Magnetic Stimulation of the Human Brain with Low-Intensity Field

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Abstract: The most popular means of depression treatment nowadays are psychotherapy, antidepressant medication and recently adopted transcranial magnetic stimulation (TMS) of the human brain. To overcome their disadvantages we are investigating an application of low-field magnetic stimulation (LFMS) to depression treatment. The 3D electromagnetic models of both TMS and LFMS have been developed in COMSOL Multiphysics. The head is modeled so that various tissues are represented by homogeneous concentric spheres of different size. Concurrently we are developing a realistic model of the human head with the help of Simpleware software. Obtained LFMS model shows that a current density in the order of 0.1 mA/m^2 can be induced up to 10 mm deep into the brain, what makes it possible to draft a technical specification on the stimulation device.

Keywords: depression treatment, TMS, LFMS, electromagnetic modeling, image processing

1. Introduction

Depression is a neuropsychological disorder, affecting over a hundred million people worldwide. The reports of the World Health Organization are projecting it to become the second leading cause of disability by the year 2012 [1]. As well a part of the motivation for the project comes from the literature review, which reveals LFMS of the human brain as an under-researched area [2]. The depression treatment market shows substantial annual growth over the last decade and today it amounts to billions of dollars a year. The most commonly used forms of treatment are psychotherapy and medication. Noninvasive transcranial magnetic stimulation has been adopted recently as well. But the problem is: drug- and therapy-resistant forms of depression exist; antidepressants have adverse side effects; and TMS as a complex multipurpose system has disadvantages in cost and clinical use. Therefore, we propose to implement low-field magnetic stimulation in a stimulator device as a competitor suitable for easy and safe use.

2. Materials and Methods

The work is based on the proven influence of low-intensity electromagnetic fields on biological cells [2]. We are taking into account the disputes regarding effects in complex systems. Our research is devoted to the investigation of a possibility to use LFMS in depression treatment. The first stage of the project is the development of a theoretical background. The outcome here is technical specifications of the stimulator. By means of 3D electromagnetic modeling of LFMS, we are selecting appropriate stimulation parameters, such as operating current waveform. The layered-sphere model has been used initially, but MRI/CT-based human head model is being developed.

2.1 Electromagnetic theory

Resonant electric circuits are able to produce differently dumped output current waveforms which are called monophasic, biphasic, or polyphasic excitation signals in terms of stimulator devices. An ordinary TMS stimulator in Figure 1 works as follows: a kV source is charging a mF capacitor and when charging is completed, it is rapidly discharging onto the stimulating coil, which creates a very strong electromagnetic field for some microseconds.

The fundamental theoretical basis of both TMS and LFMS is the Maxwell's classical electromagnetic theory. According to Ampere's law, an alternating current flowing in the coil produces a time-varying magnetic field (1). In the

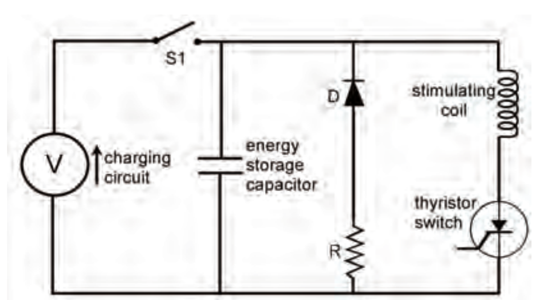

Figure 1. Schematic of magnetic stimulator from [3].

agreement with Faraday's law, this magnetic field subsequently generates a time-varying electric field (2) represented as currents induced in the head, as it follows from Ohm's law (3). That gives tissue excitation by depolarization of neurons via current flow through cell membranes.

$$\nabla \times \vec{H} = \vec{J} + \frac{\partial \vec{D}}{\partial t} \tag{1}$$

$$\nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t} \tag{2}$$

$$\vec{J} = \sigma \vec{E} \tag{3}$$

Considering all of the necessary boundary conditions – usually the Dirichlet condition (4) of magnetic insulation on the external boundary and the Neumann condition (5) of continuity on all of the internal boundaries – a large system of linear equations similar to (6) given for every mesh node is solved for the magnetic vector potential. Later, the magnetic field (7) and the electric field (8) can be calculated from the known magnetic vector potential.

$$\vec{n} \times \vec{A} = 0 \tag{4}$$

$$\vec{n} \times \left(\vec{H}_1 - \vec{H}_2\right) = 0 \tag{5}$$

$$\sigma \frac{\partial \vec{A}}{\partial t} + \nabla \times \left(\frac{\nabla \times \vec{A}}{\mu \mu_0} \right) = \vec{J} \tag{6}$$

$$\vec{B} = \nabla \times \vec{A} \tag{7}$$

$$\vec{E} = -\frac{\partial \vec{A}}{\partial t} - \nabla V \tag{8}$$

$$\nabla \cdot \vec{A} = 0,\ \vec{A} \rightarrow \vec{A} + \nabla \psi \tag{9}$$

If the skin effect, the proximity effect and the effect of laminations – all related to the stranded conductors with ferrite cores (coil windings) – should be left out of consideration for electromagnetic modeling, one has to use solid geometries and set almost zero conductivity for both a coil and a core. In transient 3D models containing such conductors, the gauge fixing problem appears which affects the solution time. The Coulomb gauge fixing essentially means including of one constraint and a redundant variable (9) in the core equation (6) simply to assure the uniqueness of vector and scalar potentials, which is of mathematical relevance only.

As both methods share the same underlying physics, our strategy is to build a TMS model first and evaluate it against existing publications afterwards. In a second step we implement the necessary changes to introduce LFMS.

2.2 TMS and LFMS modeling

The analytical solution for this time-dependent problem by means of Biot-Savart law (10) was not trivial. Therefore, we employed 3D finite element analysis software to conduct the actual modeling. Since the software development was not a part of our research, we decided to use the well-known publically available one – COMSOL Multiphysics based on the A-V formulation.

$$\vec{B}(\vec{r}, t) = I(t) \frac{\mu_0}{4\pi} \oint_{coil} \frac{\left(\vec{r} - \vec{r}_0\right)}{\left|\vec{r} - \vec{r}_0\right|^3} \times d\vec{l} \tag{10}$$

The LFMS and TMS models were based upon the use of the layered sphere model of the human head with the radius of 10 cm, where skin, skull, cerebrospinal fluid (CSF), and brain tissues were represented as homogeneous spheres of different diameter, concentrically embedded one inside the other. The electrical conductivity σ and the dielectric permittivity ε of human tissues were taken from [4].

In modeling we followed established guidelines [5], [6], [7]. One issue was related to the specification of an excitation current density inside a coil having a certain tilt angle relative to the xy-plane. That was solved via the cross product of a coil surface normal vector *n* and an orthogonalized current vector *r* (11).

$$\vec{J} = J\left(\vec{n} \times \vec{r}\right) \tag{11}$$

Another issue was to determine the correct solver settings. The almost zero order of the conductivity values used for human head tissues was close to those used to "simulate" stranded conductors. It made application of iterative solvers impossible due to a very long convergence time. For this reason the model was solved by means of direct solvers with increased solution time. The surrounding air domain was made larger than the explored area of interest because of the impact of the boundary condition of magnetic insulation on the modeling results.

For the initial experiments with the modeling of LFMS two sets of 4 small coils were placed at each side of the head and arranged around the points of F3 and F4 according to the international 10-20 system. A sine wave current with a peak value of 1 A at a frequency of 1 kHz was used for excitation. TMS was modeled with the most frequently used coil – figure-of-eight coil, average diameter of 5 cm each loop. A 1 ms long monophasic pulse with the peak of 6.2 kA at 130 μs was chosen as excitation current.

Whereas the fairly low frequency range used in LFMS usually causes a deep penetration depth, the studied weak fields mitigated that effect. Hence, the induced currents penetrated only a rather small depth within the head. This allowed us to consider only the eighth part of the layered sphere head model – the upper left frontal part of the head with the point of F4 shown in Figure 3. In turn, the use of only one-eighth part of the head allowed fine meshing.

2.3 Human head model

Radiological data for the development of a realistic human head model came from the second version of the Visible Human 2.0 Project, where the cadaver of a 66 years old male without pathology appears as the donor. The head can be reconstructed with a resolution of up to 0.5 mm per voxel side.

First, we converted the raw radiological data to the DICOM format. Next, there was a preprocessing stage which consisted of data crop, removal of artifacts, various data windows and levels. Then, the manual and half-automated segmentation into skin, skull, CSF, brain, and sinuses took place using masks, thresholds, filters, “magic wand” tool and confidence connected region growing. After all these steps, we need to integrate the coil set and the surrounding air domain into 3D image data. Assumptions regarding the use of 3D Slicer and Amira for this task turned out to be wrong. This is the first issue. For this reason we have chosen Simpleware software [8]. The integration was followed by the creation of surface or volume meshes for each of the segmented tissues by means of marching cubes or similar algorithm. The second issue is to find trade-off between the model quality and finite element mesh size. Preserving the complexity of internal head structures, we have to provide a reasonable solution time.

3. Results

In the course of the first stage of work, we developed and debugged the 3D models of transcranial magnetic stimulation and low-field magnetic stimulation, based upon the use of a layered sphere head model. These models, reflecting the quantity of main interest – distribution of induced current density |***J***| inside the brain sphere, represented in Figure 2 and Figure 3. For both cases, peak values of the current density induced inside the human head were registered in CSF as roughly 1 mA/m^2 for LFMS and 180 A/m^2 for TMS. It was explained by a high conductivity of CSF in a comparison to other head tissues.

The model of TMS was used for auxiliary purposes. For the figure-of-eight coil stimulation occurred under its center. Magnetic flux density |***B***| of 2.7 T were measured 5 mm below the coil surface at the intersection of the loops, and only of 1.3 T at the centers of the loops.

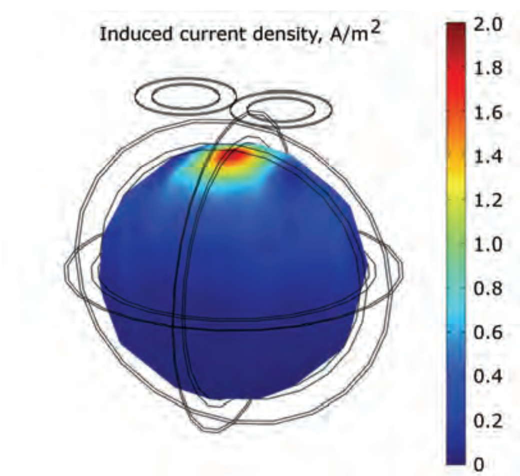

Figure 2. Model of transcranial magnetic stimulation.

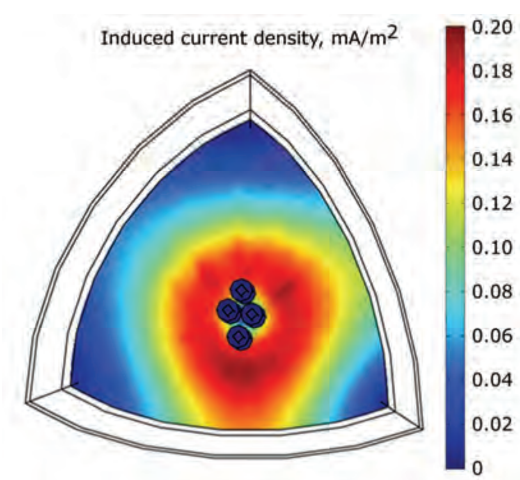

Figure 3. Model of low-field magnetic stimulation.

The model of LFMS was made precise. It consisted of approximately 30,000 tetrahedrons with quadratic shape functions, amounted to 220,000 degrees of freedom. The modeling showed that the coils were capable of generating a peak magnetic flux density $|\boldsymbol{B}|$ of 66 mT within the core, what corresponded to the electric field $|\boldsymbol{E}|$ of 41 mV/m inside the head. A current density $|\boldsymbol{J}|$ in the order of 0.1 mA/m^2 was induced up to 30 mm deep into the head along the main stimulation axis – the line drawn from the point of F4 on the head surface to its center.

The preliminary approach towards the development of the MRI/CT-based human head model shown in Figure 4 was successfully conducted. Depending on the number of segmented tissues and the quality of both segmentation and meshing, the total number of elements in the finite element model of the human head varied from 50 thousand up to 500 thousand.

Figure 4. The model of the human head.

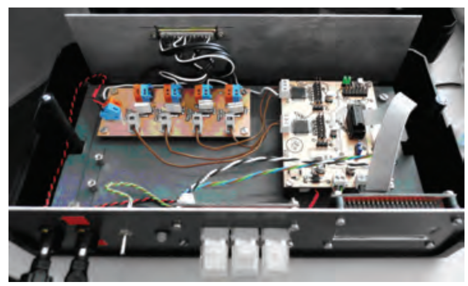

Figure 5. Prototype of the stimulator from [9].

4. Conclusion

The literature review has shown that the idea of depression treatment via LFMS is novel and worth investigating, but there are no models for it. We have developed TMS and LFMS models with the use of the layered sphere head model. With the help of the obtained models we are able to determine the relationships between the currents induced inside the human brain and an excitation current placed in a particular kind of the coil set. This information is used for the development of the stimulator prototype, shown in Figure 5. Now we are working under the development of a realistic head model, based on MRI and CT scans of a human head and designed to replace the layered sphere model.

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