Title: Optimizing the Delivery of Deep Brain Stimulation Using Electrophysiological Atlases and an Inverse Modeling Approach

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ABSTRACT:

The use of deep brain stimulation (DBS) for the treatment of neurological movement degenerative disorders requires the precise placement of the stimulating electrode and the determination of optimal stimulation parameters that optimally reduce symptoms (e.g. tremor, rigidity, movement difficulties, etc.) while minimizing undesired physiological side-effects. This study demonstrates the feasibility of determining the ideal electrode placement and stimulation amplitude by performing a patient-specific multivariate optimization using electrophysiological atlases and a bioelectric finite element model of the brain. Future work involves optimization validation clinically and improvement to the accuracy of the model.

Preferred Presentation Type: Either

Keywords: Deep brain stimulation, Finite element modeling, Optimization.

PURPOSE

Deep brain stimulation (DBS) is a potentially effective treatment for neurological movement degenerative disorders like Parkinson's disease and Dystonia. The treatment, however, is still in its developmental stages and its mechanism is still not fully understood. Currently, electrode positions are determined based on intraoperative observations from trial stimulations using intraoperative electrodes. Permanent postoperative electrodes are then implanted at those pre-determined positions and stimulating parameters explored during postoperative programming. Both types of electrodes function by stimulating subcortical structures believed to affect the involuntary movements brought on by the disorders. The hypothesis is that this process may miss potentially more effective single/multi-electrodeconfigurations as an exhaustive search intraoperatively is prohibitive. The goal of this study is to perform a formal multivariate optimization for the intraoperative electrode placement and stimulation amplitude using probabilistic electrophysiological maps of the brain and a computational bioelectric model. The maps are based on an extensive collection of intraoperative patient data and are nonrigidly registered to the patient-specific preoperative images to provide the most likely candidate efficacy and undesired side-effect zones in the patient's brain [1, 2]. The optimum electrode configuration found in the intraoperative setting should provide the best initial guess towards optimizing the final postoperative therapeutic programming of the implants.

METHODS

Bioelectric Finite Element Model

A 3-dimensional finite element model of 5 intraoperative DBS electrodes inserted into brain tissue was created using COMSOL version 4.0a (COMSOL, Inc., Burlington, MA). To simulate the potential distribution resulting from stimulation, Laplace's equation for conductive media was used,

$$\nabla \cdot (-\sigma \nabla V) = 0 \quad (1)$$

where σ is the conductivity and V is the potential. In this preliminary work, the brain tissue geometry was represented as a cylinder consisting of about 80,380 tetrahedral elements and assumed to be homogeneous and isotropic with conductivity of 0.3 S/m [3]. Since the primary focus of this study is to optimize the electrode(s) placement and amplitude(s) of stimulation, capacitive effects were neglected and electrostatic conditions were assumed which allowed for tractable computation time using the multi-physics solver COMSOL linked with MATLAB (MathWorks, Inc., Natick, MA). The 5 DBS electrode configuration (FHC, Inc., Type D: Differential microTargeting Electrode)involves a central electrode with the remaining 4 electrodes being placed a distance of 2 mm anterior, posterior, lateral, and medially, respectively. Each electrode consisted of a conducting contact, an insulating shaft and a larger grounded cannula (Figure 1). To simulate a distant ground, the sides of the brain cylinder were specified to have a Dirichlet boundary condition of V = 0. Current sources were assigned to the 5 contactsand allowed to vary in magnitude and position. Since the 5-electrode implant method is constrained to move along insertion tracks, variability in position is a one degree of freedom translation in the direction of depth. A full remeshing of the geometries occurred with each adjustment in electrode depth.

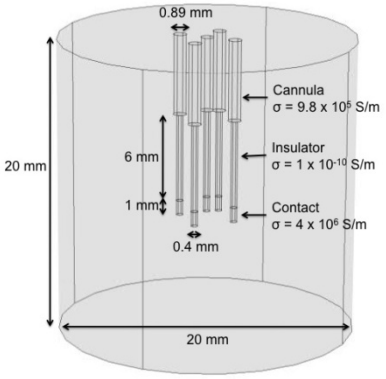

Figure 1. Model of the 5 intra-operative DBS electrodes within the cylindrical brain tissue geometry. The conducting contacts are at the tips and separated from the thicker grounded cannula by the insulating shaft in between.

Optimization

Desired stimulation efficacy zones from efficacy map (***E***) and undesired side-effect zones from side-effect map (***S***) are physiologically triggered when the brain tissue potential at those locations becomes elevated above a certain tissue activation voltage (TAV) level (TAV = -0.7 V [4]). The goal of the optimization is to position and power the 5 electrodes such that the electric potential distribution produced is sufficient to activate high-efficacy zones for therapeutic benefit while avoiding activation of the side-effect zones. Towards this goal, the objective function for minimization was written as,

$$\boldsymbol{min}\{\boldsymbol{G}(\boldsymbol{A_i})\} = \mathbf{1} - \frac{\sum_{i=1}^{N} \boldsymbol{E_i'} \boldsymbol{A_i}}{\mathbf{1}+\sum_{i=1}^{N} (\mathbf{1}-\boldsymbol{E_i'}) \boldsymbol{A_i}} + \frac{\sum_{i=1}^{N} \boldsymbol{S_i'} \boldsymbol{A_i}}{\mathbf{1}+\sum_{i=1}^{N} \boldsymbol{A_i}} \quad (2)$$

where ***E'*** and ***S'*** are the normalized efficacy and side-effect maps (values range from 0 to 1 with values of unity indicating high efficacy or high side-effect, respectively) and are interpolated to 3D image volume grid associated with the patient. Normalization by the maximum value in each map was required to equalize the

weighing factors from both maps. ***A*** represents a binary mask of the tissue activated volume determined by the electric potential solved by COMSOL. Specifically, with each candidate depth and electrode amplitude, COMSOL is invoked to calculate the potential field which is then interpolated onto the same 3D image volume as the probabilistic maps. The electric potentials at the *i'th* voxel over *N* voxels are used to generate a binary mask whereby all regions above the TAV are assigned unity. The general construction of the objective function in Eq. 2 is to select configurations that attempt to improve the ratio of activated efficacious regions over those that are not efficacious while simultaneously penalizing configurations that improve the ratio of activated side-effect regions over the activated regions.

The global minimization function *patternsearch* in MATLAB was used for the multivariable optimum search. It has the potential to avoid local minima by being set-based method instead of gradient-based. Briefly, a set of points for evaluation is first determined and their objective functions calculated and polled to find their minimum. If a minimum is found, then polling is successful and the domain for the next set of points is decreased. Otherwise, the domain is increased to expand the search area. The process is repeated until the convergence tolerance to the objective function is reached. The initial guess for electrode depths was set at the center of the maps and at half maximum amplitude (-7.9mA) for all electrodes. The optimization was constrained with lower and upper bounds for electrode depthat -5 and +5 mm, respectively from the initial implant depth. Their amplitudes were constrained from -15.9 to 0 mA.

RESULTS

The optimum depth and amplitude for the 5 electrodes are tabulated in Table 1. No power was needed for the center, anterior and posterior electrodes. For the lateral electrode, even though power was delivered, the electrical potential generated was not sufficient to activate the nearby brain tissue, but it was high enough to influence the tissue activation shape at the medial electrode. Figure 2 shows the optimized brain tissue activation regions (based on the optimum configuration in Table 1) overlaid with efficacy and side-effect maps of a candidate patient. Despite having no single electrode trajectory path that passes through the heart of the efficacy region (circled in Figure 2a), the optimization routine is able to find the next most efficacious location while avoiding the high side-effect regions. Additionally, in data not reported here, simulated efficacy and side-effect maps were generated to further validate Eq. 2.

Table 1.Optimum depth and amplitude for the 5 electrodes.

	Center	Anterior	Posterior	Lateral	Medial
Depth [mm]	5.00	5.00	2.50	-0.31	3.59
Amplitude [mA]	0.0	0.0	0.0	-1.2	-2.0

BREAKTHROUGH WORK

There has been research in the simulation of DBS via finite elements methods [5,6], but no work to our knowledge has involved the optimization of the surgical procedure itself via a coupled modeling/probabilistic map inverse framework as performed here.

CONCLUSIONS

Computational multivariate optimization of electrode placement and amplitude in DBS based on electrophysiological atlases is feasible and can be easily calculated as part of the trajectory planning steps. Ultimately, this additional bit of information may provide the best patient-specific electrode configuration for

use during preoperative planning, intraoperative navigation and postoperative programming phases. Future work involves improving the accuracy of the models with more realistic tissue properties and simulating more realistic stimulation settings with time dependent analysis. Lastly, further testing of the objective function and validation with clinical observations will have to be performed too. Nevertheless, this paper offers an exciting new modeling framework within the field of DBS therapeutic delivery.

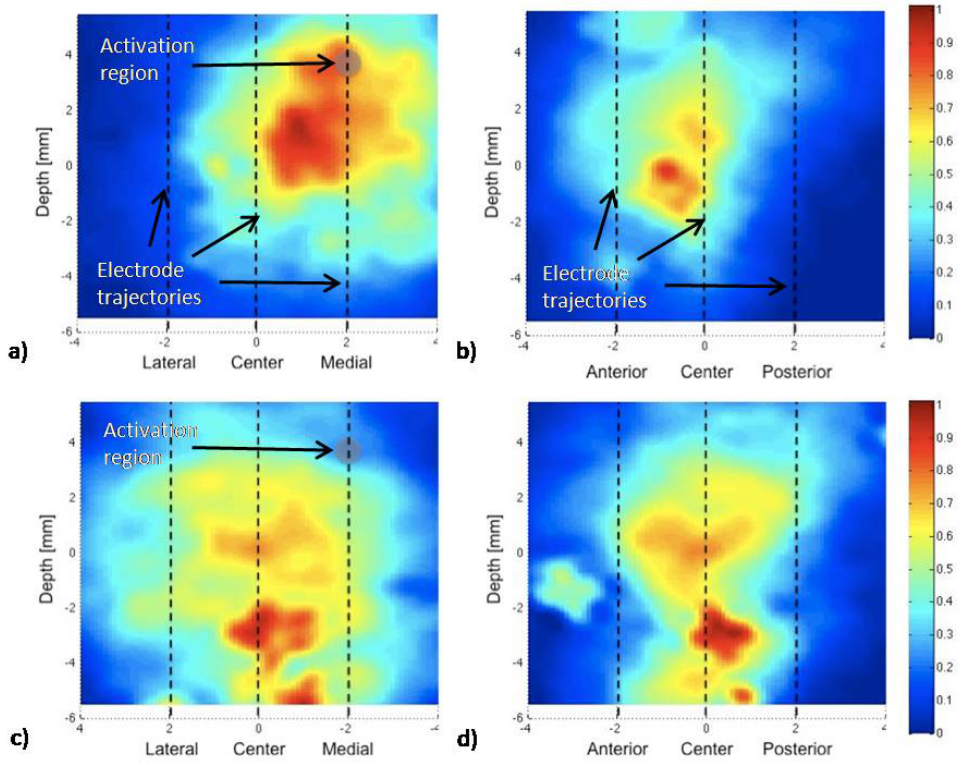

Figure 2. Cross-sectional views of the optimized brain tissue activation region (in grey) overlaid with the (a-b) efficacy and (c-d) side-effect map (colored). Unity is at the highest efficacy or side-effect. Dashed lines represent the electrode trajectories.

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