Histograms of multi-component T_2 relaxation imaging in multiple sclerosis: Characterization and comparison with histograms from diffusion tensor imaging.

S. H. Kolind[1], C. Laule[2], I. Vavasour[2], B. Mädler[3], A. Rauscher[2], V. Devonshire[2], J. Hooge[2], J. Oger[2], P. Smyth[2], A. Traboulsee[2], W. Moore[2], D. Li[2], and A. MacKay[2]

[1]Physics, University of British Columbia, Vancouver, BC, Canada, [2]University of British Columbia, [3]Philips Medical Systems, Vancouver, BC, Canada

Introduction: Using multi-component T_2 relaxation, the myelin water fraction (MWF, the ratio of the short T_2 signal to the total signal in the T_2 distribution, which reflects myelin content[1-3]) and the geometric mean T_2 of the intra/extracellular water pool (GMT_2) can be calculated[4, 5]. MWF and GMT_2 provide information about multiple sclerosis (MS) which is complementary to other techniques, such as diffusion tensor imaging (DTI)[6]. In this study, use of a recently developed 3D multi-echo T_2 relaxation sequence provided a 5-fold increase in coverage[7, 8], allowing histogram analysis for a more thorough characterization of MWF and GMT_2 in MS normal appearing white matter (NAWM) and lesions than has previously been possible, as well as more extensive comparisons to DTI-derived metrics.

Methods:

MRI Experiments: 13 patients with relapsing-remitting MS (10 female, 3 male; median EDSS = 2.5 (range 1.0-6.0); mean age = 40yrs (range 28-57yrs); mean disease duration = 8.5yrs (range 0.5-27yrs)) and 11 healthy age and gender matched controls were scanned on a Philips Achieva 3.0T system. The 3D T_2 relaxation sequence utilized a 90º excitation pulse followed by 32 slab-selective refocusing pulses flanked by gradient crusher pulses (7 slices, 32 echoes, TR = 1200ms, voxel size = 0.94x1.88x5mm, 10ms echo spacing)[8]. The DTI data, centered at the same location as the T_2 relaxation scan, used a single-shot EPI sequence (13 slices, TR = 2000ms, TE = 55ms, voxel size = 2.1x2.5x5mm, SENSE factor = 2.0, δ = 13.2ms, Δ = 27.4ms, b = 0 & 1000s/mm^2, 16 directions, 2 averages). Additional scans included a T_1-weighted turbo field echo (TFE) and FLAIR scans for segmentation of normal white matter (NWM) for controls, and NAWM and lesion for MS patients.

Data Analysis: MWF was the area under the T_2 distribution from 0-40ms divided by the total area, and GMT_2 was the mean T_2 on a log scale for 40ms<T_2< 200ms. The diffusion data was registered to the T_2 relaxation data, and fractional anisotropy (FA), mean diffusivity (<D>) and parallel and perpendicular diffusivities ($\lambda_{\parallel}$= largest diffusion eigenvalue and $\lambda_{\perp}$ = average of the 2 smaller eigenvalues) were calculated. Histograms were created for the slices corresponding to the centre 5 slices of the T_2 relaxation acquisition. Spearman rank correlation coefficients (R) were used to assess correlations and group comparisons were evaluated using a two-tailed Student's t-test.

Results and Discussion:

Histograms: Fig 1 illustrates the average histograms across all MS patients and all controls for NAWM/NWM and MS lesion. The MWF histograms showed good separation between NAWM and NWM. The MWF MS lesion histogram had a significant shift in peak location to lower values and a lower average MWF value than NWM. Changes in average MWF and MWF histograms for individual MS patients did not mirror changes in histograms of DTI metrics. Examination of $\lambda_{\parallel}$ and $\lambda_{\perp}$ histograms provided more information about changes in MS histograms compared to controls than only considering the more commonly reported FA and <D> histograms; $\lambda_{\perp}$ and <D> histograms detected significant differences between NAWM and NWM that were not detected by FA and $\lambda_{\parallel}$.

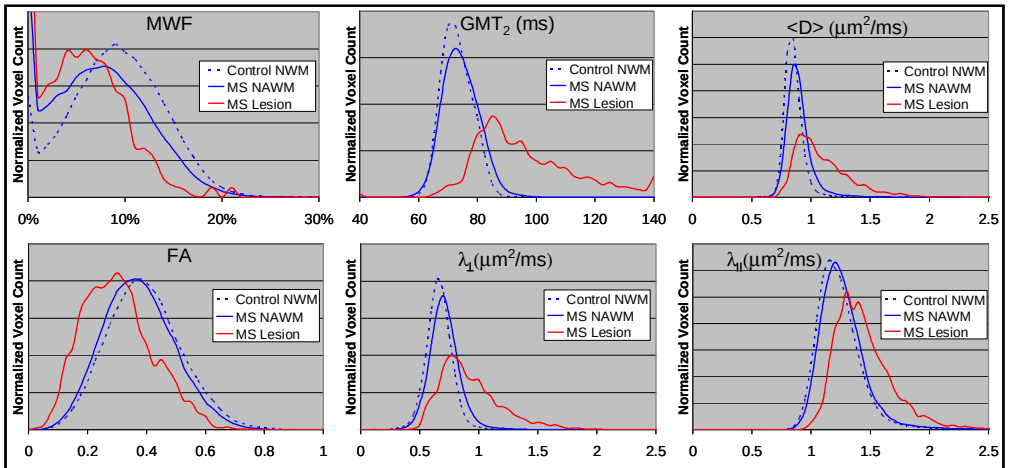

Fig 1: Normalized average histograms for NWM (dashed blue line) across the 11 control subjects, and for NAWM (solid blue line) and lesion (solid red line) across all 13 MS subjects, for T_2 relaxation-derived metrics (MWF and geometric mean T_2) and DTI-derived metrics (<D>, FA, $\lambda_{\perp}$, and $\lambda_{\parallel}$).

Correlations with disability: EDSS correlated with MWF NAWM average value (R = -0.57, p = 0.02) and the percentage of zero MWF values (R = 0.58, p = 0.04) but not with DTI metrics. Disease duration was correlated with peak height for <D> NAWM and $\lambda_{\perp}$ NAWM.

Correlations between MR-derived metrics: None of the histogram metrics for MWF or GMT_2 were significantly correlated with any of the DTI histogram metrics in NAWM, but in NWM, several histogram metrics were related between MWF and FA. Conversely, no correlation was found between GMT_2 and DTI histogram metrics in NWM, but several significant relationships were found in lesion.

Conclusion: MWF and GMT_2 histograms were different for MS patients compared to controls, and thus can be used to observe subtle changes in NAWM myelination. Furthermore, MWF histogram parameters correlated with disability. DTI metric histograms differed significantly from MWF histograms, therefore applying multiple MR techniques with different sensitivities to the many pathological features of MS may provide greater insight into MS pathophysiology.

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