# Voxel Based Analysis and Reconstruction of Spectroscopic Imaging Data

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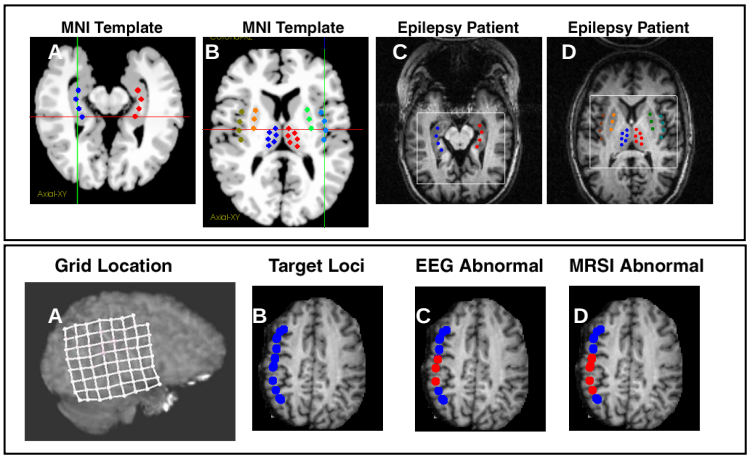
**Introduction:** Although the co-registration of fMRI and anatomical imaging data to a common atlas for analysis and interpretation is common, most spectroscopic imaging studies are still analyzed using large arrays of reconstructed data and manual selection of target loci. Due to the low spatial resolution of most spectroscopic imaging studies (0.5-1.0cc), significant partial volume effects can occur when the SI grid is poorly aligned with the anatomy. Similarly significant user bias/variability can also occur during the manual selection the target regions. Notably, there are also few reports for multimodal co-registrations of spectroscopic imaging data with other imaging data such as CT, SPECT and PET. To overcome these limitations we have implemented a strategy where the exact loci of the target SI voxels are automatically determined from non-rigid co-registration of the subject's anatomical images into a reference space (Montreal Neurological Institute Standard Brain, MNI) or images from the same subject but from other imaging modalities. The SI data are then reconstructed from those exact loci using a voxel shifting method to provide anatomically accurate placement. We have applied these methods to investigate: 1) the extent of asymmetric subcortical metabolic abnormalities in patients with temporal lobe epilepsy and 2) the relationship between regions with abnormal EEG and decreases in NAA in patients with neocortical epilepsy.

**Methods:** All data were acquired at 4T using a Varian INOVA console and a quadrature head coil. The hippocampal and subcortical data were collected using a modified LASER sequence (10mm thickness, 80x100mm in-plane FOV selection) in combination with two dimensions of phase encoding (24x24, FOV=192x192mm, 19.2 min). For the correlations with intracranial EEG studies MRSI data was acquired with similar parameters, but without in-plane selection, allowing the cortical periphery to be sampled. Lipid suppression for these studies was obtained using an inversion recovery preparation, TIR=265ms prior to excitation.

Images were co-registered using Bioimage Suite, an NIH supported integrated multiplatform image analysis utility (www.bioimagesuite.org). For the spectroscopic imaging of subcortical loci, the target loci were determined within the MNI standard brain space. The MRS images were co-registered into this space using both rigid/affine and non-rigid transformations. The non-rigid registration was determined using a parameterized tensor b-spline grid with uniform control point spacing. For the intracranial EEG reconstructions, electrode contacts were determined with the post-op CT space and transformed into the pre-op MRS space. Due to the location of the electrodes on the surface of the brain for the intracranial studies (i.e. ½ of the SI voxel outside of the brain), the loci were automatically shifted into the brain (1 SI voxel radius) along the normal to the brain surface. Statistical analyses were performed using a three way ANOVA, with corrections for multiple comparisons.

**Results:** Figure 1 displays images showing the target loci in the MNI reference space, and a co-registered example from a patient with temporal lobe epilepsy. There is good agreement between the loci despite the presence of atrophy on the ipsilateral (left) hippocampus. Pooling data across n=10 epilepsy patients demonstrated : 1) a significant decline in NAA in the ipsilateral hippocampi, thalami and insula in comparison to their contralateral loci (Table 1) and 2) a regional specific decline in the anterior hippocampus in comparison to the posterior hippocampus ($p<0.001$). Displayed in Figure 2 are images showing the location of a grid of intracranial electrodes in a patient with neocortical epilepsy (2a), the loci of the reconstructed SI voxel corresponding to the grid electrodes represented within the SI slice (2b). The EEG contacts from the grid associated with seizure onset within this slice are shown with filled circles (2c). Analysis of all grid loci within the slice (after correction for gray matter content) revealed significant reductions in NAA/Cr ($p<0.05$ in comparison to controls, solid circles, 2d) which are in excellent agreement with the loci of EEG associated with seizure onset.

**Figure 1 (Left Top) 1a and 1b show the locations for analysis on the MNI standard brain, 1c and 1d display the co-registered locations on the patient images.**
**Figure 2 (Left Bottom) 1a displays the EEG grid location in 3D, 1b displays the target locations corresponding to the EEG grid location in this slice (blue circles), 1c displays the electrodes associated with seizure onset (red circles) and 1d displays the metabolically abnormal regions ($p<0.05$) (red circles).**




| Table 1 | NAA/Cr | | |
|---|---|---|---|
| | ipsi | contra | p (ipsi<contra) |
| **Hippocampus** | 1.16 | 1.24 | 0.002 |
| **Thalamus** | 1.46 | 1.5 | 0.05 |
| **Insula** | 1.28 | 1.37 | 0.008 |
| **Putamen** | 1.41 | 1.39 | 0.43 |

**Conclusions:** Co-registration and reconstructions of SI data using voxel shifting techniques with a standard atlas allows for automatic, accurate and bias free selection and reconstruction of target loci. This enables cross sectional patient studies to be compared directly. For temporal lobe epilepsy patients significant asymmetries in NAA subcortical structures outside of the temporal lobes were detected. For neocortical epilepsy co-registration of the SI data with CT images to detect the location of intracranial electrodes allows the metabolic information from the SI data set to be compared with the corresponding EEG characteristics.