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ORIGINAL ARTICLE

COMETS: A MATLAB Toolbox for Simulating Local Electric Fields Generated by Transcranial Direct Current Stimulation (tDCS)

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Abstract
Purpose Three-dimensional (3D) numerical computation of electric fields generated by transcranial direct current stimulation (tDCS) has widened our insight into the underlying mechanisms of current conduction, accelerated the development of novel electrode montages, and enabled more accurate field concentrations to targeted brain areas. However, there is no well-established field simulator specifically designed to analyze electric fields due to tDCS.
Methods We developed a MATLAB-based toolbox, *COMETS* (COMputation of Electric field due to Transcranial current Stimulation), for simulating local electric fields generated by tDCS. Since *COMETS* has a simple and interactive graphical user interface, users can readily simulate various electrode configurations, sizes, and orientations without coding any MATLAB scripts. *COMETS* evaluates 3D cortical current distributions based on the electrostatic finite element method (FEM).
Results Although only a standard human head model is provided in the current version, users may import their own head model datasets for specific research. For advanced 3D visualization of the resultant cortical current distributions, output data can also be exported to readily accessible ASCII-format data files. The toolbox package is freely available at http://www.COMETStool.com for noncommercial and academic uses.
Conclusions It is expected that our toolbox *COMETS* can contribute to popularizing the numerical analysis of cortical stimulation current in the field of noninvasive electrical brain stimulation.

Keywords Transcranial direct current stimulation (tDCS), Finite element method (FEM), Electrostatic field, MATLAB toolbox, *COMETS*

INTRODUCTION

Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that can modulate cortical excitability by transmitting direct current (DC) between a pair of scalp electrodes [1-4]. Extensive studies have shown that anodal and cathodal DC stimulation can facilitate and inhibit cortical excitability, respectively, although the exact underlying mechanisms have not yet been revealed [5, 6]. Since the late 1990s, tDCS have been studied in a variety of clinical fields as a potential treatment modality for neuropsychiatric diseases and neurological disorders including stroke, depression, epilepsy, Alzheimer's disease, chronic pain, and Parkinson's disease [4, 7-12] Although the effect of tDCS is similar to that of repetitive transcranial magnetic stimulation (rTMS), tDCS has garnered attention from the neuroscience field because of its advantages over rTMS, including better mobility, increased safety, and lower cost [4, 6].

Since no imaging modality can image the cortical electric field distribution generated by tDCS, electric field distributions are generally estimated from computer-based numerical field simulations [13-19]. Indeed, computer-based tDCS analyses have many virtues. Since it is difficult to precisely predict modulated cortical areas due to the non-uniform conductivity values of head compartments and the edge effect [14], realistic three-dimensional (3D) numerical simulations can help researchers determine electrode locations that elicit

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increased stimulating currents at target brain areas. Recent studies have achieved enhanced field concentrations in target brain areas by using 3D electric field analyses [20-22], actualizing customized and individualized noninvasive brain stimulation. Moreover, 3D field simulations based on the finite element method (FEM) elucidated the underlying mechanisms of current conduction [13, 14, 16, 20, 23-25], accelerated the development of new electrode montages [16, 17, 19, 20], and decreased the amount of massive experimental studies needed to verify the safety of DC stimulations [18]. However, because there has been no open software package designed to simulate electric fields generated by tDCS, only a few research groups could use this important technology.

In the present study, we developed a MATLAB toolbox, *COMETS* (COMputation of Electric field due to Transcranial current Stimulation), for simulating local electric fields generated by tDCS. *COMETS* has interactive graphical user interfaces (GUIs), enabling even inexperienced users to simulate various electrode montages, sizes, and orientations without coding any MATLAB script. *COMETS* is based on an FEM program coded with Fortran 90, which was also used in our previous tDCS simulation studies [17-19]. Although only a standard human head model is provided in the current version, advanced users may import their own head model datasets for their specific purposes. The remainder of this paper introduces implemented methods and representative examples of the *COMETS* toolbox.

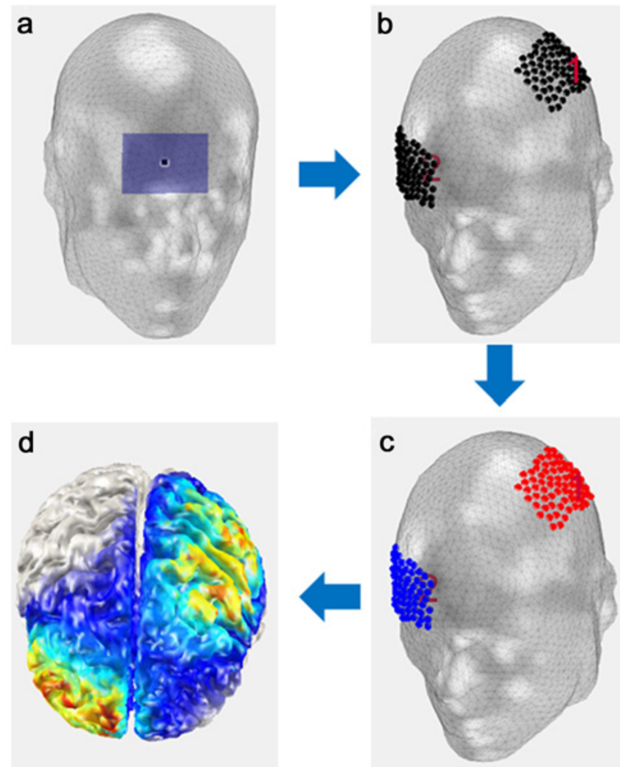

Fig. 1. Procedure of *COMETS* toolbox: (a) center locations, sizes, and orientations of rectangular electrodes are determined on the scalp surface, (b) two rectangular electrodes are mapped onto the curved scalp surface and nodes included in the electrode area are selected, (c) different input current values (unit: mA) are assigned to each electrode, (d) electric field distribution on the tessellated cortical surface is evaluated and visualized.

METHODS

Overview of the toolbox

COMETS requires a MATLAB environment but does not need any supplementary MATLAB toolboxes such as the signal processing toolbox, spline toolbox, or statistical toolbox. The GUIs of *COMETS* allow users to intuitively analyze electric field distributions on the cortical surface without MATLAB scripting. Users can select various locations for cathode and anode electrodes and also adjust the size and orientation of each electrode. Fig. 1 shows the *COMETS* toolbox procedure. First, the center locations, sizes, and orientations of rectangular electrodes are determined on a scalp surface tessellated with triangular elements (upper left panel). Second, two rectangular electrodes are mapped onto the curved scalp surface considering a geodesic distance, and scalp nodes included in the electrode areas are selected (upper right panel). Third, users can assign different input current values (unit: mA) to each electrode (lower right panel). Last, electric field distribution on the tessellated cortical surface is evaluated and visualized (lower left panel). Users can probe the resultant field quantities at any selected cortical vertex and also select various visualization options, such as show/hide electrode locations, toggle on/off 10-20 EEG electrode locations, show/hide electrode numbers, show/hide scalp surface, show/hide cortical surface, and show/hide/adjust color bar. There are also useful options for controlling the visualized images, including 3D rotate, move, zoom in/out, adjust degree of transparency, turn light on/off, change background color, view/hide mesh, and view/hide axis (grid and axis-marker). Fig. 2 shows two *COMETS* GUI modes, one for setting cathode and anode electrodes (Fig. 2a), and the other for visualizing output field distribution on the cortical surface (Fig. 2b). The electrode locations used for a specific simulation can be saved into a MATLAB .MAT file and can be reloaded at any time. ASCII-format output files that can be imported in the commercial 3D visualization program Tecplot® (Tecplot Inc., WA, US) or the free 3D visualization program MeshViewer (http://mview.sourceforge.net) are automatically generated in the main folder of the toolbox after each finite element analysis.

Generation of a head-cortex model

The human head model embedded in the *COMETS* toolbox

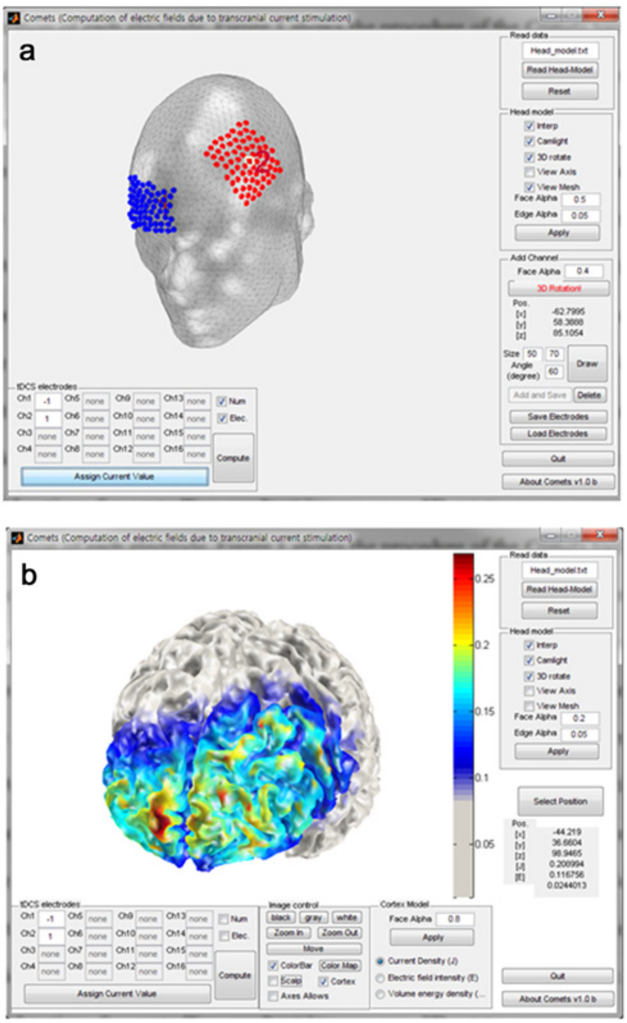

Fig. 2. Two graphical user interface (GUI) modes: (a) a GUI mode for setting cathode and anode electrodes, (b) a GUI mode for visualizing output field distribution.

was extracted from the standard Montreal Neurological Institute (MNI) brain atlas [26]. A three-layer boundary element model consisting of the scalp, and outer and inner skull boundaries as well as a sophisticated cortical surface model were extracted from MRI T1 images of the standard brain atlas using CURRY6 for windows (Compumedics, Inc., El Paso, TX, US). The integrated model was tessellated with volumetric tetrahedral elements using the open-source mesh generation software package TetGen (http://tetgen.belios.de), which is based on the constrained Delaunay tetrahedralization (CDT) approach [27].

Since the inhomogeneous electrical conductivity distribution of a human head cannot be accurately estimated even with the best imaging modalities, well-known effective electrical conductivity values of head structures were used. Effective electrical conductivity values for the scalp, skull, and CSF regions were set as 0.22, 0.014, and 1.79 (S/m), respectively [28]. The conductivity difference between CSF and the brain was ignored because of the increased complexity of the finite element model that eventually led to a considerably increased computational burden. Indeed, this simplification has been a widely-accepted assumption in the field of electroencephalography (EEG) forward problems (e.g., CURRY6 also adopts this assumption, according to Fuchs [29]). Electric field intensity and current density on the sophisticated cortical surface model were calculated by linear interpolation of finite element analysis results. Resolution of the analysis model was determined after careful consideration of computational time. The finite element model consists of 13,914 nodes and 80,592 tetrahedral elements, while the cortical surface model is composed of 25,945 cortical vertices and 52,052 triangular elements. It takes 35 seconds to compute field distribution on the cortical surface with an Intel Core2Quad 2.83 GHz 4G-DRAM personal computer. Advanced users can generate their own head models using individual subjects' MRI data or other standard brain atlases. Conversion programs are also provided in the *COMETS* toolbox download webpage. Fig. 3 illustrates the overall procedures of model generation and computation.

3D Finite element method

3D FEM was adopted to analyze the electric field intensity and current density inside a human head produced by tDCS. Considering direct current conduction, the following electrostatic Laplace equation was used as the governing FEM equation:

$$\nabla \cdot (\sigma \nabla V) = 0\,, \tag{1}$$

where σ and V represent electrical conductivity and electric potential, respectively. A first-order finite element formulation and incomplete Cholesky conjugate gradient (ICCG) matrix solver [30] were used. The convergence criterion of ICCG was $|\mathbf{A}\boldsymbol{x} - \mathbf{b}| / |\mathbf{b}| < 1.0 \times 10^{-14}$, where $\mathbf{A}$, $\boldsymbol{x}$, and $\mathbf{b}$ represent the stiffness matrix, the unknown vector, and the forcing vector, respectively. Two electrode pads were modeled as two sets of surface nodes, each with different Dirichlet-type boundary values, -1 V and 1 V, respectively. Electric field intensity and current density were evaluated for every volumetric tetrahedral element using the solution of (1) and then transformed into a node-wise form by linear interpolation. The total injection current value was computed by integrating the total current density under each surface electrode pad area. The average difference between total injection currents of the two electrodes was less than 5% of the absolute injection current value in the simulations. Based on linearity between the total injection current and the current density at each node, current density vectors in the entire analysis domain were scaled by a ratio of the target injection current

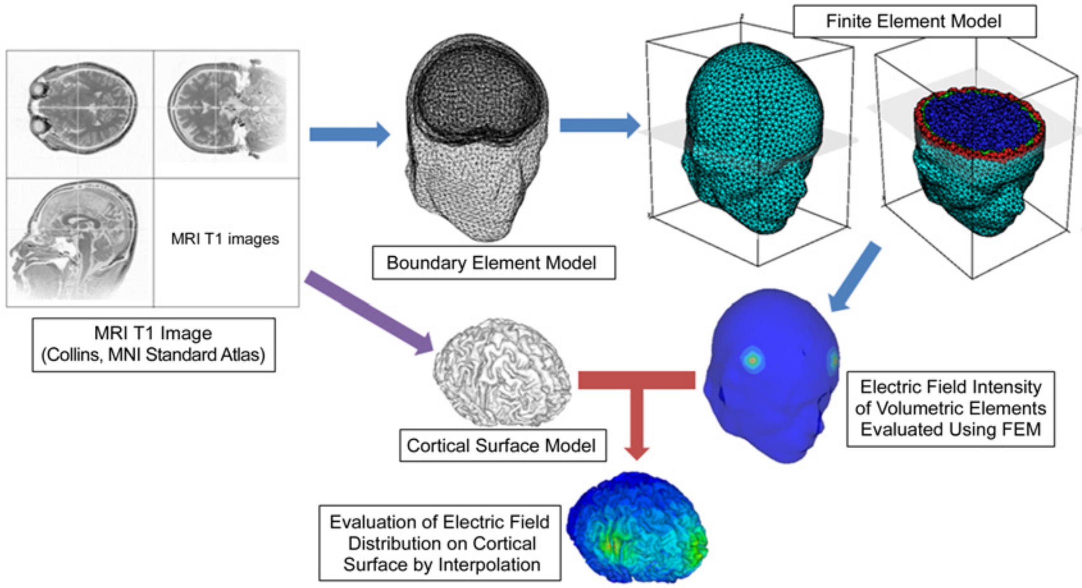

Fig. 3. Overall procedure for model generation and analysis. Finite element model for analysis was generated from the boundary element model extracted from MRI T1 images. Electric field distribution on the cortical surface was evaluated by interpolating the electric field intensity of volumetric elements.

(e.g., 1 mA) to the computed total injection current. This led to a result for constant current injection through a pair of electrode pads (e.g., injection current of each pad: 1 mA and -1 mA, respectively). All numerical analyses were performed using an optimized in-house FEM program coded using Fortran 90 [17-19].

RESULTS

This section introduces three representative examples that illustrate the potential applications of the *COMETS* toolbox, which are: 1) Simulation for finding optimal electrode configuration to facilitate excitability of foot motor area; 2) Finding electrode locations that increase current density at a specific target point; and 3) Investigating the influence of different anatomical structures upon the resultant electric field distribution.

Simulation for finding optimal electrode configuration

In this example, *COMETS* was used to compare cortical current distributions simulated for three different electrode configurations to increase the excitability of the foot motor area. Fig. 4 shows three different electrode configurations and the resultant cortical current density distributions evaluated using *COMETS*. In all three simulations, the anode electrode (size: 5 × 7 cm) was attached at the vertex of the scalp (Cz location). In Figs. 4a-c, cathode electrodes (size: 5 × 7 cm) were attached at the left supraorbital area, right mastoid process, and neck, respectively. Since the current version of *COMETS* can only visualize the superficial cortical surface, current density distributions on the medial wall were visualized by importing and processing an ASCII-format *COMETS* output file in Tecplot®. The color map range for medial views was set differently from that used in *COMETS* to highlight current distributions on the medial wall. When the reference (cathode) electrode was attached to the right supraorbital area, as shown in Fig. 4a, the maximum electric field was generated at a location slightly outside the target area (right below the active electrode) toward the reference electrode. This phenomenon has been reported in many previous computer simulation studies [14, 15, 22]. Conversely, when extracephalic reference electrodes were assumed, as in Figs. 4b and 4c, the resultant cortical current distributions were not significantly different from each other. In addition, larger current densities were generated around the foot motor area than when the cephalic reference electrode was used. These results are in accordance with those of our previous studies that investigated the influence of extracephalic reference electrodes on current distributions inside the human body [18]. A comparison of the two cases (Figs. 4b and 4c) showed that deeper areas were stimulated when the reference electrode was attached to the neck. Likewise, *COMETS* can simulate and compare a variety of electrode configurations. This will help researchers find appropriate electrode configurations for specific tDCS applications.

Finding electrode location that increase current density at a target

As already illustrated, maximum current density may not be

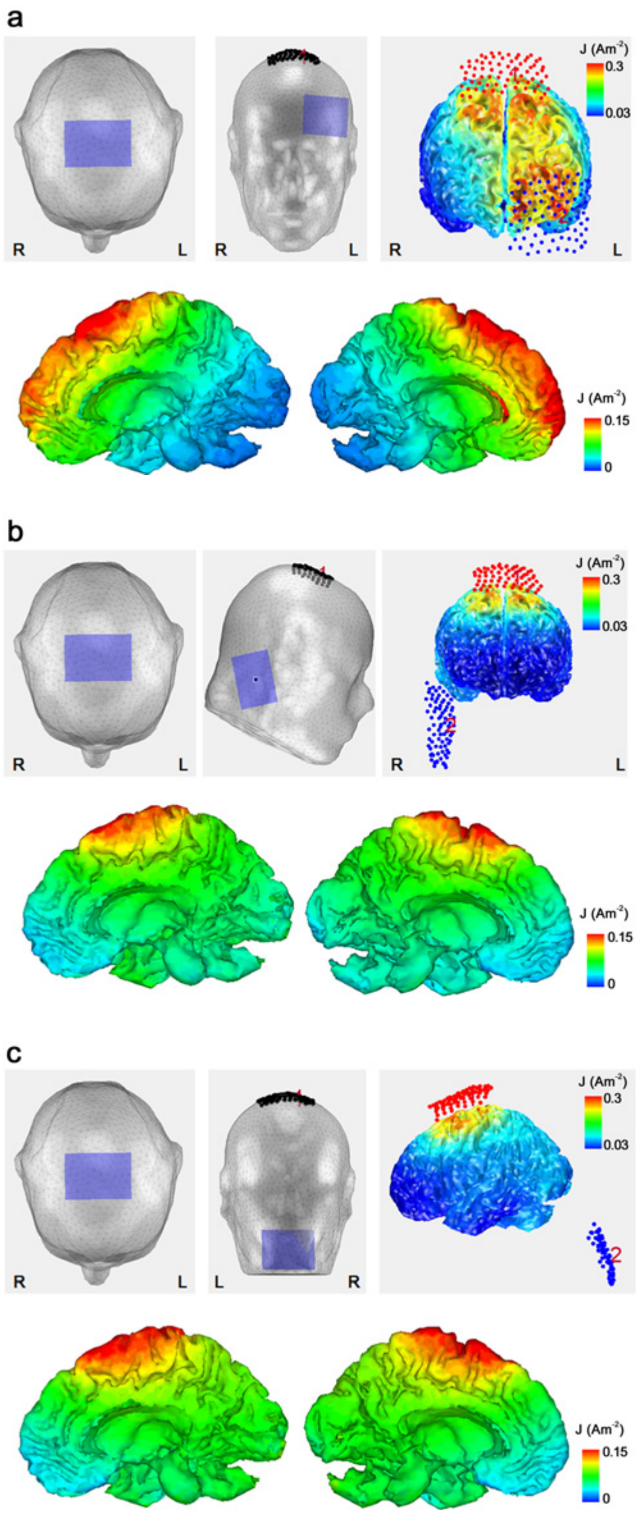

Fig. 4. Current density distributions evaluated using *COMETS* toolbox for three different electrode configurations. In all three simulations, the anode electrode was attached at the vertex of the scalp (Cz location). Cathode electrodes were attached at (a) left supraorbital area, (b) right mastoid process, and (c) neck. In each figure, the upper three panels show the electrode locations and the current density distributions on the outer cortical surface, and the lower figures show the current distributions on the medial wall of cerebral cortex. 'R' represents 'Right' and 'L' represents 'Left'.

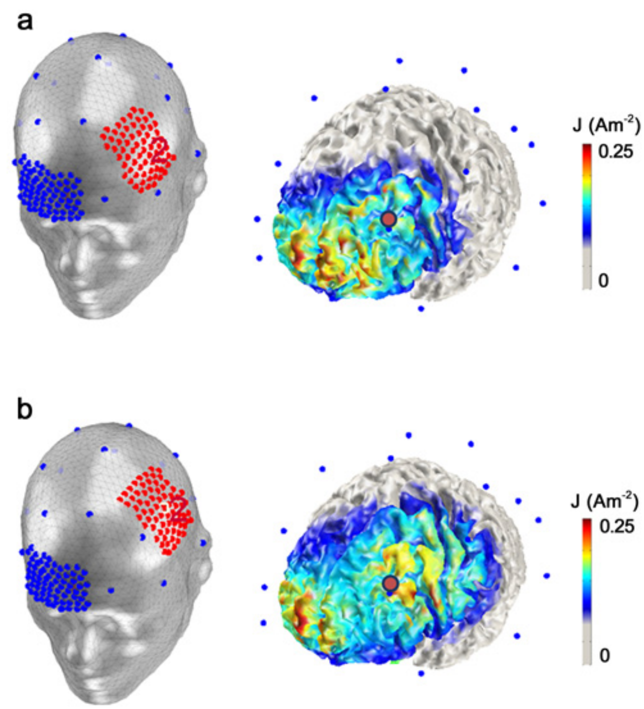

Fig. 5. Examples demonstrating changes in cortical current density distributions due to variations in anode electrode location. In both simulations, the cathode was attached at the right supraorbital area and the anodes were attached at (a) F3 and (b) FC3 locations. In Figs. (a) and (b), the left panel shows the electrode locations on the scalp surface and the right panel shows cortical current density distribution. The red dot with a black border represents the target cortical area (right below F3 location: inferior dorsolateral prefrontal cortex).

formed directly below the active electrode, especially when two electrodes are located at a close distance [15, 18]. Electric field simulation using *COMETS* can be utilized to find electrode locations that increase current density at a target position. Fig. 5 shows two examples of analysis results obtained with *COMETS*. In both simulations, the cathode electrode was attached at an identical location (right supraorbital area) using the *COMETS* "save/load electrode locations" function. The target cortical area was below the F3 electrode (international 10-20 system) and roughly corresponded to the inferior dorsolateral prefrontal cortex (DLPFC). Fig. 5a shows cortical current density distribution when the anode electrode was attached at the F3 location according to the international 10-20 system. Both anode and cathode electrodes were 5 × 7 cm. As shown in the figure, resultant current density was mainly distributed between the two electrodes. Conversely, when an anode electrode was attached at the FC3 location (middle of F3 and C3), higher current density was formed around the target position, as shown in Fig. 5b. Current density values at the target location (marked as a red dot with a black border line on the cortical surface) were probed using the "probing values at a specific location" function. The current density of the first case (anode at F3) was 0.163 A/m^2, whereas that of the second case (anode at FC3) was 0.186 A/m^2. This shows that an anode electrode attached at FC3 can transmit more direct currents to the cortical area below the F3 location than an electrode attached directly at the F3 location. This example demonstrates how *COMETS* can be used to find an electrode location that increases the transmitted current at specific target locations.

Influence of anatomy on electric field distribution

Recent advances in modeling and computational methods have enabled customized and individualized transcranial DC stimulations, as shown in a recent review article by Bikson [31]. *COMETS* can import individual head-cortex models generated using external modeling software. In the current version, *COMETS* can only import finite element head models generated using TetGen and cortical surface models exported from CURRY6 or CURRY7. In a later version, more head-cortex model variety could be incorporated based on user requests. Fig. 6 shows examples of field analysis results obtained from *COMETS*, in which analysis models were generated from MRI T1 data of two healthy subjects (both males, 22 and 21 years old) who participated in a simple tDCS experiment. The experiments were performed in the rehabilitation department of Samsung Medical Center in Korea. Participants provided written consent, and the Samsung Medical Center Institutional Review Board (IRB) approved the study protocol. Participants underwent a 3-back verbal working memory task [32] before and after a 20-min tDCS session. In the experiments, the cathode electrode was attached at the right supraorbital area and the anode electrode was attached at the F3 location because the target cortical region was the left DLPFC. The F3 location was determined using CURRY6 software and imported to *COMETS*. The cortical current density distributions of both models showed clear differences, particularly around the left DLPFC area. The first analysis result (Subject 1, Fig. 6a) showed higher current density around the left DLPFC than the second analysis result (Subject 2, Fig. 6b). Average current density values around the left DLPFC of Subjects 1 and 2 were 0.176 A/m^2 and 0.144 A/m^2, respectively. It is noteworthy to mention that different cortical current distributions originated mainly due to the different anatomical structures of individual head and cortices, which can only be considered with 3D electric field analyses. Interestingly, behavioral data also showed that Subject 1 had significantly enhanced working memory task performance (accuracy improved from 64% to 86%) than Subject 2 (accuracy was not changed and remained at 47%). Although no conclusions can be drawn from these examples due to the limited sample size, they demonstrate that the relationship between stimulation current delivered to a specific cortical area and change in cortical excitability might be investigated in future studies using *COMETS*.

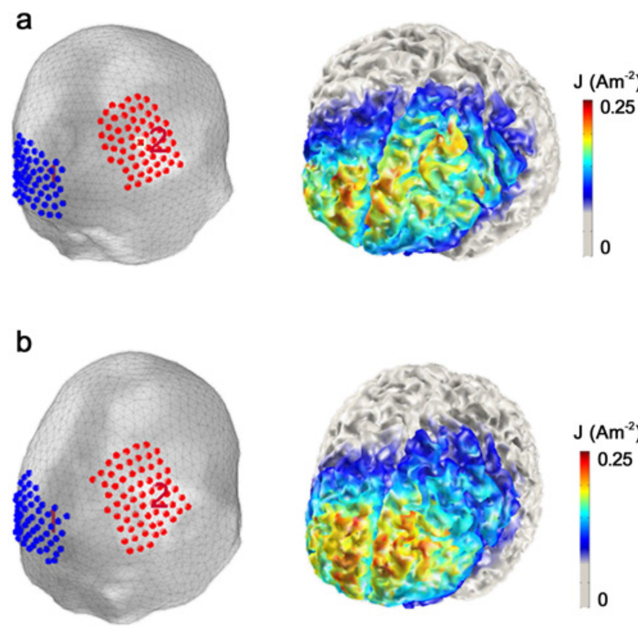

Fig. 6. Cortical current distributions analyzed using *COMETS* toolbox: Results shown in Figs. (a) and (b) were obtained using individual anatomical data from two healthy subjects. Cathode electrode was attached at right supraorbital area and anode electrode was attached at F3 location.

DISCUSSIONS

Numerical analyses of electric fields generated by tDCS have played an important role in recent tDCS studies. Since it is difficult to accurately predict the cortical areas modulated by tDCS due to non-uniform head compartments and the edge effect, most researchers have relied on their experience, previous literature research, and intuition to determine locations for attaching tDCS electrodes. 3D electric field analysis can help researchers to determine optimal electrode locations based on simulated cortical current distribution [15, 17]. In addition, a numerical analysis of the electric field may provide insight into the underlying mechanisms of tDCS that cannot be investigated through experimental studies [14, 16, 18]. A series of recent studies have reported successful 3D simulation of stimulation current delivered from tDCS to the brain. However, only a few research groups could access this new technology using commercial field analysis software because there is no electric field simulation software specifically designed for tDCS.

We have developed a new Matlab toolbox named *COMETS* that can be used to simulate current density distribution from a pair of rectangular electrode pads attached to the scalp. The friendly interface of *COMETS* allows even novice MATLAB users to access various functions. As demonstrated in a series of examples, *COMETS* can be utilized to simulate various electrode configurations and to find optimal electrode locations that increase current density at a target cortical region. In addition, advanced users can use the individual head-cortex model for their research purposes. *COMETS* can also be used to educate practitioners about the cortical current distributions delivered from tDCS electrodes.

Although advanced users can import their own head-cortex models to *COMETS*, the originally embedded standard head-cortex model does not have sufficiently high spatial resolution. The main reason for this rather simplified head model was to reduce the overall computational time required for practical applications. In the current version, *COMETS* cannot be used to analyze local electric fields in deep brain structures [33] or to simulate current distributions when skull defects or lesion sites are present in the analysis model [16]. *COMETS* also does not include the sponge (electrode) layer in the analysis domain because new finite element models must be generated for different electrode configurations due to altered model geometry. If new finite element models need to be generated at every simulation, the potential applications of *COMETS* shown in this article might not be possible in practice. Since the sponge layer passively delivers currents from the electrodes to the scalp, the normalized distributions of cortical stimulation currents are not affected by omitting this layer. However, absolute cortical current density values would be slightly decreased when the sponge layer (electrical conductivity of this layer is generally assumed to be 1.4 S/m) is included in the analysis domain. Although the resolution and complexity of analysis models do not always equate with clinical values [34], we will consider adopting more options for simulating high-resolution head-cortex models for refined research purposes in future versions of *COMETS*.

New functions will be also adopted in future versions of *COMETS*. Recently, some research groups have tried to simultaneously stimulate multiple cortical areas using multiple tDCS channels (e.g., http://neuroelectrics.com/about_tdcs/tcs-multi-channel-use). This function will be considered in the next version of *COMETS*. Because the *COMETS* toolbox is executed in a Matlab environment, visualization of the resultant cortical current distributions is rather slow and its function is limited. The next version of *COMETS* will incorporate an independent post-processing program coded with C++ and OpenGL for enhanced visualization of cortical current distribution.

The *COMETS* toolbox can be downloaded for free from the title page of the Computational Neuroengineering Laboratory in Hanyang University (http://cone.hanyang.ac.kr) or from http://www.COMETStool.com for non-commercial and academic uses. The toolbox can only be used for research and education purposes, not for medical purposes. A manual describing the details of toolbox use is included on the download page. We invite users to provide feedback for improving the toolbox by emailing COMETStool@gmail.com. We hope that our toolbox can contribute to popularizing the numerical analysis of cortical stimulation current in the field of noninvasive electrical brain stimulation.

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CONFLICT OF INTEREST STATEMENTS

Jung YJ declares that s/he has no conflict of interest in relation to the work in this article. Kim JH declares that s/he has no conflict of interest in relation to the work in this article. Im CH declares that s/he has no conflict of interest in relation to the work in this article.

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