Electric Stimulation of the Nervous System: a dosimetric study for the DBS application

***Fernando Maggio*[1], *Marta Parazzini*[2], *Micaela Liberti*[1], *Alessandra Paffi*[1] , *Francesca Apollonio*[1], *Paolo Ravazzani*[2], *Guglielmo D'Inzeo*[1]**

[1]ICEmB @ Department of Electronic Engineering "Sapienza" University of Rome, Via Eudossiana 18, 00184, Italy, maggio@die.uniroma1.it, liberti@die.uniroma1.it, Paffi@die.uniroma1.it, apollonio@die.uniroma1.it, dinzeo@uniroma1.it

[2] CNR @ Institute of Biomedical Engineering, Piazza Leonardo da Vinci 32, 20133, Milano, Italy, marta.parazzini@biomed.polimi.it, paolo.ravazzani@polimi.it

Abstract

Deep Brain Stimulation (DBS) is an increasingly common treatment for Parkinson's disease, showing a positive effect on motor functions and more generally on the activities of daily living of the patient. However, further studies are needed to investigate how DBS works, being this aspect not completely clear. In order to obtain a better knowledge of the technique, in this paper a 2D electromagnetic model and a 3D geometrical model of the anatomical region involved in the electrical stimulation have been developed. Moreover, the influence of a 2D conducting domain, based on a simplified shape of human body, on the distribution of the fundamental electric quantities inside the brain target area is evaluated.

1. Introduction

The Deep Brain Stimulation (DBS) is a successful technique in reducing symptoms of several movement disorders, including essential tremor (ET) and it is an effective treatment for advanced Parkinson's disease [1].

The clinical outcomes with DBS technique are analogous to those achieved by an ablative surgical lesion, suggesting that DBS works by blocking the pathological neural information between interconnected brain region, specifically in basal ganglia [2]. The main advantages of DBS over surgical lesions are its ability to modulate stimulation parameters and its reversibility [3]. Although the health-related quality of life of patients is actually improved by the technique, the precise mechanism of DBS functioning remains not well understood [1-3].

In order to investigate the mechanism of action of DBS, the first goal is to characterize the electric potential and the activating function generated inside the brain by the stimulation.

In this context, a previous work, by the authors, has evaluated the influence of domain dimensions on the distribution of the electric potential and activating function through a 2D conducting box with different sizes, and the role of ground positioning by considering different boundary conditions along the box sides [4]. Moving from those results, in this work, a synthetic 2D geometric structure based on a simplified model of the head, neck, trunk, and a 3D model of the neuroanatomical targets of stimulation derived from magnetic resonance imaging (MRI) are developed.

Purpose of this study is, therefore, to characterize the influence of a more realistic modeling on the distribution of the fundamental electrical quantities, mainly involved in the neuronal stimulation. In this way, it will be possible to correctly correlate the distribution of the fundamental electric quantities inside the targets with neuronal activities.

2. Materials and Methods

Clinic experience singles out the Subthalamic Nucleus (STN) as the more suitable target for the electrical stimulation of the brain [1]. The STN is located ventral to the thalamus including the zona incerta (ZI) and the Fields of Forel (FF), dorsal to the Substantia Nigra (SN) and medial to the Internal Capsule (IC); all these structures together are referred as neuroanatomical target (NAT). For sake of clarity, materials and methods are discussed into two subsections regarding 2D and 3D models, respectively. In the first section, a complete 2D electromagnetic model is described, together with the electrical quantities used for quantifying the stimulation of the brain regions. In the second one, the whole procedure, adopted for obtaining a 3D NAT model, crucial for an accurate and complete analysis of the electrical stimulation, is shown.

2.1 The 2D Model

In this study, the 2D model of of the NAT has been adopted as a rectangular region surrounding the stimulating electrode (fig. 1A); it encompasses the STN, the IC, the SN and part of the Ventral intermediate nucleus of the thalamus (Vim). The 2D neuroanatomical shapes (Fig. 1) are obtained from image segmentation of human stereotaxy atlas [5]. The electromagnetic characterization of the NAT is given following the approach proposed by Kuncel in [6]. All the regions are modeled as grey matter (conductivity: σ = 0.2 S/m), except for IC whose anisotropy is taken into account (σ = 1 S/m, parallel to the fibers, σ = 0.1 S/m, perpendicular to the fibers) [7].

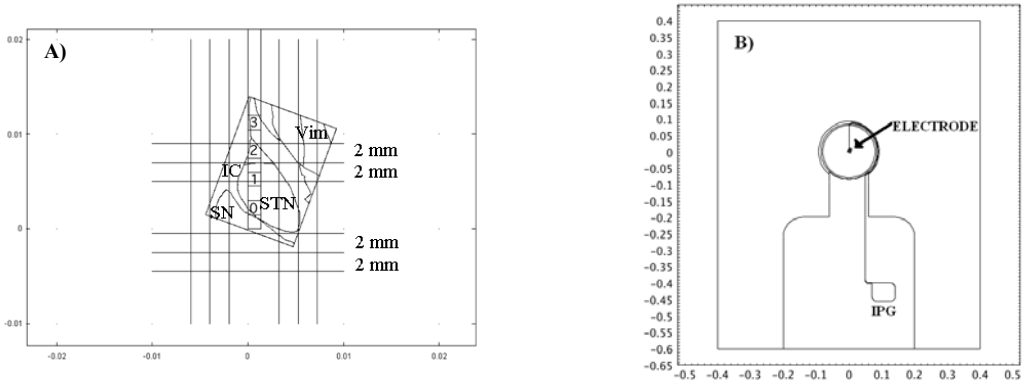

Fig. 1. A) 2D region of NeuroAnatomical Target, where the electrode with the four contacts is visible with the main region of interest: Subthalamic Nucleus (STN), Internal Capsule (IC), Substantia Nigra (SN) and part of the Ventral intermediate nucleus of the thalamus (Vim). B) Anthropomorphic model: the IPG and the electrode are visible, the 2D NeuroAnatomical target is located around the electrode like in Fig.1. The head is a multilayered sphere without the skin between the skull and the neck.

The NAT has to be placed into a 2D conducting domain which can be simply a square or rectangular box [4] or a more realistic geometry approximating a human body shape. In this work, a simplified model of head, neck and trunk, with heterogeneous tissues, is considered, called anthropomorphic model (Fig 1B). The head is modeled as three concentric circumferences [8] delimiting three regions constituted by brain (σ = 0.09 S/m), skull (σ = 0.02 S/m) and skin (σ = 0.0002 S/m), moving from the inner one. The neck and the trunk are characterized by muscle conductivity (σ = 0.26 S/m). The anthropomorphic model is inserted in a bounding box (80 x 100 cm^2) filled with air, and the boundary conditions are set to electric insulation (continuity of normal components of current density).

The stimulating electrode, inserted in the NAT, is modeled as a real quadruple DBS electrode (Medtronic DBS 3387 (Medtronic, Inc, Minneapolis, MN) [9]) consisting of four equally spaced platinum electrode contacts (σ= $8.6*10^6$ S/m) numbered from 0 to 3 (Fig. 1A). The implantable pulse generator (IPG) is placed in the trunk ad is modeled as a titanium box ($\sigma = 24*10^8$ S/m) considering the dimension of a real IPG device (about 7.0 x 5.5 cm^2).

At the boundary between head and neck, the skin is removed to better model the conducting pathway from head to IPG. Once the electromagnetic model is carried out, the Laplace equation is solved to determine the electric potential (V) distribution in the analysis domain using the commercially available software package Comsol Multiphysics v.3.2 (Comsol Inc) [4]. Because the main frequency of DBS signal is in the range 120-180 Hz [9], the problem is treated as a quasi-static one and the conductivities of tissues are evaluated at 120 Hz [4]. As reported by several studies [1,6,10], clinically effective DBS of STN in PD is typically achieved with a unipolar stimulation. Therefore, Contact 0 is set to V = −1 V and the ground (V = 0 V) is placed on the IPG [9].

Results are based on the evaluation of the electrical potential (V) and the activating function [11] (AF) along a series of vertical lines passing through and around the NAT, equally spaced of 2 mm (Fig. 1A), and representative of neural fiber direction.

2.2 The 3D model

As already mentioned, the STN represents the most common anatomical target for DBS treatment of PD. Nevertheless, STN neurons send their axons to the globus pallidus (Gp) which carries output from Caudate Nucleus

(Cd) and Putamen (Pt) to the Thalamus (Th) [1,12]. In this context, in order to account for the complexity of the stimulated system, a 3D geometrical model of all anatomical structures in the basal ganglia region was carried out.

With respect to the 2D case, the procedure for obtaining an accurate description of the brain targets is not straightforward and requires to manage a lot of information. The model is developed on the basis of a pre-operative magnetic resonance imaging (MRI) data. Starting from a patient specific MRI data, a medical imaging software package Mimics v.10.0 has been used to translate MRI data into the 3D model.

The whole procedure to create the 3D geometrical model is quite complex and consists in two fundamental steps. From the MRI data set, it is necessary to select precise slices in which the anatomical nuclei implicated in the electric stimulation are clearly visible. In each chosen slice, the segmentation of the images is done pixel by pixel with the aid of brain atlas [16] to identify borders of nuclei not directly visible in the slices. In this way 3D volumes of the nuclei are created by interpolating between these contour lines using the Mimics MedCad Module.

The stimulating lead is the DBS electrode used in the 2D model. It is modeled as a cylinder made up of four metal contacts each with a diameter of 1.27 mm, height 1.50 mm and separation between the contacts of 1.50 mm [9]. Its position is defined by stereotaxic coordinates atlas with respect to anterior commissure (AC), posterior commissure (PC), and mid-commissural (MC) point and is realistically located in the posterior subthalamic nucleus [12]. The realized 3D geometrical model is importable in the software package Comsol Multiphysics v.3.2. Before solving the electromagnetic problem, the model must be characterized from a dielectric point of view and inserted in a conducting domain which can be a cubic box, a sphere or a realistic head again obtainable from MRI data.

3. Results

Moving from previous results carried out by the group, the influence of a different shape of the conducting domain is evaluated comparing the distributions of V and AF around the electrode, obtained with the Antropomorphic Model, and a rectangular box model 80x100 cm^2, grounded on the base side.

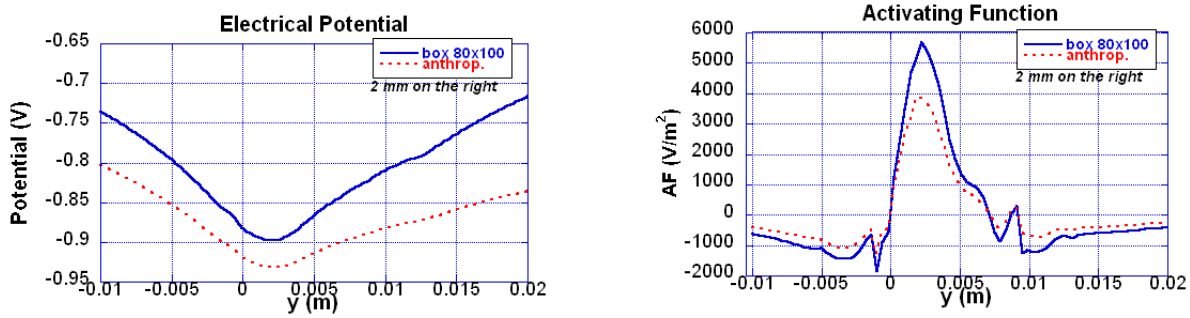

Fig. 2. Electric potential and activating function along a line passing 2 mm on the right of the active contact, for a 80x100 box model bottom grounded and Anthropomorphic Model.

Figure 2 depicts V and AF evaluated along a line passing 2 mm on the right of the active contact (Contact 0 as shown in fig.1A). In all cases, V and AF for the rectangular box model are higher than for the Anthropomorphic one, even though their trend are quite similar. These data suggest that even a variation in the shape of the conducting domain can strongly influence the values of both V and AF and thus the possible activation of nervous fibers near the electrode.

Regarding the 3D model of neuroanatomical nuclei, the geometrical model derived from MRI data as described in section 2.2, is imported in the software package Comsol, leaving unchanged the relative distances between the structures, their size and their positions. Figure 3 shows the anatomical nuclei present in the model. Thalamus (red one) is located lateral-dorsal to STN (violet); Globus Pallidus (blue) is located lateral to Putamen (green) that, in turns, is located dorsal to Caudate (orange). All nuclei are surrounded by the IC. Successive step towards a complete 3D solution of the stimulation problem is assigning the values of the electrical conductivities for each nucleus (Fig. 3), taking into account both isotropic and anisotropic behaviors of the tissues.

As a first analysis, the conducting domain can be chosen as a cube whose dimensions and ground position can be varied in order to evaluate their influence on the electrical quantities distribution inside the anatomical nuclei. This model can provide a more realistic quantification of the electrical potential and the activating function in the brain region, leading to an accurate analysis of their correlation with the neural responses.

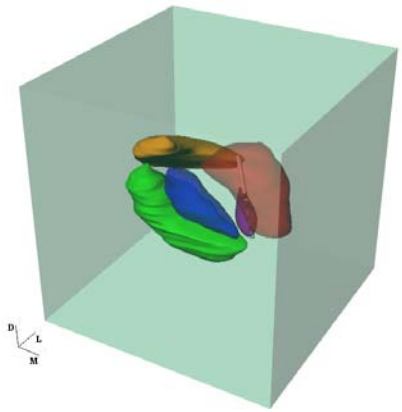

Fig. 3. 3D model of the basal ganglia, the DBS electrode and the conducting domain shaped as a cubic box. Caudate nucleus is in green, Globus Pallidus in blue, Caudate Nucleus in orange, SubThalamic Nucleus in violet and Thalamus in red. The 4-contact electrode (in black) is located lateral to STN. Each legs of the 3D scale is long 5mm, where D stand for dorsal, L for lateral, M for medial.

4. Conclusion

The clinical success of the DBS technique masks a substantial lack of knowledge of the action mechanism. In this sense, an accurate modeling of the anatomic structure involved into the electrical stimulation allow a complete analysis of the problem. In this work a complete 2D electromagnetic model and a 3D geometrical model has been described. The procedure to create the 3D geometrical model has been also illustrated. Further studies will provide a precise characterization from a dielectric point of view, taking into account both isotropic and anisotropic properties of the tissues in the model. After this, we can solve the 3D electromagnetic problem, so a more realistic quantification of the electrical potential and the activating function in the brain region is possible.

5. References

1. T. Parsons, S. A. Rogers, A. J. Braaten, S. P. Woods, A. I. Tröster, "Cognitive sequelae of subthalamic nucleus deep brain stimulation in Parkinson's disease: a meta-analysis," *Lancet Neurol.,* 2006, pp. 578-588..
2. A. M. Lozano, N. Mahant, "Deep brain stimulation surgey for parkinson's disease: mechanisms and consequences," *Parkinsonism Related Disorders,* 2004, pp. 49-57.
3. C.C. McIntyre, W.M. Grill, D.L. Sherman, N.V. Thakor, "Cellular effects of deep brain stimulation: Model-based analysis of activation and inhibition", *J. Neurophysiol*., 2004, pp. 1457-1469.
4. M. Liberti, F. Apollonio, A. Paffi, M. Parazzini, F. Maggio, T. Novellino, P. Ravazzani, G. D'Inzeo, "Fundamental Electrical Quantities in Deep Brain Stimulation: Influence of Domain Dimensions and Boundary Conditions," *proceedings of the 29th Annual Int. Conf. IEEE. EMBS*, Lyon, France, Aug. 2007.
5. G. Schaltenbrand, W. Wahren, "Atlas for Stereotaxy of the Human Brain," *2nd ed., Thieme*, Stuttgart, 1977.
6. A. M. Kuncel and W. M. Grill, "Selection of stimulus parameters for deep brain stimulation", *Clin. Neurophysiol.*, 2004, pp. 2431-2441.
7. Gabriel C., Gabriel S., Corthout E., "The dielectric properties of biological tissues: I. Literature survey," *Phys. Med. Biol.,* 1996, pp. 2231–2249.
8. S.Rush, D.A. Driscoll, "EEG electrode sensitivity-an application of reciprocity", *IEEE Transactions on Biomedical Engineering*, 1969, pp. 15-22.
9. Medtronic DBS™ Implant Manual 2006: lead kit for deep brain stimulation.
10. C.C. McIntyre, S. Mori, D.L. Sherman, N.V. Thakor, J.L. Vitek , "Electric field and stimulating influence generated by deep brain stimulation of the subthalamic nucleus", *Clin. Neurophys.* 2004, pp. 589–595.
11. F. Rattay, "Analysis of models for external stimulation of axons," *IEEE Trans. Biomed.,* 1986, pp. 974-977.
12. S. Miocinovic, M. Parent, C. R. Butson, P. J. Hahn, G. R. Russo, J. L. Vitek, C.C. McIntyre, "Computational analysis of subthalamic nucleus and lenticular fasciculus activation during therapeutic deep brain stimulation", *J Neurophysiol.*, 2006, pp.1569-1580.