Purpose:We utilize the DTI indices of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) to investigate 14 normal subjects with the specific genes that increase (APOE e2) and that decrease (APOE e4) the age of onset of Alzhiemer's Disease.

Methods:DTI acquisitions were performed in clinically acceptable scan times and thus had a low signal-to-noise ratio. The DTI data was denoised with a total variation regularization algorithm prior to affine and nonlinear registration to generate a common reference frame for the image volumes of all subjects. Region of interest (ROI), voxel-based analysis (VBA), and tract based spatial statistics (TBSS) were performed on the aligned ADC and FA maps to identify differences in the cohorts segregated by these alleles as well as segregated by mean age of the group.

Results:VBA on the denoised tensor data identified regions of reduced FA (primarily in the genu which was confirmed by ROI analysis) in the APOE e4 cohort compared to the APOE e2 cohort. The most consistent results were obtained for VBA using the denoised tensor and anisotropic smoothing prior to statistical testing. In contrast, isotropic smoothing identified regional differences for small filter sizes alone, emphasizing that this method introduces bias in FA values for higher smoothing kernel sizes. TBSS did not identify any regional differences in the white matter tracts and this may be related to the small localized area of change (found by VBA and ROI methods) that may not be detectable when analyzing voxels averaged normal to the tract.

Conclusions:The current findings are consistent with the age trajectories of the transverse relaxation rate studies of APOE ϵ2 and ϵ4 cohorts. The relaxometry study confirms the current DTI study that the late myelinating regions such as the genu are more susceptible to age-related myelin breakdown and this was associated with APOE status.