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The Effect of Spatial Resolution on Structural Connectome Analysis

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Introduction: Structural connectivity analysis was recently introduced as a comprehensive method to investigate the characteristics of white-matter fiber networks in the human cortex **[1]**. Because of its promising potential to help identify biomarkers for neurodegenerative diseases, it has rapidly become an active area of neuroimaging research. Structural connectome analysis essentially aims at classifying cortical fibers obtained from diffusion tensor imaging (DTI) based on topological information derived from high-resolution T1-weighted MRI **[2]**. Truthful depiction of the connectome therefore heavily relies on the quality and completeness of the DTI data. As such, it is prone to inherent limitations of conventional diffusion acquisition techniques and post-processing algorithms. In particular, the inability to disambiguate complex fiber pathways in highly convoluted cortical folds can be detrimental to the reconstruction of the structural connectome. For example, short U-fibers connecting adjacent areas are often missed or mischaracterized. Fiber incoherence can also lead to the creation of spurious connections or even to an underestimation of fiber density whenever tracts are terminated before reaching the grey/white matter interface **[3]**. Advanced DTI techniques such as HARDI/DSI/PAS may overcome these issues by estimating multiple tensors within a given voxel, but they can be prohibitively time-consuming, and still cannot resolve curved fibers or differentiate crossing from kissing bundles. In comparison, sufficiently high spatial resolution (e.g., 1 mm^3) may be the only viable solution to potentially address both issues. In this work, we compare structural connectomes obtained from data acquired at increasing spatial resolutions (3mm^3, 2mm^3 and 1mm^3), and report the effect of spatial resolution on the FA connectivity matrix **[4]**.

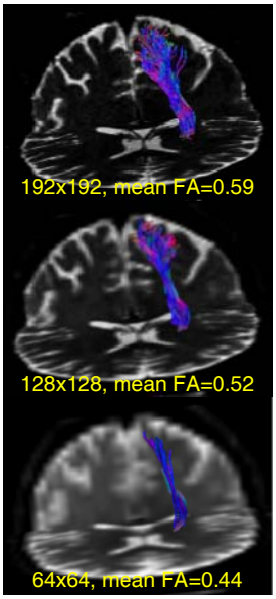

Fig.1 Reconstruction of the Cerebro-Spinal Tract (CST) at 1, 2 and 3 mm^3

Methods: Three sets of axial EPI DTI datasets (SENSE factor 2, TE/TR=73/15000ms, FOV=24cm, b=1000s.mm^2, 2 b0+15 directions) with increasing matrix sizes of respectively 64x64 (nex=1, #slices=30), 128x128 (nex=4, #slices=60), 192x192 (nex=8, #slices=100) were acquired on a healthy volunteer using a GE 3T 750 system equipped with an 8-channel head coil. Head motion within each set was corrected using FSL's FLIRT and taken into account in the b-matrix calculation. An additional 1mm^3 T1-weighted FSPGR scan was collected in the same session and fed into the Freesurfer recon-all pipeline to automatically label each hemisphere into 66 anatomical regions. Structural networks were reconstructed for each resolution using the CMTK toolkit. Connectivity matrices were subsequently derived for a finer parcellation to reveal anatomical discrepancies across the 3 datasets **[5]**.

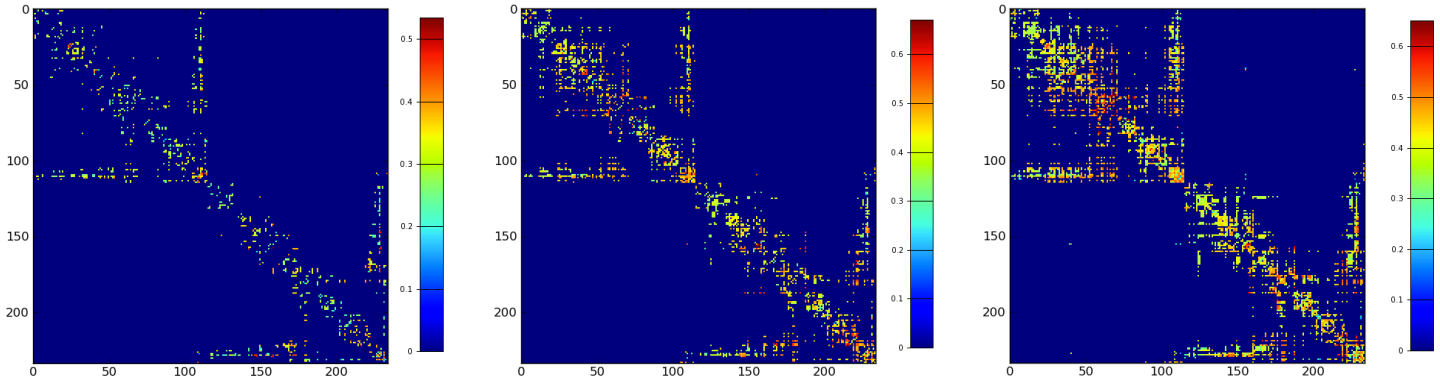

Fig.2 Matrices of mean FA between all pairs of n=234 ROIs respectively obtained from left to right for the 4mm3, 2mm3 and 1mm3 datasets. The upper left and lower right blocks of the matrix respectively represent connections in the right and left hemisphere.

Discussion: Fig.1 illustrates the levels of fiber tracking improvements at the boundary between the white matter and the cortex as the spatial resolution increases. Fig.2 provides further evidence that spatial resolution has a direct impact on the FA connection matrix. The higher-resolution matrix (right) reveals more highly weighted connections, as assessed by the higher mean FA along the cortico-cortical tracts. This result is consistent with the expected FA increase resulting from a diminution of fiber incoherence within smaller voxels. Furthermore, the 1x1x1mm^3 connectome captures connections, which are missed at lower resolutions.

Conclusion: Our results show that structural connectome reconstruction benefits greatly from increasing the spatial resolution of the DTI acquisition. Although 1mm^3 resolution is stretching the limits of currently available 2D acquisition methods in terms of SNR per unit time at 3T, we anticipate that advanced full brain 3D high-resolution Diffusion Tensor Imaging acquisition schemes will play a central role in helping to achieve the goals of the Human Connectome Project.

References: 1. Sporns et al. PLOS Comput Biol 2005;1:4 **2.** Kaiser Neuroimage 2011;57:892 **3.** Gigandet et al. PLOS1 2008;3:12 **4.** Hagmann et al. PLOS Biol 2008;6:7 **5.** Gerhard et al. Front Neuroinf 2011;5:3 **Acknowledgements:** This work was supported in part by NIH grant T32EB001040-08