Published in final edited form as:

J Neurosci Methods. 2008 September 15; 174(1): 106–115. doi:10.1016/j.jneumeth.2008.06.02.

Localization of neurosurgically implanted electrodes via photograph-MRI-radiograph coregistration

Sarang S. Dalal^{a,b}, Erik Edwards^{a,e}, Heidi E. Kirsch^d, Nicholas M. Barbaro^{c,d}, Robert T. Knight^e, and Srikantan S. Nagarajan^{a,b}

^a Biomagnetic Imaging Laboratory, Department of Radiology, University of California, San Francisco, CA 94143-0628, USA

^b Joint Graduate Group in Bioengineering, University of California, San Francisco and University of California, Berkeley, USA

^c Department of Neurological Surgery, University of California, San Francisco, CA 94143-0112, USA

^d Department of Neurology, University of California, San Francisco, CA 94143-0138, USA

^e Helen Wills Neuroscience Institute and Department of Psychology, University of California, Berkeley, CA 94720-3190, USA

Abstract

Intracranial electroencephalography (iEEG) is clinically indicated for medically refractory epilepsy and is a promising approach for developing neural prosthetics. These recordings also provide valuable data for cognitive neuroscience research. Accurate localization of iEEG electrodes is essential for evaluating specific brain regions underlying the electrodes that indicate normal or pathological activity, as well as for relating research findings to neuroimaging and lesion studies. However, electrodes are frequently tucked underneath the edge of a craniotomy, inserted via a burr hole, or placed deep within the brain, where their locations cannot be verified visually or with neuronavigational systems. We show that one existing method, registration of postimplant CT with preoperative MRI, can result in errors exceeding 1 cm.

We present a novel method for localizing iEEG electrodes using routinely acquired surgical photographs, X-ray radiographs, and magnetic resonance imaging (MRI) scans. Known control points are used to compute projective transforms that link the different image sets, ultimately allowing hidden electrodes to be localized, in addition to refining the location of manually registered visible electrodes. As the technique does not require any calibration between the different image modalities, it can be applied to existing image databases. The final result is a set of electrode positions on the patient's rendered MRI yielding locations relative to sulcal and gyral landmarks on individual anatomy, as well as MNI coordinates. We demonstrate the results of our method in eight epilepsy patients implanted with electrode grids spanning the left hemisphere.

Keywords

Subdural electrodes; Intracranial electroencephalography; Electrocorticography; Epilepsy surgery; 3-D localization; Coregistration; Surface rendering; X-ray; CT; MRI

Email address: E-mail: sri@radiology.ucsf.edu (Srikantan S. Nagarajan).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1 Introduction

Intracranial electroencephalography (iEEG) is indicated in potential neurosurgical patients when noninvasive diagnostic techniques prove inconclusive (Bancaud et al., 1965). Most of these patients have medically intractable epilepsy, requiring long-term invasive monitoring to localize seizure foci as well as to prevent resection of critical brain areas that would result in cognitive deficits or paralysis (Wyler et al., 1988; Lesser et al., 1991). These recordings also provide rare but highly valuable data to test basic hypotheses in neurophysiology and cognitive neuroscience. Furthermore, iEEG is a promising avenue for the development of neural prostheses designed to aid patients with brain or spinal cord damage resulting from trauma, stroke, or neurodegenerative diseases (Leuthardt et al., 2006; Santhanam et al., 2006; Hochberg et al., 2006).

Accurate localization of iEEG electrodes is critical for planning resective surgery as well as for relating iEEG findings to the larger neuroimaging literature. Direct visual observation of electrode positions, perhaps supplemented by neuronavigational systems (Barnett et al., 1993) or recorded with digital photography (Wellmer et al., 2002; Mahvash et al., 2007), provides the most reliable information. However, many electrodes are tucked underneath the edge of a craniotomy or guided into locations deep within the brain, and so their final locations relative to brain anatomy are not precisely known since they cannot be visually verified. In some procedures, electrodes may be inserted into the subdural space via a small burr hole.

Postimplant radiographs (X-rays) are routinely ordered at most epilepsy centers, and while they are high-resolution, they are nevertheless flat 2D projections that give little indication of underlying brain anatomy. They are typically used to visualize the approximate extent and curvature of the implanted electrode arrays. Simple measurements can be performed to estimate rough electrode positioning on anatomy (Fox et al., 1985; Miller et al., 2007). However, variable magnification and distortion as well as inherent variability in anatomy and X-ray configuration between patients may reduce the accuracy of these measurements.

Many epilepsy centers obtain postimplant computed tomography (CT) scans to visualize the 3D configuration of the electrodes. However, CT has poor soft tissue contrast and brain structures are very difficult to discern, especially in the presence of severe streaking artifacts caused by the electrodes themselves. Therefore, CT scans must be coregistered to preoperative magnetic resonance imaging (MRI) scans in order to visualize electrode positions on brain anatomy (Grzeszczuk et al., 1992; Winkler et al., 2000; Nelles et al., 2004; Hunter et al., 2005). However, the resolution of CT is often poor, resulting in partial volume effects. Additionally, the brain may shift considerably following the electrode implant (Hastreiter et al., 2004; Miyagi et al., 2007), contributing to significant errors in the coregistered locations of electrodes. These disadvantages are compounded by the fact that CT can be uncomfortable and sometimes risky for implanted epilepsy patients, and monitoring must be stopped during the exam. Finally, head CT delivers approximately 200 times the radiation dose of a lateral skull radiograph (Wall and Hart, 1997).

Some groups acquire postimplant MRI scans, which can visualize brain anatomy with high fidelity. Unfortunately, many electrodes can be difficult to see on them (Bootsveldt et al., 1994); furthermore, from MRI scans published in the literature (Schulze-Bonhage et al., 2002; Kovalev et al., 2005; Sochůrková et al., 2006), it seems likely that electrodes on arrays with spacing tighter than 1 cm would be indistinguishable. Susceptibility artifacts from the electrode material may also distort the images. MRI is also relatively expensive, and, as with CT, many epilepsy centers consider postimplant MRIs to be unjustifiably risky.

We present a procedure and algorithm for localizing electrodes implanted into the brains of neurosurgery patients and for interactively linking a 3D preoperative MRI with a 2D postimplant radiograph and surgical photographs. The method provides a more robust estimate of electrode positions than previously possible. Additionally, we use the transformation matrices to create an interactive viewer that links coordinates on the MRI, photograph, and radiograph; this both verifies goodness of fit as well as assists identification of other structural features on the radiograph by corresponding them to 3D locations on the patient's MRI.

2 Methods

2.1 Patients and Electrodes

Eight intractable epilepsy patients (referred to as GP1 – GP8) were implanted with subdural electrodes for the purpose of planning resective surgery. Electrode implants were guided strictly by clinical indications and research recordings were approved by the Committees on Human Research at the University of California, San Francisco and the University of California, Berkeley. The electrodes were 4 mm diameter platinum-iridium disks with a 2.3 mm contact width, embedded within a Silastic sheet (Ad-Tech Medical, Racine, WI, USA). The center-to-center spacing between electrodes was 10 mm. Grid electrodes consisted of 64 electrodes arranged in an 8×8 square and placed on the surface of left frontotemporal cortex in all patients. Electrode grids were sewn to the dura to minimize movement after placement. Supplemental 4×1 or 6×1 electrode strips (10 mm spacing) were also placed on the cortical surface in some patients.

2.2 Medical Images

High-resolution T1-weighted MRI scans were acquired with a FSPGR sequence at a resolution of 0.43×1.5×0.43 mm on a 3 T scanner (GE, Milwaukee, WI, USA). Lateral skull film radiographs were obtained in 6 patients, and digitized at approximately 0.15×0.15 mm. Postimplant CT scans were acquired on GP1 and GP2 at a resolution of 0.43×0.43×3.75 mm.

Digital photographs were taken of the craniotomy both prior to and following placement of the electrodes using a consumer-grade camera (except GP1, who only had a post-placement photograph). The camera was handheld roughly 50 cm away from the exposed cortex and oriented approximately orthogonal to it.

2.3 MRI Processing

Skull and scalp tissue were stripped from the structural MRIs with the Brain Extraction Tool (Jenkinson et al., 2005, <http://www.fmrib.ox.ac.uk/analysis/research/bet/>). This segmented volume was used to determine the coordinates of points on the brain surface as well as create rendered brains with MRICro (Rorden and Brett, 2000, <http://www.sph.sc.edu/comd/rorden/mricro.html>).

2.4 Registration of Surgery Photographs

Two photographs are typically taken during surgical implantation of the electrode array—one showing the exposed brain (*anatomical photograph*, Figure 1b) and one showing the electrode grid on top of the brain (*grid photograph*, Figure 1a). The plastic and cabling of the electrode grid partially occludes the view of the brain anatomy underneath it; therefore, it is useful to transfer the coordinates of the electrodes seen in the grid photograph to the anatomical photograph. Fortunately, matching two photographs of the same scene taken with an uncalibrated camera is a 2D homography problem that is well-studied in the field of computer vision; given at least four matched point pairs called *control points*, a *projective transform* may be computed to map any given point from one photograph to the other (Abdel-Azziz and

Karara, 1971; Hartley and Zisserman, 2004). The projective transform automatically corrects for the inherent change in perspective and distance expected from two photographs taken at different moments with a handheld camera. In the case at hand, several control points can easily be chosen on the two photographs, including prominent features of blood vessels, distinct corners of the craniotomy, fixed sutures, and other stationary surgical hardware.

Given N pairs of control points with coordinates $\mathbf{a}_i \equiv (x_i, y_i)$ from the first photograph and $\mathbf{b}_i \equiv (u_i, v_i)$ from the second photograph, the projective transform may be computed as follows: First, the coordinates are normalized with transforms $\mathbf{T}_1$ and $\mathbf{T}_2$, respectively, such that the centroid for each group is (0,0) and the mean distance from the origin is $\sqrt{2}$ for each set of points. Let us define $\tilde{\mathbf{a}}_i \equiv \mathbf{T}_1[\mathbf{a}_i \ 1]^T$ and $\tilde{\mathbf{b}}_i \equiv \mathbf{T}_2[\mathbf{b}_i \ 1]^T$, with $\tilde{\mathbf{a}}_i = (\tilde{x}_i, \tilde{y}_i, 1)$ and $\tilde{\mathbf{b}}_i = (\tilde{u}_i, \tilde{v}_i, 1)$. The coordinate vectors are augmented with unity as a scaling factor, which will become important later.

Then, the discrete linear transformation (DLT) algorithm can be used to determine the 3×3 projective transform $\tilde{\mathbf{P}}$ that best maps $\tilde{\mathbf{a}}$ to $\tilde{\mathbf{b}}$ (Abdel-Azziz and Karara, 1971; Hartley and Zisserman, 2004):

$$\tilde{\mathbf{P}} = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & 1 \end{bmatrix} \quad (1)$$

where the entries in $\tilde{\mathbf{P}}$ can be determined by solving the following $2N \times 8$ system:

$$\begin{bmatrix} \tilde{x}_1 & \tilde{y}_1 & 1 & 0 & 0 & 0 & -\tilde{u}_1\tilde{x}_1 & -\tilde{u}_1\tilde{y}_1 \\ 0 & 0 & 0 & \tilde{x}_1 & \tilde{y}_1 & 1 & -\tilde{v}_1\tilde{x}_1 & -\tilde{v}_1\tilde{y}_1 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \tilde{x}_N & \tilde{y}_N & 1 & 0 & 0 & 0 & -\tilde{u}_N\tilde{x}_N & -\tilde{u}_N\tilde{y}_N \\ 0 & 0 & 0 & \tilde{x}_N & \tilde{y}_N & 1 & -\tilde{v}_N\tilde{x}_N & -\tilde{v}_N\tilde{y}_N \end{bmatrix} \begin{bmatrix} p_{11} \\ p_{12} \\ p_{13} \\ p_{21} \\ p_{22} \\ p_{23} \\ p_{31} \\ p_{32} \end{bmatrix} = \begin{bmatrix} \tilde{u}_1 \\ \tilde{v}_1 \\ \tilde{u}_2 \\ \tilde{v}_2 \\ \vdots \\ \tilde{u}_N \\ \tilde{v}_N \end{bmatrix} \quad (2)$$

When $N > 4$, the system is overdetermined, but may be solved in a least squares sense using singular value decomposition. Then, in order to apply the transform to the original coordinate spaces, the normalization transforms must be applied to $\tilde{\mathbf{P}}$:

$$\mathbf{P} \equiv \mathbf{T}_2^{-1} \tilde{\mathbf{P}} \mathbf{T}_1 \quad (3)$$

Finally, $\mathbf{P}$ may be applied to any point $\mathbf{m} \equiv (m_x, m_y)$ from the first image to estimate the corresponding point $\hat{\mathbf{n}} \equiv (\hat{n}_u, \hat{n}_v)$ on the second image:

$$\begin{bmatrix} k\hat{n}_u \\ k\hat{n}_v \\ k \end{bmatrix} = \mathbf{P} \begin{bmatrix} m_x \\ m_y \\ 1 \end{bmatrix} \quad (4)$$

Note that after applying the transform to (m_x, m_y) , the first two elements of the output vector must be divided by the third, k , to yield $(\hat{n}_u, \hat{n}_v)$. This effectively removes any perspective

distortion; in fact, if P defines an affine transform, then the mapping is distortionless by definition and $k = 1$.

The transform requires matching of fixed landmarks (*fiducials*) between the two photographs; in this application, features on visible portions of the brain, blood vessels, and fixed surgical hardware may be used as landmarks for control points. The computed transform can then estimate the coordinates on the anatomical photograph corresponding to any point from the grid photograph. Therefore, the transform is applied to the coordinates of all visible electrodes in the grid photograph. This method does not require that the two photographs be taken with identical parameters (e.g., the angle, distance, and zoom/focus settings need not be the same).

2.5 Photograph-MRI Registration

The locations of visible electrodes from the photograph can then be manually annotated on a high-resolution MRI surface rendering of the patients brain. This yields a set of 3D coordinates of known electrode positions in MRI space (Figure 1c). This process may be assisted with the use of a 3D-2D projective transform (see Section 2.6 below), or a feature matching algorithm may help automate this step (e.g., Yuan et al., 2004).

2.6 MRI-Radiograph Registration

The projective transform used above to register two photographs of the same scene may be extended to a more general “camera” problem (Abdel-Azziz and Karara, 1971). A photograph is a projection of 3D “world” points onto a 2D image plane; light rays from the photographed scene converge onto a focal point behind the image plane (film or digital sensor). Note that radiography is a special case of the camera problem in which the focal point is actually the X-ray source; the X-rays then *diverge* before being absorbed by the imaged object or the film/sensor (image plane) behind it. Fortunately, most camera geometry principles and formulae are readily generalizable to the case of radiography with the proper assignment of polarities to various parameters. Thus, in our case, the 3D world data is represented by the MRI and the photographic projection is represented by the X-ray image. It should be noted that due to the fan beam configuration of typical clinical X-ray sources, an affine transform—which assumes parallel rays—would result in greater registration errors.

Given at least six control points matching 3D world locations to a 2D image plane, a 3×4 projective transform may be computed to map *any* 3D location to the image. (Abdel-Azziz and Karara, 1971; Hartley and Zisserman, 2004). In practice, ten or more well-distributed control points are needed to generate a reliable transform. It is difficult to find that many uniquely identifiable yet nonplanar point correspondences given a standard MRI and uncalibrated radiograph. Other approaches require calibration of the X-ray system (including precise measurement of the position and orientation of the X-ray source relative to the patient) and/or placement of additional external markers that can be observed in both sets of images (e.g., Gutiérrez et al., 2005). These methods are cumbersome to implement in clinical practice and cannot work for typical existing data.

However, electrodes are clearly visible on radiographs (Figure 1d) and many of their 3D positions are known from the above photograph-MRI registration. Therefore, several known 3D-2D point correspondences exist from the visible electrodes. With the addition of some potentially clear anatomical landmarks (e.g., nasion, auditory canals, teeth, and upper vertebrae), enough control points can be defined to create a viable projective transform between the MRI and the radiograph. As a sanity check, the transform can confirm the location of the X-ray source, which in a typical clinical setting is 100 cm from the head. The transform can then be applied to the X-ray positions of the electrodes.

We start with N pairs of control points with coordinates $\mathbf{a}_i \equiv (x_i, y_i, z_i)$ from the MRI and $\mathbf{b}_i \equiv (u_i, v_i)$ from the radiograph. As with the 2D projective transform, the coordinates should be normalized with transforms $\mathbf{T}_1$ and $\mathbf{T}_2$, respectively, such that each set of coordinates has a centroid that falls on the origin and is distributed with a mean distance of $\sqrt{3}$ for the 3D coordinates and $\sqrt{2}$ for the 2D coordinates. Let us define $\tilde{\mathbf{a}}_i \equiv \mathbf{T}_1[\mathbf{a}_i \ 1]^T$ and $\tilde{\mathbf{b}}_i \equiv \mathbf{T}_2[\mathbf{b}_i \ 1]^T$, with $\tilde{\mathbf{a}}_i = (\tilde{x}_i, \tilde{y}_i, \tilde{z}_i)$ and $\tilde{\mathbf{b}}_i = (\tilde{u}_i, \tilde{v}_i)$.

An expanded form of the DLT algorithm can be used to determine the 3×4 projective transform $\mathbf{P}$ that best maps $\tilde{\mathbf{a}}$ to $\tilde{\mathbf{b}}$ (Abdel-Azziz and Karara, 1971; Hartley and Zisserman, 2004):

$$\tilde{\mathbf{P}} \equiv \begin{bmatrix} p_{11} & p_{12} & p_{13} & p_{14} \\ p_{21} & p_{22} & p_{23} & p_{24} \\ p_{31} & p_{32} & p_{33} & 1 \end{bmatrix} \quad (5)$$

where the entries in $\tilde{\mathbf{P}}$ can be determined by solving the following $2N \times 11$ system:

$$\begin{bmatrix} \tilde{x}_1 & \tilde{y}_1 & \tilde{z}_1 & 1 & 0 & 0 & 0 & 0 & -\tilde{u}_1\tilde{x}_1 & -\tilde{u}_1\tilde{y}_1 & -\tilde{u}_1\tilde{z}_1 \\ 0 & 0 & 0 & 0 & \tilde{x}_1 & \tilde{y}_1 & \tilde{z}_1 & 1 & -\tilde{v}_1\tilde{x}_1 & -\tilde{v}_1\tilde{y}_1 & -\tilde{v}_1\tilde{z}_1 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \tilde{x}_N & \tilde{y}_N & \tilde{z}_N & 1 & 0 & 0 & 0 & 0 & -\tilde{u}_N\tilde{x}_N & -\tilde{u}_N\tilde{y}_N & -\tilde{u}_N\tilde{z}_N \\ 0 & 0 & 0 & 0 & \tilde{x}_N & \tilde{y}_N & \tilde{z}_N & 1 & -\tilde{v}_N\tilde{x}_N & -\tilde{v}_N\tilde{y}_N & -\tilde{v}_N\tilde{z}_N \end{bmatrix} \begin{bmatrix} p_{11} \\ p_{12} \\ p_{13} \\ p_{14} \\ p_{21} \\ p_{22} \\ p_{23} \\ p_{24} \\ p_{31} \\ p_{32} \\ p_{33} \end{bmatrix} = \begin{bmatrix} \tilde{u}_1 \\ \tilde{v}_1 \\ \tilde{u}_2 \\ \tilde{v}_2 \\ \vdots \\ \tilde{u}_N \\ \tilde{v}_N \end{bmatrix} \quad (6)$$

Again, in practice the system will be overdetermined (given $N > 6$), so singular value decomposition can be used to find the least squares solution. Next, $\tilde{\mathbf{P}}$ is denormalized so that it may be applied to the original coordinate spaces:

$$\mathbf{P} \equiv \mathbf{T}_2^{-1} \tilde{\mathbf{P}} \mathbf{T}_1 \quad (7)$$

Finally, $\mathbf{P}$ may be applied to any MRI point $\mathbf{m} \equiv (m_x, m_y, m_z)$ to estimate the corresponding point on the radiograph $\hat{\mathbf{r}} \equiv (\hat{r}_u, \hat{r}_v)$:

$$\begin{bmatrix} k\hat{r}_u \\ k\hat{r}_v \\ k \end{bmatrix} = \mathbf{P} \begin{bmatrix} m_x \\ m_y \\ m_z \\ 1 \end{bmatrix} \quad (8)$$

As with the 2D-2D case, the first two elements of the output vector must be divided by the third, k , to remove projective distortion and obtain $(\hat{r}_u, \hat{r}_v)$.

An interesting property of the projective transform $\mathbf{P}$ is that the estimated position of the focal point $\mathbf{f}$ (i.e., the X-ray source) may be directly calculated from it. For the present application,

this serves as a sanity check to ensure that the transform is consistent with the X-ray acquisition specifications. Let us define:

$$M \equiv \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{bmatrix} \quad (9)$$

and

$$p_4 \equiv [p_{14} \quad p_{24} \quad p_{34}]^T \quad (10)$$

such that $P = [M \ p_4]$. Then, the focal point is known to be

$$f = -M^{-1}p_4 \quad (11)$$

Indeed, if M is singular, $\|f\| = \infty$ and therefore P would define an affine transform, which assumes parallel rays with no convergence (i.e., an infinite focal length).

In practice, the DLT method for 3D-2D registration is somewhat sensitive to noise and inaccuracy in the given control points, and the computed X-ray source location is subject to some uncertainty along the axis perpendicular to the X-ray image plane. However, with only knowledge of the distance and approximate direction of the X-ray source, Levenberg-Marquardt optimization (Levenberg, 1944; Marquardt, 1963) may be used to adjust the displacement parameters in the normalization transform T_1 to ensure a reasonable estimate of f and, by extension, P .

Applying the projective transform P maps every 3D MRI point to a 2D radiograph point. We are interested in mapping the radiograph points to the MRI as well, but since P is a 3×4 matrix, P^{-1} is not defined. However, a form of the inverse projective transform does exist! Intuitively, all points on a line passing through the focal point f must map to a single point on the radiograph. Therefore, applying the inverse projective transform to a point on the radiograph should backproject to a *line* in MRI space. For a non-affine projective transform, the line equation is known to be (Hartley and Zisserman, 2004):

$$l(r, \mu) = M^{-1} \left(\mu \begin{bmatrix} r^T \\ 1 \end{bmatrix} - p_4 \right) \quad (12)$$

where $r \equiv (r_u, r_v)$ is the radiograph coordinate to be backprojected, and μ is a parameter that determines position along the backprojected line.

If the electrodes are known to be on the brain surface, then their coordinates are easily found by backprojecting each electrode's X-ray location and finding the intersection with the set of MRI points comprising the brain outline (Figure 1e,f).

It should be noted that large backprojection errors may arise in areas where the brain curves sharply away from the X-ray image plane. For example, when backprojecting to the bottom of the temporal lobe from a lateral radiograph, small errors along the superior-inferior axis of the brain may result in large displacement along the left-right axis. Additionally, electrodes are sometimes placed at depth within the brain. In these cases, known electrode spacing can be used to constrain the solution. Alternatively, if multiple X-ray views are available, projective

transforms can be computed for each of them; these electrodes can then be localized by computing the intersection of their back-projections from each X-ray view.

2.7 Transformation to Canonical Coordinate System

Given a set of electrode positions on a patient's individual 3D MRI space, it is quite straightforward to transform them to a standard coordinate system such as the Montreal Neurological Institute (MNI) template (Evans et al., 1993; Mazziotta et al., 2001). We used SPM2 (<http://www.fil.ion.ac.uk/spm>) to generate the nonlinear spatial transformation function using the preoperative MRI. The transform was then applied to the electrode coordinates determined from X-ray backprojection to obtain corresponding MNI coordinates. After conversion to Talairach coordinates (<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>), the Talairach Daemon (<http://ric.uthscsa.edu/projects/talairachdaemon.html>) may be used to corresponding anatomical labels from the Talairach atlas (Talairach and Tournoux, 1988). Note that since many epilepsy patients have unusual brain anatomy, it is especially important to use spatial normalization only to obtain standardized coordinates; functional activations should be rendered on an individual's MRI rather than a standard template.

2.8 Interactive Navigation

Another 3D-2D projective transform can be synthesized to map MRI surface points onto the anatomical photograph, using the electrode positions from Section 2.5 and/or distinct anatomical features as control points. We have created an interactive navigation tool that uses this MRI-photograph transform along with the the MRI-radiograph transform to allow a user to select any point on the MRI and immediately see that point's corresponding projection on the radiograph and photograph (Figure 2). Conversely, selecting a point on the radiograph defines a corresponding point on the photograph and a line (i.e., the X-ray path) on the MRI. Finally, if MNI spatial normalization has been performed, corresponding MNI coordinates and anatomical labels can be displayed.

2.9 Performance Evaluation

2.9.1 Accuracy of MRI-Radiograph Projective Transform—To evaluate the performance of the proposed technique, particularly for electrode locations that are not used as control points, we selected one patient (GP6) for further analysis. Since it is not possible to definitively validate the computed coordinates for electrodes that are located beyond extent of the craniotomy, another projective transform was generated using six of the 47 visible electrodes, along with four anatomical fiducials (superior orbital ridge, left and right auditory canals, and the vertex). This effectively simulates a scenario with a smaller craniotomy that exposes only these six electrodes, providing a means to assess the accuracy of the remaining 41 locations computed using the proposed technique. The coordinates found from X-ray backprojection were compared with the photograph-derived coordinates not used to compute the transform, as well as the set of backprojected coordinates resulting from using all 47 visible electrodes plus the 4 anatomical fiducials.

2.9.2 CT-MRI Coregistration—GP1 and GP2 had CT scans in addition to high-resolution preoperative MRI scans; GP1 additionally had a postimplant lateral radiograph. CT-MRI coregistration was performed with SPM2 using a normalized mutual information algorithm. (Simple fiducial-based coregistration was first attempted with unsatisfactory results.) The quality of coregistration was visually verified by ensuring good agreement of skull shape between the CT and MRI. Electrode coordinates were found using our proposed method and compared with the electrode positions derived from the coregistered CT scan. 3D renderings of CT electrode positions on the MRI were created with MRICro. Figures showing coregistered

CT/MRI slices were generated with OsiriX (Rosset et al., 2004, <http://homepage.mac.com/rossetantoine/osirix/>).

3 Results

The photographs, radiographs, and final annotated brain renderings for all eight patients are shown in Figure 3. The total time for image registration, annotation, and rendering was typically 5 hours per patient as performed by a trained researcher/technician.

3.1 Performance Evaluation

One patient's image (GP6) was selected for further analysis to validate algorithm performance. Electrode locations found by computing projective transforms based on all visible electrodes had a mean discrepancy of 1.5 mm (s.d. 0.5 mm, max 2.7 mm) when compared to the photograph-derived coordinates (Figure 4, blue points). Using only a subset of six electrodes to compute the projective transform, the output electrode locations yielded only a mean discrepancy of 2.0 mm (s.d. 1.0 mm, max 4.6 mm) from the photograph-based positions (Figure 4, yellow points).

3.2 CT-MRI Coregistration

As shown in Figure 5, coregistration of the postimplant CT with the preimplant MRI did not yield a satisfactory solution for either patient. Even though the skull and intact right hemisphere were well-registered, several surface electrodes coregistered to locations more than 1 cm deep into brain tissue on the MRI in both patients (Figure 5, column 1). Another CT-MRI overlay (Figure 5, column 4) clearly shows that the ventricles, midline, and exposed cortical surface shifted considerably. These displacements are likely due to the craniotomy, associated swelling, and the thickness of the cables and electrodes themselves.

Therefore, it was necessary to project electrode locations from the CT to the brain surface. Figure 6 compares the results of this procedure to electrode locations from the surgical photograph. For GP1, the discrepancy of CT-based electrode positions with the photograph-based positions averaged 7.5 mm (s.d. 2.5 mm), with a maximum error of 14.5 mm. For the other patient (GP2), the discrepancy averaged 4.3 mm (s.d. 2.1 mm), with a maximum error of 7.6 mm. In both cases, upon removal of the grid implant, the surgeon (NMB) confirmed that the grid had not shifted from the implant photograph. Additionally, iEEG recordings from these patients showed patterns consistent with the photograph-based electrode locations, such as phase reversals across the Sylvian fissure as well as auditory and motor responses in expected areas (Canolty et al., 2006,2007;Dalal et al., 2008).

4 Discussion

We have presented a method for registration of electrode positions from standard medical images. In summary, pre-implant and post-implant digital photographs are registered with each other via a projective transform. Next, the pre-implant photograph, now annotated with the visible electrode positions, is used to manually annotate the corresponding anatomy on an MRI rendering of the brain. These visible electrodes are then used to compute another projective transform between the MRI and the radiograph. Finally, backprojection using this transform reveals the locations of occluded electrodes.

We have demonstrated that our procedure outputs an accurate localization of electrode positions and does not require additional imaging procedures that add risk, radiation exposure, and expense to standard practice. Our technique makes use of digital photographs and high-resolution MRIs that have only recently been incorporated into the standard of care for epilepsy

surgery patients. Precise knowledge of the X-ray configuration, placement of additional fiducial markers on the patient, and special calibration are not required. Most importantly, as the input images required are already collected by most neurosurgery centers, the technique can be quickly implemented and introduced to clinical use as well as applied to archived images from past patients for research use.

We have also shown that a popular technique for electrode localization, coregistration of postimplant CT scans with preoperative MRI scans, may not provide accurate results. The thicker slices usually obtained with standard clinical CT scanners result in significant partial volume averaging and coarse resolution along the superior-inferior axis. Furthermore, coregistrations may be unreliable since simply performing a craniotomy is known to significantly deform brain tissue (Hill et al., 1998; Roberts et al., 1998); particularly for patients implanted with chronic electrodes, swelling and the thickness of the electrodes along with associated hardware can contribute to further brain tissue displacement relative to the preoperative MRI. While the same issues may arise with our technique since we are also registering postimplant images with preoperative structure, we expect their impact to be less significant since the algorithm fits only the portion of the brain covered by electrodes and incorporates highly reliable information from the surgical photographs. Therefore, the various projective transforms involved may effectively absorb some brain deformation.

We have applied our method to register superficial electrodes, for which the estimated solution is the intersection of the X-ray backprojection with the cortical surface. The localization of deep electrode arrays can also be accomplished if the depth of the shallowest electrode contact is used to choose the displacement along the backprojected line from the cortical surface. The remaining electrodes can then be computed similarly using known electrode spacing. If additional X-ray views are available, depth electrode locations may instead be localized by computing separate projective transforms for each X-ray. The solution would then be the intersection of the multiple backprojected lines for a given electrode.

While having a full set of high-quality image data (photographs, MRI, and radiograph) increases confidence in the results, the presented technique is still useful if some images are poor or missing altogether. As anatomy is still identifiable through the Silastic electrode sheet in a good-quality post-implant photograph, the pre-implant photograph is not strictly necessary, though it does ease the procedure to have it. Without a radiograph, MRI-photograph registration can be performed, and the position of hidden electrodes can be estimated from known electrode spacing and brain curvature (e.g., see results for GP7 shown in Figure 3(b)). MRI-radiograph coregistration can still be performed in the absence of surgical photographs with an estimate of a few electrode positions on the MRI and the use of other anatomical features as control points. (This last scenario likely would not provide results better than CT-MRI registration, but provides an option in the event of an archived patient dataset in which no photographs or CT are available.) Finally, at any point in the process, electrode locations can be manually adjusted to account for information from other sources such as known electrode spacing, CT coregistration, or coordinates from surgical navigation devices.

One metric to evaluate the quality of the solution for hidden electrodes in individual patients would be to examine the spacing of estimated electrode locations. Since electrode spacing is generally known, a large disagreement would suggest a suboptimal solution. In this event, however, the electrode spacing can then be used to constrain the solution and provide a satisfactory result, even in regions of high brain convexity where a small error in X-ray coordinates can result in large backprojection errors.

Much of the time required for our procedure was spent simply converting between different image formats and manually transcribing coordinates; manual annotation of visible electrodes

and landmarks on the various images also consumed a large proportion of time. However, with further development, all required procedures can be implemented as an integrated software package, and it should be possible to automate the image annotation procedures. We expect this could reduce overall rendering time to less than 2 hours per patient.

The algorithm presented is a valuable complement to existing medical imaging software that fuses different imaging modalities (e.g., existing software coregisters MRI and CT or MRI and PET). It would be useful as part of a suite of programs specifically intended for the diagnostic imaging and monitoring of neurosurgery patients with implanted electrodes. We have found that our interactive navigation tool to be clinically useful to aid in the positive identification of structures of interest on the X-ray and photograph; it could also be suitable in an educational setting to help students connect neuroanatomy with radiographs, photographs, MRI slices, and MRI renderings.

Acknowledgments

The authors would like to thank Paul A. Garcia and David S. Filippi for acquisition of surgical photographs, Robert G. Gould and Jim Buescher for helpful information on X-ray acquisition protocols, Kenneth E. Hild II for insightful discussions on algorithmic topics, and Susanne M. Honma for critical assistance in tracking down the medical images and personnel necessary for this project. We also thank Johanna M. Zumer and Edward F. Chang for their helpful comments on this manuscript. SSD was supported in part by NIH Grant F31 DC006762.

References

- Abdel-Azziz, Y.; Karara, H. Direct linear transformation from comparator coordinates into object space coordinates in close-range photogrammetry. *Papers from the 1971 ASP Symposium on Close-range Photogrammetry*. American Society for Photogrammetry; Falls Church, VA. Jan. 1971 p. 1-18.
- Bancaud, J.; Talairach, J.; Bonis, A. *La stéréo-électroencéphalographie dans l'épilepsie*. Masson; Paris: 1965.
- Barnett GH, Kormos DW, Steiner CP, Morris H. Registration of EEG electrodes with three-dimensional neuroimaging using a frameless, armless stereotactic wand. *Stereotact Funct Neurosurg* 1993;61:32–38. [PubMed: 8197325]
- Bootsveldt K, Träber F, Kaiser WA, Layer G, Elger CE, Hufnagel A, Gieseke J, Reiser M. Localisation of intracranial EEG electrodes using three dimensional surface reconstructions of the brain. *European Radiology* 1994;4:52–56.
- Canolty RT, Edwards E, Dalal SS, Soltani M, Nagarajan SS, Kirsch HE, Berger MS, Barbaro NM, Knight RT. High gamma power is phase-locked to theta oscillations in human neocortex. *Science* 2006;313:1626–1628. [PubMed: 16973878]
- Canolty RT, Soltani M, Dalal SS, Edwards E, Dronkers NF, Nagarajan SS, Kirsch HE, Barbaro NM, Knight RT. Spatiotemporal dynamics of word processing in the human brain. *Frontiers in Neuroscience* 2007;1(1):185–196. [PubMed: 18982128]
- Dalal SS, Guggisberg AG, Edwards E, Sekihara K, Findlay AM, Canolty RT, Berger MS, Knight RT, Barbaro NM, Kirsch HE, Nagarajan SS. Five-dimensional neuroimaging: Localization of the time-frequency dynamics of cortical activity. *NeuroImage* 2008;44
- Evans AC, Collins DL, Mills SR, Brown ED, Kelly RL, Peters TM. 3D statistical neuroanatomical models from 305 MRI volumes. *Proc IEEE Nucl Sci Symp Med Imaging Conf* 1993;3:1813–1817.
- Fox PT, Perlmuter JS, Raichle ME. A stereotactic method of anatomical localization for positron emission tomography. *J Comput Assist Tomogr* 1985;9(1):141–153. [PubMed: 3881487]
- Grzeszczuk R, Tan KK, Levin DN, Pelizzari CA, Hu X, Chen GTY, Beck RN, Chen C-t, Cooper M, Milton J, Spire JP, Towle VL, Dohrmann GJ, Erickson RK. Retrospective fusion of radiographic and MR data for localization of subdural electrodes. *J Comput Assist Tomogr* 1992;16(5):764–773. [PubMed: 1522271]
- Gutiérrez, LF.; Shechter, G.; Lederman, RJ.; McVeigh, ER.; Ozturk, C. Distortion correction, calibration, and registration: Towards an integrated MR and X-ray interventional suite. In: Galloway, RL.; Cleary, KR., editors. *Proceedings of the SPIE Medical Imaging Conference*. Vol. 5744. 2005. p. 146-156.

- Hartley, RI.; Zisserman, A. Multiple View Geometry in Computer Vision. Vol. 2. Cambridge University Press; 2004.
- Hastreiter P, Rezk-Salama C, Soza G, Bauer M, Greiner G, Fahlbusch R, Ganslandt O, Nimsky C. Strategies for brain shift evaluation. *Med Image Anal* 2004;8:447–464. [PubMed: 15567708]
- Hill DL, Maurer CR, Maciunas RJ, Barwise JA, Fitzpatrick JM, Wang MY. Measurement of intraoperative brain surface deformation under a craniotomy. *Neurosurgery* 1998;43:514–526. [PubMed: 9733307]
- Hochberg LR, Serruya MD, Friehs GM, Mukand JA, Saleh M, Caplan AH, Branner A, Chen D, Penn RD, Donoghue JP. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* 2006;442:164–171. [PubMed: 16838014]
- Hunter JD, Hanan DM, Singer BF, Shaikh S, Brubaker KA, Hecox KE, Towle VL. Locating chronically implanted subdural electrodes using surface reconstruction. *Clin Neurophysiol* 2005;116(8):1984–1987. [PubMed: 16000256]
- Jenkinson, M.; Pechaud, M.; Smith, S. Eleventh Annual Meeting of the Organization for Human Brain Mapping. 2005. BET2: MR-based estimation of brain, skull and scalp surfaces.
- 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;26:1078–1083. [PubMed: 15891163]
- Lesser, RP.; Gordon, B.; Fisher, RS.; Hart, J.; Uematsu, S. Subdural grid electrodes in surgery of epilepsy. In: Lüders, HO., editor. *Epilepsy Surgery*. Raven; New York: 1991.
- Leuthardt EC, Miller KJ, Schalk G, Rao RPN, Ojemann JG. Electrocorticography-based brain computer interface—the Seattle experience. *IEEE Trans Neural Syst Rehabil Eng* 2006;14:194–198. [PubMed: 16792292]
- Levenberg K. A method for the solution of certain nonlinear problems in least squares. *Quart Appl Math* 1944;2:164–168.
- Mahvash M, König R, Wellmer J, Urbach H, Meyer B, Schaller K. Coregistration of digital photography of the human cortex and cranial magnetic resonance imaging for visualization of subdural electrodes in epilepsy surgery. *Neurosurgery* 2007;61:340–4. [PubMed: 18091249]discussion 344
- Marquardt DW. An algorithm for least-squares estimation of nonlinear parameters. *SIAM J Appl Math* 1963;11:431–444.
- Mazziotta J, Toga A, Evans A, Fox P, Lancaster J, Zilles K, Woods R, Paus T, Simpson G, Pike B, Holmes C, Collins L, Thompson P, MacDonald D, Iacoboni M, Schormann T, Amunts K, Palomero-Gallagher N, Geyer S, Parsons L, Narr K, Kabani N, Le Goualher G, Boomsma D, Cannon T, Kawashima R, Mazoyer B. A probabilistic atlas and reference system for the human brain: International Consortium for Brain Mapping (ICBM). *Philos Trans R Soc Lond B Biol Sci* 2001;356:1293–1322. [PubMed: 11545704]
- Miller KJ, Makeig S, Hebb AO, Rao RPN, denNijs M, Ojemann JG. Cortical electrode localization from X-rays and simple mapping for electro-corticographic research: The “Location on Cortex” (LOC) package for MATLAB. *J Neurosci Methods* 2007;162:303–308. [PubMed: 17343918]
- Miyagi Y, Shima F, Sasaki T. Brain shift: an error factor during implantation of deep brain stimulation electrodes. *J Neurosurg* 2007;107:989–997. [PubMed: 17977272]
- Nelles M, König R, Kandyba J, Schaller C, Urbach H. Ko-registrierung von mrt vor und CT nach der implantation subduraler gitterelektroden. *Zentralbl Neurochir* 2004;65(4):174–179. [PubMed: 15551181]
- Roberts DW, Hartov A, Kennedy FE, Miga MI, Paulsen KD. Intraoperative brain shift and deformation: a quantitative analysis of cortical displacement in 28 cases. *Neurosurgery* 1998;43:749–58. [PubMed: 9766300]discussion 758
- Rorden C, Brett M. Stereotaxic display of brain lesions. *Behav Neurol* 2000;12:191–200. [PubMed: 11568431]
- Rosset A, Spadola L, Ratib O. OsiriX: an open-source software for navigating in multidimensional DICOM images. *J Digit Imaging* 2004;17:205–216. [PubMed: 15534753]
- Santhanam G, Ryu SI, Yu BM, Afshar A, Shenoy KV. A high-performance brain-computer interface. *Nature* 2006;442:195–198. [PubMed: 16838020]

- Schulze-Bonhage AHJ, Huppertz HJ, Comeau RM, Honegger JB, Spreer JM, Zentner JK. Visualization of subdural strip and grid electrodes using curvilinear reformatting of 3D MR imaging data sets. *AJNR Am J Neuroradiol* 2002;23:400–403. [PubMed: 11901007]
- Sochůrková D, Rektor I, Jurák P, Staněák A. Intracerebral recording of cortical activity related to self-paced voluntary movements: a Bereitschaftspotential and event-related desynchronization/synchronization. SEEG study. *Exp Brain Res* 2006;173:637–649. [PubMed: 16544136]
- Talairach, J.; Tournoux, P. Co-Planar Stereotaxic Atlas of the Human Brain. Thieme, Stuttgart; Germany: 1988.
- Wall BF, Hart D. Revised radiation doses for typical X-ray examinations. Report on a recent review of doses to patients from medical X-ray examinations in the UK by NRPB. *Br J Radiol* 1997;70:437–439. [PubMed: 9227222]
- Wellmer J, von Oertzen J, Schaller C, Urbach H, König R, Widman G, Van Roost D, Elger CE. Digital photography and 3D MRI-based multimodal imaging for individualized planning of resective neocortical epilepsy surgery. *Epilepsia* 2002;43:1543–1550. [PubMed: 12460257]
- Winkler PA, Vollmar C, Krishnan KG, Pfluger T, Brückmann H, Noachtar S. Usefulness of 3-D reconstructed images of the human cerebral cortex for localization of subdural electrodes in epilepsy surgery. *Epilepsy Res* 2000;41:169–178. [PubMed: 10940618]
- Wyler AR, Walker G, Richey ET, Hermann BP. Chronic subdural strip electrode recordings for difficult epileptic problems. *J Epilepsy* 1988;1:71–78.
- Yuan X, Zhang J, Buckles BP. Evolution strategies based image registration via feature matching. *Information Fusion* 2004;5(4):269–282.

Fig. 1.

Complete procedure for registration of electrodes from photographs, MRI, and X-ray. (a) Photograph showing position of grid implant. Cables entering the bottom left and bottom right corners of the craniotomy connect to electrode strips. (b) Photograph taken immediately before grid placement clearly showing anatomical features. A projective transform with the photograph in (a) is computed with several manually selected point correspondences, such as blood vessel features, craniotomy edges, and stationary surgical hardware. The transform were then applied to electrode positions from (a) and superimposed. (c) MRI-based brain rendering with electrode positions transcribed from the photographs. (d) Lateral radiograph showing electrode positions (dark dots) along with electrode cabling. The green circles outline the

electrodes with 3D locations known from the previous photograph-MRI registration step; these two sets of coordinates were used as control pairs to generate the MRI-radiograph projective transform. (e) The projective transform can be used to compute the location of the X-ray source and trace the path of X-rays that generated the image for each electrode location. Surface electrodes are known to be at the intersection of these rays with the cortical surface. (f) The final rendering showing electrode positions confirmed by the photograph (in white) and those determined solely by backprojection (grid electrodes in blue, strip electrodes in yellow). Note that the strip electrodes A1–A4 and B1–B4 are difficult to see at the contrast level chosen for the shown radiograph.

Fig. 2.

Interactive navigation is possible with the photograph, MRI, and radiograph linked via projective transforms. The crosshairs on each image indicate the same brain location, in this case, the inferior tip of a large parietal encephalomalacia in GP4.

Fig. 3.
The photographs, radiographs, and final renderings for all 8 of the included patients

Fig. 4.

Evaluation of registration for the same patient shown in Figure 1 (GP6). Known electrode positions from the photograph are shown as red dots, and the results from using the projective transform with all known electrode positions are depicted in blue. Since it is not possible to validate the location of hidden electrodes, a subset of six visible electrodes (boxed in yellow) were chosen to compute another projective transform. This transform was then applied to all X-ray locations, with the backprojection solution shown in yellow. The results from just these six electrodes agree closely with the known photograph-based positions as well as the results from the complete projective transform (blue dots).

Fig. 5.

Comparison of preoperative MRI and postimplant CT in two patients. First column: Coregistration of postimplant CT (in color) with preoperative MRI (grayscale); even though registration of the skull, scalp, and right hemisphere is good, many surface electrodes on the coregistered CT land more than 10 mm deep on the MRI in both patients. Second column: Another slice of the CT scan adjusted for contrast to visualize the ventricles. Third column: The corresponding MRI slice. Fourth column: The same MR (color) slice overlaid on the CT (grayscale); note the displacement of the whole brain, including a clear shift of the ventricle and midline, indicating significant brain deformation.

Fig. 6.

(a) Comparison of electrode registration with the proposed technique and from CT-MRI coregistration for GP1. The red splotches are the CT-derived positions; their shape is determined from intensity-based segmentation of the CT. The translucent white disks indicate positions known from the surgical photographs, while the yellow disks indicate positions backprojected from the X-ray. The CT-derived positions are considerably displaced posteriorly relative to the photograph-verified positions. (b) Surgical photograph for this patient. (c) and (d) show similar images for GP2.