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A Comparative Study of the 3D Precentral Gyrus Model for Unipolar and Bipolar Current Stimulations

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Abstract— **Cortical stimulation (CS) is an appealing method for treating stroke and other disorders by promoting functional recovery. It is necessary to study the effect of different cortical stimulation types through numerical simulations in order to understand the underlying mechanism. In this paper, we simulated four types of invasive CS – unipolar ECS (epidural CS), bipolar ECS, unipolar SCS (subdural CS), and bipolar SCS – to investigate and compare the effects of stimulation types. Current stimulation was considered to increase the observability of the comparison between ECS and SCS. The simulation results obtained from the 3D precentral gyrus model showed ECS and SCS had similar current density distributions with higher stimulated current. However, the differences between bipolar and unipolar stimulation are significant with higher stimulated current. As stimulated current increased, unipolar CS penetrated deeper and wider regions than bipolar CS, so it can be more effective for functional recovery.**

I. INTRODUCTION

Cortical stimulation (CS) has been widely used to treat stroke and other disorders by promoting functional recovery [1-4]. Recent studies have reported that performed CS via an invasive or noninvasive approach is more effective than other extensive therapies. Invasive CS has shown better performance than noninvasive CS, especially in chronic pain and movement disorders [1, 2]. With invasive CS, there is no report to discuss parameters, such as the location of implanted electrodes and polarity of electrodes, in a solid computational way. It means such parameters are usually determined at clinician's discretion.

Invasive CS can be classified as epidural cortical stimulation (ECS; electrode located above the dura mater) and subdural cortical stimulation (SCS; electrode placed on the cerebral surface), depending on the location of the implanted electrode. ECS is more generally used due to a lower risk and higher success rate than SCS [1]. SCS is also needed because ECS cannot stimulate some patients who have advanced cortical atrophy due to duro-cortical separation.

In addition to the location of the electrode, it is necessary to determine the polarity of each electrode for stimulation. Implanted electrodes can have either the same polarity or opposite polarity. When electrodes have the same polarity, it is called unipolar CS; otherwise, it is called bipolar CS. Several references noted that unipolar stimulation is more effective than bipolar stimulation for improving the motor performance of stroke patients in practical CS [3, 4, therein]. The researchers experienced that unipolar stimulation reaches deeper regions than bipolar stimulation, but this has not been clearly studied on the computational domain. In this work, we would like to investigate how each method (SCS or ECS, unipolar or bipolar) yields current density distribution (CCD) effectively and assess how they differ.

In recent our work [5], SCS and ECS were numerically simulated using voltage stimulation to understand the differences between them. However, it was difficult to observe differences in the current density between ECS and SCS because the output current from electrodes made it hard to be consistent. In the voltage stimulation, a constant current condition could be not controlled because the conductivity beneath the electrode differs between ECS and SCS. Therefore, voltage stimulation is difficult to analyze to understand the difference between ECS and SCS.

Previous studies have shown the effects of unipolar and bipolar CS [6, 7]. However, their focus was not on comparing bipolar and unipolar stimulation, [6] and the comparison was enforced under SCS, but ECS [7]. For these reasons, in this work, we simulated four types of invasive CS – unipolar ECS, bipolar ECS, unipolar SCS, and bipolar SCS – to study the effects of stimulation types and differences among them. We numerically experimented with the current stimulation so that we can fix the output current of electrodes to increase the observability of the comparison between ECS and SCS. For assessing efficiency of CS, from current density distributions we quantified the volume and depth of the brain region on which neurons excited by passive stimulation exist.

II. METHODS

In this section, we describe the computational models. The three-dimensional computational models for ECS and SCS we used is described in Section II.A, the setup for unipolar and bipolar stimulations and electrodes are addressed in Section II.B, and the analysis method using the quantitative approach is described in Section II.C.

A. Modeling of 3D computational models

The three-dimensional computational models are restricted to the precentral gyrus and surrounding sulci and gyri. The models consist of white matter, gray matter, cerebrospinal fluid (CSF), dura mater, and skull, as displayed in Fig. 1. The model dimensions and conductivities are obtained from the literature and are tabulated in Tables 1 and 2, and the dimension of our computational models is 13.4 x 12 x 12 cm^3.

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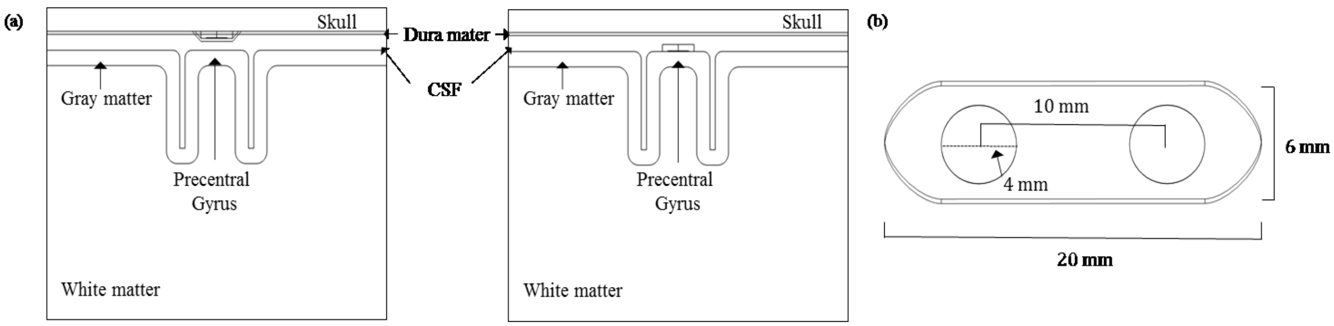

Figure 1. The 3D computational model: (a) cross-section of the extracted ECS model; (b) cross-section of the SCS model; (c) strip electrode.

One 6 x 20 mm^2-sized strip electrode is then epidurally or subdurally implanted. The electrode (4 mm diameter) is attached with 10-mm contact spacing that is referenced by a Wyler subdural grid electrode array configuration (Ad-Tech Medial Instruments, Racine, WI, USA).

TABLE I. CONDUCTIVITIES OF TISSUES AND ELECTRODES [8]

Compartment	*Conductivity (S/m)*
Substrate conductivity	0.1×10^{-9}
Electrode conductivity	9.4×10^{6}
Skull	0.01
Dura mater [9]	0.065
CSF	1.65
Gray matter	0.276
White matter	0.126

TABLE II. MODEL DIMENSION OF TISSUES AND ELECTRODES [7, 10]

Property	*Dimension (mm)*
Skull thickness	5
Dura mater	0.5
CSF	2.6
Gray matter thickness	2.5
Precentral gyrus width	12
Central sulcus width	1
Precentral sulcus width	1
Central sulcus depth	16
Precentral sulcus depth	16
Electrode thickness	0.1
Substrate thickness	1.8

B. Parameters of the electrodes for comparison

There are three types of parameters for the simulations: 1) placement of electrodes (SCS or ECS); 2) current stimulation or voltage stimulation; and 3) the polarity of each electrode.

Comparison of both SCS and ECS were first performed under current stimulation (to our best knowledge, they have not yet been compared under the same stimulated current). The SCS electrodes were more deeply located than those of the ECS. Although SCS is riskier than ECS, SCS has been considered as an efficacious method with the exception of its risk. In addition, SCS has been known to have a lower performance rate than ECS [1]. However, the differences in these two approaches have not been shown clearly to date. By simulating both SCS and ECS under the constant current condition, we expect to have a better understanding of their characteristics.

It is suitable to compare simulation results for current stimulation when the same current is stimulated. However, the output current from the electrode cannot be fixed in the voltage stimulation and also changes under various conditions, such as conductivity and geometry. Hence it is not easy to compare the simulation results with voltage stimulation due to the different stimulated current. For the polarity of each electrode, we use both unipolar and bipolar stimulation. Several references noted that unipolar stimulation is more effective in improving the motor performance of stroke patients in practical CS than bipolar stimulation [3, 4] because unipolar stimulation tends to stimulate deeper regions than bipolar stimulation. However, to our best knowledge, this has not been clearly studied. Here we investigate such phenomenon further and show how unipolar and bipolar stimulations differ.

In this work, the stimulation currents are considered for two cases. One is below 1 mA, and the other is above 1 mA. The empirical parameter of the input current is below 6.5 mA [11] with stimulation up to 15 mA [12], suggesting that human brains accommodate higher stimulated currents. In this paper, we investigated varying simulated currents (from 0.2 to 1.0 mA and from 1.0 to 9.0 mA) to observe the tendency of lower and higher input currents.

C. Quantitative measurement

We analyzed the effect of the cortical simulations using a quantitative interpretation in terms of the current density and estimated the volume and depth of the region that is evoked so as to excite neurons (i.e., the effective volume and depth [5]). The effective volume and depth represent quantities that are above 50% of the threshold of current density. The threshold was defined by the minimum value needed to excite neurons in the motor cortex, considered as 2.5 A/m^2 in the literature [13]. In practical cases, 50% or less of the threshold has usually been used in CS in order to avoid seizure. In this study, we selected the percent of the threshold as 50%, which lies in the range of the practical usage case.

The effective volume and depth were measured in both the gray and white matter, and the effective depth just beneath the electrode surface was computed. The Dirichlet boundary condition (grounded) was applied to all boundaries except the

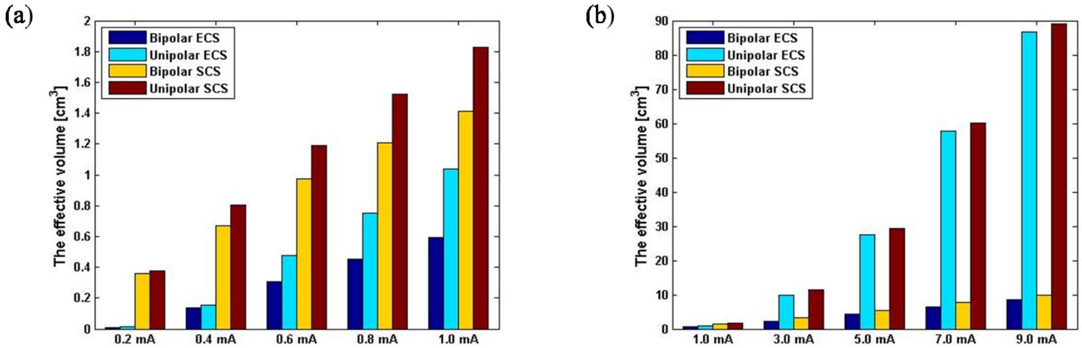

Figure 2. The effective volumes of four type of invasive CS are (a) in the 0.2 to 1.0 mA range and (b) in 1.0 to 9.0 mA range.

upper boundary of the skull for unipolar CS, but all sides were insulated for bipolar CS.

III. Experiments and Results

We performed numerical experiments and observed the characteristics and differences of the four types of invasive CS – unipolar ECS, bipolar ECS, unipolar SCS, and bipolar SCS – by increasing the stimulated current.

A. Configuration of the simulations

We used a desktop computer (Inter i7 Quadcore CPU at 3.4 GHZ, 64 bit OS, and 16 GM RAM) for the computation, and the finite element models were implanted in COMSOL Multiphysics (Version 4.2; Burlington, MA). The number of total tetrahedral mesh elements was about 250,000, and it did not affect the analysis of effective volume. When we increased or decreased the number of mesh elements by four times, the effective volume was changed 5% or less. For accurate computation, we used the linear direct solver with LU decomposition, which took about 50 seconds for each model.

B. SCS versus ECS

First, we compared unipolar SCS and ECS. The difference between the SCS and ECS volumes shown for low current input [Fig. 2(a)] was considerable, but both effective volumes became similar for high current input [Fig. 2(b)]. The ratio of ECS to SCS volumes was 56.7% under 1.0 mA, but it became 97.5% under 9.0 mA. The ECS increase rate grew quickly in terms of the effective volume, and the differences became smaller as the stimulated current increases. The differences between the SCS and ECS volumes were less than 10% when the input current was over 5.0 mA. The effective depth of ECS was 5.4 times larger than that of SCS under 0.2 mA, but the differences in depths decreased with higher stimulated current, similarly to the effective volumes. The differences in the SCS and ECS depths were less than 10% under 7.0 mA, decreasing as the stimulated current increased.

The comparison between bipolar SCS and ECS showed the similar tendency in regards to effective volume, but the overall value was lower than in the unipolar approach because the increase rate of the bipolar SCS and ECS volumes was quite smaller than the unipolar SCS and ECS volumes. The differences between the SCS and ECS volumes were less than 20% with the 7.0 mA input current. The effective depth of ECS was 2.0 times larger than that of SCS under 1.0 mA. However, the differences of depths became gradually smaller with higher stimulated current.

C. Unipolar versus bipolar stimulation

The current density distribution (CDD) of both unipolar and bipolar CS is illustrated in Fig. 3. The CDD of unipolar stimulation seems to spread wider, and the bipolar stimulation looks more concentrated in comparison. Unipolar and bipolar stimulation showed close amount of high magnitude of CDD with 1 mA, but their differences increased as stimulated current got higher.

The effective volume of unipolar CS was much bigger than that of bipolar CS, and the differences in volumes increased (Fig. 2). The effective volume of unipolar SCS was almost the same as that of the bipolar SCS volume with 0.2 mA, but it was more than three times when the simulated current was above 3.0 mA. The differences between depths also increased with higher stimulated current. The increase rates of the effective depths were two and four times for bipolar and unipolar SCS, respectively, from 1.0 to 9.0 mA. Due to a low increase rate of the effective depth of bipolar SCS, it could not penetrate the deep region of the brain, whereas unipolar SCS was able. The comparisons of unipolar and bipolar CS are in a similar pattern for both ECS and SCS.

D. Comparison with four types of invasive CS

We simulated invasive CS under lower and higher stimulated currents (below or above 1.0 mA). When stimulated current was below 1.0 mA, SCSs had bigger effective volumes than ECSs though the increasing rates of each were different [Fig. 2(a)]. However, since the effective volume of unipolar ECS increased considerably, unipolar ECS and SCS had similar effective volumes from 3.0 to 9.0 mA [Fig. 2(b)]. The effective depth of SCSs had bigger value than ECSs until 3.0 mA stimulated current. The unipolar ECS became similar with unipolar SCS at stimulated current above 5.0 mA.

IV. Discussion

In this paper, we compared four types of invasive CS: SCS, ECS, unipolar CS, and bipolar CS. Compared with ECS, the

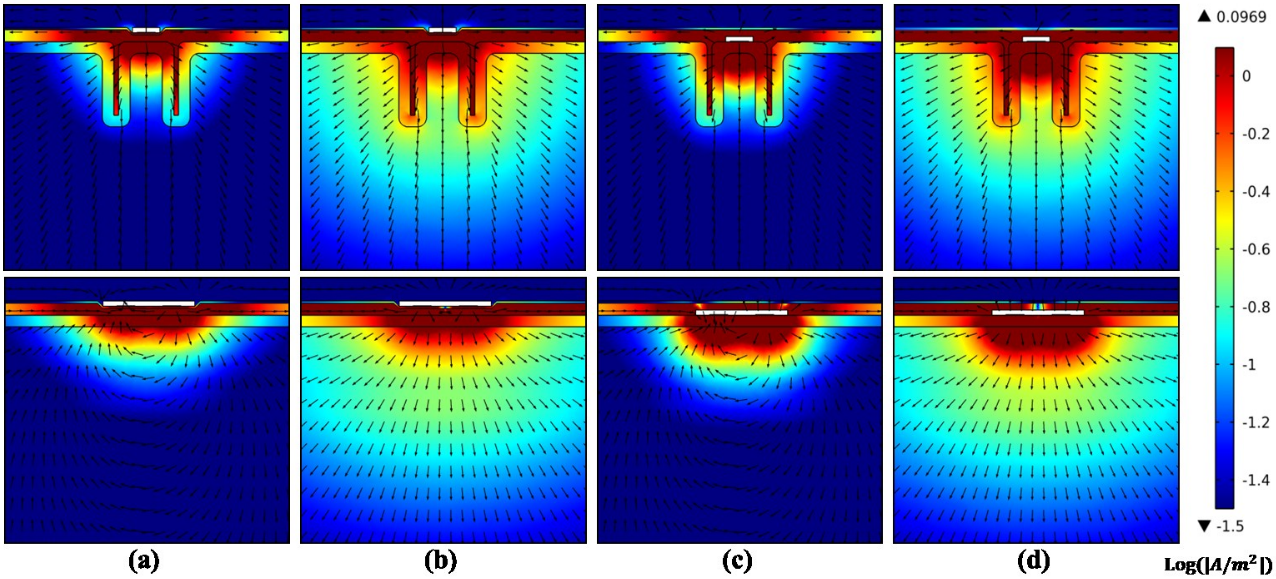

Figure 3. The current density distribution generated by 1.0 mA. The above pictures are cross-sections of model made perpendicular to extrusion direction, and the below pictures are parallel to the extrucsion direction; these are through the middle of the electrodes. (a) Bipolar ECS, (b) Unipolar ECS, (c) Bipolar SCS, (d) Unipolar SCS

electrode for SCS was located deeper, so we expected that SCS would cover a wider and deeper cortical area than ECS. In a previous study, SCS was found to be more effective, and the differences between the effective volumes and depths increased as the injection voltage increased [5]. However, the result in this paper was the opposite results found in [5] because when the same constant voltage was injected, ECS and SCS led to different output currents, as the conductivities below the implanted electrode differed. Under a constant stimulated current, the differences between volumes and depths were quite small, and the differences became smaller as the stimulated current increased.

Several researchers have reported that unipolar stimulation performed better than bipolar stimulation in practical CS [3, 4]. These researchers assumed that unipolar stimulation can reach a deeper region, but that assumption has not been verified. In this paper, we simulated both approaches and showed that unipolar stimulation penetrated deeper and wider than bipolar stimulation. According to the numerical results, the differences between volume and depth increased as the value of the stimulated current increased. Unipolar stimulation may stimulate the larger brain cortical region, indicating that unipolar stimulation can enhance the chances of obtaining a therapeutic effect. Therefore, unipolar stimulation can be more effective for functional recovery than bipolar stimulation.

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