

# Transforming Electrocortical Mapping Data into Standardized Common Space

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## Key Words

Epilepsy Surgery

Imaging

Montreal Neurological Institute Space

SPM2

Subdural Grid Electrodes

Talairach Atlas

3-D CT

3-D MRI

## ABSTRACT

Subdural grid electrodes are implanted routinely for the pre-surgical work up of epilepsy. While different approaches are available, many centers, including ours, visualize electrode locations by co-registering pre-operative 3-D MR images with post-implantation 3-D CT images. This method allows the determination of the electrode positions in relation to the individual patient's anatomy, but does not easily allow comparison across patients. The goal of this study was to develop and validate a method for transforming electrode positions derived from 3-D CT images into standardized space. We analyzed data from twelve patients with subdurally implanted electrodes. Volumetric CT and MRI images were co-registered and then normalized into common stereotactic space. Electrode locations were verified statistically by comparing distances between the anterior commissure and a representative sampling of 8 electrode sites per patient. Results confirm the accuracy of our co-registration method for comparing electrode locations across patients.

## INTRODUCTION

Subdural grid and strip electrodes are used routinely to localize seizure foci and to map language and motor cortex prior to seizure surgery. The exact localization of implanted electrodes in relation to underlying brain structures is important for individualized pre-surgical planning. Different imaging modalities such as plain x-rays, CT, MRI or intra-operative photography have been used to determine the grid position in relation to the patient's cerebral cortex.<sup>1-5</sup> While all of these methods have advantages as well as disadvantages, many centers, including ours, choose to superimpose the patient's post-operative 3-D CT scan onto his or her pre-operative 3-D MRI scan for the purpose of visualizing the electrodes. This technique allows the dis-

play of all electrode positions in relation to the patient's individual brain anatomy and at the same time minimizes electrode and motion artifacts which may limit post-implantation MRI scans.<sup>4,6</sup>

Cortical mapping results are of clinical importance for individual patients because they can provide information about the location of eloquent cortex. On a larger scale they can also contribute to our knowledge of brain organization and re-organization in epilepsy patients if compared across subjects. Group comparisons require that electrode positions can be stated not only in relation to an individual patient's anatomy but also as coordinates in a common reference space. In the area of functional imaging, in particular fMRI, the Talairach 3-D coordinate system as well as the Montreal Neurological Institute (MNI) space have become the standard reference spaces for reporting brain locations across individuals.<sup>7-8</sup> As a result, many software programs are available that automatically transform high resolution MR-images onto group templates.<sup>9</sup>

Reporting the locations of subdural grid electrodes visualized on 3-D CT images as coordinates in a standard reference space has been less straightforward. The goal of this study was therefore to devise a method for transforming electrode positions derived from 3-D CT images into a standard Talairach space.

## MATERIALS AND METHODS

### Subjects

We retrospectively analyzed data from 12 patients with epilepsy (6 male, 6 female, age range 16 to 59 years) who had subdural grid electrodes placed covering the left temporal lobe. 3-D MRI and 3-D CT data sets acquired from June 2000 to December 2005 were used. All patients pro-

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This work was presented in part at the Annual Meeting of the American Epilepsy Society (AES) in December 2005.

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Received: January 5, 2007; accepted: January 24, 2007.

vided informed written consent for participation in research studies.

### Clinical procedures

In accordance with our clinical protocol, all patients undergoing grid implantation had volumetric (3-D) MRI scans prior to surgery and a volumetric (3-D) CT scan the day after electrode implantation. The subdural grids consisted of 1.5-mm-thick, soft silastic sheets embedded with platinum-iridium electrodes (4 mm diameter, 2.3 mm diameter exposed surface) that were equally spaced 1 cm center-to-center (Adtec, Racine, WI, USA). The pre-operative MRI data sets (1 to 1.8 mm coronal slice thickness) were acquired on a Siemens or GE 1.5 Tesla scanner using a volumetric SPGR sequence. Post-operative CT data sets (1mm axial slice thickness) were acquired on a Toshiba or GE CT scanner. Data were then transferred in digital imaging and communication (DICOM) format from the MR and CT scanners to a Linux work station and displayed in Curry 4.6 (Compumedics Neuroscan, El Paso, TX, USA). Using this software, post-implantation CT and pre-implantation MRI data were then automatically co-registered after manually identifying the nasion, right and left pre-auricular notch which served as fiducials. Individual electrodes were identified and 3-D reconstruction of the co-registered CT and MRI was performed. The electrodes were then visualized on a surface rendering of the brain for the clinical purposes of correlating subdural EEG findings and the results of cortical stimulation mapping with the patient's individual gyral anatomy.

### Co-registration and normalization

Image sets co-registered in Curry 4.6 cannot be transferred into a data format suitable for normalization to a standardized template. Therefore, we opted to automatically co-register our patients' MRI data in SPM2 and perform the normalization on the automatically co-registered data. For this purpose, data sets acquired in the fashion described above were transferred in DICOM format to a Linux workstation. Using MRicro (<http://www.sph.sc.edu/cmd/rorden/mricro.html>), data were converted into ANALYZE format and transferred to a SUN workstation. Subsequent image processing was carried out in SPM2 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm2/>). CT data were co-registered onto the MRI data from the same patient using a six-parameter rigid body transformation. The pre-implantation MRI was then normalized onto the standard brain of the Montreal Neurologic Institute (MNI) included in SPM2 using the default parameters for normalization. Simultaneously, the co-registered 3-D CT scan was also normalized using the parameters derived from the normalization of the 3-D MRI. Data were transferred back to our Linux workstation. Images could then be displayed in MRicro. By linking (yoking) several windows, each patient's MRI, CT as well as a 3-D rendering of the MRI with a CT overlay could be visualized simultaneously for

the easy identification of electrodes of interest. Since all datasets were co-registered and transformed into MNI space, MRicro displayed the MNI coordinates of selected data points. Talairach coordinates could then be calculated from the MNI coordinates using the `mni2tal` matlab function (<http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mni-space.shtml>).

### Verification

To verify our results, we used co-registered, but not normalized, CT and MRI images. Using MRicro these images were converted into an 8-bit format and visualized in Curry 4.6. Displaying the results of both types of co-registration in the same program (Curry 4.6), allowed us to directly compare electrode locations derived from the two methods.

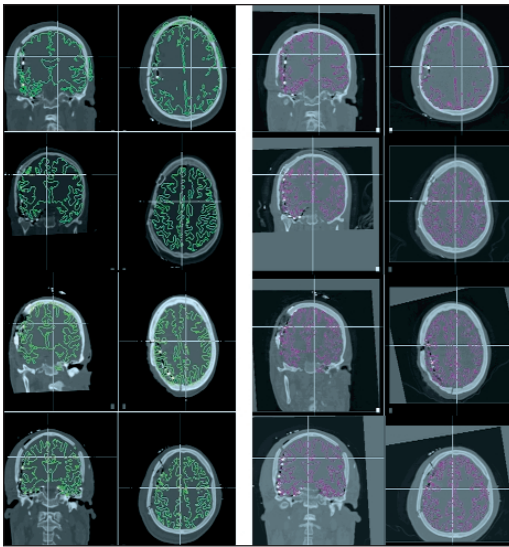
### Statistical analysis

For the statistical analysis, we compared distances between selected electrode positions and the anterior commissure (AC) in the Curry and SPM data. We identified 8 electrodes on each patient's CT and computed their distances in millimeter to the superior and posterior borders of the AC (the origin of Talairach space) on the co-registered MRI. To obtain a representative sampling of the grid, we chose the 4 corner electrodes as well as 4 electrodes in the row located over the superior temporal gyrus. We calculated *t* from paired *t*-tests for each of the 8 electrode locations. Then the beta error was determined for each location at an alpha error level of 0.01. A type II error (beta error) is analogous to a false-negative result during diagnostic testing: No difference is shown when in "truth" there is one. Testing for the probability of a type II error therefore established the likelihood of failing to observe a difference between the two methods when in truth there is one.

### RESULTS

Automatic co-registration of 3-D CT and 3-D MRI datasets using SPM2 was straightforward. Figure 1 compares the two co-registration methods for each of 4 typical patients. The figure shows the brain outline generated from the patient's own MRI superimposed onto the co-registered CT of the same patient. When the co-registration was performed in Curry, the brain outline is shown in green, while a pink brain outline denotes that the co-registration was performed in SPM. Figure 2 shows the reconstruction for one patient from the Curry-generated (green electrodes) and the SPM-generated (pink electrodes) co-registrations displayed on that same patient's native (original) MRI. Figures 1 and 2 document the precision of the automated alignment with SPM.

Multiple paired *t*-tests comparing the distance between the anterior commissure and any one of the 4 corner electrodes of the grid, as well as any one of 4 electrodes overlying the superior temporal gyrus, in the Curry- and SPM-generated data sets did not reveal any statistically significant differences (all  $t < 1$ ) (Table 1). Tests of different electrode sites are not independent since all electrodes were



**Figure 1.** Alignment verification of the co-registration performed using Curry 4.6 (green) and the co-registration using SPM 2 (pink) for 4 typical patients. The outline of the brain derived from the patient's MRI scan is superimposed onto the same patient's CT scan in the patient's native (original, individual) space. All images are displayed in Curry 4.6.

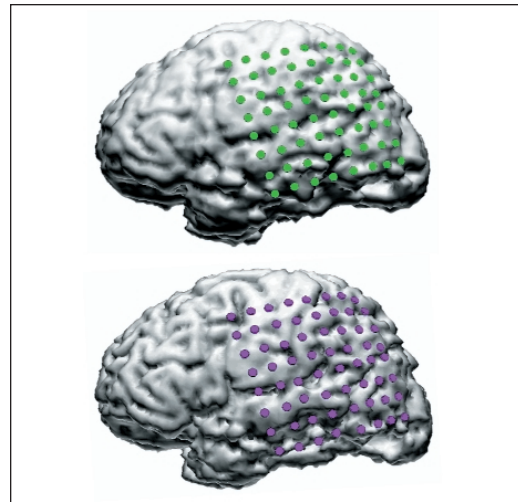
**Table 1**

*t*-values and beta errors (for alpha <0.01) for the statistical comparison of measurements from the anterior commissure to selected electrode locations across 12 patients

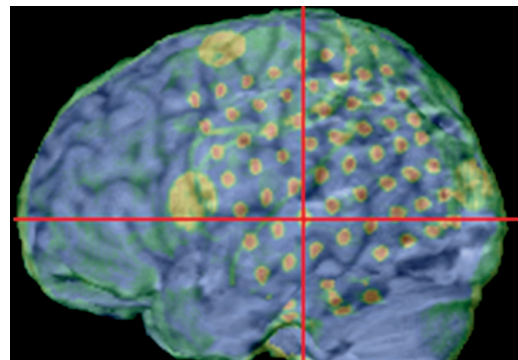
|     | <i>t</i> -value | Beta for alpha < 0.01 |
|-----|-----------------|-----------------------|
| TR  | 0.40169004      | 0.01270525            |
| BR  | 0.02910297      | 0.01001364            |
| TL  | 0.21760600      | 0.01077167            |
| BL  | 0.44580815      | 0.01336297            |
| ST1 | 0.00945879      | 0.01000144            |
| ST2 | 0.04459183      | 0.01003204            |
| ST3 | 0.02811058      | 0.01001273            |
| ST4 | 0.40177280      | 0.01270641            |

TR = top right, BR = bottom right, TL = top left, BL = bottom left; ST = superior temporal

physically linked together. By testing electrodes from the corners of the grid we aimed to target those electrodes which were more likely to show significant differences between the two methods. In addition, we calculated the beta error to show that both co-registration methods provide similar results. Beta errors ranged from 0.01 to 0.013 (Table1). Figure 3 shows the brain of the same patient shown in Figure 2, now transformed into MNI space. After warping into MNI space, the 3-D rendering of the brain



**Figure 2.** Comparison of the 3-D reconstruction of the data sets of a typical patient in the patient's native space. Green electrodes denote that co-registration was performed using Curry 4.6, pink electrodes denote that the co-registration was performed using SPM2.



**Figure 3.** 3-D rendering of the brain MRI and superimposed CT of the same patient shown in Figure 2, now in MNI space. Co-registration and transformation into standard stereotactic space were performed using SPM2. The 3-D rendering of the patient's CT superimposed on the patient's MRI in MNI space are displayed in MRICro. Electrode positions can easily be identified. (note that the large circles represent metallic burr hole covers.)

image was generated in MRICro and the 3-D rendering of the CT was displayed as an image overlay.

**DISCUSSION**

Our results demonstrate that MNI or Talairach coordinates for grid electrode positions derived from post-operative 3-D CT data can be determined employing several easy, automated steps. We were further able to show that SPM2, freely available software, reliably performs the co-registration of CT and MRI datasets. Co-registration is the

critical step of the procedure, since the subsequent normalization simply applies the same parameters to both the MRI and the CT. The images can then be rendered in 3-D, superimposed and displayed in MRICro, another freely available software package. While we used the commercially available package Curry 4.6, to visualize the 3-D reconstruction in this study our main aim in doing so was to be able to compare our routine clinical procedure for co-registration with our new method.

Advances in neuroimaging have provided new techniques for the visualization of implanted grid electrodes used in the pre-surgical work up of epilepsy patients. In particular, methods involving co-registration of pre-operative MRI scans, which provide superior anatomical detail with postoperative MRI or CT scans for electrode visualization, have increasingly been used. Advantages and disadvantages of the two methods for the purpose of electrode localization in the individual patient are discussed elsewhere.<sup>2-5</sup> Our center, like others,<sup>6,10</sup> has successfully performed co-registration of the patient's pre-operative MRI with his or her post-operative CT in our pre-surgical evaluation.

A multimodal approach like this, for which CT and MRI are used together for electrode localization, can make inter-subject comparisons and group analyses more difficult. Previous electrocortical mapping studies often discussed their group data by showing several or all of the individual patient's results separately in the individual patient's native (original) space or in a sketch thereof.<sup>11-13</sup> However, this approach is limited in that it does not allow a direct group comparison. Other investigators used standardized, schematic 2-D brain representations to demonstrate group results. This involves visually identifying areas of cortex underlying the electrodes of interest and then calculating the equivalent location on a standardized 2-D template.<sup>14</sup> In this case, visual judgments increase the risk of human error. When electrodes are placed stereotactically, they can be identified on the individual patients' stereotactic scheme and then anatomically localized using the proportional Talairach atlas and a schematic display.<sup>10,15</sup> While this method is accurate, a schematic 2-D display does not provide the same anatomical detail as a display on a normalized 3-D brain image in MNI or Talairach space. Edwards et al.<sup>16</sup> employed intraoperative electrode localization with the help of an infrared probe and a coregistered pre-operative MRI. MRI snapshots were taken and electrode positions were then displayed on the 3-D rendering of the standardized Montreal Neurological Institute (MNI) brain. However, this process only allows identification of those electrodes that are exposed by the craniotomy.

By contrast, our method allows the accurate co-registration of post-operative 3-D CTs and pre-operative 3-D MRIs with subsequent transformation of all electrodes into three dimensional standardized space. The statistical comparison of the co-registration procedure showed no significant differences whether this step was performed with SPM or with Curry — a software package we have relied on for clinical purposes for years. In addition, the probability for a type II error was very low. Our method is easy, the critical steps are automated and can be performed using freely available software. Our original goal was to determine the MNI and Talairach coordinates for electrodes located over lateral temporal cortex, but our algorithm can be used to display CT-derived electrode positions in any brain region including deeper structures like the hippocampus.

One of the limitations of our study is that co-registration with Curry cannot be viewed as the "gold-standard" of co-registration. However, our center has a significant amount of experience with this type of co-registration since we routinely use Curry 4.6 to superimpose the patient's post-operative CT with their pre-operative MRI for clinical purposes. A recent report by Sebastiano et al.<sup>17</sup> describes and verifies a Matlab routine for the automatic co-registrations of pre-operative MRI and post-operative CT for electrode visualization. Since SPM is a Matlab based program, Sebastiano's report lends further validation to the feasibility and accuracy of our automated co-registration with SPM. Unlike Sebastiano et al.<sup>17</sup> we purposefully did not choose intraoperative photographs to validate our method, because this would have limited us to the statistical comparison of the electrodes' locations in the center of the grid, since corner electrodes are often not exposed by the craniotomy. Comparison of the location of corner electrodes is more meaningful, since these electrodes have the highest likelihood of showing differences between our new method and the reference method. We avoided post-operative MRI scans because, in our experience, electrode artifacts limit their usefulness.

Finally, we believe our method has the potential to facilitate a multimodal approach to the study of cognition on a broader scale. Not only does it provide an automatic transformation of CT-derived electrode position into common space, but it also has the potential to allow functional MRI (fMRI) and electrocorticographic group data to be displayed together. This should allow for exciting new possibilities in the study of cognitive function in the epilepsy population.

#### ACKNOWLEDGMENTS

This study was supported by NIH grants R01-DC005645 (DB), R21-DC007490 (DB) and R01-NS40596 (NEC).

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