Moments of the T2 spectrum as a marker of resolving edema in new MS lesions

Sneha Pandya[1], Elizabeth Monohan[2], Michael Dayan[1], Susan A. Gauthier[2], and Ashish Raj[1]
[1]*Radiology, Weill Cornell Medical College, New York, NY, United States,* [2]*Neurolgy, Weill Cornell Medical College, New York, NY, United States*

Purpose: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system for which novel therapies to stimulate remyelination are being developed. Our laboratory has developed a fast technique to quantify the myelin water signal from multi-echo multicomponent T_2 relaxometry, which uses T2prep 3D spiral pulse sequence **(FAST-T2**) to enable whole brain coverage in only 10 minutes [1], and a spatially constrained non-linear multi-Gaussian T2 algorithm [2]. This mapping method overcomes the lower signal-to-noise ratio (SNR) and increased artifacts introduced by the fast spiral pulse sequence. In order for FAST-T2 to be utilized as an accurate measure of myelin change in remyelination clinical trials, we must first address the impact of resolving edema in acute MS lesions on MWF change estimates. Acute MS lesions have an increase in extracellular water or edema, and this can preferentially affect the intra-/extra-cellular water compartment, which is represented by subtle shifts in the intermediate T2 peak. In this preliminary study we propose new measures based on moments of T2 spectra that are sensitive to changes in edema and provide addition information to a single myelin water fraction number. By combining the proposed moments with MWF maps we hope to obtain a more accurate measure of myelin change within the acute stage lesion development.

Methods: T_2 relaxometry involves inferring from exponentially decaying T2-weighted MR data the distribution of tissue T2 ("T2 spectrum") [3]. Spectral components with T2 values ranging from 10 to 50ms have been assigned to myelin water trapped between myelin bilayers, and approximately 100ms for intra- /extra-cellular water. We model these two pools by Gaussian distributions [2] and determine first and second moments of the intermediate peak. These low-order statistics can help us to comprehend underlying phenomenon causing T2 shift and underestimation of myelin in acute lesions induced by edema or axonal loss. We hypothesize that these phenomena involve increase of water in the intermediate compartment, leading the intermediate T2 peak to increase in height and shift to higher T2. Let $T_2(t)$ be the T2 spectrum over an interval of 5-300ms. We define the following restricted moments of this distribution within the intra-/extra-cellular T2 range [t1, t2]:

First moment $M_1 = \int_{t1}^{t2} T_2(t)tdt$ (Eq 1), Second moment $M_2 = \int_{t1}^{t2} T_2(t)t^2dt$ (Eq 2); where t1 = 50 ms, t2 = 150 ms

Data analysis: T2 relaxometry analyses were performed in MATLAB R2011b. Brain images were analyzed after the removal of skull (very short T2) and fluid (very long T2) signals. Whole brain MWF maps were obtained using our recently proposed technique [1, 2], and first and second moment maps were obtained using Eq 1 and 2. A recently developed automated data processing pipeline based on the SPM8 toolbox and FSL software was used to co-register the spiral T2 weighted images with the T1 weighted anatomical images. The transformations obtained from the multi-step registration procedure were then applied to the computed MWF maps.

Results: Figure 1a and b shows MWF maps of a patient with enhancing lesions scanned 6 months apart. Timepoint1(TP1) MWF map shows an acute left periventricular (LP) enhancing lesion with significant recovery of MWF, as seen in MWF map from Timepoint2(TP2). This recovery in MWF might be assumed to be remyelination. Figure 1c shows the T2 spectrum of LP region (red window in Fig1a and b) from TP1 and TP2. Spectrum from TP1 clearly shows rightwards shift of intra-/extracellular T2 peak (red curve) suggesting of possible underestimation of myelin content, which from literature is assumed to be because of presence of edema [4]. Similar example is demonstrated in Figure 2, showing T2 spectrum of a left frontal chronic (> 2 yrs) lesion (red window), where there is no change associated, either with MWF or height/location of intermediate T2 peak.

Conclusion and Discussion: We calculated both the moments for proof of concept, however suspect that M2 will be more useful in detection of subtle edema in lesions that are smaller or no longer enhancing. Resolving edema is likely to influence the accuracy of MWF as an estimate of true myelin change. In this study, we demonstrate the obvious shift in the intermediate T2 peak in an acute MS lesion as compared to a chronic lesion, which is consistent with the known differences in levels of edema between these lesion types. We provide a quantitative method to exploit the subtle shifts within lesions, specifically M1 for more acute lesions and M2 for lesions which are smaller and new lesions that are no longer enhancing. Moments can be utilized as a more sensitive measurement for resolving edema within new MS lesions and which can be utilized with MWF to provide a more accurate assessment of true myelin change.

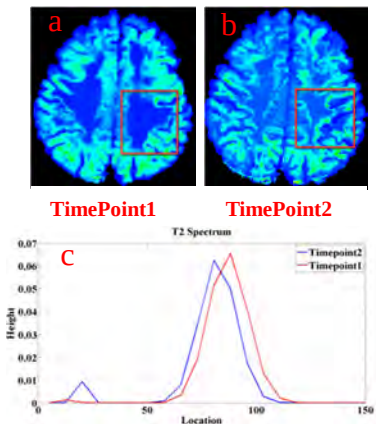

Figure 1: Example of a patient with acute lesion (a), with possible remyelination because of suspected resolution of edema (b). In c we show a T2 spectrum showing shift in intermediate T2 peak and increase in height because of edema (red curve)

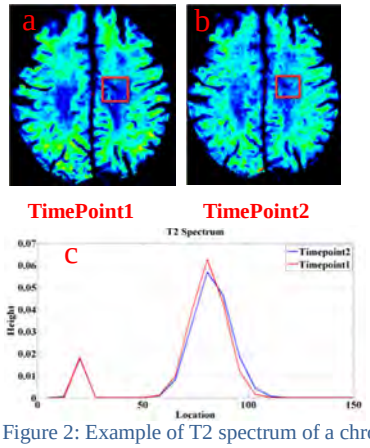

Figure 2: Example of T2 spectrum of a chronic lesion in a patient scanned 7 months apart. Note almost no change in MWF and location/height of intermediate T2 peak.

References:
[1] Nguyen TD, et al. Magn Reson Imgaging. 2012; 67(3):614-621
[2] Raj A, Pandya S, et al. PloS one. 2014;9(6):e98391 [3] Whittall K, Mackay, et al. Magn Reson Med. 1989;84:134–152
[4] Barnett MH, et al. Ann Neurol. 2004;55:458-468.