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BrainRuler-a free, open-access tool for calculating scalp to cortex distance

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Dear editors

We are writing to notify the community of *Brain Stimulation* readers about “BrainRuler”- a free, open-access tool available to efficiently quantify the distance between a specified position outside of the skull and the cortical gray matter below the skull (“scalp-cortex distance”). All documentation is located on the Wiki (<http://brainruler.wikispaces.com/>). The scripts are present on Matlab Central File Exchange (<https://www.mathworks.com/matlabcentral/fileexchange/61847-brain-ruler>). We encourage users to provide feedback and to announce any new scripts they have created on our Wiki. We hope that this serves as a platform to share ideas on improving this program and developing new techniques.

The non-invasive brain stimulation (NIBS) community needs a standardized, efficient approach to quantify the distance between the scalp and the cortex, as this is a critical metric to determining the dosage of NIBS delivered to an individual. The strength of an electrical or magnetic field decays exponentially at distances greater than the diameter of the coil (up to a rate of $1/r^3$, wherein ‘r’ is the distance from the origin to the target). Consequently, an individual’s scalp to cortex distance is directly related to the dosage of NIBS that will be delivered to the cortex. The relationship between the strength of a magnetic field and distance was derived from Ampere’s law and extended by Maxwell in 1861 [1]. The influence of this principle and the physics of NIBS techniques is elegantly described in numerous textbooks written by scientific leaders in the brain stimulation field [2,3].

Unfortunately, however, before the routine acquisition of MRI scans in NIBS research (an approach which has become increasingly common as commercial neuronavigation tools are available), it was difficult to incorporate this fundamental metric of scalp-cortex distance into NIBS research and clinical practice. The association between scalp-cortex distance and motor threshold is well established. Previous groups have reported significant correlations between motor threshold and scalp-cortex distance [4], with estimates that up to 50% of the inter-subject variance in motor threshold is related to distance alone [5] and estimates that the motor threshold increases 2.8% for each millimeter of distance [6].

As the field has grown, we now face several challenges: 1) TMS is routinely being applied to cortical areas that do not generate a measureable behavioral output (e.g. the lateral and

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medial prefrontal cortex, the cerebellum, and the parietal and temporal cortex), 2) many potential cortical targets are proximal to biophysical structures with high inter-individual variability (e.g. frontal sinuses, subdural CSF, and subcutaneous fat), and 3) many NIBS techniques induce electromagnetic fields but do not induce action potentials (e.g. transcranial direct current stimulation) such that, even when positioned over the motor cortex, it is difficult to determine the strength of the field at the cortex.

To address some of these concerns, we have developed a free, open access tool which will enable NIBS investigators to rigorously and efficiently calculate the distance from a point of origin outside of the scalp to gray matter beneath the origin. Through this tool the field can now take advantage of scalp-cortex distance as a supplemental technique to determine the strength of the electromagnetic field delivered to an individual. We have evaluated the accuracy of this tool to calculate scalp-cortex distance at two different cortical locations in comparison to scalp-cortex distances manually drawn by an experienced technician. The data set included individuals with a history of drug and alcohol dependence (associated with cortical atrophy) and age-matched controls [7]. Scalp-cortex distances were calculated for two cortical locations (F3, dorsolateral prefrontal; Fp1, ventral medial prefrontal). The inter-rater reliability (intra-class correlation coefficient) of the manual drawings was 0.81 for F3 and 0.85 for Fp1. The reliability between this automated tool and the technician was 0.92 for F3, and 0.95 for Fp1.

The tool is currently implemented in MATLAB as a set of scripts that run behind an easy to use graphical user interface (Fig. 1). For inputs, it prompts the user to load an anatomical MRI image and locate the area of origin outside of the scalp (e.g. a fiducial on the surface of a TMS coil, a landmark on the scalp used for surgical guidance, or an arbitrary user-defined position outside of the skull). An optional dura mater subtraction tool used to mitigate the impact of dura thickening on threshold measurements. In addition, the user can opt to modify a set of default threshold values used for the calculation (e.g. tolerance for gray matter boundaries, threshold for dura and skull). As outputs, the program produces a graphical representation of the boundaries and vectors estimated and a table containing: 1) minimum distance from the origin to cortex, 2) average minimum distance in a predefined window of cortex and 3) average CSF volume between the scalp and cortex within the window. Additional outputs include: 4) average skull thickness, 5) minimum skull thickness, 6) shortest fiducial to scalp distance, 7) shortest fiducial to cortex distance, and 8) shortest fiducial-to-fiducial arc length (a measurement of the shortest arc outside of the skull between two fiducials).

Some of the challenges we aimed to overcome in developing an automated program included the presence of diffuse dural thickening in several participants (which is bordered by cerebrospinal fluid - CSF - on both sides), epidural venous dilations, sinus shape and contrast, and spatial irregularities in the skull. We encourage the NIBS community to help us optimize this tool and refine these scripts as they utilize it for various patient populations. Future versions of this software tool will likely include measurements of CSF volume and basic projections of the magnetic and electrical field emanating from the point of origin. This open access approach has been critical to the development of many neuroimaging analysis tools now routinely utilized in research (e.g. Statistical Parametric mapping).

Our hope is that, moving forward, for all NIBS studies (e.g. TMS, TDCS, TES) in which an MRI scan is available, investigators will routinely calculate, report, and include TMS coil-cortex distance as a parameter in their estimations of dosage delivered to an individual.

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Fig. 1.

The graphical user interface for BrainRuler. As outputs, the program produces a graphical representation of the boundaries and vectors estimated and a table containing: 1) minimum distance from the origin to cortex, 2) average minimum distance in a predefined window of cortex and 3) average CSF volume between the scalp and cortex within the window. Additional outputs include: 4) average skull thickness, 5) minimum skull thickness, 6) shortest fiducial to scalp distance, 7) shortest fiducial to cortex distance, and 8) shortest fiducial-to-fiducial arc length (a measurement of the shortest arc outside of the skull between two fiducials).