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D O V S , U A , B , L , P R , G , A , N
D P , P U , H R , H , B , C
D S E S , U A , S S , A , N
D M , U A , S S , A , N
S O V S , U W , C S W, W , ON, C N L G

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Academic Edi or: Zhengchao Dong

A ke iss e in he eld of nonin asi e brain s im la ion (NIBS) is he acc ra e locali a ion of scalp posi ions ha correspond o arge ed cor ical areas. e c rren gold s andard is o combine s r c ral and f nc ional brain imaging i h a commerciall a ailable ne rona iga ion s s em. Ho e er, ne rona iga ion s s ems are no commonplace o side of speciali ed research en ironmen s. Here e describe a echniq e ha allo s for he se of par icipan -speci c f nc ional and s r c ral MRI da a o g ide NIBS i ho a ne rona iga ion s s em. S rface mesh represen a ions of he head ere genera ed sing Brain Vo ager and ec ors linking ke ana omical landmarks ere dra n on he mesh. O r echniq e as hen sed o calc la e he precise dis ances on he scalp corresponding o hese ec ors. ese calc la ions ere eri ed sing ac al meas remen s of he head and he echniq e as sed o iden if a scalp posi ion corresponding o a brain area locali ed sing f nc ional MRI.

1.

Nonin asi e brain s im la ion (NIBS) echniq es s ch as repe i i e ranscranial magne ic s im la ion (rTMS) and ranscranial direc c rren s im la ion (DCS) allo for he emporar mod la ion of ne ral ac i i i hin he h man brain. rTMS in ol es he ind c ion of eak elec rical c rren s i hin arge ed regions of he cor e ia brief, ime- ar ing magne ic elds prod ced i h a hand-held coil [ ]. DCS emplo s head-mo n ed elec rodes, hich allo for a eak direc c rren o in erac i h he nderl ing cor e [ ]. NIBS can be sed o in es iga e he role of indi id al brain areas in speci c cogni i e, beha ioral, or percep al processes [ ]. In addi ion, hese echniq es are being in es iga ed from a clinical perspec i e and c rren e idence s gges s ha NIBS ma be applicable o he rea men of m l iple ne rological and ps chia ric disorders [,].

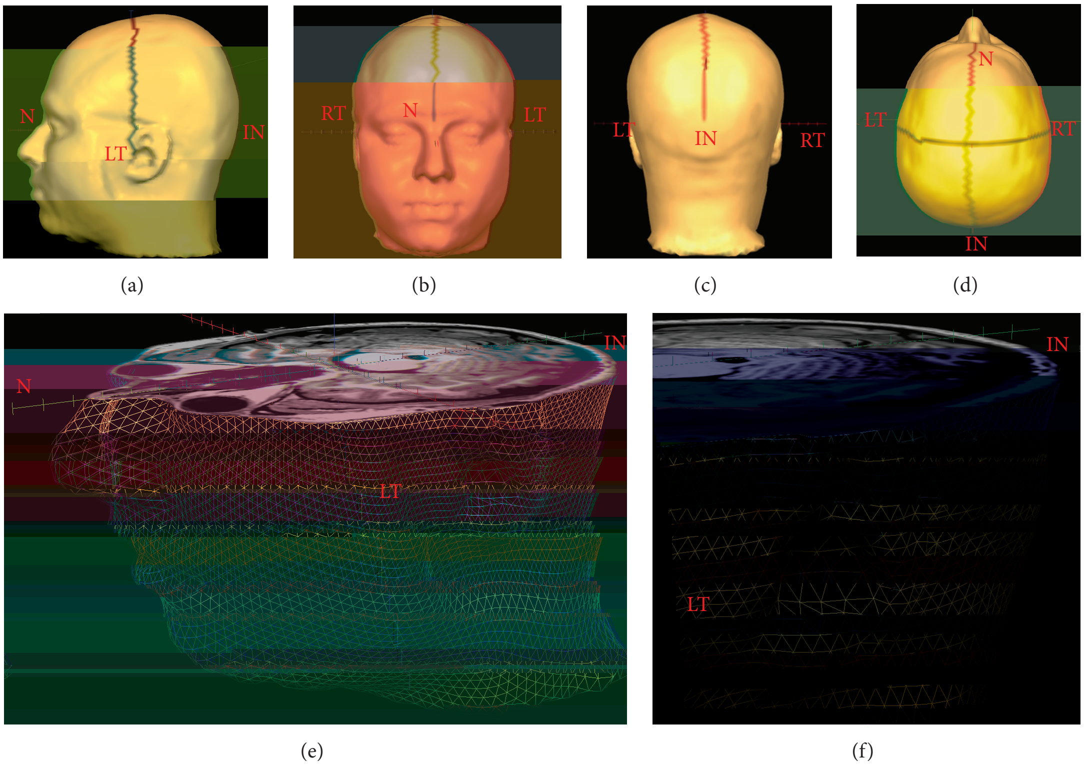
S dies in ol ing he se of NIBS begin b selec ing a arge brain area for s im la ion. is process is picall informed b e idence from brain imaging, animal ne ro-ph siolog , or s dies in ol ing ne rological pa ien s. S bse-q en s eps incl de he selec ion of appropria e s im la ion parame ers and ens ring ha he s im la ion is deli ered o he correc brain area. is la er poin is par ic larl impor an as he s im la ion e ec s are mos prono nced in close pro imi o he rTMS coil and DCS elec rodes [ ]. erefore, acc ra e, par icipan -speci c locali a ion of s im-la ion si es on he scalp is req ired for op imal s im la ion [ ].

A n mber of approaches can be sed o iden if he correc scalp posi ion for s im la ion. Single p lse TMS can be sed o ac i a e speci c regions of he primar mo or cor e , res l ing in mo or e oked po en ials (MEPs) i hin he corresponding peripheral m scle [ ]. e scalp loca ion that evokes the strongest MEP can then be used as the location for rTMS or tDCS. A comparable technique also exists for the visual cortex, whereby single pulse TMS of the occipital pole can be used to evoke the percept of a phosphene [ ]. The scalp location that induces the most robust phosphene or a phosphene in a specific visual field location can be used for visual cortex stimulation. A similar technique can be used for motion sensitive, extra-striate visual area V5, whereby TMS can be used to induce moving phosphenes [ ]. It has been shown that this technique is in good agreement with localization of V5 using functional magnetic resonance imaging [ ]. However, it is not possible to use this approach outside of the motor and visual cortices because most brain regions do not produce active neurophysiological or perceptual effects in response to single pulse TMS.

An alternative technique for identifying participant-specific stimulation sites on the scalp is the 10-20-electrode system, which was originally designed for positioning EEG electrodes [ ]. This approach defines a grid of positions on the scalp that are separated by 10% or 20% of the distance between anatomical landmarks such as the nasion and the inion. This approach has been used successfully in a large number of brain stimulation studies; however, the mapping of particular 10-20 system locations to specific brain areas can vary across participants [ ].

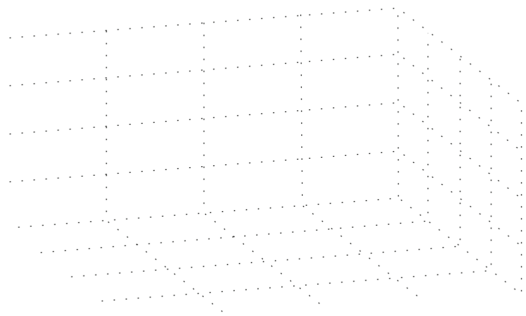
Another alternative is to use structural and functional brain imaging techniques to localize specific brain areas in individuals with millimetre resolution. A number of frameless stereotactic navigation systems exist for real-time coregistration of a participant to their own MRI images. Tools such as a pointer or a TMS coil can also be registered within the volume. These systems typically involve ultrasound devices or infrared cameras and a number of reference targets mounted on the head and NIBS apparatus. When used in combination with structural and functional MRI images these neuronavigation systems allow for precise identification of the scalp position corresponding to a particular brain area [ ].

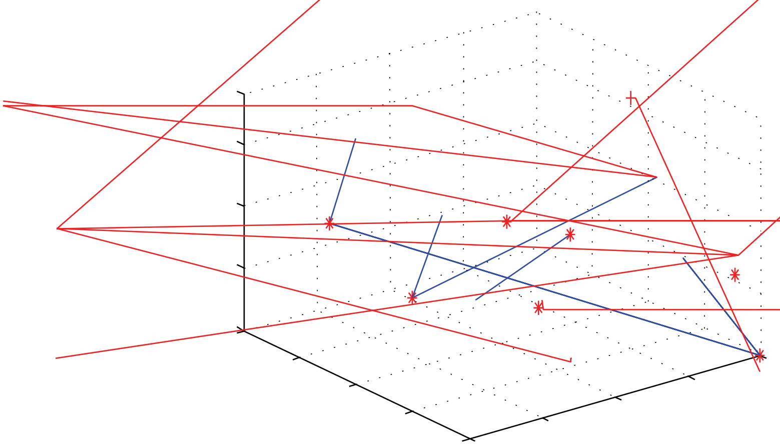
The combination of brain imaging and a neuronavigation system is the current gold standard in the field of NIBS [ ] and may improve the results of NIBS-based therapeutic interventions [ ]; however, there are some disadvantages. These include difficulty in using these systems for studies of posterior brain areas that can fall outside of the neuronavigation system's field of view and, most importantly, the high cost of these systems, which can exceed . Techniques have been described that allow NIBS to be targeted using generic MRI datasets [ ] or when structural but no functional MRI data are available for individual participants [ ]. Furthermore, techniques for identifying optimal scalp locations for stimulation based on individual participant's neuroanatomy are also available [ ]. However, each of these approaches requires the use of a neuronavigation system. Here we describe a technique that allows the use of individual structural and functional MRI to guide NIBS in the absence of a neuronavigation system. The approach is based on vectors drawn on a mesh that is morphed to participant-specific MRI data. These mesh vectors are then transposed to the participant's head by converting them to head measurements anchored to anatomical landmarks. We report comparisons between measurements made using our technique and actual head measurements. We also give an example of how the technique can be used in combination with fMRI to localize a stimulation site for visual area V5 in a single subject. Visual area V5 was chosen for this example as it can be readily localized using fMRI and the corresponding scalp position cannot be identified based on a single anatomical landmark. Therefore, a number of measurements

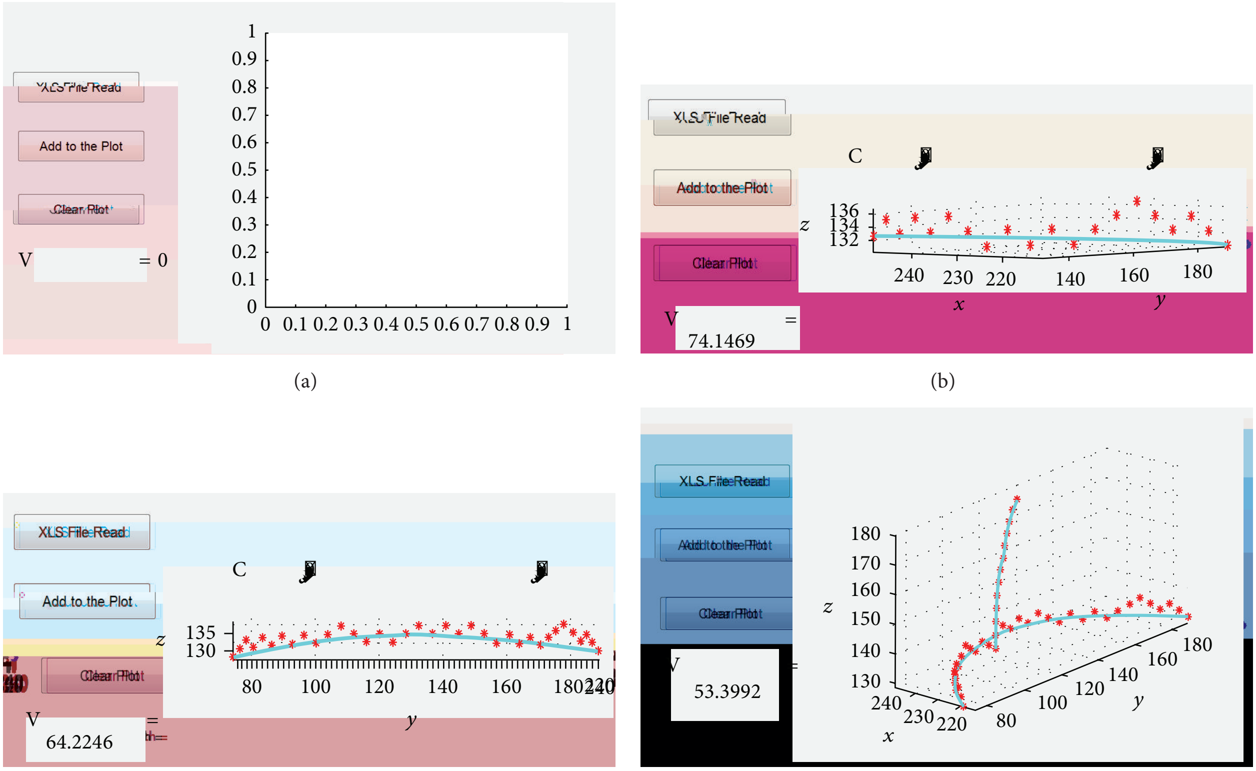


F : A D mesh morphed o he s r c ral MRI da a of a represen a i e par icipan . Panels (a) (d) sho he ana omical landmarks ha ere sed as anchor poin s for scalp dis ance calc la ions marked on a T - ol me s rface mesh crea ed sing Brain Vo ager. N: nasion, RT and LT: righ and le ragi, respec i el , and IN: inion. e lines connec ing he ana omical landmarks are pa ches of in eres (POIs) dra n in Brain Vo ager ha link adjacen riangles in he mesh. Panels (e) and (f) sho close- p ie s of he mesh i ho he s rface coloring. e mesh has been c a iall a he le el of he inion. e smoo h s rface of he head is represen ed sing riang lar elemen s and each of hese elemen s is de ned b i s ricorners.

s bro ines i hin Brain Vo ager. A general linear anal sis as cond c ed and he res l s ere is ali ed as -maps on he ana omical image. Area V as iden i ed as a






XLS File Read
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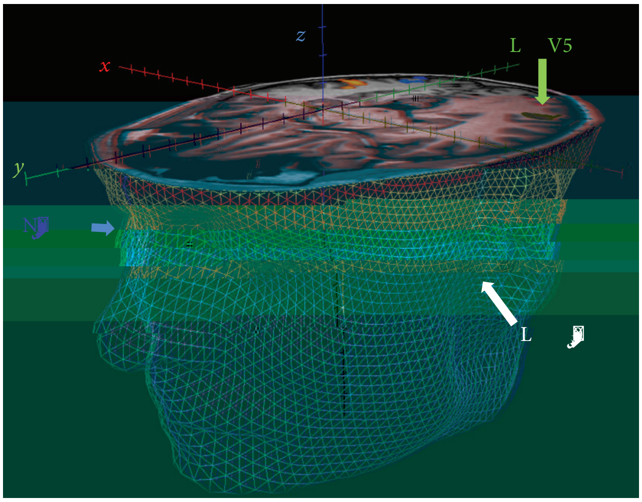
(a) (b) (c) (d)



F : Locali a ion of a scalp posi ion abo e V in he le hemisphere. e a ial c hro gh he Brain Vo ager mesh as posi ioned o re eal he mos ac i e o el in le V . e lines dra n on he mesh sho he POIs ha ere sed o iden if he scalp loca ion corresponding o le V . Bl e: nasion o rans erse plane, hi e: rag s o rans erse plane, red: in ersec ion of nasion ec or and rans erse plane o in ersec ion of rag s ec or and rans erse plane, and green: e ension of he ec or o he scalp posi ion abo e area V . Orange regions indica e areas of f nc ional ac i a ion in response o he V locali a ion scans. See he main e for a de ailed descrip ion of his proced re.

no s ppor ed. is iss e is also rele an o he se of ne ron a iga ion s s ems. Selec ion of he op imal s im la ion si e is a comple process as he elec rical c rren genera ed b NIBS echniq es in erac s i h he head and brain ana om in a s ha are niq e o each par icipan [ ]. A n mber of echniq es for iden if ing op imal NIBS si es based on MRI da a ha e been de eloped. ese co ld be combined i h o r approach for ransposing s im la ion si es o he head o f r her impro e he arge ing of NIBS hen ne rona iga ion s s ems are no a ailable.

e a hors declare ha here is no con ic of in eres s regarding he p blica ion of his paper.

A

is ork as s ppor ed b gran s from Marsden F nd of he Ro al Socie of Ne Zealand o Ehsan Vaghe and from he Heal h Research Co ncil, Uni ersi of A ckland, Fac l De elopmen Research F nd, and A ckland Medical Research Fo nda ion o Benjamin ompson.

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