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Patient-specific models and simulations of deep brain stimulation for postoperative follow-up

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***Abstract*— Deep brain stimulation (DBS) is an established treatment for Parkinson's disease (PD). The success of DBS is highly dependent on electrode location and electrical parameter settings. In this study patient-specific computer models of DBS were used for postoperative follow-up in three PD patients who suffered from stimulation induced hypomania, dysarthria, and uncontrollable laughter respectively. The overall aim of the study was to relate the anatomical aspect of the electric field to the effects and side effects of stimulation. The simulations showed the anatomical distribution of the electric field for all the patients and the results were in agreement with previous reports regarding these side effects of stimulation. It was demonstrated that patient-specific models and simulations of DBS may be useful for postoperative follow-up of DBS.**

Keywords— **Deep brain stimulation, patient specific, finite element method, dysarthria, hypomania**

I. Introduction

Deep brain stimulation (DBS) is used for improving the motor signs in movement disorders such as medically refractory Parkinson's disease (PD). Despite the effectiveness of DBS there are many unanswered questions regarding the clinical effects and side effects of this therapy. It is well known that significant improvement of motor signs may be accompanied by parallel negative effects on other functions, such as speech. Improved control of the distribution of the electric field is essential for improving the outcome of this therapy. In order to provide a visual feed-back of the anatomical distribution of the electric field we have previously developed a method for setting up 3-dimensional patient-specific finite element computer models of DBS where the electric field can be simulated and visualized [1]. In the present study such patient-specific computer models of DBS were used for postoperative follow-up in three PD patients who suffered from stimulation induced hypomania, dysarthria, and uncontrollable laughter respectively. The overall aim of the study was to relate the anatomical aspect of the simulated electric field to the effects and side effects of stimulation.

II. Materials and methods

A. Patient-specific models and simulations

Patient-specific finite element computer models of bilateral DBS in the subthalamic nucleus (STN) were set up for each of the three patients. Preoperative T2 weighted stereotactic magnetic resonance images (MRI) was used to create models of each brain, and postoperative stereotactic MRI was used to position the DBS electrodes at their true positions in the brain-models. In order to allot realistic electrical properties to the models, each preoperative MRI voxel was classified into material groups, such as grey matter, white matter, and cerebrospinal fluid. The classified MRI voxels were then allotted isotropic electrical conductivity properties at a frequency of 130 Hz from Andreuccetti's online database [2]. A random neuronal orientation was assumed, thus isotropic electrical conductivity values were used. Two DBS electrodes with a radius of 0.635 mm and contact lengths of 1.5 mm separated by 0.5 mm (Model 3389 DBS™ Lead, Medtronic, Inc. USA) were modelled and positioned in each brain model. The distribution of the electric potential in the vicinity of the electrodes was calculated using the equation for steady currents [3]:

$$\nabla \cdot J = -\nabla \cdot [\sigma \nabla V] = 0 \ (\mathrm{A\ m^{-3}}) \qquad (1)$$

where J is the current density (A m^{-2}), σ the electrical conductivity (S m^{-1}), and V the electric potential (V). The electric field was visualized in three dimensions with isolevels at 0.2 V/mm together with the anatomy on two-dimensional colour-coded axial and coronal slices. The contours of the electric field isolevels were traced onto the axial and coronal slices and anatomical structures were identified with help from an atlas presented in Gallay et al. [4].

B. Case 1: Dysarthria

This PD patient was enrolled in a study where speech and movement was assessed during a variety of electrical DBS settings [5]. Speech intelligibility and movement were evaluated during monopolar STN stimulation with an electric potential of 0, 2, and 4 V (off, low and high amplitude stimulation). The evaluation of speech consisted of sustained vowel phonation "ah" for three repetitions, Assessment of Intelligibility for the Dysarthric Speech, and a 60-seconds monologue about a subject of the speaker's choice. Following the speech recordings, movement was evaluated using the Unified Parkinson's Disease Rating Scale part three (UPDRS-III). The patient was withdrawn from his anti-parkinsonian medication the night before the day of investigation. The pulse width and frequency remained unchanged at 60 µs and 130 Hz. Subsequent every change of amplitude the patient rested for 15 minutes before the next evaluation. The electrode contacts located closest to the centre of the STN were used as active electrode contacts. In order to identify the contacts closest to the centre of the STN, the postoperative MRI, where artefacts produced by the electrodes are visible, were studied using the FrameLink Planning Station™ (Medtronic, Minneapolis, MN, USA). The electric field was simulated for 2 V and 4 V electric potential settings which were used during the assessments (Table 1). The frequency and pulse length was kept at 130 Hz and 60 µs for both electrical settings.

Table 1 Electrical settings and clinical effects

Left contact (Electric potential)	Right contact (Electric potential)	Speech intelligibility	UPDRS-III	Side-effects
0 (2 V)	5 (2 V)	70 %	33	None
0 (4 V)	5 (4 V)	20 %	33	Dysarthria

C. Case 2: Hypomania

This PD patient was treated with bilateral DBS in the STN after unsatisfying medical treatment. Stimulation-induced hypomania appeared a few days after a revisit to the clinical centre where the electrical settings were readjusted for optimization of the clinical effects. After adjustment of the electrical settings, movement as measured by UPDRS-III was slightly improved from 32 to 21. However, introduction of hypomania made these settings unusable. The electric field was simulated and visualized for both the electrical settings that induced hypomania and did not induce hypomania (Table 2). The frequency and pulse length was 145 Hz and 60 µs before adjustment. After the adjustment the pulse length of the right electrode contact was changed to 90 µs.

Table 2 Electrical settings and clinical effects

Left contact (Electric potential)	Right contact (Electric potential)	UPDRS-III	Side-effects
1 (3.6 V)	5 (3.5 V)	32	None
0 (3.5V)	4 (3.5 V)	21	Hypomania

D. Case 3: Uncontrolled laughter

This PD patient, who was treated with STN DBS after unsatisfactory medical treatment, was also enrolled in the study where speech and movement was evaluated during a variety of electrical DBS settings, as briefly described in Case 1. When high amplitude stimulation at 4 V was turned on the patient started to laugh uncontrollable. During these electrical settings the patient also experienced stimulation induced dysarthria. The electric field was simulated for 2 V and 4 V electric potential settings which were used during the assessments (Table 3). The frequency and pulse length was kept at 130 Hz and 60 µs for both electrical settings.

Table 3 Electrical setting and clinical effects

Left contact (Electric potential)	Right contact (Electric potential)	UPDRS-III	Side-effects
2 (2.0 V)	6 (2.0 V)	34	None
2 (4.0 V)	6 (4.0 V)	26	Laughter, Dysarthria

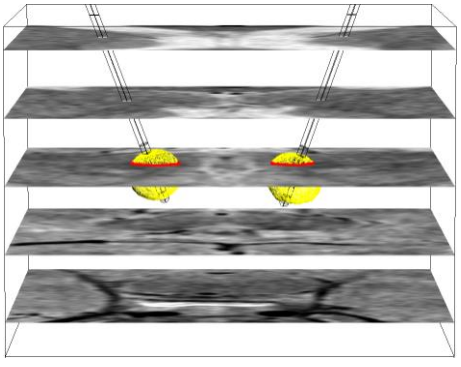

Fig. 1 Patient-specific simulation of DBS. The electric field has been visualized with isolevels at 0.2 V/mm. The isolevels were traced onto the axial and coronal images. This is illustrated with red colour in this figure.

III. Results

The electric field was simulated for all three patients and the electric field isolevel at 0.2 V/mm was traced onto axial and coronal images. The traced isolevels were colour-coded according to the appearance of side-effects where white colour refers to an electric field that did not induce side-effects and red colour to an electric field that did induce side-effects (Fig. 1).

A. Case 1: Dysarthria

The patient suffered from acute stimulation-induced impairment of speech intelligibility during high amplitude stimulation (Fig. 2). This patient had active electrode contacts positioned slightly ventral, posterior and medial to the centre of the STN. The simulations showed that the electric field isolevel covered a major part of the fasciculus cerebello-thalamicus (fct) during high amplitude stimulation. Movement as measured by the UPDRS-III was improved during both low and high amplitude settings compared to off stimulation. In this particular patient the motor score was the same during both high and low amplitude stimulation.

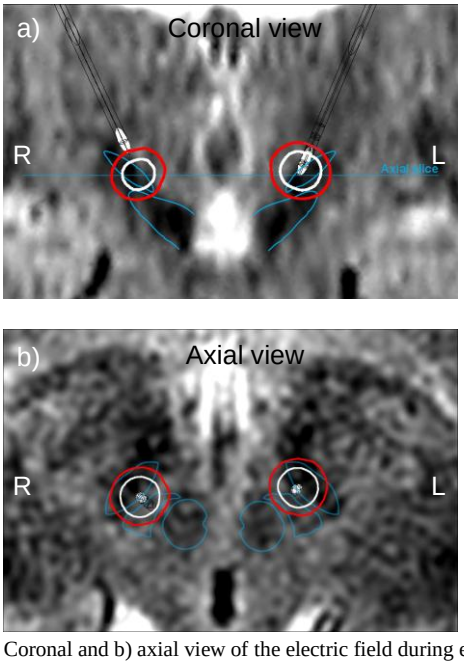

Fig. 2 a) Coronal and b) axial view of the electric field during electrical settings that induced dysarthria (red) and that did not induce dysarthria (white). The approximate boundaries of the red nucleus, the fasciculus cerebello-thalamicus, and the STN have been traced with blue colour.

B. Case 2: Hypomania

This patient suffered from reversible stimulation-induced hypomania. The active electrode contacts that were used during the conditions that induced hypomania were positioned slightly medial and ventral in the STN area. The simulations showed an electric field isolevel that reached down into the substantia nigra (Fig. 3). Movement was slightly improved during the electrical settings that induced hypomania compared to the electrical settings which did not induce hypomania.

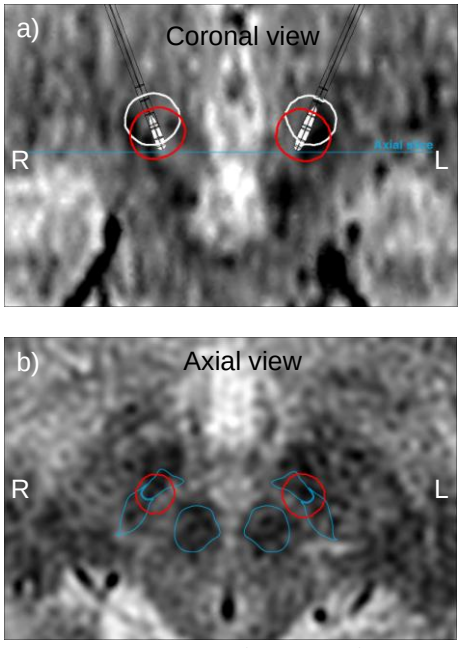

Fig. 3 a) Coronal and b) axial view of the electric field during electrical settings that induced hypomania (red) and that did not induce hypomania (white). The approximate boundaries of the red nucleus, the substantia nigra pars reticulata, and the STN have been traced with blue colour.

C. Case 3: Uncontrolled laughter

Acute uncontrolled laughter was induced during high amplitude stimulation in the STN. In addition to laughter the patient suffered from acute stimulation-induced dysarthria. The simulations showed that the electric field isolevel generated by the right electrode was located far ventral in the STN area and covered part of the substantia nigra. The electric field isolevels generated by both electrodes also covered a major part of the fct during high amplitude stimulation (Fig. 4). There was a greater improvement in movement during high amplitude stimulation than during low amplitude stimulation.

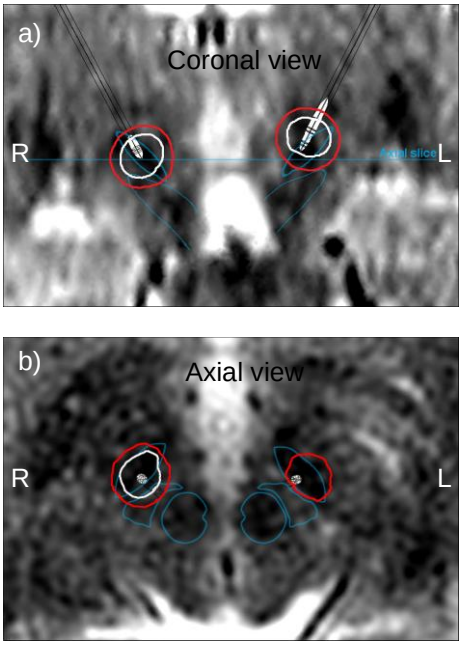

Fig. 4 a) Coronal and b) axial view of the electric field during electrical settings that induced uncontrolled laughter and dysarthria (red) and that did not induce these side-effects (white). The approximate boundaries of the red nucleus, the fasciculus cerebello-thalamicus, and the STN have been traced with blue colour.

IV. Discussions

There are several findings of this study. In case 1, speech intelligibility was impaired when the 0.2 V/mm electric field isolevel, from active electrode contacts positioned ventral, posterior and medial to the centre of the STN, covered a major part of the fct. Stimulation-induced speech impairments during STN DBS has often been attributed to lateral stimulation of the motor limb in the internal capsula, the corticobulbar fibers [6]. During stimulation of the corticobulbar fibers there is usually a change of sustained phonation and other acoustical parameters. These characteristics were not seen in this study. In a study by Plaha et al. [7] stimulation related dysarthria were seen in patients with active electrode contacts positioned medially in the STN area. They believed that stimulation of fibres from the fct that control movements of the vocal cords was likely the cause of the dysarthria. This is in agreement with the present study. In case 2, hypomania was introduced during electrical settings that generated an electric field isolevel that reached down into the substantia nigra. Ulla et al. [8] reported that one patient who had benefited from bilateral DBS in the STN for PD, suffered from acute and reproducible manic behavior. They believed their patient was stimulated in the substantia nigra. This is in agreement with the present study where the electric field isolevel covered part of the substantia nigra. Uncontrolled laughter and speech impairments were introduced by the stimulation in case 3. The electric field generated by the right electrode reached down into the substantia nigra, and the electric field isolevels generated by both electrodes covered a major part of the fct during high amplitude stimulation. Mirthful laughter has been reported in a study by Krack et al., 2001 [9] during bilateral stimulation at the most ventral contacts with an electric potential of 3.6 V, a pulse-width of 90 µs, and a frequency of 160 Hz.

V. Conclusions

It was demonstrated that the anatomical distribution of the simulated electric field could be visualized and related to the reported effects and side effects of stimulation. Patient specific models and simulations may in the future become a useful tool for postoperative investigations of DBS.

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