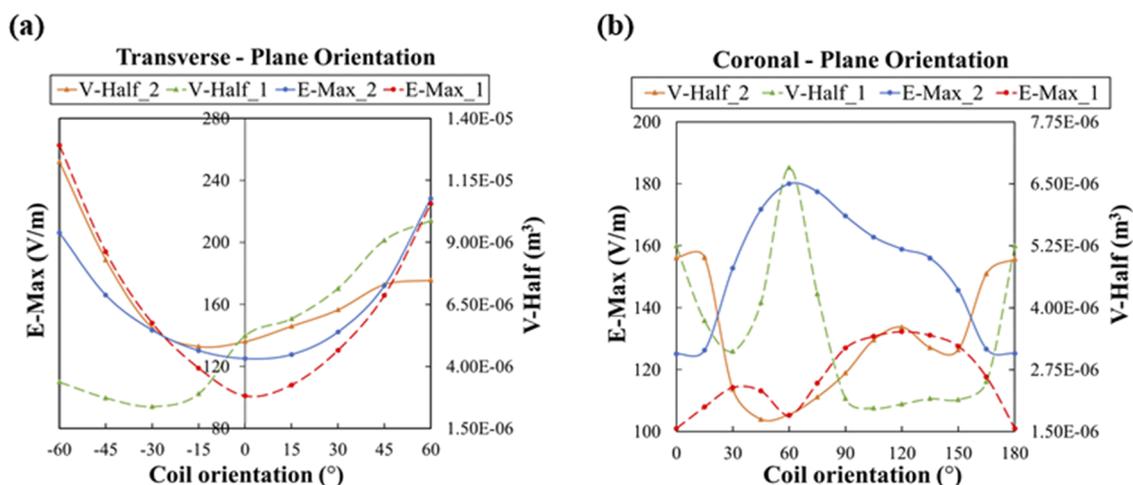


FIG. 3. Comparison of Coil orientation effect on the E-Max and V-Half of the head model 1 and 2 along the (a) Transverse and (b) Coronal plane.

highest E-Max is achieved with this orientation, and a 60.74 % decrease in V-Half. For the head model 2, the initial (without any orientation) E-Max and V-Half value was 125.1 V/m and 5.01e-06 m³ respectively. The highest E-Max occurred at 60° with a value of about 180.01 V/m (43.89 % increase from initial value), while the smallest V-Half occurred at 45° with a value of 1.75e-06 m³ (65.06 % decrease from the initial value). The V-Half at 60° was 1.85e-06 m³ (63.13 % increase), while the E-Max at 45° was 171.69 V/m (37.25 %). Both 45 and 60° can be considered good orientation for the head model 2 since they have a higher E-Max and lower V-Half than the initial value. However, 60° is considered an optimal orientation since the highest E-Max is achieved with this orientation.

IV. CONCLUSION

In this study, the effect of coil orientation and positioning of the QBC was studied on two head models. Each head model exhibited different distributions of induced E-Field with coil orientation along the transverse and coronal plane, thereby confirming the effect of coil orientation on E-Field distribution. This study provides an understanding to clinicians and researchers about the effect of the QBC positioning and orientation on the E-field distribution so they can assess its potential for different neurological and psychiatric disorders.

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DATA AVAILABILITY

The data that support the findings of this study are available within the article.

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