

# *Application of Diffusion Tensor Imaging to Brain Gray and White Matter*

## ABSTRACT

In the present work we explore the gray and white matter applicability of diffusion tensor imaging (DTI). To evaluate effect of ferritin-bound iron on gray matter contrast in DTI, we created an *in vitro* model consisting of agarose gel phantoms doped with ferritin, and validated our results *in vivo* on 29 healthy volunteer subjects 19–80 years of age in the basal ganglia. We further explored the application of DTI to amyotrophic lateral sclerosis (ALS) and multiple system atrophy (MSA); neurodegenerative diseases with gray and white matter pathophysiological components. In the ALS study, 33 patients and 30 age- and sex-matched controls were recruited, while the MSA study included 20 probable MSA subjects (10 MSA-P, 10 MSA-C) and 20 age- and sex-matched controls.

We found that ferritin-bound iron may make a significant contribution to DTI scalars in gray matter regions of the brain, mediated by eigenvalue repulsion. This has important implications for DTI studies targeting gray matter regions, especially in adolescence and in diseases associated with altered brain-iron load. In ALS, we found altered diffusion in the corona radiata and callosal body, and changes in  $R_2$  in the caudate nucleus and frontal white matter. In MSA, we observed widespread white matter changes associated with a positive clinical history of cerebellar manifestations, while altered DTI metrics in the putamen were associated with a positive clinical history of parkinsonian manifestations. The diagnostic potential of MRI in MSA may be greatly extended by applying DTI and evaluating changes primarily in the putamen and middle cerebellar peduncle, reaching very high sensitivities and specificities.

Keywords: magnetic resonance imaging, diffusion-weighted imaging, diffusion tensor imaging, multiple system atrophy, amyotrophic lateral sclerosis