The Virtual Patient Simulator of Deep Brain Stimulation in the Obsessive Compulsive Disorder Based on Connectome and 7 Tesla MRI Data

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Abstract— **We present work in progress on the virtual patient model for patients with Deep Brain Stimulation (DBS) implants based on Connectome and 7 Tesla Magnetic Resonance Imaging (MRI) data. Virtual patients are realistic computerized models of patients that allow medical-device companies to test new products earlier, helping the devices get to market more quickly and cheaply according to the Food and Drug Administration. We envision that the proposed new virtual patient simulator will enable radio frequency power dosimetry on patients with the DBS implant undergoing MRI. Future patients with DBS implants may profit from the proposed virtual patient by allowing for a MRI investigation instead of more invasive Computed Tomography (CT) scans. The virtual patient will be flexible and morphable to relate to neurological and psychiatric conditions such as Obsessive Compulsive Disorder (OCD), which benefit from DBS.**

Keywords-virtual patient simulator; VPS; deep brain brain stimulation; DBS; obsessive compulsive disorder; OCD; MRI; CT; MRI safety; specific absorption rate; SAR; connectome; 7 Tesla MRI

I. INTRODUCTION

A. MRI safety in Deep Brain Stimulation (DBS)

Many DBS patients will require regular MRI examinations throughout the course of their lives since MRI is often the diagnostic tool of choice for monitoring structural changes in the brain. Because of safety concerns to the patients approximately 300,000 people per year are denied MRI and the associated health implants such as Implantable Cardioverter Defibrillator (ICD) and DBS leads as well as guide wires and catheters. One of the main concerns of use of MRI for DBS implants is related to potential RF – heating [1]. The Radiofrequency (RF) waves used in MRI to elicit signal from the brain tissue interact with the conductive leads generating potentially high induced currents ("antenna effect") and related increased RF power deposition at the tip of the leads [2]. Several cases of permanent neurological injury were recently reported [3]. The conditions in which currently DBS are indicated for MRI are extremely restrictive. In these patients it is only possible to image with head coils, so that any other part of the body is contraindicated. Also, only transmit-receive heads coil are indicated and the current state-of-the-art MRI receive coils multichannel coils are completely contraindicated. In the near future, the use of MR imaging in these patients will become more and more problematic following the manufacturer guidelines. This is of the upmost importance for the 300,000 people who are denied MRI.

B. Lack of a gold standard DBS Virtual Patient Simulator (VPS)

The state-of-the-art numerical DBS modeling is based on a wire or set of wires, which represents the virtual DBS implant, superimposed to healthy human brains [4]. Several numerical models for electromagnetic analysis of DBS have been proposed [5-9]; however they are incomplete since they do not take in consideration an accurate anatomical modeling of the structures involved in the stimulation, anisotropic dielectric constants, information about head perfusion and the tissue scar from the surgery. Therefore, we need knowledge about the i) anatomy, ii) conductivity and permittivity along x, y, z, iii) blood vessels and iv) encapsulating tissue around the electrodes.

C. Importance of structural MRI-based modeling

The Ventral Capsule/Ventral Striatum (VC/VS) in the Anterior Limb of the Internal Capsule (ALIC, which is approximately 20 mm long in its dorsoventral extension and 2-5 mm wide mediolaterally at the coronal sections where the nucleus accumbens is present) is currently a target for DBS in Obsessive-Compulsive Disorder (OCD) (Medtronic, Minneapolis, MN) (Fig.1). Importantly, a small structure within this large territory, namely the ventromedial Prefrontal-Basal Ganglia (vmPFC-BG) tract is thought to be a more specific target for this procedure in OCD. The latter is a relatively small fiber bundle, of about 2 mm diameter, which courses approximately 4-5 mm above the nucleus accumbens interconnecting ventral prefrontal cortex with basal ganglia [10].

D. Importance of Connectome-based modeling

Anisotropy of electrical properties of tissue arises in nerve and muscle fibers which consist of bundles of long, parallel myelinated elements. Diffusion Tensor Imaging

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(DTI) data will be used to model tissue anisotropic conductivity. In general, we will convert the acquired diffusion tensor **D** into a complex relative permittivity tensor ε* using a simple linear transform $\boldsymbol{\varepsilon}^* = \frac{\varepsilon^*}{d} \cdot \mathbf{D}$ where ε* is the tissue complex relative permittivity [11] and d is the diffusivity. Our preliminary data (Fig. 1B) show that Connectome MRI data (voxel size: 2 × 2 × 2 mm^3) could be reliable in identifying the fiber tracks connecting vmPFC and BG. The gradient strength determines the sensitivity, accuracy, and resolution of diffusion imaging. The connectome MRI is a new scanner purpose-built for diffusion MRI with ultra-high gradients of 300 mT m^{-1}, more than three times stronger than any previously achieved in human subjects. The new Connectome scanner at the A. A. Martinos Center has reduced read out time , increased time-efficiency, and improved structural resolution with reduced diffusion time. Recent data show that this technology allows for enhanced sensitivity and resolution of white matter imaging and MRI tractography of 5-10 fold over any other human DTI or High-Angular Resolution Diffusion Imaging (HARDI) such as the Diffusion Spectrum Imaging (DSI) technology. We will be generating fiber tracks by using spatial information derived from high spatial resolution ex-vivo diffusion imaging (voxel size: 100 μm isotropic). Finally, VPS with DBS have been proposed for real time MRI surgical guidance, we propose to develop a post-operative VPS tool for safe MRI.

E. Importance of Computed Tomography Angiography (CTA)-based modeling

Heat transport in biological tissues, which is usually expressed by the Pennes bio-heat equation, is a complicated process since it involves thermal conduction in tissues, convection and perfusion of blood (delivery of the arterial blood to a capillary bed in tissues). We propose to model the heat transfer from the blood to the tissue (q_p) in the Pennes bio-heat equation as a term proportional to the temperature difference between the arterial blood entering the tissue and the venous blood leaving the tissue. A total of continuous 15 minutes exposure to heating may result reversible thermal lesions occur at 42–44°C, and irreversible lesions occur at temperatures greater than 45°C. At higher temperatures, the thermal damage depends on both the temperature levels and the time of exposure. Since ex-vivo CTA is a standard tool in micro vasculature modeling, we will use CTA with contrast agents containing large barium or iodine particles to elucidate vascular tissues in 3D.

F. Importance of Tissue Scaring around the DBS Electrode

Chronically implanted recording electrodes provoke an immune reaction against them. The histopathological finding is that of gliosis and spongiosis around the electrode track, which forms an encapsulation layer referred to as the "glial scar". This reactive glial tissue which surrounds the implanted electrodes is approximately 200 μm thick and progressively isolated the electrode from surrounding neurons modifying the electric field and acts as a natural neuro protector against heating of the electrode tips. We will model the conductivity and permittivity of the scar tissue at the frequency of interest (124 MHz). The scar tissue will affect the bio-heat modeling behaving as a thermal insulating shield, thus improving the accuracy of the model.

G. Impact of the new RF pulse

The issue of heating of implants during MRI has been studied [12] and analytical solutions (Green's function) to the problem have been proposed for simple geometries. Modifications of the implant leads and wires for reducing the RF-induced heating have been proposed introducing chokes or special geometrical paths of the wire. However, all of these leads design modifications may be not appropriate for patients who already have DBS implants, since replacing the original leads with these modified safer leads requires major brain surgery. Since the heating due to conductive wires depends on the phase distribution of the MRI transmit field, the modification of the transmit field to minimize the electric field in and around the implant to minimize the RF pickup of the DBS wire is critical.

II. METHODS

A. Overview of study design

The study is based on *ex-vivo* analysis of collected 7 Tesla (7T) T2* and Connectome diffusion MRI data.

(a) <u>*Structural T2* 7 Tesla MRI*</u> The model is generated by segmenting 21 different brain structural entities on the *ex-vivo* structural MRI, as well as 28 non-brain structural entities following the approach described in Makris and colleagues [13]. This *ex-vivo* brain consisted of MRI data of a hemisphere fixed in Periodate-Lysine-Paraformaldehyde (PLP) using the following parameters: T2*-W, 100 μm^3 isotropic resolution, TR/TE/flip=40ms/20ms/20°, 1600×1100×896 matrix. Segmentation of OCD-DBS target-related cerebral structures, specifically the putamen, caudate nucleus, nucleus accumbens and anterior limb of the internal capsule were manually outlined (on a re-sampled dataset at 1 mm isotropic spatial resolution of the original *ex-vivo* high-resolution (100 μm^3 isotropic resolution) dataset acquired at 7 Tesa) using the segmentation methods by Filipek [14] and Makris [15], which have been developed and validated at the MGH Center for Morphometric Analysis, and have been implemented in several clinical studies (Fig. 1A). The VC/VS in the ALIC is currently a target for DBS in OCD (Medtronic). Importantly, a structure within this large territory, namely the vmPFC-BG tract is thought to be a more specific target for this procedure in OCD. This is a relatively small fiber bundle, however, by reaping the benefits of the high-resolution dataset, we will segment the ALIC/VS as follows. The anterior limb of the internal capsule is delimited medially by the head of the caudate nucleus, laterally by the putamen and ventrally by

the nucleus accumbens. These structures were delineated by direct visualization using intensity-based contours in the Cardviews software system). *(b) Connectome DSI data* are transformed into DTI data to estimate complex relative permittivity tensor $\hat{\varepsilon}^* = \frac{\varepsilon^*}{d} \cdot \mathbf{D}$, introduced above. The vmPFC-BG tract is delineated using diffusion Connectome data as shown in Fig. 1B. DTI/DSI data are visually validated by comparing the computed fiber tracks with since the VPS is meant to be used for 3T scanners with head transmit birdcage coil, where the quasi-static approximation applies. Finally, the simulations are tested by following the same procedure for the published CHEMA model [4] and running the FDTD simulations described in this paragraph. This data are then resampled at 1mm^3 and compared with our published results and [4] only if the error of the 10g - averaged SAR data is within 20% the test is considered passed.

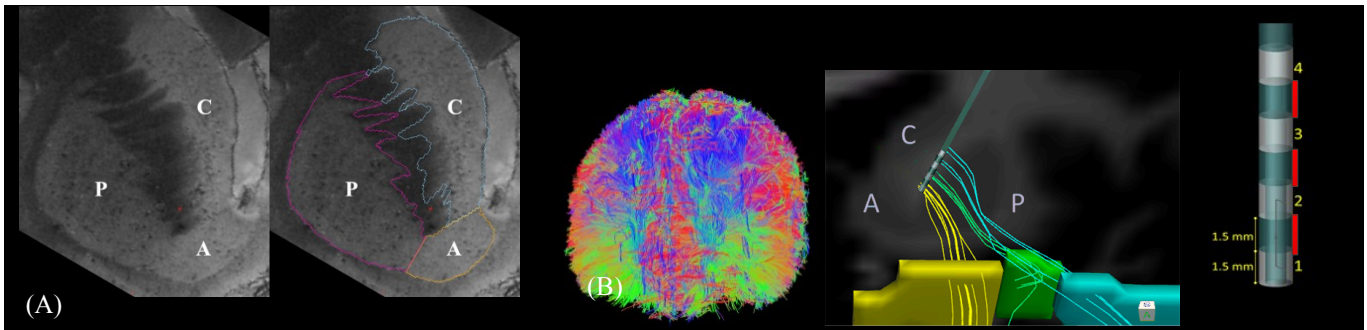

Fig. 1. (A) *Coronal section at the C.A.P. (Caudate-Accumbens-Putamen) level of a 7T high-resolution (100 µm3 isotropic) ex-vivo human dataset showing detailed anatomy of the VC/VS target area (cross-hair in red) within the anterior limb of the internal capsule.* ***(B) :*** *(left) DSI connectome data set, (middle) electrode placement in the VC/VS target area traversed by fibers (yellow fibers) of the ventromedial prefrontal-basal ganglia tract at the C.A.P. coronal slice. The latter fibers stem from the ventromedial prefrontal area (yellow block). (A=nucleus accumbens, C=caudate nucleus, P=putamen), and (right) electrode geometry with the proposed embedded thin solid state temperature sensor film (red).*

anatomical atlases with particular emphasis to the basal ganglia region as shown in Fig. 1A. Finally, DTI/DSI data provide detailed information on the fiber tract connectivity between the ventromedial prefrontal cortex and basal ganglia that is useful for DBS programming [16] and basic neuroscience research.

B. Numerical Model of Deep Brain Stimulation implant

One or two bilateral implants, as shown by the post-operative MRI, are modeled as insulated wire(s) connected to the left and/or right targets in the head [3]. The wires are modeled as a Perfect Electrical Conductor (PEC) and the dielectric is modeled as Teflon. A four-electrode connection [16] and the scar tissue are modeled in full detail reaping the benefits of the proposed 100 µm^3 isotropic resolution based on the actual Medtronic electrode set that will be used. The four electrodes are modeled as PEC and the scar tissue is modeled with the known dielectric properties. We model only the head without the shoulders,

III. RESULTS

Our preliminary results are principally in identification and segmentation of the OCD target structures for DBS using high-resolution T2*-W and diffusion spectrum MRI data and electromagnetic simulations for MRI safety. Given that this is work in progress our pilot data provide a basis for validation and completion of the VPS database.

In Fig. 1 (A and B), we show data from a manual segmentation procedure to outline the different anatomical structures related to the VC/VS target area derived from a high-resolution 7 Tesla dataset and DSI-based tractography. In Fig. 2, we present a geometrical model of the coil array and the VPS model [13] with examples of different parallel transmit excitation phases and the resulting B_1 maps (nT/ampere) [18].

IV. DISCUSSION

Clinical work in obsessive-compulsive disorder (OCD) indicates that several compulsive behaviors in this disorder

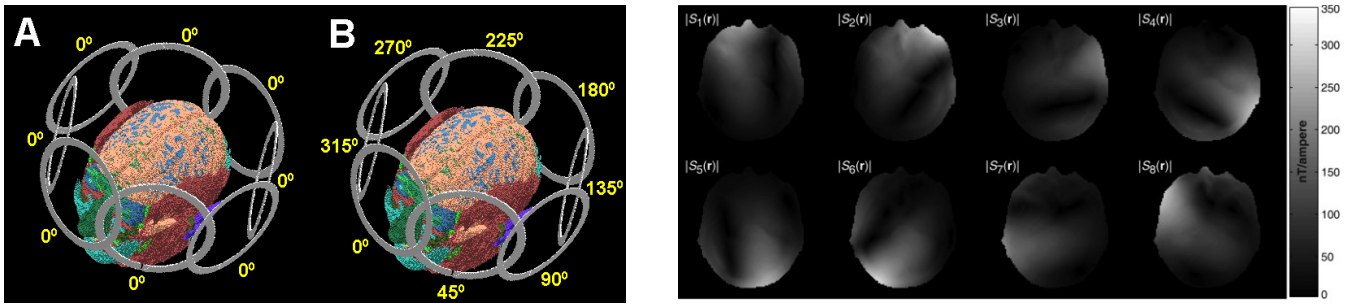

Fig. 2 (Left) Geometrical model of the coil array and our model [13] with examples of null (A) and uniform (B) $\vec{\varphi}$ vectors [17]. (Right) 8-channel transmit phase array FDTD B_1 maps (nT/ampere) of the center transverse slice of our model when each channel is driven with a 1-ampere peak-to-peak 300-MHz sinusoid [18].

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are related to avoidance of putative dangerous situations. The neural system that mediates avoidance is the same one that also underlies reward-seeking and comprises (anterior cingulate/orbital)-Basal-Ganglia (BG) connections. DBS is a therapeutic procedure aiming to change activity in fronto-basal ganglia circuits by injecting electrical stimulation in the Ventral Anterior Internal Capsule (VA-ALIC) and adjacent Ventral Striatum (VS), i.e., nucleus accumbens septi. In many OCD patients the benefits of DBS as a therapy outweighs the risks of surgery. However, there have been reports of serious accidents associated with magnetic resonance imaging (MRI)-related heating [3]. OCD patients with DBS would benefit from regular MRI examinations, as MRI is often the diagnostic tool of choice to diagnose injury due to trauma or evaluate comorbidities (e.g., stroke, cancer, etc.). The Food and Drug Administration (FDA) has approved the use of DBS leads by restricting the use to transmit head only coils and fields up to 1.5 Tesla. However, excluding the use of 3 Tesla systems severely limits MRI as a diagnostic tool. There are over 75,000 patients with DBS implants worldwide and only approximately one patient in twenty is assessed with (FDA restricted) MRI. In this pilot study investigating the VPS application in patients with DBS implants we gathered preliminary results on the anatomical characterization of the OCD target structures for DBS using high-resolution 7 Tesla and Connectome MRI data and performed electromagnetic simulations for MRI safety. VPS are realistic computerized human models that allow medical-device companies to test new products earlier, helping the devices get to market more quickly and cheaply according to the FDA. We envision that the proposed new OCD VPS will enable radio frequency (RF) power dosimetry on patients with DBS implants undergoing MRI. Based on VPS dosimetry, we will be able to modify ad hoc the MRI parameters to allow for MRI acquisition on patients with DBS implants in situ. Future OCD patients with DBS implants may profit from the proposed VPS by allowing for a MRI investigation instead of more invasive computerized tomography (CT) scans.

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