Sensitivity of Transcranial Electric Stimulation to Tissue Conductivities Using Non-intrusive Polynomial Chaos Expansion

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Predictions of effects from transcranial electric stimulations rely on simulations with computer models and therefore quantitavily depend on conductivity definition. We aimed to analyze the sensitivity of the induced current density distribution on conductivity variations by means of a generalized polynomial chaos (gPC) expansion approach. Non-intrusive simulations were performed in a realistic three compartment finite element method model. The polynomial chaos coefficients were calculated by a regression approach with total order expansion. The results demonstrate highest differences in the current density distribution for variations of the skull and soft tissue conductivities at the edge and underneath the stimulation electrodes. The computed sensitivity of the current density distribution to uncertainties in the choice of conductivity values, here assessed for the first time with gPC, allows for a safer prognosis of the effect of transcranial electric stimulation.

Index Terms—**finite element method, sensitivity analysis, regression analysis, transcranial current stimulation**

I. INTRODUCTION

TRANSCRANIAL ELECTRIC STIMULATION (tES) is a non-invasive technique to excite or inhibit neuronal activity of a target brain area, which is applied in clinical therapy and scientific research. Electrical current with strength around 1 mA is applied by typically two rubber electrodes (anode, cathode) of several square centimeters in size. Targeting a certain brain area involves the adaptation of electrode design and positioning.

Electrical fields in realistic head models are numerically calculated in finite element method (FEM) models. The FEM models are derived from individual magnetic resonance imaging (MRI) data of the head. The simulated electric fields are used for targeting brain areas in tES applications.

Simulations of electric fields in volume conductor models rely on definitions of the electrical conductivities for the different conductor compartments (tissue layers). The determination of exact conductivity values for living human tissue is a challenging task, which has been addressed in several studies. Therefore, a variety of conductivity values for each tissue can be found in literature [1],[2].

The selection of certain conductivity values and their interaction influence the simulation results and therefore the stimulation prediction. Hence, an uncertainty analysis of the impressed electric field appears imperative for interpretations that are more meaningful.

To the best of our knowledge, we use for the first time a generalized polynomial chaos (gPC) expansion approach to analyze the influence of conductivity uncertainties in the soft tissue, skull and scalp compartments on the induced current density in the framework of tES.

II. MATERIAL AND METHODS

A. Volume conductor modeling

A structural magnetic resonance imaging data set from a male volunteer (age 22) provided the base for realistic volume conductor modeling. The brain extraction tool from the FSL suite [3] was used to segment the tissue boundaries of inner and outer skull as well as scalp and FreeSurfer tools [4] to finalize the compartment masks. Stimulating rubber electrodes with an edge length of 7 cm x 5 cm were modeled in a 4 mm dilated scalp mask. The anode was placed over the left primary motor cortex and the cathode was placed over the right frontopolar cortex. Figure 1 shows the volume conductor model.

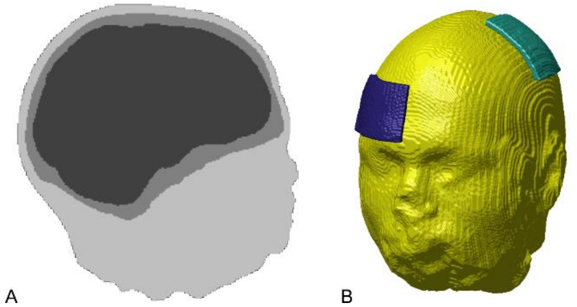

Fig. 1. Volume conductor model. A: Slice of head with soft tissue (dark gray), skull (intermediate gray) and scalp (light gray). B: Rendered skin surface (yellow) with anode (green) and cathode (blue).

Combined and labeled masks were meshed using the freely available SimBio-Vgrid[1] software. The FEM model comprised 4.3 million hexahedral elements with 4.4 million nodes.

B. The non-intrusive polynomical chaos expansion approach

In tES simulations, the quasi-static approximation to Maxwell's equations is justified which leads to the Laplace

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[1] The SimBio-Vgrid mesh generator: www.rheinahrcampus.de/~med-sim/vgrid/index.htm

equation for the electric scalar potential inside the head $\nabla(\sigma\nabla\phi) = 0$ with the conductivity σ and the electric potential ϕ. The current density $\vec{j} = -\sigma\nabla\phi$ was computed in all elements from the approximated potential at the nodes in the open source software SimBio [5] with an input current strength of 1 mA.

For the first time in a tES simulation study, the conductivities were modelled as independent and uniformly distributed variables with five representations each. The conductivities, $\sigma_{\text{soft tissue}}$, σ_{scalp}, varied from 0.165 S/m to 0.495 S/m. The conductivity of the skull, σ_{skull}, varied from 1/80 [1] to 1/15 [4] of 0.33 S/m. The coefficients for the gPC expansion of order five were determined by a regression approach [6],[7].

III. RESULTS

Overall 125 simulations with all possible combinations of the conductivity configurations for soft tissue, skull and scalp lead to the results exemplarily shown in Fig. 2 and Fig. 3. The depicted slice was selected such that edge effects directly connected to the cathode electrode can be observed. The top row in Fig. 2 shows the mean current density and demonstrates highest current densities connected to the electrode edges in the scalp layer and underneath the electrode edges in the soft tissue compartment. The standard deviation in the targeted soft tissue compartment is in the order of one percent underneath the electrode edges.

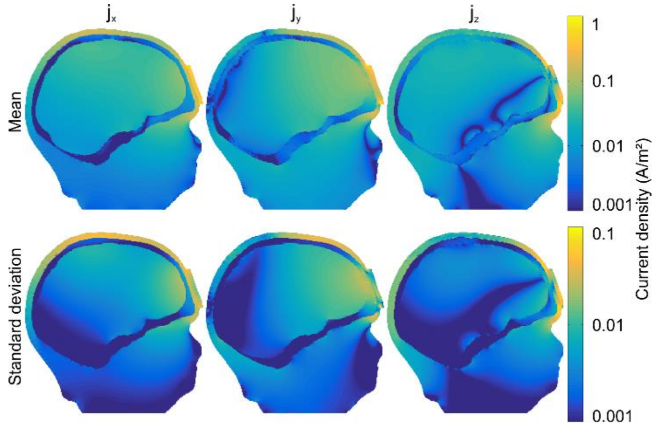

Fig. 2. Top row: mean current density values. Bottom row: standard deviation of the current density. Please note the logarithmic scaling.

Figure 3 shows the global derivative based sensitivity coefficients in absolute values on a logarithmic scale [7]. The global derivative based sensitivity coefficients were computed in Matlab (The Mathworks, Natick, USA) without parallelization in approx. 40 min on a compute server with 24 CPUs and 128 GB of memory. These coefficients indicate how strong and at which point in space the current density variance is affected by the variations of the electrical conductivity of soft tissue, skull and scalp, respectively. Variation of the skull conductivity resulted in the largest effects (compare middle row with top and bottom row) followed by the soft tissue and scalp conductivity changes. The global sensitivity coefficients for scalp are approximately a factor of 10 smaller compared to the other two sensitivity coefficients. Prominently, the areas in the close vicinity of the electrodes are most affected. Dark blue lines in y- and z-components of the current density and the sensitivity components indicate change of sign.

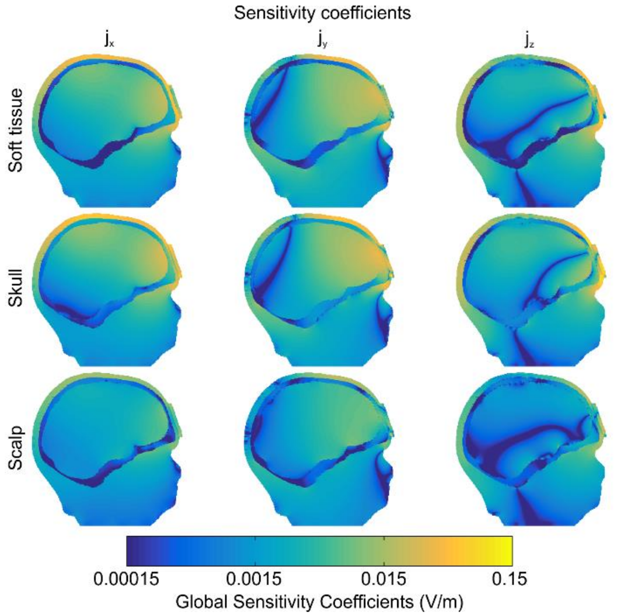

Fig. 3. Distribution of absolute global derivative based sensitivity coefficients for soft tissue (top row), skull (middle row) and scalp (bottom row) conductivity variations. Please note the logarithmic scaling.

IV. DISCUSSION

Simulations of tES with conductivity variation by means of gPC expansion for skin, skull and soft tissue demonstrated high sensitivity of electric field distribution in soft tissue on skull conductivity in contrast to the less affected magnetic field from the skull layer conductivity in TMS [7].

Our results demonstrate that predictions of tES effects in model simulations are sensitive to uncertainties in conductivity values. Since real conductivity configurations can vary due to several factors such as individual anatomy and constitution, it is useful to perform simulations with a range of conductivity values in multiple combinations to capture several possibilities of the impressed electric currents in the brain. Our future work will include more realistic conductivity representations by beta distributions and their respective representation through Jacobi polynomials.

V. REFERENCES

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The German ministry of Science supported this work (3IPT605A & X).