T2 Relaxometry

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Target audience: Neurologists and clinicians involved in neurodegenerative and demyelinating diseases; basic scientists interested in quantifying white matter, particularly myelin content in the brain within a clinically feasible acquisition time.

Purpose: To introduce a new software pipeline for performing clinically feasible and routine quantitative myelin imaging via T2 Relaxometry, with specific application to demyelinating diseases like Multiple Sclerosis [1]. T2 Relaxometry uses multi-echo T2weighted images to separate the contribution of various tissue components in the brain, thereby quantifying the myelin content. We have developed a fully automated pipeline in MATLAB featuring 3 steps: a) fast 3D T2-prepared spiral MR sequence for rapid multi-echo T2 imaging, b) a new post-processing technique obtaining T2 distributions and myelin fractions, and c) fully automated atlas-based coregistration, segmentation and parcellation pipeline to enable cross-subject voxel-based analysis. The overall pipeline is depicted in Fig 1. This analysis pipeline will be made publically available to facilitate routine myelin imaging and statistical analysis in common space.

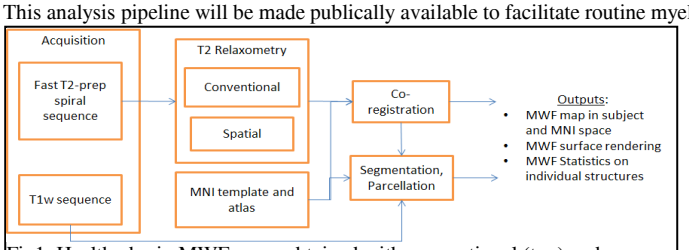

Fig1. Healthy brain MWF maps obtained with conventional (top) and proposed spatial (bottom) algorithms.

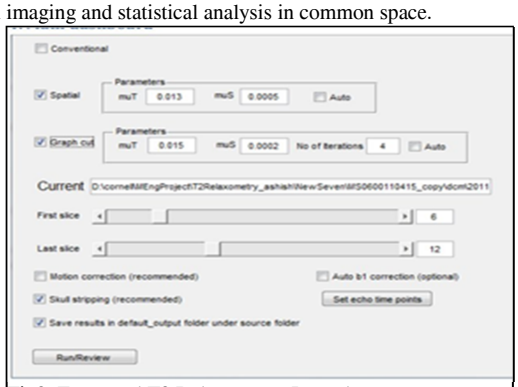

Fig2. Front-end T2 Relaxometry Launcher

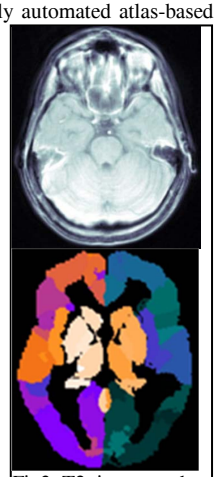

Fig3. T2 image and MNI parcellation

Method: The individual processes therein are described below.

a) ***Image Acquisition***: Following [4], a custom-designed fast 3D (28 slices, 5 mm thickness) multi-echo T2-prep spiral sequence was developed and tested at 3T (GE HDxt 15.0, GE Healthcare). We acquired 16 logarithmically spaced echoes between 5 ms to 300 ms, for a total scan time of 10 mins - one of the fastest T2 relaxometry sequences.

b) In ***T2 relaxometry***, acquired multi-echo T2 data are fit to a model consisting of multiple components exponentially relaxing at different T2 time constants. Unfortunately, this is a hard numerical problem due to ill-posedness of the problem [2], leading to myelin maps which are excessively sensitive to noise and are frequently difficult to interpret diagnostically. This problem is accentuated by the low SNR spiral scans we wish to work with. We have implemented a new way of solving the inverse problem in T2 relaxometry by imposing spatial smoothness constraints (following [3]) and by restricting the relaxing T2 distribution to 2 Gaussian-shaped peaks corresponding to myelin water and intra/extra-cellular water. The method works by minimizing a non-convex cost function of the form (details in another abstract): $\widehat{\boldsymbol{\theta}_{\mathbf{ex}}} = \arg\min_{\boldsymbol{\theta}_{\mathbf{ex}}} \|\mathbf{A}_{\mathbf{ex}}\mathcal{G}(\boldsymbol{\theta}_{\mathbf{ex}}) - \bar{\mathbf{y}}\| + \mu_T\|\boldsymbol{\theta}_{\mathbf{ex}}\| + \mu_S\|D_S\boldsymbol{\theta}_{\mathbf{ex}}\|$. Minimizaion was performed by an iterative non-linear least squares solver written in MATLAB. The Jacobian of the objective is calculated in advance and its sparsity is exploited to speed up computations. MWF was defined as the 1st Gaussian strength divided by overall signal. The method greatly improves robustness to noise, reduces spatial variations and definition of white matter fiber bundles in the brain. This allows it to be used on fast but low-SNR spiral acquisitions which take only 10 minutes for whole brain coverage.

c) ***Volumetric pipeline***: Subject's T2 images (Fig 3) are co-registered to subject's T1 image, which is then coregistered to the T1 template from the Montreal Neurological Institute (MNI). These transformations are applied to the computed MWF maps. The cortex is parcellated into 68 regions using pre-labeled MNI atlas (Fig 3). Mean MWF values are computed for each region, split further into the cortical ribbon and adjacent white matter. All code was written in MATLAB using SPM codebase.

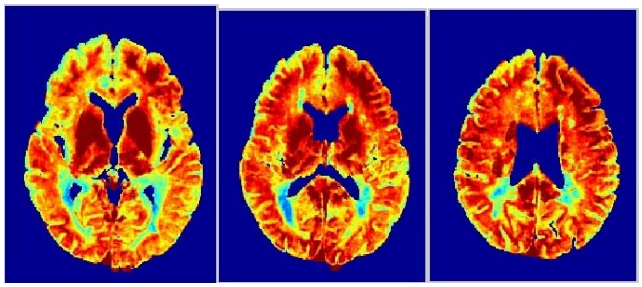

Fig4. 3 axial slices from whole brain spatial MWF map of an MS patient. Note excellent depiction of demyelinating lesions and of normal WM. Colors range from 0 to 0.2

Results: We tested the pipeline on 10 MS patients. Myelin water fraction (MWF) maps were computed using both conventional [1] and proposed spatial algorithms. An axial MWF slice shown in Fig 4 indicates improved definition of callosal and peripheral white matter and great delineation of MS lesions. The coefficient of variation between different regions for all 10 subjects was computed, and found to be quite small (0.1-0.2), which indicates consistent and spatially homogeneous estimates of MWF. Fig 4 shows MWF statistics generated by the software: histogram of regional MWF averaged across all subjects. Clearly, MWF in WM has a higher distribution than GM, and the two are statistically well separated, with p<0.01. **Execution time**: the entire pipeline takes approx. 2 hours for the whole brain.

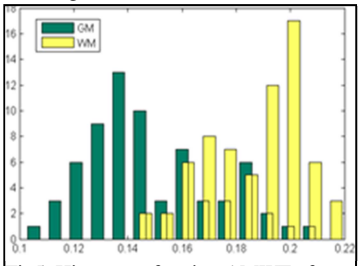

Fig5. Histogrm of regional MWF of each ROI averaged over 10 subjects

Conclusions: This fully automated pipeline has the potential to bring T2 relaxometry into the realm of clinical feasibility. It uses 2 highly novel techniques – a fast spiral MR sequence and a fast spatial processing algorithm, whose combined effect results in consistent and noise-free myelin maps. The volumetric pipeline enables detailed investigations of the spatial distribution of MWF, and since it is coregistered in common MNI space, it allows voxel-based analysis across subjects.

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[1] Laule et al, J Neurol 2004;251(3):284-293
[2] Graham et al, Magn Reson Med 1996;35(3)
[3] Kumar et al, Magn Reson Med 2012;68(5):1536-43.
[4] Nguyen et al, Magn Reson Med. 2012;67(3):614-2