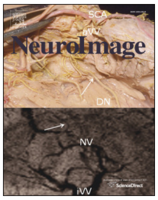
YNIMG-12712; No. of pages: 7; 4C: 5, 3, 4

NeuroImage xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



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Three-dimensional localization of cortical electrodes in deep brain stimulation surgery from intraoperative fluoroscopy

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ARTICLE INFO

Article history:
Received 10 August 2015
Accepted 25 October 2015
Available online xxxx

Keywords:
Deep brain stimulation (DBS) surgery
Electrocorticography (ECoG)
Electrode localization
Fluoroscopy
Image coregistration
Movement disorders

ABSTRACT

Electrophysiological recordings from subdural electrocorticography (ECoG) electrodes implanted temporarily during deep brain stimulation (DBS) surgeries offer a unique opportunity to record cortical activity for research purposes. The optimal utilization of this important research method relies on accurate and robust localization of ECoG electrodes, and intraoperative fluoroscopy is often the only imaging modality available to visualize electrode locations. However, the localization of a three-dimensional electrode position using a two-dimensional fluoroscopic image is problematic due to the lost dimension orthogonal to the fluoroscopic image, a parallax distortion implicit to fluoroscopy, and variability of visible skull contour among fluoroscopic images. Here, we present a method to project electrodes visible on the fluoroscopic image onto a reconstructed cortical surface by leveraging numerous common landmarks to translate, rotate, and scale coregistered computed tomography (CT) and magnetic resonance imaging (MRI) reconstructed surfaces in order to recreate the coordinate framework in which the fluoroscopic image was acquired, while accounting for parallax distortion. Validation of this approach demonstrated high precision with an average total Euclidian distance between three independent reviewers of 1.65 ± 0.68 mm across 8 patients and 82 electrodes. Spatial accuracy was confirmed by correspondence between recorded neural activity over sensorimotor cortex during hand movement. This semi-automated interface reliably estimates the location of temporarily implanted subdural ECoG electrodes visible on intraoperative fluoroscopy to a cortical surface.

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Introduction

Subdural electrocorticography (ECoG) electrodes are useful clinical tools for functional mapping and seizure monitoring that can also provide detailed temporal and spatial information valuable for cognitive neuroscience research. Recent studies have employed the temporary implantation of subdural ECoG electrodes during deep brain stimulation (DBS) electrode implantation surgeries in order to simultaneously record cortical ECoG and subcortical single unit and local field potential (LFP) activity in the intraoperative setting. Initial findings using this technique suggest that patients with movement disorders, including Parkinson's disease (PD) (de Hemptinne et al., 2013, 2015; Crowell et al., 2012; Whitmer et al., 2012) and essential tremor (ET) (Air et al., 2012), have abnormal oscillatory activity recorded within the structures in the sensorimotor network. However, the lack of a reliable method for localizing the ECoG electrodes on the cortical surface in the absence of intraoperative computed tomography (CT) scanning is a limitation for the expansion of this important research opportunity. The accurate localization of these electrodes is essential for relating the recorded ECoG signals to the anatomical structures responsible for generating them.

Effective methods for the localization of subdural ECoG electrodes have been developed for clinical and research use in patients with medically refractory epilepsy. One common method uses post-operative CT to visualize implanted electrode locations that are then coregistered to their corresponding locations in pre-operative magnetic resonance imaging (MRI) space (Azarion et al., 2014; Hermes et al., 2010; Tao et al., 2009; Ken et al., 2007; Wang et al., 2013). Three-dimensional stereotactic coordinates for each electrode can then be determined on an individual reconstructed MRI. Other methods verify the electrode locations visually on the exposed brain surface with either surgical photographs or a neuro-navigational system and additionally leverages known electrode spacing to calculate the locations of non-exposed electrodes (Dalal et al., 2008; Yang et al., 2012). However, since the subdural

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http://dx.doi.org/10.1016/j.neuroimage.2015.10.076
1053-8119/© 2015 Published by Elsevier Inc.

Please cite this article as: Randazzo, M.J., et al., Three-dimensional localization of cortical electrodes in deep brain stimulation surgery from intraoperative fluoroscopy, NeuroImage (2015), http://dx.doi.org/10.1016/j.neuroimage.2015.10.076

ECoG electrodes used during DBS surgeries are only implanted temporarily and are not visible within the cranial opening, intraoperative imaging represents the only opportunity to visualize the implanted subdural electrodes. Upper extremity somatosensory evoked potential phase reversal mapping can also be used to functionally localize ECoG electrodes to the upper extremity representation of the somatosensory cortex in the post-central gyrus, but cannot localize electrodes to non-somatosensory areas of cortex. Of the options for intraoperative imaging, fluoroscopy is most often used during DBS surgeries to verify the final DBS lead position in relation to the stereotactic arc center, since intraoperative CT is not readily available in many DBS programs.

Determining the three-dimensional locations of subdural electrodes from a two-dimensional fluoroscopy image, however, is problematic due to a lack of depth information in the dimension orthogonal to the image orientation. It is possible to regain this dimension by overlaying and aligning the 2-D fluoroscopic image and corresponding 3-D anatomy to recreate the coordinate framework under which the fluoroscopic image was acquired. Many previous cortical electrode localization methods performed this coregistration by assuming that the fluoroscopic image was acquired at a perfectly lateral view (Rowland et al., Q3 2014; Miller et al., 2007a, 2007b). This assumption may imprecisely fixe rotation along all coordinate axes, limiting the ability to accurately localize cortical electrodes to a particular gyrus. One method that does account for rotation in two of the three coordinate axes utilizes post-operative fluoroscopic images in multiple orientations (Miller et al., 2010), although typically this is cumbersome in the intraoperative setting. These methods also either rely on manual placement of the reconstructed MRI within the inner skull contour (Rowland et al., 2014) or approximate alignment using the anterior–posterior commissure (AC-PC) and inioglabellar line (Miller et al., 2007a, 2007b, 2010), which Q4 can introduce error to the resulting electrode locations. All previous methods additionally do not account for the distortion introduced by the parallax effect implicit in fluoroscopic images, which unrealistically magnifies objects closer to the X-ray source.

We developed a semi-automated method to localize subdural electrodes on a three-dimensional reconstructed brain using intraoperative fluoroscopy obtained during DBS electrode implantation. This method aligns coregistered pre-operative CT and post-operative MRI surfaces with an intraoperative fluoroscopic image in a manner that recreates the coordinate framework of the fluoroscopic image and simulates the parallax distortion to provide accurate and reliable electrode location estimations on the cortical surface. The reproducibility of this method was validated using multiple independent reviewers, and the accuracy of these estimations were confirmed using observed functional cortical activity.

Materials and methods

Patients

Eight patients undergoing DBS electrode implantation for the treatment of movement disorders were included in this study (7 male, 1 female, 64.4 ± 1.9 years, mean ± SE). Patient diagnoses included PD ($n = 5$) and ET ($n = 3$). DBS electrode targets were either the subthalamic nucleus (STN; $n = 4$) or the internal globus pallidus (GPi; $n = 1$) for patients with PD, and the ventral intermediate (Vim) nucleus of the thalamus ($n = 3$) for patients with ET. Six patients underwent bilateral implantation, and two patients underwent unilateral implantation.

Patients additionally had standard subdural ECoG electrodes implanted to record cortical activity for research purposes and provided informed consent for this research, which was approved by the University of Pittsburgh Institutional Review Board (#13110420). Subdural ECoG electrodes were either six or eight linear contact strips of 4 mm-diameter platinum-iridium contacts with a 2.3 mm-diameter exposed contact area and 1 cm center-to-center electrode spacing (AdTech, Racine, WI, USA). In one patient, a higher density electrode array (28 contacts, 2 mm diameter, 4 mm spacing; AdTech, Racine, WI, USA) was implanted along with a standard 8-contact electrode. Six patients had the subdural ECoG electrodes implanted on the right hemisphere, and two patients were implanted on the left. In all 8 patients, a total of 9 electrode strips over 8 hemispheres and 82 contacts were used in this analysis.

Electrode placement

Subdural ECoG electrodes were placed through the burr hole after opening the dura, but before guide tube insertion. The electrodes were aimed posteriorly to direct the distal end of the strip electrode over sensorimotor cortex, often in close approximation to the hand knob, as viewed on a cortical reconstruction in the surgical planning software (BrainLab). In one patient, an additional strip electrode was directed frontally towards the dorsolateral prefrontal cortex. Following guide tube insertion, fibrin glue was used to temporarily seal the burr hole. Once the DBS electrode was implanted, a lateral fluoroscopy image was acquired to confirm correct placement of the DBS electrode in the vertical (z-axis) and anterior–posterior (y-axis) axes. The fluoroscopic image captured the locations of the implanted subdural ECoG electrodes and at least two pin tips of the stereotactic frame. Upon confirming the placement of the DBS electrode, the subdural ECoG electrode was removed, and the DBS electrode was locked into place. Following the procedure, a post-operative MRI was obtained for additional confirmation of DBS electrode position.

Imaging data acquisition

Standard, clinically indicated imaging for DBS surgeries was used and included (1) a pre-operative stereotactic CT obtained after placement of the Leksell frame, (2) an intraoperative lateral fluoroscopic image (512 × 512 pixels, General Electric, OEC 9900), and (3) a post-operative MRI (1.5 T, Siemens Allegra). Pre-operative stereotactic CT images were acquired in contiguous axial slices with 1.5 mm thickness (General Electric, 9800). Both the pre-operative CT and intraoperative fluoroscopy were acquired with the stereotactic frame in place. MRI scans were high-resolution T1-weighted volumetric fast spoiled gradient echo (FSPGR) images (slice thickness = 1.5 mm, repetition time = 33.33 ms, echo time = 6 ms, flip angle = 35°), our standard post-operative protocol.

Image processing

All raw images were converted from the DICOM format of the scanner to NIfTI (Neuroimaging Informatics Technology Initiative) formatting and resliced with the Freesurfer image analysis suite (Dale et al., 1999). After conversion, the pre-operative CT was coregistered to the post-operative MRI using the normalized mutual information approach and then resliced in the Statistical Parameter Mapping (SPM) package (SPM12, http://www.fil.ion.ucl.ac.uk/). The accuracy of the registration was then visually verified for each patient.

Using a custom graphical user interface (Supplementary Fig. 1) within MATLAB software (The MathWorks Inc., Natick, MA, USA), DBS electrode tract locations on the post-operative MRI were visualized slice by slice as a localized reduction in signal intensity (Fig. 1A). The tracts were marked along their entire length on every other axial slice (2 mm spacing). The developed interface allows users to visualize NIfTI images in either the coronal, sagittal, or axial sections and selects desired landmarks. Using this interface, the tips of the four pins on the stereotactic frame that secure the frame to the patient's head were marked on the pre-operative CT slice images (Fig. 1B). A high-resolution reconstructed three-dimensional cortical surface model was created for each patient from post-operative MRI images using the Freesurfer suite (Dale et al., 1999). This surface was imported into MATLAB with the Freesurfer toolbox as a triangulated rendering for

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