A Comparison of the Reliability of Two Techniques for White Matter Segmentation in a Clinical DTI Study

K. R. Padgett[1], C. S. Garvan[2], K. M. Crandall[3], T. A. Black[4], F. D. Eyler[5], M. Behnke[5], C. M. Leonard[3], I. M. Schmalfuss[6], S. J. Blackband[3]

[1]Medical Physics, University of Florida, Gainesville, Florida, United States, [2]Biostatistics, University of Florida, Gainesville, Florida, United States, [3]Neuroscience, University of Florida, Gainesville, Florida, United States, [4]AMRIS, University of Florida, Gainesville, Florida, United States, [5]Pediatrics, University of Florida, Gainesville, Florida, United States, [6]Radiology, Univeristy of Florida, Gainesville, Florida, United States

Introduction: Developing a reliable, valid segmentation technique for DTI datasets poses many technical issues. While manual tracing techniques of segmentation closely mimic the radiologist's interpretation it is susceptible to poor intra and inter operator reliability (1). Conversely, fully automated segmentation techniques are robust in reproducing regions of interest (ROIs), but are more open to segmentation artifacts. Semi-automated segmentation techniques are hypothesized to be more reliable than hand drawn methods but less susceptible to segmentation artifacts. The purpose of our study was to demonstrate the superiority of a semi-automated segmentation over the hand drawn method in regard to intra-rater reliability.

Methods: Fractional anisotropy (FA) maps were generated from diffusion tensor images (DTI) sets collected on a Siemens 3T Allegra head scanner equipped with gradients capable of 40mT/m. A spin-echo diffusion weighted EPI pulse sequence was utilized as the six direction DTI sequence with b values= 0, 250, and 1000 s/mm^2, FOV = (210 mm)^2, matrix = 128^2, slice thickness = 3.5 mm, TR = 4200 ms, TE = 90 ms, and NEX = 4 yielding an acquisition time of 4 min. Two raters (one neuroanatomist and one MRI researcher) applied different segmentation procedures to the same white matter structures. The ROIs studied in the anterior-posterior commissure (AC-PC) plane included callosal and projection fibers recorded for each side separately. Anatomical structures studied 8mm above the AC-PC plane were the genu, splenium, and internal capsule with the results noted for each side separately as well. The hand drawn and a semi-automated segmentation method were employed for each region by both raters independently. The intra-rater reliability was determined using intraclass correlations (ICC) (2, 3). The ICC divides the "between subjects" variance by the sum of "between subjects" variance and "within subjects" variance. If the two measurers agree with each other, the "within subjects" variance will be small and the ICC will be close to 1.

Segmentation Procedures: The hand drawn segmentation was completed on 22 subjects. Using the processed FA images the user would segment the structures of interest by following a set of anatomical rules. An example of these anatomical rules may be found for the genu of the corpus callosum on the right and an example ROI is shown in figure 1. This procedure is followed for each structure of interest followed by the tabulation of the measures of interest from these ROIs.

<u>Genu Hand Drawn Anatomical Rules</u>

1) Determine the midline using the anterior and posterior aspects of the longitudinal fissure.
2) Starting at the midline, bisect the genu of the corpus callosum
3) Laterally follow the boundary between the genu and the lateral ventricle.
4) To determine the lateral border of the genu make a 45-degree line (towards midline) from the intersection point of the anterior internal capsule and the genu.
5) Medially follow the boundary between the genu and the gray matter of the frontal lobe connecting to the bisection in step 1.

The region shrink segmentation was completed on 10 randomly chosen subjects by both researchers in order to test the reliability of the technique before its implementation on all the datasets. The region shrink method requires two criteria to operate, an encompassing region in which the entire structure is contained and a pixel intensity threshold provided by the user. The encompassing region is drawn around the entire structure of interest also enclosing much of the unwanted surrounding gray matter and ventricle. The computer shrinks in from the encompassing region one pixel at a time until the pixel threshold is encountered. The anatomical rules for the genu encompassing region are similar to that of the hand drawn method except that large amounts of gray matter and CSF are included in the encompassing region. Rigorous rules are still used to define the white matter on white matter borders. An example of an encompassing region and subsequent ROI may be seen in figure 1.

The pixel intensity thresholds were chosen carefully for each structure of interest. A high threshold resulted in a ROI not resembling the structure. A low threshold allowed significant gray matter and CSF signal contamination of the white matter ROI. The distribution of FA pixel intensities of white matter compared with the distributions of pixel intensities of CSF and gray matter were quite separate from each other, but the distribution of whole brain pixel intensities was continuous due to volume averaging. The approach used to decide threshold levels was to set the threshold at the highest level that still maintained the shape of the structure of interest. A threshold at this level should provide an ROI without extensive volume averaging. This procedure of selecting the highest threshold that maintained the shape was completed for each structure on 10 randomly selected subjects. The thresholds used for the entire population were created by averaging the pixel threshold for each structure from the 10 subjects. Table 1 lists the pixel threshold values used to segment out each structure.

Results & Discussion: The hand drawn method relied heavily upon subjective user decisions to outline the structure of interest. The ICC for this technique was poor, approximately 0.38 (full results are listed on table 1). While the anatomical structure of interest was identified easily, the borders of the structure were difficult to reproduce and were the main contributing factor to the poor reliability results. The lack of defined guidelines for pixel intensity inclusion / exclusion was the likely cause.

In contrast, the ICC for the semi-automated shrink method was almost perfect with 0.94 (for full results seen table 1). The greatest potential for error using this method was at the time of defining the encompassing region. While the ROIs were mainly bordered by gray matter or ventricle most also formed a boundary with some white matter, as seen in the genu shown in figure 1. These white matter on white matter junctions most likely caused the minor errors in the reliability. The creation of rigorous anatomical rules to define such junctions minimized these errors. While manual segmentation is a common technique, requires little investment to setup a protocol, and is easy to implement, semi-automated techniques require less time for segmentation, produce similar results, and achieve superior reliability.

<u>References & Acknowledgements:</u> NIH support from DA05854 & the National High Magnetic Field Laboratory, also thanks to Ann Welch (Project Director), Tamara Warner (Research Fellow), Wei Hou, and Vijay Komaragiri (Biostatisticians). [1] Clarke LP, et al., Magn Reson Imaging, 13, 343-368, 1995. [2] Howell DC, et al., Intraclass Coefficient, Web Reference, 2002. [3] Ott RL, Book: An Introduction to Statistical Methods and Data Analysis, Belmont, Wadsworth, 1992.

Structure	Hand Drawn ICC	Region Shrink ICC	Region Shrink Thresholds FA
Right Genu	0.16	0.91	0.45
Left Genu	0.41	0.96	0.45
Right Anterior IC	0.46	0.94	0.38
Left Anterior IC	0.31	0.96	0.38
Right Posterior IC	0.55	0.92	0.40
Left Posterior IC	0.40	0.98	0.40

Table 1: A comparison of reliability for two different segmentation techniques and the thresholds used for the region shrink technique. The region shrink ICC values are all above 0.90, which is substantially better than for the hand drawn technique. IC represents Internal Capsule.

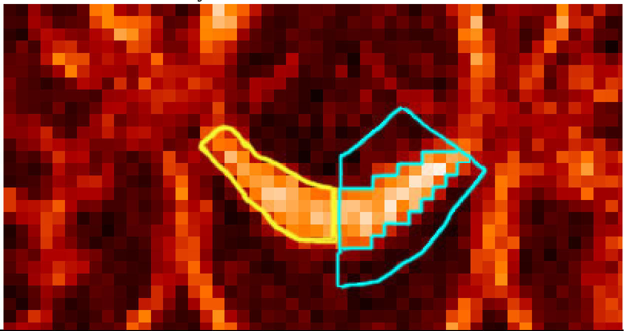

Figure 1: The two segmentation techniques applied to the genu of the corpus callosum. The yellow ROI is an example of the hand drawn technique. The outer blue ROI is the encompassing region and the inner blue ROI is the final region shrink ROI.