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Journal of Neuroscience Methods 162 (2007) 303–308

JOURNAL OF NEUROSCIENCE METHODS

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Cortical electrode localization from X-rays and simple mapping for electrocorticographic research: The "Location on Cortex" (LOC) package for MATLAB

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Received 20 November 2006; received in revised form 13 January 2007; accepted 17 January 2007

Abstract

Medically refractory epilepsy accounts for more than 30% of the epilepsy population. Scalp EEG electrodes have limited ability to localize seizure onset from deep structures and implantation of subdural electrodes with long term monitoring provides additional information. Apart from clinical application, this patient population provides a unique opportunity for acquiring electrocorticography data in research paradigms. We present a method for rapid localization of electrodes using lateral and anterior–posterior X-rays. Skull landmarks and proportions are used for co-registration with the standardized Talairach coordinate system. This MATLAB-based "Location on Cortex" (LOC) package facilitates rapid visualization of clinical and experimental data in a user-friendly manner.

Keywords: Electrocorticography; ECoG; Electrode localization; X-ray; Talairach coordinates; Imaging; Standardization

1. Introduction

Medically refractory epilepsy affects more than 30% of the epilepsy population (Kwan and Brodie, 2000). One significant clinical challenge is the accurate localization of seizure onset. Scalp EEG electrodes are limited in their ability to localize seizure onset from deep structures, and implantation of subdural electrodes with long term monitoring provides additional seizure localization information (Lesser et al., 1991). In addition to the clinical application of subdural electrodes, long term electrocorticographic monitoring provides a unique opportunity for acquiring data in research paradigms. In order to accurately interpret the seizure onset and to interpret electrocorticography data for research paradigms, the three-dimensional location of the electrodes must be known. Although intra-operative photographs of subdural grids provide locations for electrodes on exposed cortex (see supplemental figure), they do not provide information for electrodes passed beyond the limits of the cranial exposure. These electrodes may be located with post-operative CT or MRI (Kovalev et al., 2005; Wellmer et al., 2002), but this process requires sophisticated image acquisition preoperatively and postoperatively and these image studies are often unavailable. Post-operative X-rays, however, are ubiquitous and readily accessible. The method and the associated package presented here address the need for a fast, reliable co-localization technique to locate and standardize radio-opaque electrodes from anterior–posterior (AP, also called 'coronal') and lateral X-rays.

This MATLAB (The MathWorks, Inc.) based "Location on Cortex" (LOC) package uses skull landmarks and proportions for co-registration with the standardized Talairach coordinate system. The Talairach coordinate system defines the origin as the anterior commisure (AC) and the anterior–posterior (y) axis as the line connecting the anterior and posterior commisures (AC/PC line). The x axis is perpendicular to the y axis in the axial plane, and the z axis is normal to the x–y plane(Talairach and Tournoux, 1988).

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0165-0270/$ – see front matter
doi:10.1016/j.jneumeth.2007.01.019

Skull landmarks visible on the lateral X-ray may be used to approximate the Talairach axes. The line segment drawn from the glabella to the inion (GI line) is parallel to the AC/PC line (Fox et al., 1985; Friston et al., 1989). The y axis is defined as the AC/PC line. The x axis is the direction of left–right symmetry and the z axis is perpendicular to the GI line, and thus normal to the x–y plane. The origin is defined in the x direction as the center of the skull on AP X-rays. In the z direction, it is defined as 21% along the perpendicular line segment corresponding to the maximum distance between the GI line and the inner table of the superior surface of the skull. In the y direction, the distance from the posterior inner table of the skull to the anterior inner table along the y axis is normalized to 173 mm, and the origin is taken at 115 mm anterior to the midpoint of this line. The y axis is positive anterior to the origin, the x axis is positive on the patient's right, and the z axis is positive superior to the origin.

To interpret the location of subdural electrodes for clinical analysis and inter-patient comparison, the patient's brain is normalized to standard dimensions. By making the assumption that the inner table of the skull matches the brain surface, the maximum x, y, and z coordinates of the inner table of the skull can be normalized to a template brain volume. Furthermore, the position of any radio-opaque objects within this volume can also be normalized to the template brain. The AFNI template brain is routinely used in imaging research and is available in Talairach coordinates (Brett et al., 2002; Collins et al., 1994; Holmes et al., 1998; http://afni.nimh.nih.gov/). Its maximum x, y, and z dimensions are 138 mm, 173 mm, and 116 mm, respectively. Normalization to this template brain allows clinicians and researchers to interpret electrocorticographic data with reference to this standardized brain atlas.

2. Methods

This technique was implemented on patients enrolled in an electrocortigraphic research study at the University of

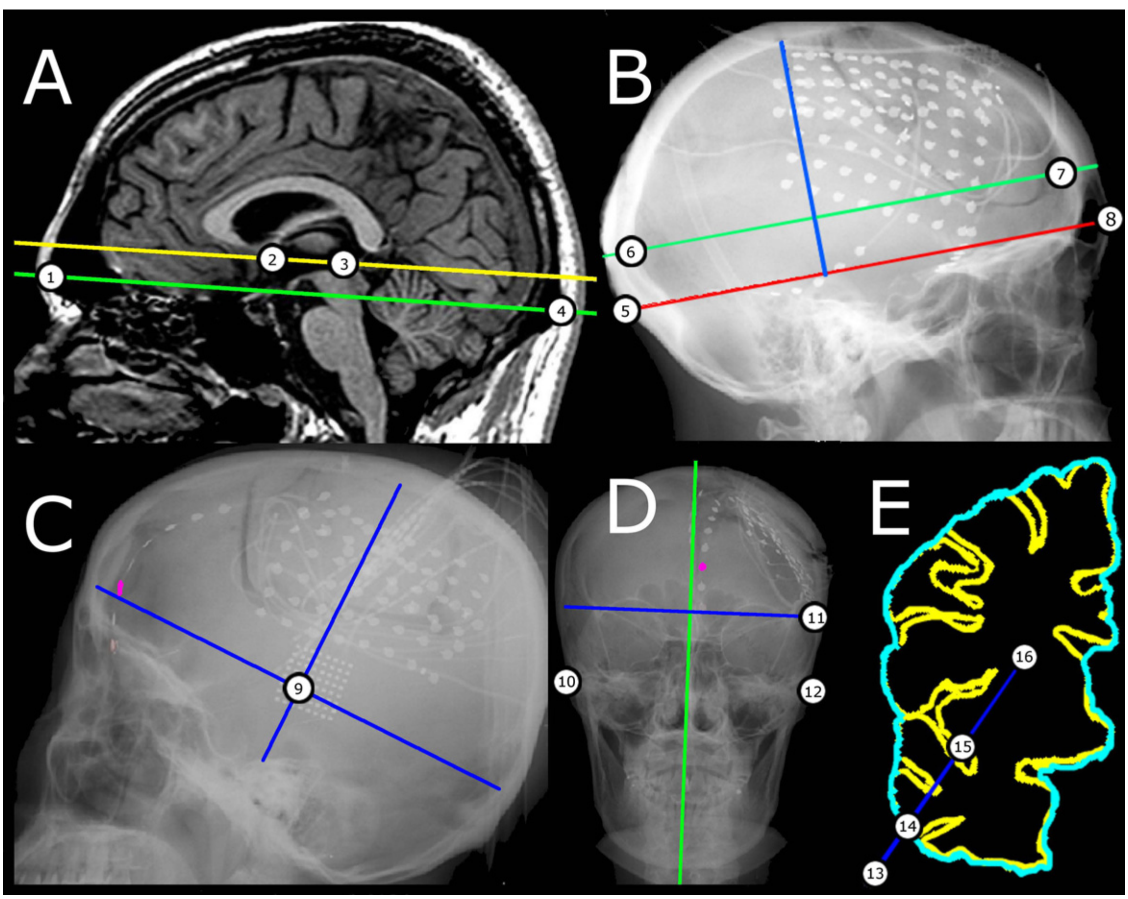

Fig. 1. (A) The anterior commisure–posterior commisure (AC–PC) line (2–3) defines the Talairach y axis, shown in yellow on a patient MRI. The glabella–inion (GI) line (1–4) is parallel to AC–PC line and the glabella (1 and 8) and inion (4 and 5) are therefore used to approximate the AC–PC line. (B) X-ray image of the same patient. The y axis (6–7, teal) is positioned parallel and superior to the GI line (5–8, red), 21% along the length of the longest perpendicular line segment joining the GI line to the skull's inner table (perpendicular line, blue). The distance between posterior and anterior inner tables of the skull (6–7) along the y axis is scaled to template dimensions. (C) The y–z origin, the estimated position of the AC, is defined 115 mm anterior of the midpoint (9) of the line segment between the two skull tables. (D) A vertical line segment is drawn that perpendicularly bisects a user-defined line segment joining two symmetric structures (10 and 12). The x, y, z origin is defined as the intersection of this line segment with the y–z origin defined on the lateral projection. The maximal biparietal distance measured on the AP X-ray (11) is scaled to the template brain. (E) Points that do not fall on the cortex after identification using the AP and lateral X-rays (e.g. 13 and 15) may be projected to the surface of cortex by switching to spherical coordinates, with the center of mass of the surface template (shown in light blue) as the origin (16). The point on the surface template (14) for this solid angle (dark blue line) defines the replacement location, which is converted to standard Talairach coordinates. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

Washington Regional Epilepsy Center. As part of standard clinical practice, subdural platinum electrode arrays with 1 cm center-to-center separation were implanted for seizure localization (AdTech, Racine, WI). Digital skull X-rays were obtained for clinical purposes to localize the subdural electrodes. These X-rays were stored and analyzed as part of a pre-approved research protocol supervised by the University of Washington Institutional Review Board.

The X-ray images were converted to JPEG or BMP format and used with the Location on Cortex (LOC) package for MATLAB, freely downloadable from the EEGLAB site (Swartz Center for Computational Neuroscience, 2006, see http://sccn.ucsd.edu/eeglab/plugins.html).

The orthogonal axes in Talairach space were calculated using skull landmarks. The user identifies the glabella and inion, and the inner table of the skull. Complementary bilateral structures on the AP X-ray (for example, the mandibular condyles) are used to define the x origin.

Using the inner table of the skull to approximate the dimensions of the surface of the brain, the axes are linearly scaled to match the MNI template brain in Talairach coordinates. This is done by resizing the width of the brain to 138 mm, the anterior–posterior length of the brain to 173 mm and the positive z axis to a length of 75 mm.Radio-opaque electrodes present on the patient's skull X-rays are co-registered to the template brain surface. Interpolation to a cortical shell template may be used to simplify this process (Lancaster et al., 1999), facilitating the localization of positions off of the cortical surface by telescoping. A convex shell template is generated from the model brain by radially smearing each point, both in the polar direction and the azimuthal direction (see Fig. 1E where the shell is shown in cross section). Cortical surface locations in regions of low curvature from the lateral perspective require localization only the lateral X-ray, since a given y and z coordinate uniquely determine an x coordinate on the surface of the template shell (Fox et al., 1985). In regions of high curvature (e.g. orbitofrontal, occipital, and subtemporal locations), small changes in y and z position produce large changes in the estimated x coordinate. In these cases, the user must also define each electrode location on the AP X-ray to calculate the set of x-coordinates.

By our assumption that the inner table of the skull matches the brain surface, the coordinate triplets may not be precisely on the surface of the template brain. By representing these locations using polar coordinates, they may be radially telescoped to the surface of the convex hemispheric template with the same solid angle. This is illustrated in cross-section in Fig. 1, inset (E).

The LOC package includes graphical rendering functions to present the electrode locations on the surface of the AFNI template brain. Unrestricted three-dimensional rotation is possible to visualize the electrode locations.

An interleaved face and house picture presentation paradigm was used in conjunction with the LOC package to identify subtemporal face processing areas (Fig. 2). An interleaved

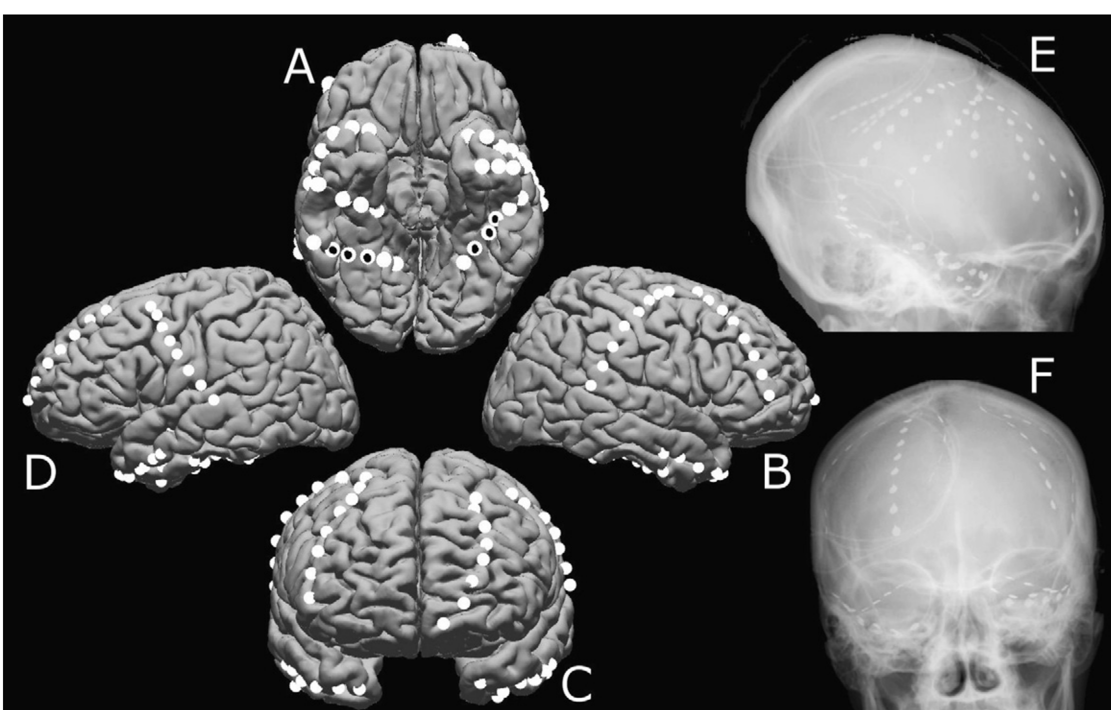

Fig. 2. (A–D) Localization of strip electrodes calculated from lateral (E) and AP (F) X-rays. (A) The functional localization of fusiform gyrus face recognition area in a patient with bitemporal electrode strips. The patient was shown pictures of faces or houses, and areas showing a selective N170 response for face stimuli were identified. Bilateral changes were observed in the electrodes shown with black dots (located at (−41, −27, −22) (−37, −35, −23) (−30, −43 and −17) on the left and (28, −48 and −16), (38, −47 and −21), (47, −44 and −24) on the right). These locations correspond with previously published data for the fusiform face area (Kanwisher et al., 1997).

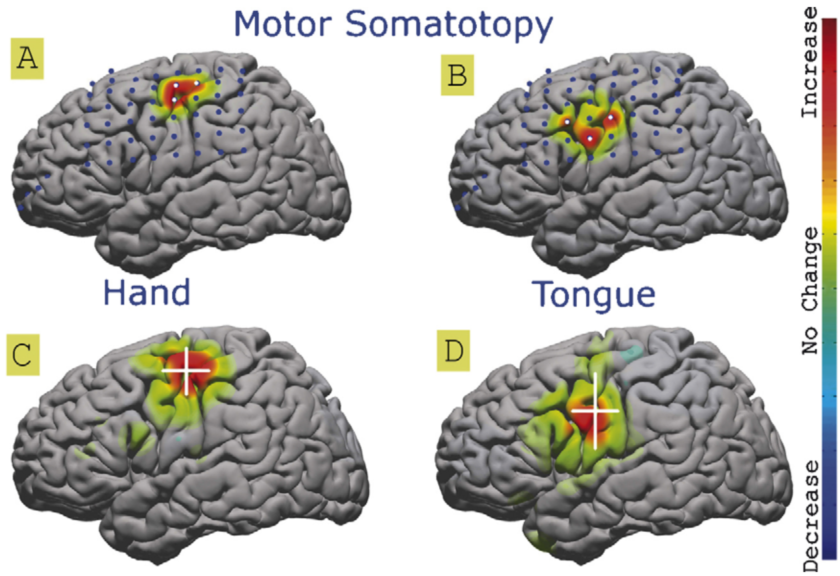

Fig. 3. Gaussian interpolated maps for hand (A and C) and tongue (B and D) changes associated with a movement task in a single patient (A and B) and cohort average (C and D). Yellow and red surface colors indicate power increases in the 76–100 Hz frequency band during this task. Blue dots indicate electrode locations and white dots highlight electrodes with a statistically significant response after Bonferroni correction ($p \ll 0.01$). All highlighted motor electrodes are located within the primary motor area, Brodmann area 4 (Fox and Uecker, 2005). (A) The highlighted electrode coordinates for the hand movement task are (−47, −25 and 57), (−44, −14 and 56), and (−42, −3 and 55). (B) The highlighted electrode coordinates for the tongue movement task are (−60, −3 and 30), (−57, −13 and 40), (−53, 8 and 38). Published coordinates of the activation area center-of-mass based on fMRI data are (−36 ± 3, −22 ± 4 and 58 ± 3) for hand and (−52 ± 3, −5 ± 3, and 29 ± 6) for tongue (Alkadhi et al., 2002). Thus, the observed activation areas in these patients flank the center-of-mass area reported from fMRI data. Insets C and D illustrate the results of hand and tongue area mapping averaged across a large cohort ((C) hand, $n = 17$ and (D) tongue, $n = 14$) and projected to the left hemisphere for all patients. The mean electrode positions were $y = -15 \pm 11$ mm, $z = 52 \pm 11$ mm for hand movement, and $y = -9 \pm 11$ mm, $z = 31 \pm 18$ mm for tongue movement. The white cross represents the mean position and variance along each axis.

movement and rest task where subjects performed 3 s blocks of hand or tongue movement followed by 3 s of rest was used with the LOC package to identify hand and tongue rolandic cortex. Maps of the cross-correlation strength of power changes (between movement and rest) at each electrode in a cortical ensemble are shown in Fig. 3.

To assess the precision of resulting locations and inter-user reproducibility of this method, two of the authors independently calculated the subdural electrode positions using the LOC package.

3. Results

This technique was used on 17 patients enrolled in an electrocortigraphic research study at the University of Washington Regional Epilepsy Center. We present the results for 4 patients as a demonstration of the technique. Figs. 1–3 demonstrate how the LOC program may be used to localize electrodes and visualize electrocorticographic data.

To examine how reproducible the calculation of electrode positions was with this method, two of the authors independently calculated positions in four subjects. For two subjects, the lateral X-ray was used to calculate the location of a 64-electrode grid array. The mean distance between calculated positions was 1.3 mm (S.D.: 2.1 mm) for the first subject and 1.2 mm (S.D.: 0.7 mm) for the second subject. Two other subjects had a total of 36 electrodes each in frontal, sub-temporal, and occipital sites. Electrode locations were calculated from a combination of the lateral and AP X-rays. The mean distance between calculated positions was 3.5 mm for the third subject (S.D.: 2.5 mm) and 3.6 mm (S.D.: 2.4 mm) for the fourth subject. The diameter of each electrode was 4 mm. These results suggest that the method is highly reproducible, with a standard error smaller than the width of each electrode.

The plotting functions of the LOC package may be used to present electrode locations and render electrocorticographic data onto the template brain surface. For example, electrodes found to be significant for some effect may be highlighted, as shown in Fig. 2 where face-specific and visually responsive electrode locations are identified. Simple enumeration of electrode number for identification of relevant areas may be used to compare electrode locations with known functional areas in standardized coordinates. Alternatively, superposition of weighted kernels at each electrode locus presents continuous spatial distributions of electrocorticographic change with a particular task. When the changes in cortical potential with movement are examined both in a single case and in a large cohort, spatial normalization tightly localizes these changes to coordinates in sensorimotor cortex (Fig. 3).

4. Discussion

This Location on Cortex (LOC) package facilitates the rapid localization of subdural electrode arrays onto a standardized template brain volume. Once familiar with the procedure, the average time to localize a 64-contact grid using lateral

X-ray only, or a 20 contact subtemporal strip array using AP and lateral X-ray is 5–10 min. Co-registration of electrode locations by individual calculation takes an hour or more for a 64-contact grid using a lateral X-ray. Calculation of Talaraich axes using both AP and lateral X-rays may take considerably longer, and 3D telescopic interpolation is not feasible by hand.

The major limitations of this technique are the quality of the skull X-rays and the assumptions made based on these X-rays. Differences in X-ray technique may affect the differential magnification of electrodes and skull landmarks. Also, the electrode location calculations assumes the X-rays are directly lateral and AP (i.e., without rotation). Deviations from this assumption may be corrected by rotating all measurements appropriately if the axis and magnitude of rotation is known. Furthermore, the angle of the AP X-ray may affect the amount of superposition of subtemporal electrodes, creating challenges for identifying individual electrodes.

Scaling of the patient's X-ray to match the template brain is limited to the three cardinal directions without oblique correction. This linear transformation limits the accuracy of electrode localization, but the functional results in our patients agree well with known cortical organization, as demonstrated in Figs. 1 and 2.s

Cross-subject variability and postoperative brain shift also limit the accuracy of this technique. The inner table of the skull is used as a surrogate for the cortical surface in calculations; this does not take into account the possible shift in brain shape after implantation of subdural electrode arrays that may result in the electrode locations being mapped to subcortical locations on the template brain. Telescopic projection onto the surface of the template brain is required to reduce this error. Co-registration onto a template may ultimately be limited by cross-subject cortical variability, such as regional differences in cortical cytoarchitecture (Rajkowska and Goldman-Rakic, 1995), or functional variability in, for example, the location of language cortex (Ojemann et al., 1989).

If specialized pre-operative MRI imaging sequences are available, the patient's own brain can be used for the volumetric template using brain extraction algorithms (Dale et al., 1999; Kovalev et al., 2005). This requires normalization of the brain volume to Talairach dimensions. A custom shell can be generated from this, and cortical locations calculated accordingly. These cortical locations plotted on this particular brain will be displayed as biologically precise cortical phenomena, with associated Talairach coordinates to compare with known functional areas.

5. Conclusion

The Location on Cortex (LOC) package implements a rapid and reliable method of estimating the coordinates of radio-opaque markers such as subdural electrocorticography electrodes. The open source LOC package can also be used to visualize clinical and experimental data in a quantitative fashion with reference to a standardized brain template. This tool can be readily implemented in clinical research settings in which invasive electrophysiology is recorded during the treatment of patients with medically refractory seizures or other brain pathologies.

Acknowledgements

KJM is funded by the Poncin award, the NIH MSTP grant, a Neurosurgical Training Grant through the University of Washington and the Packard award via RPNR. AOH is funded by the Epilepsy Foundation through the generous support of Abbott Laboratories. JGO is funded by NS41272. SM is funded in part by the Swartz Foundation. The National Institute for Mental Health (RO1-NS497293) supports the continued development of the open source EEGLAB environment.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jneumeth.2007.01.019.

References

Alkadhi H, Crelier GR, Boendermaker SH, Golay X, Hepp-Reymond MC, Kollias SS. Reproducibility of primary motor cortex somatotopy under controlled conditions. AJNR Am J Neuroradiol 2002;23:1524–32.

Brett M, Johnsrude IS, Owen AM. The problem of functional localization in the human brain. Nat Rev Neurosci 2002;3:243–9.

Collins DL, Neelin P, Peters TM, Evans AC. Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. J Comput Assist Tomogr 1994;18:192–205.

Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage 1999;9:179–94.

Fox M, Uecker A. Talairach Daemon Client (2.0). 2005. http://ric.uthscsa.edu/projects/talairachdaemon.html.

Fox PT, Perlmutter JS, Raichle ME. A stereotactic method of anatomical localization for positron emission tomography. J Comput Assist Tomogr 1985;9:141–53.

Friston KJ, Passingham RE, Nutt JG, Heather JD, Sawle GV, Frackowiak RS. Localisation in PET images: direct fitting of the intercommissural (AC-PC) line. J Cereb Blood Flow Metab 1989;9:690–5.

Holmes CJ, Hoge R, Collins L, Woods R, Toga AW, Evans AC. Enhancement of magnetic resonance images using registration for signal averaging. J Comp Asst Tomogr 1998;22(2):324–33.

Kanwisher N, McDermott J, Chun MM. The fusiform face area: a module in human extrastriate cortex specialized for face perception. J Neurosci 1997;17:4302–11.

Kovalev D, Spreer J, Honegger J, Zentner J, Schulze-Bonhage A, Huppertz HJ. Rapid and fully automated visualization of subdural electrodes in the presurgical evaluation of epilepsy patients. AJNR Am J Neuroradiol 2005;26:1078–83.

Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314–9.

Lancaster JL, Fox PT, Downs H, Nickerson DS, Hander TA, El Mallah M, et al. Global spatial normalization of human brain using convex hulls. J Nucl Med 1999;40:942–55.

Lesser R, Gordon B, Fisher R, Hart J, Uematsu S. Subdural grid electrodes in surgery of epilepsy. In: Luders HO, editor. Epilepsy surgery. New York: Raven Press; 1991. p. 399–408.

Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurg 1989;71:316–26.

Rajkowska G, Goldman-Rakic PS. Cytoarchitectonic definition of prefrontal areas in the normal human cortex: II. Variability in locations of areas 9 and 46 and relationship to the Talairach Coordinate System. Cereb Cortex 1995;5:323–37.

S. Swartz. Center for Computational Neuroscience. EEGLAB—Open Source Matlab Toolbox for Electrophysiological Research; 2006. http://www.sccn.ucsd.edu/eeglab/.

Talairach J, Tournoux P. Co-planar stereotaxic atlas of the human brain. Thieme; 1988.

Wellmer J, von Oertzen J, Schaller C, Urbach H, Konig R, Widman G, et al. Digital photography and 3D MRI-based multimodal imaging for individualized planning of resective neocortical epilepsy surgery. Epilepsia 2002;43:1543–50.