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INTERFERENTIAL TRANSCRANIAL MAGNETIC STIMULATION: A COMPUTER MODELING STUDY

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Abstract

Interferential approach to magnetic stimulation of excitable tissues refers to the creation of a therapeutic, low frequency electric field "beat" from the superposition of two slightly different non-stimulating higher frequency fields induced by time-varying magnetic fields. The goal of this study was to investigate the ability of interferential transcranial magnetic stimulation (iTMS) to create electric fields that can preferentially stimulate the deep structures of the brain. The electric field distributions induced by time-varying magnetic fields were simulated using a three-dimensional finite element model of the human head. A newly proposed 'umbrella' coil design, coupled with the interferential technique, showed promise for producing interferential current density fields with peak values deep within the brain. The simulations demonstrated that the specific location of the peak interferential current magnitudes depended on the location of the contributing coils. In addition to varying the location of the coils, by altering the relative amplitude of the currents in the coils by 300%, we found a shift in the location of the peak interferential current density of 1 to 2 cm. These results are promising and support the iTMS technique as a potential candidate for non-invasive deep brain stimulation.

Introduction

Transcranial magnetic stimulation (TMS) is a relatively new medical therapeutic technique which uses current – carrying coils placed on the surface of the scalp to induce electric currents in the patient's neural circuitry.[1] This developing technology is proving valuable in the study, diagnosis and therapy of the brain.[3] By causing the coherent firing of neurons in the stimulated area as well as increased sensitivity to input from surrounding neurons, TMS may offer potential treatments for a variety of brain disorders such as chronic pain, epilepsy and depression.[3]

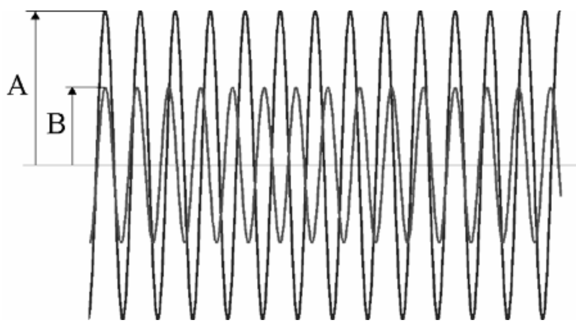
Current techniques are only able to stimulate the most superficial regions of the cerebral cortex. The amplitude of the magnetically induced electric field is always largest near the coil and decreases rapidly with distance from the coil. Hence, TMS studies rely on stimulation of the superficial regions of the brain, such as the motor cortex. Many new studies and therapies for difficult neurological conditions would be possible if stimulation of focused regions deep within the brain were available. For example, stimulation of the *substantia nigra* region could be useful in treating Parkinson's disease, while stimulation of the limbic system may allow adjustment of sleep and wakefulness patterns.[3]

In this paper we propose and explore a novel TMS technique based on interferential fields, which may be capable of stimulating internal regions of the brain without stimulating more superficial layers. The interferential approach to tissue stimulation is based on creating a low frequency electric field "beat" from the superposition of two slightly different non-stimulating medium-frequency fields. It has been shown for direct electric field stimulation using contacting electrodes that the low frequency beat signal is able to stimulate excitable tissues deeper inside muscles than conventional single frequency electrotherapy.[7,9,10]

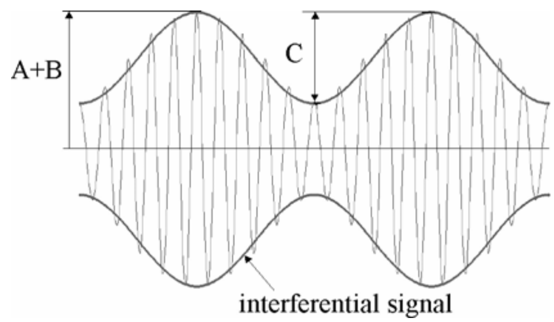
However, the interferential technique has not yet been studied for electrical stimulation induced by magnetic fields. Thus, the goal of this computer modeling study was to investigate the ability of interferential transcranial magnetic stimulation (iTMS) to create maximum amplitude "beat" electric fields in deep regions of the brain.

Interferential Fields

When two superposable sinusoidal signals co-exist in space and are separated in frequency by a small difference, the combined signal has an amplitude 'envelope' that varies at a rate inversely related to the frequency difference. Consider two signals with amplitudes *A* and *B*, at frequencies f_1 and f_2 ($f_2 > f_1$), respectively (fig. 1a). When these signals superpose, the amplitude of the resultant waveform (fig. 1b) varies sinusoidally at the difference frequency $\Delta f = f_2 - f_1$.[9,10] This phenomenon is known as beating and Δf is the beat frequency resulting from the addition of the two signals (fig. 1b). The 'beat' waveform at the difference frequency Δf is also referred to as the interferential waveform.[9,10] Excitable cells exhibit non-linear characteristics that enable the demodulation of the resulting amplitude-modulated signal, extracting the low-frequency therapeutic waveform. The amplitude *C* of the interferential waveform, defined as the peak-to-valley magnitude of the envelope of the resultant signal, is related to the amplitudes *A* and *B* of the superposed signals as $C = |A + B| - |A - B|$. The amplitude *C* of the interferential signal reaches its maximum when $A = B$. In this case, the full 100% beat effect occurs.[11]



a)



b)

Fig. 1 The phenomenon of beating: a) two sinusoidal signals with the frequencies f_1 and $f_2 = f_1 + \Delta f$ and having amplitudes A and B, respectively; b) the amplitude of the resultant signal oscillates with the beat frequency $\Delta f = f_2 - f_1$.

The mechanism whereby brain neurons are stimulated is not fully understood. It is thought that, for a long straight axon, the activation is determined primarily by the gradient of the induced electric field along the direction of the axon.[5] In contrast, for regions where axons terminate or bend, the activation function is dominated by the magnitude of the induced electric field parallel to the axon.[5,6] For the purpose of this study, we assumed that the maximum amplitude of the interferential effect at every point was responsible for eliciting a response from a neuron in iTMS.

Methods

Coils

We examined the induced electric fields produced by two known coil designs built from circular conductors that are currently used in TMS: circular coil and figure-eight' (two coils in the same plane with contact at one point)[11]. In addition, a new coil design was developed for this study. This coil is built from individual right triangular loops that are identical except for rotation around the central leg (fig. 2). The coil is characterized by the turn opening α and the length along the central axis (z axis in fig. 2). The loops of the coil are evenly distributed around the axis of rotation. Current flows through each loop in the directions indicated in fig. 2. Due to its similarity in shape with an umbrella this coil was named the ‘umbrella’ coil.

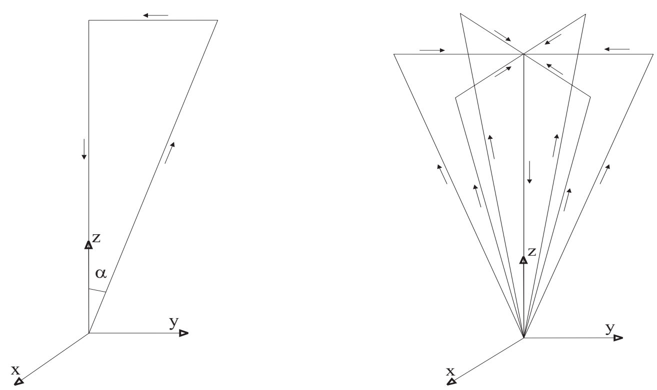


Fig. 2 The ‘umbrella’ coil configuration: a) a single triangular turn; b) ‘umbrella’ coil obtained from the combination of identical triangular loops rotated about the central axis such that the individual components are equally spaced radially. Arrows indicate the direction of current flow.

Governing Equations

In the frequency range used in this study, the electromagnetic field is approximated as quasistatic[12]. The governing equation for the electric potential ϕ is[12]

$$\nabla \cdot (\sigma \nabla \phi) = -\nabla \cdot \left(\sigma \frac{\partial \vec{A}}{\partial t} \right) \tag{1}$$

where $\vec{A}$ is the magnetic vector potential and σ is the electrical conductivity. Equation (1) is solved throughout the volume of the conducting media subject to a Neumann boundary condition on the current density J at the outer bounding surface which requires that the current density normal to the surface vanish:

$$\hat{n} \cdot \vec{J} = 0 \; (2) \tag{2}$$

The magnetic vector potential $\vec{A}$ is given by the following superposition integral

$$\vec{A} = \frac{\mu_0 I}{4\pi} \int_{\Gamma} \frac{d\vec{l}}{R} \tag{3}$$

where μ_0 is the magnetic permeability of free space (and the head), $I = I_{\max} \cos \omega t$ is the electric current intensity, $d\vec{l}$ is the wire element and $\vec{R}$ is the distance from the calculation point to the wire element along the coil.

Numerical Solutions

A realistic 3-D FEM model of the human head (fig. 3a) was constructed based on segmented MRI images taken from the database of the 3-D Slicer software (Surgical Planning Laboratory, Brigham and Women’s Hospital, Boston, MA, U.S.A.). The model contains the cranium, the cerebrospinal fluid (CSF) and the brain. Electrical conductivities were assigned to the three tissue types as follows[8]: σ_{brain} = 0.45 S/m, σ_{CSF} = 1.8 S/m, σ_{bone} = 0.005 S/m. The FEM model had 16,773 nodes and 93,203 elements (4-noded linear tetrahedrons). The magnetic vector potential $\vec{A}$ was calculated for each node in the FEM model from the superposition integral (3). For the cases where circular coils were used in the simulations, a closed form solution based on complete elliptic integrals was used.[12] To find the $\vec{A}$ field produced by the umbrella coil, the integral in equation (3) was computed numerically. Equation (1) was solved with the finite element method using I-DEAS software (SDRC, Milford, OH, U.S.A.) as described in Wang *et al*.[12]

Results

Simulation of Single Frequency Current Density Distribution

The frequency used for all single frequency simulations was 10 kHz. Figure 3b shows the magnitude of the current density field induced by a 'figure-eight' coil (4 cm diameter for each circular conductor, 500 A through each turn) placed on the right side of the head. The 'figure-eight' coil induces the highest magnitude current densities near the surface directly under the tangent point of the two circular coils.

Simulation of Interferential Current Density for Two-Coil Configurations

We computed the interferential field produced by 2 'figure-eight' coils operating at slightly different frequencies. This configuration induced fields characterized by large current density magnitudes in peripheral areas along the outer surface of the brain (not shown here). Clearly, this does not provide access to regions of the brain not currently accessible to conventional TMS.

The interferential current density distribution was also computed for configurations with two 'umbrella' coils operating at frequencies f_1=10,000Hz and f_2=10,050 Hz, respectively. In the results that follow, the interferential current density fields are scaled such that 5% of the brain volume is exposed to field magnitudes greater than or equal to the excitation threshold for neurons at 50 Hz, J_{th} = 1 A/m^2.[2,5]

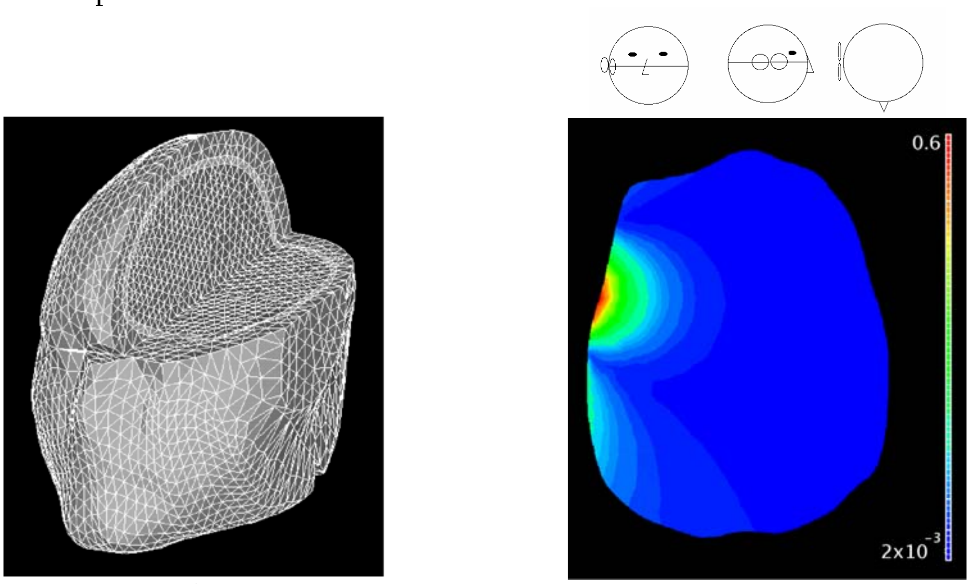
Figure 4a shows the interferential field resulting from two 'umbrella' coils, one placed at the top (T) of the head and the other on the left side (LS) of the head (T-LS configuration). These results show that the peak interferential currents are located in regions well beneath the surface of the brain. Figure 4b shows the magnitude of the interferential current distribution produced by two 'umbrella' coils placed on either side of the head, near the ears (RS-LS configuration). Again, the peak amplitude of the interferential field is deep within the brain.

Effects of Scaling Relative Coil Excitations on Interferential Fields

When the current through the coil on the top of the head is three times larger than the current through the coil on the right side of the head, the location of the peak amplitude of the interferential field shifts by approximately 1 cm towards the right side of the head (fig. 5a). Figure 5b shows the result of altering the relative amplitude of the current in coils placed on opposite sides of the head. When the current through the coil on the right side of the head is made three times larger than the current through the coil on the left side of the head, the location of peak amplitude of the interferential field shifts by approximately 2 cm towards the left side of the head.

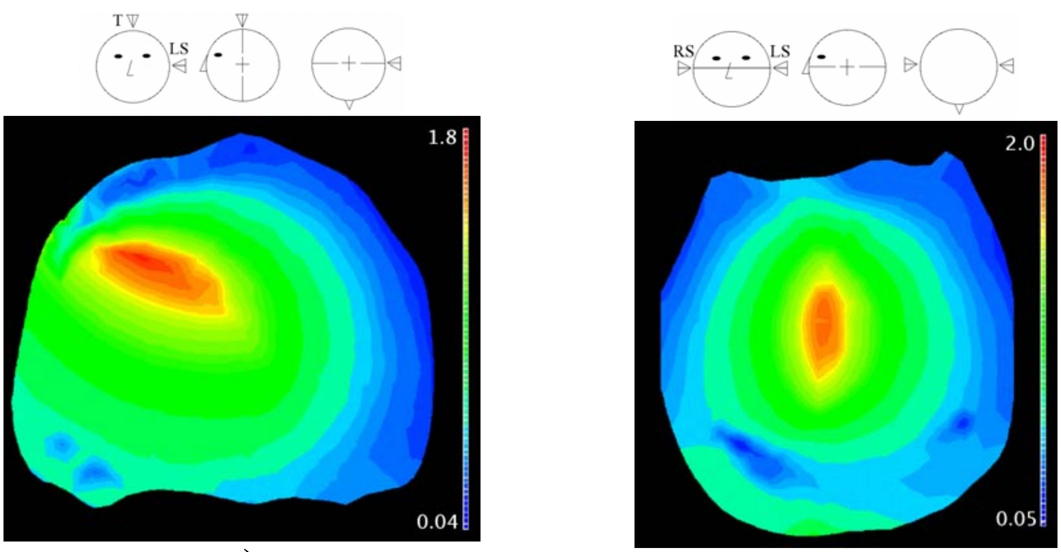
Conclusions

This paper introduced the concept of interferential magnetic stimulation and presented computer simulations of current density distributions inside the brain induced by various coil designs in single- and multiple-frequency configurations. Our results demonstrate the ability of iTMS to induce peak-amplitude fields at locations deep inside the brain, inaccessible to conventional TMS techniques. These results were achieved through a novel coil configuration, the 'umbrella' coil, which proved to be superior in an interferential configuration to circular and 'figure-eight' coils. In addition, this computational study demonstrates the ability to manipulate the location of the peak interferential current regions by changing the relative current in the coils. The results obtained are promising and support the iTMS technique as a potential candidate for non-invasive deep brain stimulation.



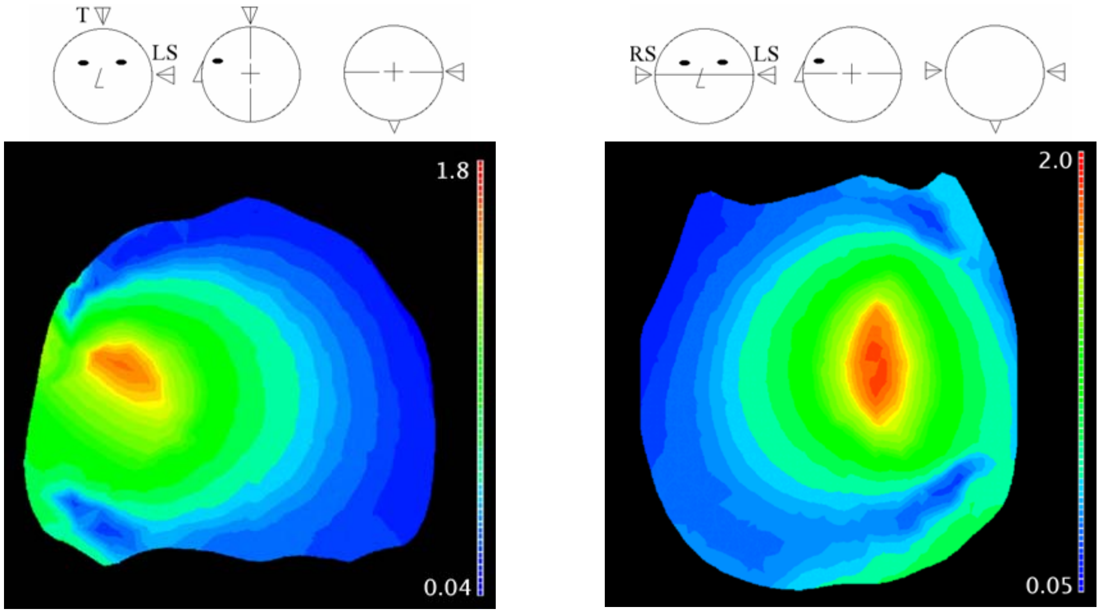
a) b)

Fig. 3 a) A cut through the finite element model of the head; b) a horizontal (axial) slice along the line in the schematic above showing the magnitude of the current density field resulting from a single 'figure-eight' coil. The coil is placed on the right side of the head, near the level of the ears (bottom-up view). The color bar show the current density magnitude in A/m^2 on a linear scale.



a) b)

Fig. 4 Interferential fields produced with two 'umbrella' coils: a) a coronal slice through the middle of the head, along the line on the schematic above, showing the magnitude of the interferential current density field resulting from the T-LS configuration (back to front view); b) a horizontal (axial) slice at the level of the ears, along the line on the schematic above, showing the magnitude of the interferential current density field resulting from the RS-LS (bottom-up view). The color bars show the current density magnitude in A/m^2 on a linear scale.



a) b)

Fig. 5 Effect of magnitude scaling on interferential fields produced with 'umbrella' coils: a) T-LS configuration. The current in the coil on the top of the head has been increased to 300% the current in the left side of the head (back to front view); b) RS-LS configuration. The current in the coil on the right side of the head has been increased to 300% the current in the left side of the head (bottom-up view). The color bars show the current density magnitude in A/m^2 on a linear scale.

Acknowledgments

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