Diffusion-weighted MRI has emerged as a powerful tool for identifying white matter (WM) pathology in neurological and psychiatric disorders. Despite the widespread application of diffusion MRI in clinical neuroscience, little is known about the physical mechanisms for diffusion changes in WM neurodegeneration. For instance it had been thought that myelin was the primary source of diffusion restriction in WM, but there is evidence that myelin is not a requirement for diffusion anisotropy (Beaulieu C, Allen PS. Magn. Reson. Med. 31: 394–400, 1994.). The objective of this project is to combine high resolution diffusion-weighted MRI, via Q-ball, and numerical simulations on realistic models of molecular diffusion in WM in order to identify the underlying physical mechanisms for diffusion anisotropy changes in WM pathology.

Regional diffusion fractional anisotropy (FA) differences between young (age=21-39 years, n=15) and middle-aged (age=40-59 years, n=9) individuals. (A) Voxel-based statistical map. (B) Region of interest analysis. From Salat DH, Tuch DS, et al. Neurobiol Aging. 2005 (in press)

Q-ball diffusion MRI of the three-way fiber crossing between the projections from the splenium of the corpus callosum (red), tapetum (blue), and optic radiation (green). The glyph at each voxel location depicts the local diffusion orientation distribution function (ODF). From Tuch DS. Magnetic Resonance in Medicine. 52: 1358-1372, 2004.

Electron micrograph (WM) of WM cross-section from corpus callosum of monkey (Peters et al., J Comparative Neurology, 442:277-291, 2002)

The tissue model is a collection of cylinders, that approximate a homogeneous regions of strong oriented fibers. Each cell includes interior and myelin sheath, which is hydrophobic. The diffusion measurements arise from a aggregate model of water molecule probabilities solved on a continuum using a finite difference scheme.

The effects of axon density/deletion on fractional anisotropy. Cells are packed according using an energy minimization scheme (Meyer et al., Shape Modeling International, To appear, 2005). The domain is periodic. Using parameters (radii, g-ratios, axon density) from published histological studies we obtain diffusion measurements which are consistent with MRI studies of homogeneous regions of oriented axons.

Supported by National Alliance for Medical Image Computing (US4 EB005149)