Published in final edited form as:

IEEE Trans Biomed Eng. 2016 September ; 63(9): 1944–1955. doi:10.1109/TBME.2015.2507572.

Preliminary Upper Estimate of Peak Currents in Transcranial Magnetic Stimulation at Distant Locations from a TMS Coil

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Abstract

Goals—Transcranial magnetic stimulation (TMS) is increasingly used as a diagnostic and therapeutic tool for numerous neuropsychiatric disorders. The use of TMS might cause whole-body exposure to undesired induced currents in patients and TMS operators. The aim of the present study is to test and justify a simple analytical model known previously, which may be helpful as an upper estimate of eddy current density at a particular distant observation point for any body composition and any coil setup.

Methods—We compare the analytical solution with comprehensive adaptive mesh refinement-based FEM simulations of a detailed full-body human model, two coil types, five coil positions, about 100,000 observation points, and two distinct pulse rise times, thus providing a representative number of different data sets for comparison, while also using other numerical data.

Results—Our simulations reveal that, after a certain modification, the analytical model provides an upper estimate for the eddy current density at any location within the body. In particular, it overestimates the peak eddy currents at distant locations from a TMS coil by a factor of 10 on average.

Conclusion—The simple analytical model tested in the present study may be valuable as a rapid method to safely estimate levels of TMS currents at different locations within a human body.

Significance—At present, safe limits of general exposure to TMS electric and magnetic fields are an open subject, including fetal exposure for pregnant women.

Index Terms

Brain Stimulation; Safety; Modeling; Analytical Models; Numerical Analysis; Finite Element Analysis

I. Introduction

Recent studies confirm the efficacy of Transcranial Magnetic Stimulation (TMS) as a non-invasive treatment of medication-resistant depression [1]–[4]. To date, a number of TMS devices such as the Neuronetics Neurostar Stimulators, the Brainsway H-Coil system, Magstim Magnetic Stimulators, and MagVenture Stimulators have been cleared by the Food and Drug Administration (FDA) for this purpose. The use of TMS might cause exposure to undesired induced currents throughout the entire body of a patient and/or a TMS operator or a nurse. Therefore, it is important to develop rigorous numerical and possibly fast analytical techniques that can safely estimate and predict the eddy current level not only in the brain, but also at various distant locations. As an example, using TMS may cause fetal exposure to undesired induced currents in pregnant patients. A considerable percentage of women experience symptoms of depression during pregnancy and develop clinical depression requiring medical intervention, and TMS has been proposed as a method to treat maternal depression while avoiding fetal exposure to drugs [5]. TMS for treatment of depression during pregnancy is an appealing alternative, but there are not enough studies to date to ensure the safety of TMS treatments for a pregnant mother and her fetus [6].

To find what are the acceptable levels of induced currents for different tissues, we refer to two guidelines [7],[8] from the International Commission on Non-Ionizing Radiation Protection. These guidelines provide recommendations on safe limits of exposure to time-varying electric, magnetic, and electromagnetic fields up to 300 GHz for both the general public and occupational cases. Induced electric fields and currents at levels exceeding those of endogenous bioelectric signals present in tissue have been shown to cause a number of physiological effects that increase in severity as the induced current density is increased. In the current density range of 10–100 mA/m², tissue effects and changes in brain cognitive functions have been reported. When induced current density exceeds 100 mA/m² for frequencies between 10 Hz and 1 kHz, thresholds for neuronal and neuromuscular stimulation are exceeded. At a higher level of exposure, severe and potentially life-threatening effects such as cardiac extra systoles, ventricular fibrillation, muscular tetanus, and respiratory failure may occur. The severity and probability of irreversibility of tissue effects becomes greater with chronic exposure to induced currents densities. The 1998 ICNIRP basic restrictions for general exposure to time-varying electric and magnetic fields for CW frequencies in the band 1–100 kHz recommend that the current density for head and trunk should be below $f/500$ mA/m² where f is the signal frequency measured in Hz. According to these guidelines, at 5 kHz frequency, the minimum exposure threshold

recommended is 10 mA/m^2 . For pulses of (effective) duration τ , the equivalent frequency to apply in the basic restrictions should be calculated as $f = 1/(2\tau)$. The above estimate can be also formulated in terms of the induced electric field by dividing the current density by local conductivity.

Induction currents in the entire human body (or bodies) caused by a TMS coil can be established in every particular case via numerical electromagnetic modeling. A numerically-accurate procedure adopted to model eddy currents within complex biological shapes is the finite-element method (FEM) or boundary element method (BEM) [9]–[16]. FEM or BEM has been previously applied specifically to TMS effects on the human head/body [13]–[15], [17]–[22]. Recently, detailed FEM computational models of the head [23] and of the entire body [24] have been developed and made available. Other methods are the finite-difference (or finite-volume) time-domain (FDTD) [25]–[35] method and quasi-analytical techniques [36]. A typical high-fidelity full-body FEM simulation with controllable accuracy and adaptive mesh refinement performed on a multiprocessor server currently requires about 5–10 hours of elapsed time for one particular geometry.

As far as the numerical computations are concerned, different body compositions (e.g. a different BMI, or a different age, or pregnancy, as well as large or metallic implants) and poses will require different human body models. There is also a growing variety of different TMS coil designs [37],[38],[36],[39]–[42], each of which in principle needs to be accurately modeled separately. Any particular coil position will require a new simulation as well. All this leads to a nearly infinite number of simulations to be performed in order to obtain general and reliable eddy current estimates. But what if we apply a simple analytical result, which uses the Bio-Savart law for the coil and Faraday's law in an unbounded homogeneous conductor, for an eddy current estimate at any particular location? Such a result is the early transcranial magnetic stimulation model [43],[44], which has been recently revisited [45].

At first sight, this analytical model seems to be useless since it severely overestimates the eddy currents in a bounded conductor with the relative dielectric constant of one. It can be shown that, for body-like conductor sizes, such a model may overestimate the true value by a few hundred times. The hidden aspect, however, is a quite large dielectric permittivity of realistic human tissues, especially at lower frequencies [46], [47]. When the actual displacement (polarization) currents and the associated polarization charges at the boundaries are taken into account, the situation may change drastically. The present study is aimed to show that the analytical model outlined above works surprisingly well as a general upper estimate of the eddy current density. This estimate applies to different body shapes, coil compositions, and different distant locations within the body, although the line integral over the coil contour still needs to be computed numerically for every observation point. The paper is organized as follows:

Section 2 formulates the analytical eddy current model and discusses all the assumptions made.

Section 3 presents an FEM computational human model and the computational testbed.

Section 4 describes an FEM analysis setup to be performed in order to prove the model and presents qualitative results.

Section 5 presents frequency-domain results over the band 300 Hz – 3 MHz and compares the FEM solution with the analytical estimate.

Section 6 presents time-domain results for a generic monophasic TMS pulse and compares the FEM solution with the analytical estimate.

Section 7 compares the FEM solution with the analytical estimate for a different coil model.

Section 8 explains the reason why the analytical model performs reasonably well.

Section 9 states the guaranteed upper estimate for the peak TMS currents and full body coverage.

Section 10 concludes the paper.

II. Upper analytical estimate of eddy currents in a heterogeneous conducting body

The upper analytical estimate of eddy currents excited in a heterogeneous non-magnetic conducting object (a human body) is based on three well-known simplifications and is rather straightforward. Recall that, after introducing the magnetic vector potential $\mathbf{A}$ so that $\mu_0 \mathbf{H} = \nabla \times \mathbf{A}$, Faraday's law of induction is transformed to [48]

$$\mathbf{E} = -\frac{\partial \mathbf{A}}{\partial t} - \nabla \varphi \quad (1)$$

Here, $\mathbf{H}(\mathbf{r}, t)$ is the total magnetic field in the body or outside, $\mathbf{E}(\mathbf{r}, t)$ is the total electric field in the body or outside, and φ is the electric potential due to surface charges residing on interfaces separating tissues with different conductivities and/or different permittivities. The electric current excited in a tissue is a combination of the conduction current, $\sigma \mathbf{E}$, and the displacement current $\epsilon \frac{\partial \mathbf{E}}{\partial t}$,

$$\mathbf{J} = \sigma \mathbf{E} + \epsilon \frac{\partial \mathbf{E}}{\partial t} \quad (2)$$

where $\sigma(\mathbf{r})$ is the local tissue conductivity and $\epsilon(\mathbf{r})$ is the local permittivity. Equation (2) will have a more complicated integral form when conductivity and permittivity are frequency-dependent. Equations (1) and (2) are exact expressions without simplification.

A. Neglecting the secondary magnetic field of eddy currents – thin limit condition

Metals are highly-conducting materials. Therefore, the skin effect becomes dominant even at low frequencies. Human tissues, on the other hand, have conductivities six to seven orders of magnitude less than metals. Therefore, they could be considered as weakly-conducting

media compared to metals. In a weakly-conducting medium, the eddy currents are small and their own (secondary or internal) magnetic field $\mathbf{H}^s$ is also small as compared to the known external large magnetic field, $\mathbf{H}^{\text{inc}}$, of the TMS coil. Thus, one has in terms of the magnetic vector potential,

$$\mathbf{A} = \mathbf{A}^{\text{inc}} + \mathbf{A}^s \approx \mathbf{A}^{\text{inc}} \quad (3)$$

Physically, (3) means that the skin layer depth, δ , is large compared to a typical body size, L , i.e. $\delta = \sqrt{2/(\omega\mu\sigma)} \gg L$. This expression is also known as the thin limit condition.

B. Neglecting the effect of free surface charges

The free surface charges (and the associated electric field) will not appear if and only if the magnetic vector potential $\mathbf{A}^{\text{inc}}$ of an exciting coil current is always *parallel* to the interfaces, i.e. when $\mathbf{n} \cdot \mathbf{A}^{\text{inc}} = 0$, where $\mathbf{n}$ is the normal vector to any interface of interest. This is indeed not the case in the human body although important analytical solutions without surface charges do exist [49]–[51]. The effect of surface charges was specifically studied in [52] and [44]. In the last paper, it was shown that a no-surface charge model always *overestimates* eddy currents in a body when compared to the more realistic situation. Further development is given in [45]. Numerical simulations indicate that the free surface charges always *reduce* the eddy current magnitude (“shorten the path” for the eddy currents). The no-surface charge model effectively makes the conducting medium homogeneous and unbound, and gives it a certain average conductivity value. In the absence of free surface charges, and in a medium with the relative dielectric permittivity equal to one, one has

$$\varphi = \text{const and } \nabla \varphi = 0 \quad (4)$$

in (1).

C. Neglecting the effect of tissue permittivity

Human tissues have varying values of the dielectric permittivity, which may be very large at low frequencies [46],[47]. As soon as the electric field is excited, the tissue medium will become polarized. This means that the bound (polarization) charges on dielectric-dielectric interfaces and the associated volume polarization currents, $(\epsilon - \epsilon_0) \mathbf{E} / t$, in the dielectric volume have to be taken into account, along with the free charges and conduction currents. The simplified model given by (4) neglects this effect entirely and does not involve the relative dielectric permittivity either.

D. Analytical estimate of eddy current density

This estimate was perhaps first formulated in an early transcranial magnetic stimulation model by Grandori and Ravazzani (the GR model) [43],[44], which disregards the secondary magnetic fields of eddy currents, neglects the free surface charges residing on conductor-conductor interfaces, and neglects the polarization charges as well as polarization currents.

As a result of these assumptions, (1)–(4) allow us to express the eddy current density in the body directly through a time-varying lumped coil current, $f(t)$, in the form

$$\mathbf{J} = -\sigma \frac{\partial \mathbf{A}^{\text{inc}}}{\partial t}, \mathbf{A}^{\text{inc}}(\mathbf{r}, t) = \frac{\mu_0 f(t)}{4\pi} \oint_C \frac{d\mathbf{l}}{|\mathbf{r} - \mathbf{r}'(l)|} \quad (5)$$

The second expression in (5) is the Bio-Savart law written in the form of a line integral for a coil having a contour C . Equations (5) are general results, which may in principle be applied to any coil geometry and any position in space, or to an array of coils using superposition. Calculation of the line integral for a given coil geometry may be accomplished via a Riemann sum or trapezoidal integration. Reference [53] presents the text of a MATLAB script that performs such a calculation for a current-carrying conductor arbitrarily oriented in space or for a number of such conductors which might form, for example, a Figure-8 coil. This script has been tested via an exact analytical solution and demonstrated an error in the eddy current magnitude below 2%. To complete the estimate in (5), the effective medium conductivity should be given. A widely-used average body conductivity value of 0.5 S/m will be employed in the following study.

III. Base FEM computational human model and computational testbed

A. Computational model

The full-body computational model employed in this study is the VHP-Female FEM computational CAD model [24],[53]. Its version 2.1 shown in Fig. S1 (and discussed in the Supplement along with a more recent version 3.0 shown in Fig. S2) has been used. Model features along with the material properties are described in Table I. The model has an improved resolution in the cranium including the continuous CSF shell around the grey matter and it has been optimized for accurate FEM modeling. The model also possesses a set of characteristics necessary for cross-platform compatibility and computational efficiency. Each triangular surface mesh of the original tissues is strictly 2-manifold (no non-manifold faces, no non-manifold vertices, no holes, and no self-intersections). No tissue mesh has triangular facets in contact with other tissue surfaces.

Between tissue surfaces, there is always a small gap representing thin membranes separating distinct tissues and numerically characterized as an “average body” tissue(s), and guaranteeing compatibility between CAD formats. At the same time, there exist tissues fully enclosed within each other.

B. Computational test bed

Maxwell 3D of ANSYS, Inc., a commercial FEM software package with adaptive mesh refinement, has been used for eddy current computations, similar to the earlier studies [14], [15].

The software takes into account both conduction and displacement currents (as well as free and polarization charges), and solves the full-wave Maxwell equation for the magnetic field, $\mathbf{H}$, in the frequency domain

$$\nabla \times \frac{1}{\sigma + j\omega\epsilon} \times \mathbf{H} = -j\omega\mu\mathbf{H} \quad (6)$$

where σ is the local medium conductivity; ϵ , μ are the local permittivity and permeability, respectively. The major difference from the full-wave case is that the phase is assumed to be constant over the volume of interest. Although Maxwell 3D also has a transient FEM solver, this solver does not take into account the displacement currents and was therefore not used. The local FEM error is the error of the divergence-free magnetic flux, $\nabla \cdot \mathbf{B}_{\text{solution}} = 0$. This term acts as a source and produces some energy. Tetrahedra with the largest local error energy (30% or so per adaptive pass) are automatically refined. The total error energy in the volume divided by the total energy of the electromagnetic field and multiplied by 100% is the energy error, which is returned each adaptive pass along with the total energy. The energy error measures the convergence of the adaptive mesh refinement process. Table II describes the computational testbed and major numerical parameters used in this study. A logarithmic frequency sweep covering the band from 300 Hz to 3 MHz has been employed over the total 22 discrete frequencies.

Such a frequency band is sufficient to model TMS pulses with the typical magnetic field rise time on the order of 0.1 ms [55],[56]. The time-pulse domain solution is constructed based on the interpolated frequency-domain data.

IV. Simulation setup. Qualitative results

A. Basic geometry setup

The base coil is a Figure-8 coil with a loop radius of 25 mm for each loop and a solid conductor (copper) diameter of 8 mm. The coil is bent so that the loop angle versus a horizontal plane in Fig. 1 is 15 degrees, similar to the Magstim BC-70 (a commercial Figure-8 coil). Five different coil positions around the motor cortex have been investigated; four of them are shown in Fig. 1a–d. In the frequency-domain solution, the sinusoidal AC coil current has the amplitude of 1 kA, although the specific amplitude value is irrelevant due to problem linearity. As shown in Fig. 1 and in Table SIa (given in the Supplement), ten observation base points have been selected within the body: 1, 2, 2a, 2b, 3, 3a, 3b, 4, 4a, and 4b. In the majority of the cases, we attempted to locate the points at such positions where the eddy currents may be expected to have relatively large values (in highly-conducting tissues and close to the boundaries). The analysis which follows is mainly represented as tables and plots for the ten observation points defined in Table SIa.

B. Full body coverage

An additional three-dimensional uniform rectangular grid of observation points shown in Table SIb (given in the Supplement) is introduced to effectively cover the entire human body in the solution space. This uniform grid includes 500,000 nodes. Among these nodes,

102,189 nodes are located inside the human body and generate meaningful current/field values. The external nodes, on the other hand, may be used to compute the electric field around the body.

C. Sensitivity analysis setup

The sensitivity analysis was performed by varying the conductivity and permittivity of an average body object of the model (a shell), which contains all inner organs/tissues and presumably has the largest influence on the final results. Both permittivity and conductivity were varied by $\pm 20\%$

D. Qualitative eddy current behavior at distant locations from the coil

While within the motor cortex itself the eddy current of the Figure-8 coil indeed peaks underneath the intersection of the two wire loops, this is certainly not the case at distant locations from the coil. As an example, Fig. 2 shows the eddy current density (A/m^2) magnitude distributions in the three different transverse planes depicted in Fig. 1 for sinusoidal coil currents at 30 kHz and 300 kHz respectively, with an amplitude of 1 kA each (coil configuration #1). Note the different color scales for each plane. The eddy current density behavior varies with changes in frequency. Compared to the 30 kHz excitation, the color scale for 300 kHz is multiplied by 20, which approximately accounts for a linear frequency increase (the factor of 10) as well as a conductivity increase.

V. Comparison between analytical and numerical results in frequency domain

A. Transfer function for the numerical solution

First, the eddy-current problem is solved numerically in the frequency domain. Next, the time-domain solution will be constructed, given the computed frequency response of the linear system (or its transfer function, which is the same) and the spectrum of the initial pulse, via the inverse discrete Fourier transform. In the frequency domain, the current coil excitation is given by a harmonic function

$$f(t) = I_0 \cos \omega t, \omega = \Omega_m, m=0, \dots, M-1 \quad (7)$$

for a number of discrete (and generally non-uniformly spaced) angular frequencies Ω_m . The problem is solved via Maxwell 3D, an FEM frequency-domain solver, for every such frequency using a frequency sweep. This operation gives us an eddy current density at any point in space within the body in the form of a complex phasor vector, $\mathbf{J}(\mathbf{r}, \omega)$, with the units of A/m^2 . The vector transfer function $\mathbf{H}_N(\mathbf{r}, \omega)$ per unit area is simply given by

$$\mathbf{H}_N(\mathbf{r}, \omega) = \frac{\mathbf{J}(\mathbf{r}, \omega)}{I_0} \quad (8)$$

This transfer function can be thought of as an eddy current passing through an area of 1 m^2 which is perpendicular to its direction with the current density given by the local expression $\mathbf{J}(\mathbf{r}, \omega)$ when the amplitude of the coil current is 1 A.

B. Transfer function for the analytical solution

Once converted to the frequency domain, (5) predicts the following form of the transfer functions (note the separation of variables):

$$\mathbf{H}_A(\mathbf{r}, \omega) = -j\omega \frac{\mu_0 \sigma}{4\pi} \mathbf{h}(\mathbf{r}), \quad \mathbf{h}(\mathbf{r}) = \oint_L \frac{d\mathbf{l}}{|\mathbf{r} - \mathbf{r}'(l)|} \quad (9)$$

C. Comparison of numerical and analytical solutions

The magnitude ratio, $R(\mathbf{r}, \omega)$, of two vector transfer functions, given by (8) and (9), respectively, is equal to the ratio of two eddy current magnitudes at point $\mathbf{r}$, when the operating frequency is ω , that is to say

$$R(\mathbf{r}, \omega) = \frac{|\mathbf{H}_A(\mathbf{r}, \omega)|}{|\mathbf{H}_N(\mathbf{r}, \omega)|} \quad (10)$$

Fig. 3 shows the ratio of eddy current density magnitudes as a function of frequency found from (10) for four different coil configurations. This ratio is always greater than one and does not exceed 23. A dip at lower frequencies is due to a rapid decrease of the relative dielectric constant in this band; it will be discussed separately in Section 8. The fifth coil configuration (which is configuration #1 with the coil rotated by 90 degrees) generated similar results. Therefore, it will not be discussed in the following text.

VI. Comparison between analytical and numerical results in time domain

A. Coil current pulse form

A variety of different TMS pulse forms has recently been suggested [55],[57],[58]. We will model a simple monophasic (monopolar) TMS pulse. Its form is aimed to approximate some common experimental monophasic TMS coil current forms [55],[56]. A biphasic pulse or a pulse of a more complicated shape can be studied similarly, using the superposition principle.

The present pulse form is characterized by two parameters: rise time τ and peak current I_0 . The coil current pulse over time interval $0 \leq t < 10\tau$ is expressed in the form:

$$f(t) = I_0 \begin{cases} \frac{4\tau(t-\tau)}{t^2} & \tau \leq t < 2\tau \\ e^{-\left(\frac{t-2\tau}{2\tau}\right)^2} & t \geq 2\tau \end{cases} \quad \text{for } \tau \leq t < 10\tau, \quad I(t) = 0 \text{ for } 0 \leq t < \tau \quad (11)$$

The derivative of the coil current pulse approximates eddy currents/electric fields induced in the body; it is given by

$$df(t)/dt = I_0 \begin{cases} \frac{4\tau(2\tau-t)}{t^3} & \tau \leq t < 2\tau \\ \frac{(2\tau-t)}{2\tau^2} e^{-\left(\frac{t-2\tau}{2\tau}\right)^2} & t \geq 2\tau \end{cases} \quad \text{for } \tau \leq t < 10\tau, I(t)=0 \text{ for } 0 \leq t < \tau \quad (12)$$

The second pulse derivative is a continuous function of t and is equal to $I_0 / 2\tau^2$ at $t = \tau$. Fig. 4a shows the coil current pulse normalized by I_0 ; Fig. 4b depicts the pulse derivative normalized by I_0 / τ . The negative phase of the pulse derivative is approximately four times longer than its positive phase. Let $f(t_n)$, $n = 0, \dots, N-1$ be pulse values at N sampling points $t_n = Tn$, $n = 0, \dots, N-1$ uniformly distributed over the time interval of interest from 0 to 10τ so that $T = 10\tau / N$. After introducing the standard form of the discrete Fourier transform, implemented, for example, in the standard MATLAB package (*fft* is an acronym for the "fast Fourier transform"),

$$F[m] = \text{fft}(f[n]) = \sum_{n=0}^{N-1} e^{-j\frac{2\pi}{N}mn} f[n], m=0, \dots, N-1$$

$$f[n] \equiv \Delta T f(t_n) \quad (13)$$

the *energy spectral density* S_{ff} of the current pulse (or of its derivative) is found as

$$S_{ff}[m] = F[m] F^*[m], m=0, \dots, N-1 \quad (14)$$

where the star denotes the complex conjugate. Fig. 4c shows the energy spectral density of the pulse derivative per 1 Hz normalized by $(I_0 / \tau)^2$. As expected, the spectral density peaks at about $0.2 f_0$ where $f_C = 1/\tau$ is the characteristic pulse frequency. At the same time, the spectrum has a significant high-frequency content due to a discontinuity of the pulse derivative. Therefore, the corresponding frequency domain analysis should include all frequencies at least up to $10 f_C$ or so.

B. Converting frequency-domain solution to time domain

The transfer function given by (8) or (9) is applied to every harmonic component of the input coil current pulse $f(t)$ separately. Those harmonics are described by the Fourier spectrum of this pulse, $F(\omega)$. The Fourier spectrum of the eddy current density, $\mathbf{F}(\mathbf{r}, \omega)$, is given at any point $\mathbf{r}$ in space by

$$\mathbf{F}(\mathbf{r}, \omega) = \mathbf{H}_{N,A}(\mathbf{r}, \omega) F(\omega) \quad (15)$$

The eddy current density itself, $\mathbf{J}_{N,A}(\mathbf{r}, t)$, is found via the inverse Fourier transform. When moving toward inverse discrete Fourier transform, (15) becomes quite a nontrivial operation. Given the DFT in the form of (13), the discrete version of (15) must have the form (we omit the sub index for the transfer function)

$$\mathbf{H}F \rightarrow \mathbf{H}[0]F[0], \mathbf{H}[1]F[1], \dots, \mathbf{H}\left[\frac{N}{2}-1\right]F\left[\frac{N}{2}-1\right], \mathbf{H}\left[\frac{N}{2}\right]F\left[\frac{N}{2}\right], \dots, \mathbf{H}^*\left[\frac{N}{2}-1\right]F\left[\frac{N}{2}+1\right], \dots, \mathbf{H}^*[1]F[N-1] \quad (16)$$

since the standard DFT describes a set of data for the following non-monotonic frequency

list: $0, \omega_0, \dots, \frac{N}{2}\omega_0, \left(1 - \frac{N}{2}\right)\omega_0, \left(2 - \frac{N}{2}\right)\omega_0, \dots, -\omega_0$. Here, $\omega_0 = 2\pi/(N \cdot T)$ is the fundamental frequency. The necessary frequency data in (16) has been extracted using linear interpolation (and sometimes extrapolation) of the transfer function $\mathbf{H}_N(\mathbf{r}, \omega)$ previously computed over the band 300 Hz – 3 MHz. The next step is given by the *ifft* (*ifft* stands for the "inverse fast Fourier transform")

$$\mathbf{J}_{N,A}(\mathbf{r}, t_n) = \text{ifft}(\mathbf{H}_{N,A}F)/\Delta T, n=0, \dots, N-1 \quad (17)$$

Note that the factor T may be omitted in both *fft* (13) and *ifft* (17). While all three components of $\mathbf{J}_A(\mathbf{r}, t)$ are exactly synchronized in time according to (9), the three components of $\mathbf{J}_N(\mathbf{r}, t)$ may be slightly offset since the phases of three components of $\mathbf{H}_N(\mathbf{r}, \omega)$ are not necessarily the same. To avoid this issue, we have synchronized the two smaller pulse components with the largest one (slightly shifted them in time). This operation might slightly overestimate the resulting vector magnitude, which is in line with our upper-estimate task.

C. Comparison between analytical and numerical results

We select $\tau = 0.1$ ms in (11), (12) which is the typical magnetic field rise time for monophasic TMS pulses [55],[56] shown in Fig. 4a,b. Fig. 5 shows the simulated (smaller) pulse form and estimated (larger) pulse form for configuration #1 at point 1. Fig. S3 and Fig. S4 (given in the Supplement) show the stimulated and estimated pulse forms for all points for configurations #1 and #4. The ratio of two peak values is also given. It can be seen that the numerically obtained pulse form is quite similar to the analytical result and to Fig. 4b. This is because the transfer function of the numerical solution in the frequency domain rather closely follows the derivative transfer function, $-\dot{j}\omega$, although some significant deviations have been observed at very low frequencies (below 5 kHz).

Table SIIa (given in the Supplement) reports numerically obtained peak eddy current densities for all coil configurations and all observation points in Fig. 1. The peak value of the coil current pulse in Fig. 4a is 1 kA and $\tau = 0.1$ ms. Table SIIb (given in the Supplement) reports the ratio of two peak pulse values (analytical versus numerical) for the same 40 datasets, respectively. Along with the pulse rise time of 0.1 ms, we also present the result for a smaller value of 0.01 ms, which can be used as an excitation in TMS coils too [57],[58].

Remarkably, the ratio of analytical and numerical pulse peaks never becomes less than one. The average value of this ratio in Table SIIa is 5.7.

D. Sensitivity analysis

The numerical sensitivity analysis has been evaluated for coil configuration 1 at the observation points given in Table SIa. Table SIIc (given in the Supplement) reports numerically obtained peak eddy current densities for all observation points in Fig. 1. Table SIId (given in the Supplement) gives the similar results for the ratio of the analytical and numerical peak pulse amplitudes. Variations in permittivity have almost negligible impact on the final result, whereas conductivity variations are somewhat more important. Overall, all results stay in line with the previous observations and indicate that the peak ratio always exceeds one and does not approach it.

VII. Testing a different coil geometry

Next, a straight Figure-8 coil with a loop radius of 52.5 mm for each loop (Magstim D70² Coil [59]) will be studied. We do not model the presumably secondary effect of the stranded conductors and replace all 11 coil windings by a solid conductor (copper) with a diameter of 8 mm. Further, we repeat the previous FEM simulations for all coil configurations and all observation points shown in Fig. 1. The corresponding simulation and comparison data is reported in Tables SIIIa and SIIIb (given in the Supplement), respectively, which are organized identical to Tables SIIa and SIIb. The peak eddy current densities for both the bent coil and the straight coil are graphically represented in Fig. 6.

VIII. Interpretation of results

A. Why is the analytical model working?

Routine FEM simulations indicate that the analytical model given by (5) could very significantly overestimate the eddy currents in a bounded conductor with the relative dielectric constant of 1. As an example, we consider here observation point 1 for coil configuration #1 in Fig. 1, assuming a “homogenized” VHP-Female v.2.1 model with constant parameters $\sigma = 0.5$ S/m, $\epsilon_r = 1$. The ratio of eddy current magnitudes for the analytical and numerical solutions in the frequency domain is given in Fig. 7a by an upper curve. The analytical eddy current now exceeds the computed FEM current density by a factor between 30 and 270 in the entire frequency domain of interest.

Next, we still assume the homogenous model but assign to its volume the frequency-dependent muscle properties (which are often considered as the “average body” properties) following references [46],[47]. The ratio of the eddy current magnitude decreases drastically

(but still exceeds one) as shown by the second lower curve in Fig. 7a. The reason for such a considerably better agreement is a very large muscle permittivity ϵ_r at lower and intermediate frequencies as shown in Fig. 7b. Other tissues possess a similar frequency behavior. The large permittivity values imply large displacement currents and, consequently, large polarization (or bound) charges at the dielectric-dielectric interfaces. These charges have the *opposite* polarity as compared to the free charges due to conduction currents. Hence, the two charge types essentially cancel each other so that the dielectric-dielectric (and conductor-conductor) interface becomes essentially neutral, which is exactly the free-space condition used by the analytical model.

Interestingly, a similar situation occurs in the antenna design field for metal patch antennas printed on high-permittivity dielectric substrates. Thus, the analytical model given by (5) provides a reasonable upper estimate of eddy currents thanks to its simplicity: the model neglects both free charges and polarization charges *simultaneously*. An attempt to improve the model by the inclusion of only free charges would probably fail. A further step toward an even better agreement compared to the second curve in Fig. 7a is probably facilitated by multiple irregular interfaces within a realistic human body.

B. Exceptions

While Table SIIb always reports the ratios of the peak pulse values greater than one, Table SIIIb for the straight coil indicates two special situations where numerical peak pulse values exceed the corresponding analytical results. A detailed analysis has shown that these special locations happen to be close to a locus of the magnetic vector potential given by (5), i.e. to a curve (or a surface) where the corresponding line integral vanishes, as does the eddy current density $\mathbf{J}$. For example, the locus of a loop of current coincides with its axis. Fig. 8a shows the magnitude of the line integral in (5) for the bent coil tested in Section 6 using a color scale.

The coil radius is now 52.5 mm. The dark (blue) color corresponds to its zero values. The locus is a curve which does not penetrate into the body deeper than two coil diameters. Therefore, Table SIIb reports the meaningful results. Fig. 8b, on the other hand, shows the absolute values of the line integral in (5) for the straight coil tested in Section 7.

The two loci seen in this figure may penetrate the entire body and hit an observation point anywhere in the body when the coil is rotated around the head. This is what happens with observation points 2a and 2b in Table SIIIb for configurations #2 and #3, respectively. The numerical solution predicts a significant eddy current, but the analytical result does not.

IX. Guaranteed upper estimate

A. Guaranteed upper estimate

In order to eliminate the loci effect for any coil type, it is suggested to find the *absolute maximum* of the line integral magnitude over a sphere surface, which is centered at the geometrical center of the coil.

Fig. S5 (given in the Supplement) shows the observation points over the sphere surface, centered at the geometrical center of the coil. The sphere radius is the distance to the observation point. Even with a few thousand test points on the sphere surface, the corresponding numerical task requires on the order of 1 s of CPU time (with a vectorized MATLAB script [53]). This maximum is then substituted in (5) instead of the local integral value and the estimate is performed. Table SIV (given in the Supplement) is a replica of Table SIIb for the bent coil obtained using this method, and so is Table SV (given in the Supplement), which is a replica of Table SIIIb for the straight coil. The method clearly overestimates the peak pulse value close to the coil (observation point 1), but otherwise it works reasonably well.

Using this method, no situation for ten base points has been found where the analytical model underestimates the induced eddy current density, either in the frequency domain or in the time domain. The average value of the ratio of analytical and numerical peak eddy currents in the time domain is approximately 10 if we exclude observation point 1 located within the cranium.

B. Results for full-body coverage

For coil configuration 1, we evaluated 102,189 extra observation nodes located within the body as described in Section IVB. We used the guaranteed upper-estimate method described above. For 134 nodes (0.13%), the ratio of analytical and numerical peak pulse values went below one. For these noncompliant nodes, the minimum peak ratio was 0.465 and the mean peak ratio was 0.817. For the remaining set of compliant nodes, the minimum peak ratio was 1.0031, the maximum peak ratio was 5210 and the mean peak ratio was 26.5407.

We explain these results by a pure numerical error close to sharp edges/corners present in the model, especially in the spinal cord and at the interface of CSF and grey matter where the conductivity is the largest. Fig. 9 illustrates one such point denoted by a red circle present in the spinal cord close to vertebra L3. Surface charge density formally becomes singular at any edge (not necessarily sharp) of a triangular mesh with non-planar triangles. For sharper edges and large adjacent triangles, this local (electrostatic) effect becomes quite significant and leads to non-physical fields/current peaks.

On the other hand, the maximum peak values occur very close to the interface between skin and air where the computed value of the current in air is not exactly zero due to a numerical smoothing effect.

X. Conclusions

In order to validate the analytical estimate for TMS eddy currents given by (5) we have performed numerically-accurate FEM simulations with one human model, two coil types, five coil positions, ten observation points, and two distinct pulse rise times, thus providing two hundred different data sets for comparison. In addition to that, we have processed the results for about 100,000 observation points of a rectangular grid containing the entire body. We have also generated about a hundred other datasets with an earlier version of the model using somewhat different coil positions. Our simulations reveal that in 98% of the cases, the

local analytical model does overestimate the peak pulse eddy current density. However, in the remaining 2% of the cases the analytical model underestimates the peak pulse eddy current density. The reason is the loci of the analytical solution discussed above.

In order to obtain the guaranteed upper estimate in every case, we have to modify (5) using the absolute maximum of the line integral magnitude over a sphere surface centered at the geometrical center of the coil with the radius R equal to the distance to the point of interest. The maximum value is to be used instead of the local value. This method neglects geometrical coil features, but still takes into account a general $1/R^3$ decay of the magnetic field from a local current source in the near-field region. It appears that this method overestimates the peak eddy currents at distant locations from a coil by a factor of 10 on average. The simple analytical model explained and tested in the present study may be valuable as a rapid method to safely estimate levels of TMS currents at different locations within the human body. An open question still remains the average conductivity value of 0.5 S/m used in (5). While this value has been justified in the present study, other CAD models (a pregnant female) might require a certain revision.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported in part by the U.S. National Science Foundation under Grant 1520168 and National Institutes of Health/National Library of Medicine Grant R43 LM012352-01A1.

Authors thank Dr. G. M. Noetscher, Mr. X. J. Jackson, Ms. T. Dolma, Mr. T. T. Trinh, Mr. J. Zhang, Ms. S. Xie, Mr. V. K. Rathi, and Mr. M. Islam, all of Worcester Polytechnic Inst., MA for their help in development of the CAD human model.

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Fig. 1.
Coil setup and observation point setup for the human model VHP-Female in Maxwell 3D FEM simulator.

Fig. 2.

Eddy current density at large separation distances from the coil at 30 and 300 kHz respectively, in the three observation planes (at 50 mm, -300 mm, and -700 mm) for coil configuration #1. Note the different color scales for each plane. The color scale for 300 kHz is exactly twenty times the color scale for 30 kHz.

Fig. 3. Ratio of eddy current density magnitudes for different coil configurations. Different curves correspond to different observation points.

Fig. 4.

(a) – Coil current pulse normalized by I_0 ; (b) – pulse derivative normalized by I_0 / τ ; (c) – energy spectral density of the pulse derivative normalized by $(I_0 / \tau)^2$ per 1 Hz.

Fig. 5. Estimated (large pulse form) and computed (smaller pulse form) eddy current density for configuration #1 at point 1. The ratio of two peak values is also given. Other coil positions generate similar results.

Fig. 6.

(a) Peak eddy current densities for all configurations and observation points for the bent coil at $\tau = 0.1$ ms ; (b) Peak eddy current densities for all configurations and observation points for the straight coil at $\tau = 0.1$ ms.

Fig. 7.

(a) – Ratio of eddy current magnitudes (analytical versus numerical solution) in a “homogenized” VHP-Female model at different conditions and (b), (c) – electromagnetic muscle properties at low and moderate frequencies.

Fig. 8. Locus of the magnetic vector potential for (a) – the bent Figure-8 coil with the radius of 52.5 mm (bending angle is 15 degrees); (b) – the straight Figure-8 coil with the same radius.

Fig. 9.
Presence of a sharp edge and corresponding noncompliant point nearby in the spinal cord shown by a red circle.

TABLE I

FEM computational human model VHP-Female v. 2.1.

Name and human subject	VHP-Female – a 60 years old female; a few known pathologies; BMI of approximately 33.5
Image source	Visible Human Project®-Female dataset (The Visible Human Project® [54]) of the National Library of Medicine
Release and vendor	VHP-Female v.2.1 2015/NEVA Electromagnetics, LLC and ECE Dept., Worcester Polytechnic Inst., USA
Individual tissues	25
Individual tissue parts	203
Triangular facets	139,450
Material properties	50 Hz – 60 GHz [46],[47], isotropic tissue materials only
Compatibility	ANSYS Maxwell 3D, ANSYS HFSS, CST MWS, FEKO, REMCOM, WIPL-D, COMSOL

TABLE II

Computational hardware/software and major project parameters.

System	18 Node Super Cluster, 2 Intel(R) Xeon(R) CPU E5-2680 2.8GHz per Node, 128 GB per Node, 56GB/s FDR Infiniband, Rocks Cluster 6.1.1 with Red Hat Enterprise Linux 2.6.32
FEM software	ANSYS Electromagnetic Suite Release16.1: ANSYS Maxwell 3D 2015.1, frequency-domain eddy current solver
HPC options	One task, twelve cores
Project adaptive frequency	10 kHz (the frequency at which the tetrahedral mesh is constructed and adapted)
External boundary conditions	Neumann (H-field is tangential to the boundary) or radiation
Execution time for five adaptive mesh refinement passes	Meshing time: 66 min Sim. time for 22 frequencies: 5 hr 50 min
Convergence history	Energy error percentage (typical): 27, 0.8, 0.12, 0.036, 0.014
Max RAM per node	107 Gbytes
Initial/final FEM mesh	450,00/1,400,000 tetrahedra