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A Dosimetric Study Comparing Intra-Operatory Microelectrode and Chronic Macroelectrode in the DBS Technique

A. Paffi, F. Apollonio, *Member, IEEE,* M. G. Puxeddu, M. Parazzini, G. d'Inzeo, *Member, IEEE,* P. Ravazzani, F. Camera, M. Liberti, *Member, IEEE*

Abstract— **To identify the target of Deep Brain Stimulation (DBS) and to choose the optimal parameters for the stimulating signal, intra-operatory microelectrodes are generally used. However, when they are replaced with the chronic macroelectrodes, the effect of the stimulation is often very different. Here, we use numerical simulations to predict the stimulation of neuronal fibers induced by microelectrode and macroelectrode placed in different positions with respect to each other.**

I. INTRODUCTION

Deep Brain Stimulation (DBS) is a successful technique for the treatment of advanced Parkinson's disease (PD) making use of the direct electric stimulation of basal ganglia in the brain [1], [2]. Different hypotheses have been done on the interaction between electromagnetic fields and the brain [3], [4], e.g. Stochastic Resonance [5]-[10], however, the precise mechanism of the DBS functioning is still unclear [1], [11].

To identify the target nucleus of DBS, i.e. the Subtalamic Nucleus (STN), and to choose the optimal parameters for the stimulating signal (amplitude, frequency, pulsewidth), intra-operatory microelectrodes are generally used. Then, the microelectrode is replaced by the chronic one (macroelectrode) fixed in the same location. Nevertheless, the stimulation with a macro- or a microelectrode not always induces similar clinical effects [12].

To explain such discrepancies, as for any bioelectromagnetic problem, the first step consists in the dosimetric evaluation [3], [13], using accurate geometric and electromagnetic models of the stimulated region, as those developed in [14]-[17].

In a previous work [18], the authors, using the 3D dosimetric model described in [17], predicted a completely different stimulation induced on a single fiber by micro and macro- electrodes. Such a result was supposed to be due to a different relative position of the fiber with respect to the active contacts of the microelectrode and the macroelectrode, respectively.

In order to extensively investigate such a hypothesis, the stimulation of the two kinds of electrodes has been numerically characterized in terms of the electric potential (V) and the activating function (AF) along groups of lines representing fibers connecting the STN to the Globus Pallidus (G_p). Two different positions for the microelectrode have been considered with respect to the macroelectrode: (1) with the same electric center (barycenter between anode and cathode); (2) with the external surfaces of the cathodes coincident. Results along some single lines have been presented in [19].

However, taking into account that the clinical effect is not determined by a single fiber, but arises from the synchronous response of groups of fibers, here, a statistical analysis has been carried out on the electric quantities along groups of lines exhibiting similar behavior.

II. MODEL AND METHODS

The 3D model (Fig. 1), implemented in the software package Comsol Multiphysics v.3.4 (Comsol Inc), has been obtained from clinician MRI data and includes the main neuronal structures involved in PD, i.e. STN, G_p, and the internal capsule (IC) [17]. STN and Gp have been modeled as nuclei of isotropic grey matter (σ= 0.2 S/m), whereas IC has been considered as a spheroid region of anisotropic white matter (σ_{yy} =σ_{xx} =0.1 S/m, σ_{zz} =1 S/m) surrounding STN and G_p. It is composed of bundles of fibers linking STN to G_p, responsible of the anisotropic behavior of the tissue along the fibers [20], i.e. approximately along the z-axis direction.

The 3D analysis domain is a cubic box (Fig. 1), 50 cm of side, filled with an isotropic medium representative of the brain tissue (σ= 0.09 S/m). This box size has been shown to be the best compromise between computational effort and solution accuracy [17], moreover it seems the most appropriate choice from an anatomical point of view being 25 cm a reasonable "average" distance between the electrode in the center of the brain and the case of the stimulator device, implanted in the sub-clavicular region.

The considered stimulating leads are: the Medtronic "3389" as the chronic one [21], and a commercial quadruple microelectrode (FHC Inc) as the intra-operatory one used during the surgical phase. Only the active contacts of the macro- and microelectrodes have been taken into account, modeled as platinum cylinder contacts ($\sigma = 8.6{\cdot}10^6$ S/m), the first ones with diameter 1.27 mm, height 1.5 mm, and

A. Paffi, F. Apollonio, M. G. Puxeddu, G. d'Inzeo, F. Camera, M. Liberti are with ICEmB at the Department of Information Engineering, Electronics and Telecommunication (DIET), Sapienza University of Rome, 00184, Rome, Italy (corresponding author phone: +390644585457; e-mail: camera@die.uniroma1.it; paffi@die.uniroma1.it; apollonio@die.uniroma1.it; mariagrazia.puxeddu@tiscali.it; dinzeo@die.uniroma1.it; liberti@die.uniroma1.it).

M. Parazzini, P. Ravazzani are with CNR Institute of Biomedical Engineering, 20133 Milan, Italy (e-mail: paolo.ravazzani@polimi.it; marta.parazzini@polimi.it).

inter-distance 0.5 mm, the second ones with diameter, height, and inter-distance of 35 μm. Considering the bipolar stimulation, for each electrode, one contact (anode) has been set to a positive voltage (1 V for the macroelectrode, 1000 V for the microelectrode) and the other one (cathode) to a negative voltage (-1 V for the macroelectrode, -1000 V for the microelectrode) (Fig. 2) [1], [21]. The ground condition has been placed on one face of the cubic box (Fig. 1), while the condition of electric insulation has been applied to the other faces [17].

Higher voltage values (1000 times higher in the absolute value) have been applied to the active contacts of the microelectrode to have comparable stimulation intensities, taking into account that the microelectrode impedance is about 1000 times higher than that of the macroelectrode.

According to the clinical practice, both contacts of the macroelectrode are placed inside the STN (Fig.1). The microelectrode is placed in two different positions with respect to the macroelectrode: with the same electric center (central), with the external surfaces of the cathodes coincident (lateral) (Fig. 2).

Due to the low frequency content of the stimulating signal (up to a few kHz), the minimum wavelength is much higher than the ganglia size (order of some cm), so the problem has been treated as a quasi-static one [14], [15] by solving the Laplace equation implemented in Comsol Multiphysics.

The responses of the neuronal tissue to the three kinds of stimulation: macroelectrode, microelectrode central, and microelectrode lateral, have been calculated in terms of V and AF along 12 lines, passing at a distance of about 2 mm from the macroelectrode contacts, and connecting the STN to the G_p through the IC (Fig. 2). The lines have been divided into two groups (Group 1-7 and Group 8-12) depending on whether they are closer to the anode or to the cathode of the macroelectrode (Fig. 2).

As for the electric potential V, for each line, the mean value and the standard deviation have been calculated in the line segment lying inside the STN; this is because the bipolar DBS is almost completely confined in the STN [19].

The AF, defined as the second derivative of the extracellular potential along a fiber [22], is a particularly interesting observable since its sing could be used to predict the fiber activation or inhibition. Indeed, moving from the classical cable theory, nervous fibers may be activated in the regions where the AF assumes positive sign and inhibited where a negative AF occurs [22].

To predict the average response of the fibers belonging to the same group, the AF along each line has been interpolated and resampled and the mean value has been calculated over the lines of the same group.

III. Results

The behavior of V along the lines exhibits its maximum or minimum value inside the STN (Fig. 3), i.e. where the line is closest to one of the active contacts. In particular, the sign of V is positive if the fiber passes close to the anode (Group 1-7) (see Fig. 3 regarding line 4) and negative if the fiber is close to the cathode (Group 8-12).

To compare the V induced by the three kinds of stimulation (macroelectrode, microelectrode central, and microelectrode lateral) on different lines, the V mean values, calculated on the line segments inside the STN, have been reported in Fig. 3, together with the standard deviations.

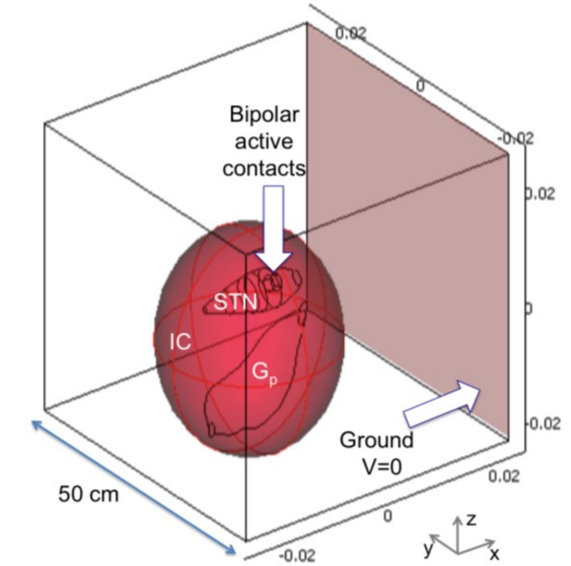

Figure 1. The 3D dosimetric model. STN, Gp and IC are immersed in a cubic box 50 cm of side. The active contacts are placed inside the STN and the ground on a face of the cube.

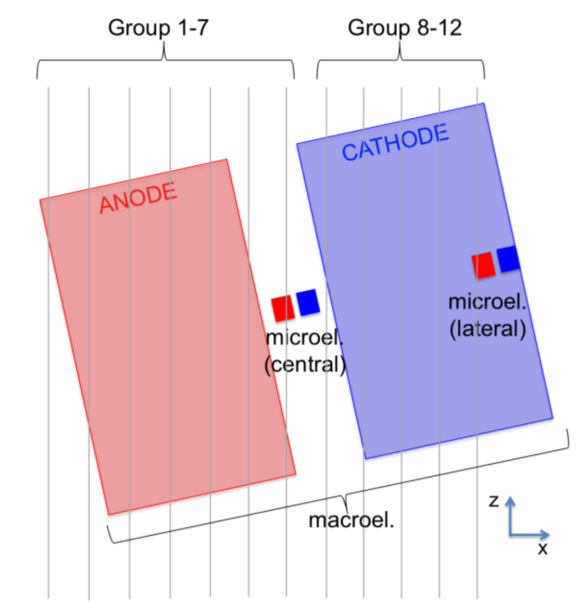

Figure 2. Relative positions of the microelectrode with respect to the macroelectrode (not in scale) and of the 12 lines grouped in two sets. Each line passes through the STN, the IC and the Gp.

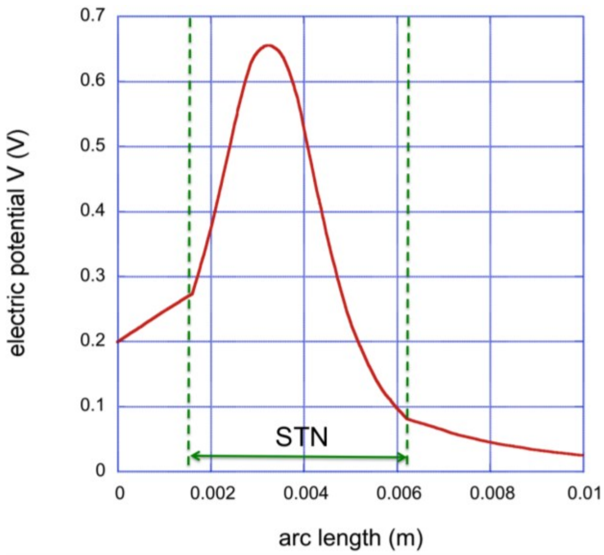

Figure 3. Electric potential V induced along the line 4 (Group 1-7) by the macroelectrode.

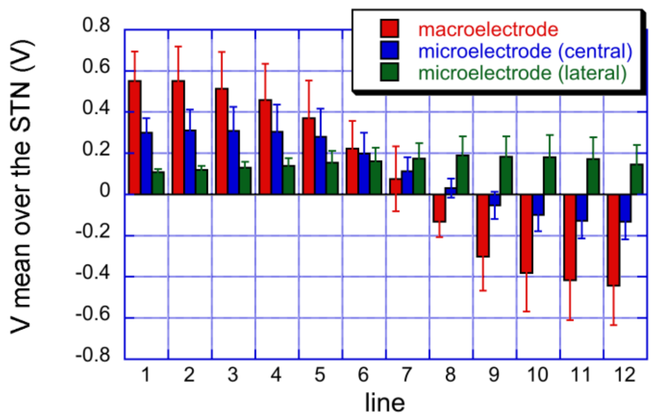

Figure 4. V mean values and standard deviations calculated for each line over the segment passing through the STN.

Results of Fig. 4 show that, for the macroelectrode stimulation, the mean V is positive for the lines of Group 1-7 and negative for the Group 8-12, in agreement with their closeness to the positive or negative active contact (Fig. 2). For the microelectrode in the central position (Fig. 2), the mean values are lower on average but show the same behavior described for the macroeletrode on the twelve lines.

The only slight difference is observable for the lines 7 and 8 that present values of V either positive or negative (line 7 for the macroelectrode stimulation and line 8 for the central microelectrode), since they are affected both by the anode and the cathode. Completely different is the case of the lateral macroelectrode, when V is always positive for each line. Thus, for the lines of Group 8-12, the sign of the stimulation is opposite with respect to those induced by the macroelectrode and the microelectrode in the central position.

As for the AF, it shows a biphasic behavior (Figs. 5 and 6), with a transition positive-negative or vice-versa, depending on the position of the fiber with respect to the active contacts (cathode and anode) of the electrode [23].

Results of Figs. 5 and 6 show the AF behaviors averaged over the lines of Group 1-7 and Group 8-12, respectively. From these behaviors it is possible to predict and compare the response of groups of fibers to the three kinds of stimulation.

Fig. 5 shows that all kinds of stimulation induce a similar response, in terms of sign of the AF, in the group of lines 1-7. As for the Group 8-12, the response induced by the lateral microelectrode is opposite with respect to that induced by the other kinds of stimulation.

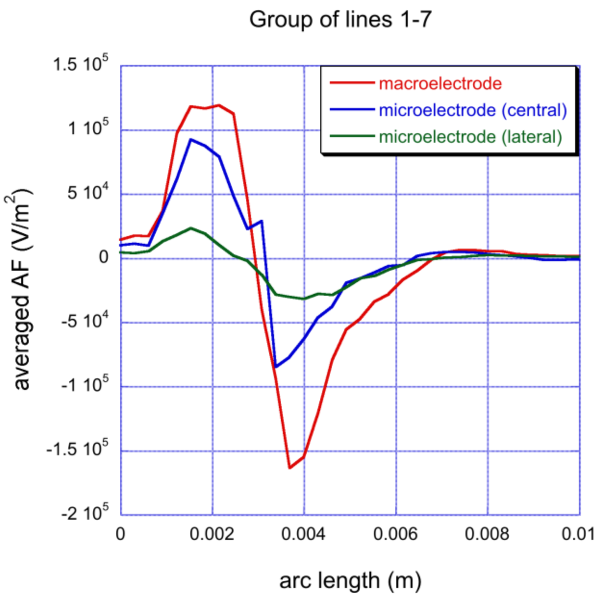

Figure 5. Average behavior of the AF over the lines of the same group (Group 1-7) for the stimulation with the macroelectrode, the central microelectrode and the lateral microelectrode.

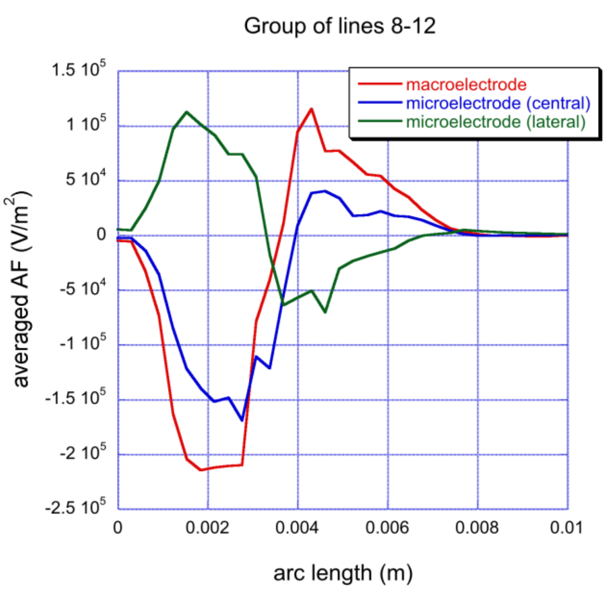

Figure 6. Average behavior of the AF over the lines of the same group (Group 8-12) for the stimulation with the macroelectrode, the central microelectrode and the lateral microelectrode.

IV. CONCLUSIONS

Results of this study indicate that the macroelectrode and the microelectrode, if positioned with coincident centers (central), induce in all groups of fibers electric stimulations with the same trends of V and AF. Conversely, when the microelectrode and the macroelectrode coincide laterally (lateral), there is a group of fibers where the two kinds of stimulation are completely opposite (Fig. 6).

This conclusion is particularly significant because it demonstrates that the response of the fibers may be completely different between the stimulations using macroelectrode (chronic) and microelectrode (intra-operatory), depending on their relative positions. Therefore, if we want the chronic electrode to produce the same effects of the intra-operative microelectrode, it will be necessary to place the macroelectrode so that its electric center coincides with that of the microelectrode. In this way it will give rise to the same average trends of V and AF along all the groups of fibers connecting the two nuclei: STN and G_p. Such an indication could be useful to improve the electrode positioning during surgical procedures.

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