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Optimizing Deep Brain Stimulation Parameter Selection with Detailed Models of the Electrode-Tissue Interface

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***Abstract*-Deep brain stimulation (DBS) is an established clinical therapy for the treatment of Parkinson's disease. However, selecting stimulation parameters for maximal clinical benefit can be a difficult and time consuming process that typically requires a highly trained and experienced individual to achieve acceptable results. To address this limitation we developed a Windows-based software package (StimExplorer) intended to aid the clinical implementation of DBS technology. StimExplorer uses detailed computer models to provide a quantitative description of the 3D volume of tissue activated (VTA) by DBS as a function of the stimulation parameters and electrode location within the brain. The DBS electric field models explicitly incorporate the capacitance of the electrode-tissue interface, tissue encapsulation of the electrode, and diffusion-tensor based 3D tissue anisotropy and inhomogeneity. The VTA is predicted with models of axonal activation resulting from the applied field. The stimulation models are tailored to the individual patient by reading in their magnetic resonance imaging (MRI) data and interactively scaling 3D anatomical nuclei to fit the patient anatomy. The user also inputs the DBS electrode orientation, location, and impedance data. The software then provides theoretically optimal stimulation parameter suggestions, intended to represent the start point for clinical programming of the DBS device. The software system is packaged into a clinician-friendly graphical user interface that allows for interactive 3D visualization. The goals of the StimExplorer system are to educate clinicians on the impact of stimulation parameter manipulation, and improve the customization of DBS to individual patients.**

I. Introduction

The realization that high frequency stimulation generates clinical benefits analogous to those achieved by surgical lesioning has transformed the use of functional neurosurgery for the treatment of movement disorders. Deep brain stimulation (DBS) is an established therapy for essential tremor, Parkinson's disease, and dystonia. In addition, DBS shows promise in the treatment of additional neurological disorders such as epilepsy, obsessive-compulsive disorder, and depression. However, the clinical successes of DBS are tempered by our limited understanding of the effects of DBS on the nervous system.

Converging theoretical [1,2] and experimental results [3] suggest that the therapeutic mechanisms of DBS may rely on the activation of axons surrounding the electrode, resulting in an override of pathological neural activity patterns [4]. However, no quantitative measures of the size and shape of the 3D volume of axonal activation generated by DBS currently exist within the clinical arena. In turn, the selection of therapeutic stimulation parameters for DBS can be a difficult and time consuming process. A recent clinical study found that the total time spent programming the stimulator and assessing DBS patients ranged from 18-36 hours per patient [5]. Further, it is infeasible to clinically evaluate each of the thousands of stimulation parameter combinations that are possible. As a result, the therapeutic benefit achieved with DBS is strongly dependent on the intuitive skill and experience of the clinician performing the programming.

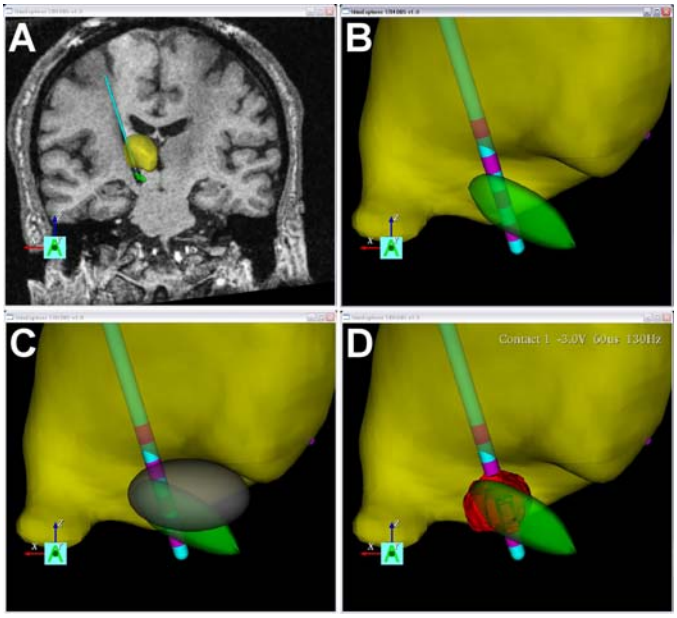

Figure 1: StimExplorer model of STN DBS. Successive screen shots from the customization of the StimExplorer software to an individual patient are displayed. A) Anatomical nuclei (thalamus – yellow; subthalamic nucleus – green) are scaled to match the MRI and the DBS electrode is placed within the context of the brain volume. B) Zoomed in region of interest. C) Black volume represents the target volume of tissue for therapeutic STN DBS for Parkinson's disease. D) Theoretically optimal stimulation parameter settings are identified (contact 1, -3V, 60μs, 130 Hz) and the resulting VTA (red) is displayed.

The fundamental purpose of DBS is to modulate neural activity with applied electric fields, but most clinicians implementing DBS technology do not have a quantitative understanding of the effects of manipulating the various stimulation parameters on the neural response to the stimulation. To address this limitation, we developed detailed computational models that accurately estimate the volume of tissue activated (VTA) by DBS as a function of the

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stimulation parameters (contact, impedance, voltage, pulse width, frequency) and electrode location in the brain [2,6,7,8,9]. However, the computational power and computer science skills necessary to effectively implement such models are not available to most clinicians. Therefore, we developed a Windows-based, clinician-friendly software package (StimExplorer) to aid the post-operative programming of DBS (Fig. 1).

II. Methods

The purpose of the StimExplorer system is to integrate our theoretical understanding of the effects of DBS into clinically useful tools for the analysis and customization of stimulation parameters for individual patients [10] (Fig. 1). Our patient-specific models of DBS consist of three fundamental components: 1) Anatomical Model, 2) Electrical Model, and 3) Stimulation Prediction. These three components are co-registered within a common coordinate and visualization system to enable analysis of the position of the electrode in the brain and the VTA generated by DBS. The software was written using VTK (Visualization Toolkit; Kitware, Clifton Park, NY) and Tcl/Tk (Tool Command Language; http://tcl.sourceforge.net). Version 1.1 of StimExplorer for DBS of the subthalamic nucleus (STN) for the treatment of Parkinson's disease (PD) is self-contained on a single DVD, and auto-installs on a PC similar to any traditional Windows software.

A. Anatomical Model

The anatomical model is developed based on pre- and/or post-operative magnetic resonance imaging (MRI) data (Fig. 1A). When the user starts the StimExplorer program they navigate to the directory containing the DICOM files of interest and load the images into StimExplorer. The user then selects the right or left side of the brain for analysis, orients the image along the midline, and defines the anterior commissure (AC) and posterior commissure (PC) in the image. The next step in the process consists of scaling and positioning 3D anatomical representations of the STN and thalamus. The anatomical nuclei are originally positioned within the context of the MRI based on the definition of the AC and PC. However, the user has the option to translate and/or scale the anatomical nuclei along the anterior/posterior, dorsal/ventral, and medial/lateral axes to enable the most accurate match possible with the MRI.

Once the anatomical model has been customized to the individual patient, the user must define the position and orientation of the DBS electrode in the brain (Fig. 1A). This can be done using stereotactic surgical coordinates, where the user inputs the X, Y, and Z location of the electrode tip relative to mid-commissural point, and defines the electrode trajectory angles relative to the sagittal and coronal planes. Or if a post-operative MRI is available the user can interactively place the DBS electrode in the electrode artifact of the image data set.

B. Electrical Model

The electrical model utilized in the StimExplorer system is based on our previous work characterizing the electric field generated by DBS and neural response to the applied stimulation [2,6,7,8,9]. The foundation of the electrical model is a high resolution diffusion tensor MRI brain atlas [11]. The electric field generated by DBS is dependent on the stimulus waveform, electrode capacitance, electrode impedance, electrode geometry (monopolar/bipolar), and the electrical conductivity of the surrounding tissue medium. The diffusion tensor data is used to estimate the inhomogeneous and anisotropic electrical conductivity of the tissue medium surrounding the STN, thereby allowing for the generation of anatomically and electrically accurate models of the electric field generated by DBS electrodes [2].

C. Stimulation Prediction

All of the DBS VTA calculations utilized in StimExplorer were performed on an 8 processor SGI Prism with 36 GB of shared memory. The conductivity tensors from the voxel-based DTI data were dynamically mapped to individual elements in a tetrahedron-based 3D FEM of the electrode and surrounding medium [2,9]. The FEM was solved; resulting in a potential distribution (V_e) in the tissue medium that was dependent on the stimulus waveform, stimulus amplitude, electrode capacitance, electrode impedance, and electrode contact selected. The neural response to extracellular stimulation is related to the second spatial derivative of the extracellular potential distribution along a given neural process ($\partial^2 V_e/\partial x^2$) [12]. Therefore, we performed thousands of simulations of the response of multi-compartment cable models of myelinated axons [13] to the applied electric field generated by DBS electrodes. These simulations were used to develop quantitative relationships that describe the threshold $\partial^2 V_e/\partial x^2$ for axonal activation as a function of distance from the electrode [2,8] (Fig. 3B). These relationships were developed for a range of stimulation parameters applicable to DBS. In turn, we calculated the $\partial^2 V_e/\partial x^2$ within the context of our human DBS FEM and defined 3D surfaces that encompass the volume where $\partial^2 V_e/\partial x^2$ was suprathreshold for axonal activation for the given stimulation parameters (contact, impedance, voltage, pulse duration, frequency). In turn, each electrode position, electrode orientation, and stimulation parameter setting has a unique VTA that can be displayed in StimExplorer as a pre-complied solution from our supercomputer simulations.

III. Results

Several studies have determined that clinically effective STN DBS for PD is typically achieved with electrode contacts located at or near the dorsal border of the STN [14,15]. We defined a 3D target VTA for STN DBS for PD that consists of the dorsal STN and the fields of Forel. For each electrode position and orientation option provided in StimExplorer, we employed a volume-based optimization algorithm to define stimulation parameter settings representative of the

theoretically optimal VTA. The optimization algorithm utilized the following equation to score each VTA:

$$Score = \frac{VTA_{in}}{Target} \; x \left(1 - \frac{VTA_{out}}{Reference}\right)$$

The theoretically optimal VTA is provided to the clinician as a suggested starting point for the programming process (Fig. 2). StimExplorer also provides the ability to visualize the VTA for any range of stimulation parameter settings for additional clinical analysis. Once the user has customized the StimExplorer system to an individual patient, they can save the MRI orientation, anatomical nuclei scaling, DBS electrode placement, and stimulation parameter settings to a file. The user can then revisit any given patient with StimExplorer by simply loading the appropriate file when starting the program.

IV. Discussion

StimExplorer uses pre-compiled results from our supercomputer simulations of DBS that explicitly account for the effects of electrode capacitance, electrode impedance, 3D tissue electrical properties of the human brain, and the neural response to applied electric fields. The stimulation results are coupled to 3D anatomical models of nuclei surrounding the electrode, and enable the clinician to interactively evaluate the effects of electrode location and stimulation parameter adjustments on the VTA. To customize the StimExplorer system to an individual patient, the clinician inputs MRI data, electrode position and orientation information, as well as the impedance of each electrode contact. Our definition of a target VTA for STN DBS allows StimExplorer to provide suggested theoretically optimal stimulation parameter settings that can represent the start point of clinical programming of the DBS device. The intended benefits of using the StimExplorer system are decreased time and effort needed to adjust the stimulation parameters to achieve the desired clinical results from the therapy. In addition, StimExplorer may decrease the level of intuitive skill necessary to perform DBS programming, provide a teaching tool on the effects of DBS, and enable a degree of standardization in programming practices across centers.

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Conflict Of Interest Statement

CRB and CCM are shareholders in IntElect Medical Inc., license holder for the neurostimulation prediction, visualization, and optimization intellectual property utilized in StimExplorer.

References

[1] McIntyre CC, Grill WM, Sherman DL, Thakor NV. Cellular effects of deep brain stimulation: model-based analysis of activation and inhibition. *J. Neurophysiol.* 2004; 91(4): 1457-69.

[2] McIntyre CC, Mori S, Sherman DL, Thakor NV, Vitek JL. Electric field and stimulating influence generated by deep brain stimulation of the subthalamic nucleus. *Clin. Neurophysiol.* 2004; 115: 589-95.

[3] Hashimoto T, Elder CM, Okun MS, Patrick SK, Vitek JL. Stimulation of the subthalamic nucleus changes the firing pattern of pallidal neurons. *J. Neurosci.* 2003; 23(5):1916-23.

[4] Montgomery EB, Baker KB. Mechanisms of deep brain stimulation and future technical developments. *Neurol. Res.* 2000; 22(3):259-66.

[5] Hunka K, Suchowersky O, Wood S, Derwent L, Kiss ZH. Nursing time to program and assess deep brain stimulators in movement disorder patients. *J. Neurosci. Nurs.* 2005; 37(4):204-10.

[6] Butson CR, McIntyre CC. Tissue and electrode capacitance reduce neural activation volumes during deep brain stimulation. *Clin. Neurophysiol.* 2005; 116: 2490-2500.

[7] Butson CR, Maks CB, McIntyre CC. Sources and effects of electrode impedance during deep brain stimulation. *Clin. Neurophysiol.* 2006; 117(2): 447-54.

[8] Butson CR, McIntyre CC. Role of electrode design on the volume of tissue activated during deep brain stimulation. *J. Neural Eng.* 2006; 3(1):1-8.

[9] Butson CR, Cooper SE, Henderson JM, and McIntyre CC. Patient-specific analysis of the volume of tissue activated during deep brain stimulation. *NeuroImage* (submitted for review).

[10] Butson CR, Maks CB, Cooper SE, Henderson JM, and McIntyre CC. Deep brain stimulation interactive visualization system. *Society for Neuroscience* 2005; 898.7.

[11] Wakana S, Jiang H, Nagae-Poetscher LM, van Zijl PCM, Mori S. Fiber tract-based atlas of human white matter anatomy. *Radiology* 2004; 230: 77-87.

[12] Rattay F. Analysis of models for external stimulation of axons. *IEEE Trans. Biomed. Eng.* 1986; 33(10):974-7.

[13] McIntyre CC, Richardson AG, and Grill WM. Modeling the excitability of mammalian nerve fibers: influence of afterpotentials on the recovery cycle. *Journal of Neurophysiology* 2002; 87(2): 995-1006.

[14] Saint-Cyr JA, Hoque T, Pereira LC, Dostrovsky JO, Hutchison WD, Mikulis DJ, Abosch A, Sime E, Lang AE, and Lozano AM. Localization of clinically effective stimulating electrodes in the human subthalamic nucleus on magnetic resonance imaging. *Journal of Neurosurgery* 2002; 97(5): 1152-66.

[15] Nowinski WL, Belov D, Pollak P, and Benabid AL. A probabilistic functional atlas of the human subthalamic nucleus. *Neuroinformatics* 2005; 2(4): 381-98.