Quantifying Neurodegeneration in Multiple Sclerosis White Matter Tracts with Diffusion Tensor Imaging

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Background
- Multiple sclerosis is characterized by focal inflammatory plaques.
- Acute contrast enhancing lesions (CEL) may interrupt association tracts spanning several different cortical regions.
- Diffusion tensor imaging (DTI) can assess tissue integrity via detecting microstructural changes in normal appearing white matter (NAWM) tracts.

Objectives
- Determine whether acute white matter CELs result in upstream/downstream damage in normal appearing tracts.
- Characterize the temporal relationship between CELs and NAWM tract damage and the effects of lesion volume and location.
- Determine whether damaged tracts can recover over time.

Method
- Monthly MRIs were collected from 75 treated relapsing MS subjects over 2 years.
- Internal capsule (IC), longitudinal fasciculus (LF), uncinate fasciculus (UF), corpus callosum (CC), and middle cerebellar peduncle (MCP) were manually segmented based on proton-density-weighted (PDW) images.
- T2 lesions within the tracts were removed to capture pure tract NAWM.
- Longitudinal DTI was determined in each NAWM tract for radial diffusivity (RD), axial diffusivity (AD), mean diffusivity (MD), and fractional anisotropy (FA).
- Changes in DTI from baseline to maximal enhancement, recovery in DTI over 6 months, lesion volume, location, and enhancement length were analyzed.

Results
- Figure 2. Spatial representation of RD of NAWM (SLF) (A) and UF (B) over time of a patient with numerous CELs. RD was at a baseline value of 0.5 at month 1, increased to 0.8 in degenerated regions at month 6, remained persistently elevated at month 12. Temporal components of both SLF and UF have most increases in RD.
- Figure 3. RD of frontal, parietal and temporal components of Superior longitudinal fasciculus on right (A) and left (B) hemispheres and right and left uncinate fasciculus (C). RD peaked 2 months after maximum Gd enhancement (+3 months after maximum number of lesions (C)). RD did not return to baseline value at month 15.
- Figure 4 (above). Maximal change in RD of SLF and UF over baseline, reflecting DTI-detectable injury within normal-appearing tracts of patients with acute CELs.
- Figure 5 (right). In tracts with ≥1 new lesions (A), there is a significance in RD increase as compared to tracts with 0 new lesions (B).

Conclusions
- More rigorous statistical analyses are forthcoming. We will be modeling for time, lesion location, relation to beginning of each acute lesion, and repeated measures within a patient.
- Preliminary analyses suggest that RD is sensitive to degenerative changes in NAWM tracts surrounding acute CELs.
- RD appears to peak 2-3 months after maximum acute CEL appearance and persists for at least 6-9 months, suggesting that significant neurodegeneration develops shortly after initial lesion formation and that the repair process may be slow.
- The extent of RD increase seems to correlate with the number of acute brain lesions and extent of white matter tract involvement.
- MS lesions may result in disability by disconnecting areas of the brain, resulting in degeneration of critical pathways.
- Results from this study will improve the understanding of etiology and patterns of CEL damage in MS with respect to white matter tracts.

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