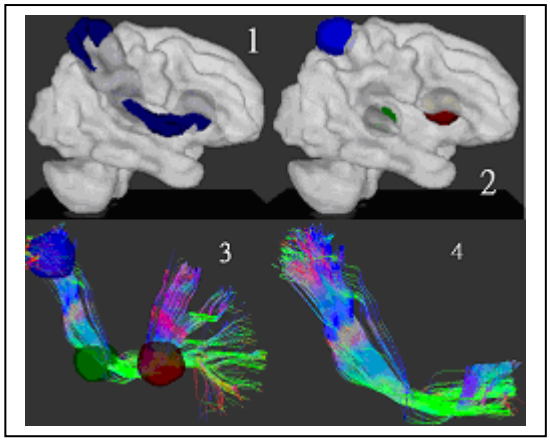
Using a mean DSI dataset and targeted ROIs can increase the specificity and reproducibility of manual tractography in DSI.

A. Nikolaidis[1], and W-Y. I. Tseng[2,3]
[1]National Taiwan University, Taipei City, Taipei, Taiwan, [2]Center for Optoelectronic Biomedicine, National Taiwan University, [3]Institute of Biomedical Engineering, National Taiwan University

Synposis: The purpose of this study was twofold: first we sought to examine whether the specificity and objectivity of DSI tractography and ROI selection can be improved; second we looked to demonstrate that using a large mean DSI dataset can be an effective method for testing the existence and shape of a highly specified clinically relevant white matter fiber tract.

Introduction: Diffusion imaging has produced significant advancements in understanding of both the anatomy of the brain as well as clinically relevant neuroanatomical differences. Unfortunately, some aspects of DSI methodology, such as region of interest selection and tractography demonstrate significant deficits in objectivity, reproducibility and specificity when compared to other techniques such as EEG and fMRI. Previous studies have recognized these problems as well [1]. The current problems with ROI selection and tractography are inextricably linked; for example, unspecific ROI selection unfailingly leads to unreliable manual tractography. Larger ROIs inevitably lead to a higher number of fibers between ROIs and a greater spatial distribution of said fibers. This causes the experimenter to apply greater subjectivity in eliminating the fibers that do not belong to the tract under question, which leads to higher inter-experimenter variability. For example, two large ROIs may have several robust fiber tracts between them; the experimenter must know which fibers to cut away and which to keep. This is all especially relevant for tractography of the frontal cortex where there exist a high number of fiber crossings. We have sought to alleviate these problems by creating a new method of ROI and tract selection.

Materials and Methods: *Subjects*- 24 individual DSI datasets were collected (100% right handed, 2 female, 8-17 years old, 12.7 mean age). *Imaging*- Images were acquired on a 3T MRI system with a 32-channel head coil (Tim Trio, Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion EPI sequence, TR/TE = 9600/130 ms, matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm^2, and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity b_{max} = 4000 s/mm^2 were sampled on the grid points in the 3D q-space with $|q| \leq 3.6$ units [2]. DSI analysis was performed based on the relationship that the echo signal S(q) and the diffusion probability density function P(r) were a Fourier pair, i.e., $S(q)=FT\{P(r)\}$. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The intravoxel fiber orientations were determined by decomposing the original ODF into several constituent ODFs [3]. Further, those primary fiber orientations were used for tractography reconstruction. Generalized fractional anisotropy (GFA) at each voxel was quantified based on the shape of the original ODF [4]. Tractography was reconstructed using a streamline-based algorithm, and the targeted tracts were selected by specific regions-of-interest (ROIs). *ROI Selection*- An ALE meta-analysis of 16 studies detailing the fMRI BOLD correlates of ADHD in children yielded 13 clinically relevant Talairach Atlas specified ROIs [5]. We then created spherical ROIs that were both centered on these coordinates and 20mm wide in diameter using WFU Pickatlas [6]. *Mean DSI Dataset*- A dataset of 60 averaged normal brains from DSI Studio was used to look for white matter tracts connecting these fMRI ROIs [7]. We performed tractography between the 13 ROIs and compiled a ranking of the most robust tracts based two criteria: the time it took for the tractography algorithm to reach 2000 fibers, and a subjective analysis of the amount of "spread" in the tract. The most robust tracts were the quickest to form with the least amount of tract "spread". ROIs were then repositioned such that the fibers passed directly through the center of the ROIs. *Tractography*- To test if our method would work on individual brains we then transformed the repositioned ROIs to each individual's brain and performed tractography on all subjects in a fronto-parietal tract (Fig 3. FA threshold <0.1, turning angle> 60, step size 1.24mm, length constraint 80-180mm, 500 fibers.) To maximize tractography objectivity, the erasure of fibers exiting the end of the ROI was the only editing performed (Fig.4).



Figures- 1: An edited fiber tract passing through the 2cm wide spherical ROIs specified in Fig. 2. Fig 3: The result of a fully automated fiber tract algorithm to 500 fibers passing through the individualized ROIs. TD x,y,z coordinates: (Top-Left) Blue- 28,-37,58. (Middle) Green- 23,18,-1. (Lower Right) Red- 27,19,0.

Results: We found that the highly specified fronto-parietal tract to exist across in all 24 datasets. Furthermore, we found that the mean DSI dataset can be used as a map for effectively and efficiently exploring white matter tracts between ROIs of functional importance yet unknown structural connectivity.

Discussion: We have demonstrated the possibility of using highly specific and functionally relevant ROIs to explore a long range white matter fiber tract in the fronto-parietal network. Furthermore, our method has demonstrated that tracts found in a mean DSI dataset can offer meaningful insight into specific previously unexplored white matter tracts, and that white matter tracts that are robust in a mean DSI dataset are also extant in individual brains. We believe that this method is important because it not only allows experimenters with varying levels of neuroanatomical knowledge to perform accurate and effective tractography, but it also allows for more accurate ROI selections and more reproducible WM tracts. Well defined ROIs, explicit fiber tract selection methods and a reduction of experimenter variability are all keys to the automation of the DSI method. Future studies should look to use mean DSI datasets in conjunction with fMRI or other imaging meta-analyses conveying the most significant ROIs for the researcher's clinical question of interest. Furthermore, future studies should look to include either TD atlas or an equivalent method of specifying ROIs in order to allow for more robust inter-study comparisons.

References: [1] Y. Zhang *et al*., Neuroimage. 2010 Vol.52 1289-1301. [2] V.J. Wedeen, *et al*., Magn Reson Med. 2005; 54:1377-86. [3] F.C.Yeh, *et al*., Proc ISMRM, 2008. [4] D.S. Tuch, Magn Reson Med ,2004 .[5] S.G.Dickstein *et al*., J. Child Psy & Psychiatr 2006; 1051–1062. [6] www.fmri.wfubmc.edu/cms/software. [7] http://dsi-studio.labsolver.org/