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# Optimization of ROI transposition for atlas-based analysis of MRI quantitative metrics in neuroimaging studies

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**Target Audience:** The strategies proposed in this study are relevant to those who wish to perform large population neuroimaging studies with varying demographic factors using automated methods to quantitatively analyze their diffusion MRI (dMRI) data.

**Purpose:** When analyzing quantitative MRI metrics in large population studies, it is convenient to have automated tools that can extract corresponding features from each individual image. This generally requires image registration and template reconstruction techniques to define ROIs on a representative atlas space. The standard approaches to define these ROIs involve: (a) using the individual images registered onto the common space during template creation or (b) transforming the ROIs back from the atlas space onto each individual subject space. Each strategy has pros and cons; approach (a) alters image statistics due to interpolation whereas in approach (b) the binary ROI images in the template space are transformed into floating point images and hence, require further manipulation. The motivations for selecting a specific approach for a given study and its effects on the analysis outcomes have mostly been disregarded in previously published studies. Here, we used dMRI data from the NIH MRI study of normal brain development (www.pediatricmri.nih.gov) to assess the contribution to overall variance in MRI metrics that is introduced by employing different ROI transposition methods. Additionally, we propose a novel ROI transformation method, which is more robust than previous approaches.

**Materials & Methods:** In this study, healthy subjects were scanned at five imaging centers on 1.5T scanners (GE or Siemens). DTI data was acquired with 3mm isotropic resolution, six diffusion sensitization directions (b=1000s/mm$^2$) plus 1 b=0s/mm$^2$ image repeated four times. 449 scans were acquired from 274 subjects (aged 15 days–22.2 years, 140 female). Diffusion MRI data was first processed with TORTOISE [1] for motion, eddy currents and susceptibility distortions. To improve the quality of subject-to-atlas registration, the computed tensors from each subject were fed into a tensor-registration based atlas creation toolkit [2] to first create several age-specific average brains (minimum of 10 scans per average). Subsequently, these age-specific average brains were registered to the atlas of 20 years-old subjects, the most representative average brain for an adult template. An expert manually drew 39 ROIs on the reference template and the ROIs were then transformed to extract Fractional anisotropy (FA) and Trace statistics from each individual subject. The issue with ROI transforming is that initially binary ROI images have values in between [0-1] after transformation and need to be thresholded to be binarized. The transformation methods involved transforming the ROIs to subject space using five different approaches: 1) using a low threshold to generate "inclusive" ROIs, 2) using a high threshold to generate "exclusive" ROIs, 3) extract image features as a weighted combination with ROI voxels as weights but without any threshold 4) using a vertex-based methods (i.e. the proposed method) and 5) using the registered images with the original set of ROIs on the atlas-image space without ROI manipulation. In the proposed method of ROI transfer, we represent the initial ROI as a set of vertices instead of binary images and transform the vertices back, in a continuous manner, back to subject space. To extract statistics from now irregular (i.e. vertex-based) ROIs, we represent each subject's tensor image as a continuous field with the method proposed in [3]. Subsequently, a uniform sampling strategy samples tensors from within the continuous ROI and the desired statistics are derived from each sampled tensor. Asymptotic growth curves of the form, $FA(age) = \alpha - \beta e^{-\tau.AGE}$ were fitted to the data extracted from each ROI method for (FA) and Trace. The mean-squares error of the fitting and the differences of the growth slopes were quantitatively analyzed.

**Results:** Figure 1 displays sample results from a large ROI at the center of the Splenium of Corpus Callosum (CC) with three of the five ROI transposition methods that we tested. With an inclusive transposition strategy, the FA values are lower than expected due to the inclusion of partial volume effects. The exclusive thresholding only includes voxels at the center of the splenium of CC and hence results in higher than normal FA values. The continuous approach results in slower growth than thresholding based method that converges to a value in between the first two methods. Thresholding based methods (inclusive/exclusive) were more susceptible to registration errors than the other three (data not presented here), whereas the continuous and atlas-space ROI statistics were mostly similar, with atlas-image based statistics showing reduced variance due to interpolation-related smoothing effects. This can also be observed from the overall fitting errors displayed in Table 1.

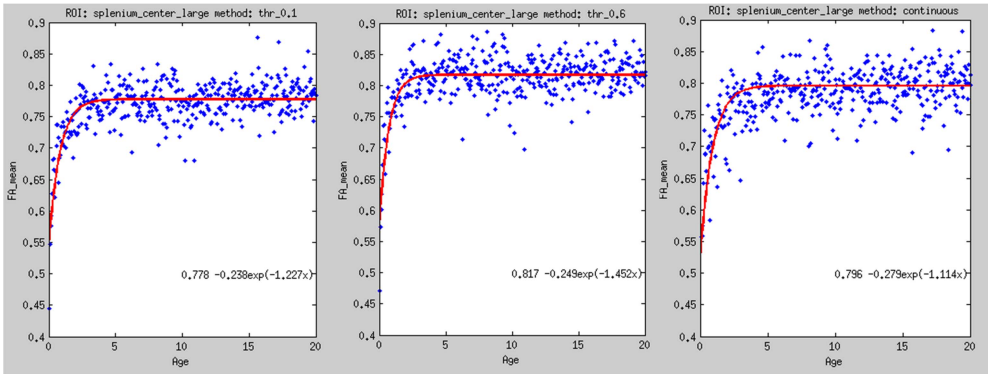


***Figure 1.*** FA growth curves from the Splenium with inclusive/exclusive thresholding and continuous ROI transformation.

| | Inc. Thresholding | Exc. Thresholding | Weighted | Continuous | Atlas Space |
|---|---|---|---|---|---|
| Overall SSE | 59.54 | 95.59 | 64.34 | 58.34 | 56.89 |

***Table 1.*** Sum of SSE of curve fitting over all 39 ROIS.

**Conclusions:** Even with the same template registration, the choice of an automatic data analysis method using ROIs can have a significant effect on the measured MRI metrics. It is important to take into account ROI location and size when considering an ROI transposition strategy.

**References: 1.** Pierpaoli C. et. al., ISMRM,2010; 2. Zhang G. et. al., TMI, 2007; 3. Pajevic S. et al, JMR, 2002.