Novel T2 Relaxometry Using Principal Components Analysis

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1. Introduction: T2-relaxometry is a promising MRI technique with wide applicability in neurological disorders like multiple sclerosis [1]. It can separate the contribution of various tissue components in the brain, thereby quantifying, for example, the myelin content of brain regions. The method works by capturing several MRI scans at different echo times, followed by a numerical fitting procedure to fit multiple components exponentially relaxing at different T2 time constants. Unfortunately, T2 relaxometry is a hard numerical problem due to ill-posedness of the problem, and extremely demanding requirement for SNR (500-1000 typically) [2]. Consequently, the T2 distributions and the resulting myelin water fraction (MWF) maps become very sensitive to noise and are frequently difficult to interpret diagnostically. Here, we propose a new way of doing T2 relaxometry by completely side-stepping the inverse problem altogether. Instead we rely on the insight that differentially relaxing components in the brain must be spatially coherent, and thus amenable to separation by principal components analysis (PCA) [3]. PCA was successful in many neuroimaging methods, especially fMRI, where it is used to resolve functionally co-activating regions. We now propose to use PCA on T2 relaxometry in much the same fashion, but this time to resolve co-relaxing components throughout the brain. This approach doesn't require fitting multi-exponential models to noisy data, and hence greatly improves noise, spatial variations and definition of white matter fiber bundles in the brain. Its execution time speed is *extremely* fast, limited only by the speed of SVD.

2. Theory: The underlying T2-relaxing tissue compartments in the brain give rise to multi-exponential decays, whose sum is the observed multi-echo MRI data. Thus at any voxel, we have $y = Ax + \varepsilon$, with $A_{ki} = \exp(-TE_k/T_2(i))$, where y is a vector of echo data, x is a vector consisting of all volume fractions of respective T2 pools, and ε captures additive noise. Lets collect signals from all voxels in the $N_v \times N_{echoes}$ matrix Y, and the desired T2 distributions in the $N_v \times N_{T2}$ matrix X. Then we can write $Y = XA$ for the whole brain. However, each matrix is rank-deficient, especially Y, which we know contains only 2-3 distinct T2 pools – fast relaxing myelin water pool, intra-cellular water pool and extra-cellular water pool. Therefore we propose to reduce dimensionality of each matrix by PCA, which performs a singular value decomposition: $Y = U \Sigma V^T, A = U_A \Sigma_A V_A^T$ (all matrices are "thin"), giving:

$$X = V_A \Sigma_A^{-1} U_A^T U \Sigma V^T$$

The thin matrix U contains the first few (3-5) principal singular *spatial* components, and V the first few *temporal* components. Examples shown in Fig 1 confirm that these components capture the principal modes of variation both spatially and temporally. From X above, we can deduce the MWF by simply summing its columns in the myelin T2 range (5-50ms) and dividing by total row sum.

3. Data and Methods: Following [4], 3D (8 slices, 5 mm thickness) multi echo spin echo (MESE) data on healthy volunteers were acquired at 1.5T (GE HDxt 15.0, GE Healthcare) using 32 echoes between 5 ms to 300 ms with echo spacing of 5 ms, for a total scan time of 32 minutes. Fast T2-prep spiral 3D (24 echoes, 28 slices, 24 mins scan time, 1.5T and 3T scanners) were also acquired [4]. Conventional regularization optimized over 50 logarithmically spaced $\mu_T \in [10^{-5}, ..., 10^{-1}]$ was obtained [1]. PCA was implemented on these data using sparse SVD function in MATLAB on a Desktop computer (2.4GHz, 4 GB RAM).

4. Results: The execution time of PCA method is *extremely* fast, taking 10s per slice, compared to 2 hours for conventional regularized least squares [1]. MWF maps from 1.5T MESE data are shown in Fig 2. Note improved definition of callosal and peripheral white matter, esp. the genu of CC. The PCA MWF maps are extremely detailed and highly specific for white matter. Fig 3 shows an MWF from the T2-prep spiral sequence at 3T, and the corresponding anatomic scan and histograms of MWF suggest reasonable agreement with conventional, except that its more biased toward higher values. Example T2 distribution is shown in Fig 4 - although it is much wider than expected, its peak is at the right place. The reason for the larger width of PCA distribution is not immediately clear, but we think it owes to the fact that we are using a single principal temporal mode to capture the entire myelin composition of the brain. The MWF contrast is again much better than the conventional one, and its anatomic agreement is good. We have not yet had a chance to perform quantitative evaluations on healthy and diseased brains, but presented evidence is visually compelling, on both 1.5T MESE data as well as 3T spiral T2-prep data.

5. Conclusions: Our results demonstrate that use of spatial constraints allows the reconstruction algorithm to handle much lower SNR data. Also, we expect that the MWF extracted using our spatial algorithm would have better reproducibility in inter-site and intra-site studies.

[1] Laule et al, J Neurol 2004;251(3):284-293   [2] Graham et al, Magn Reson Med 1996;35(3)
[3] Friston et al, Philos Trans R Soc B 355(1393):135-46   [4] Nguyen et al. Proc ISMRM 2011;233
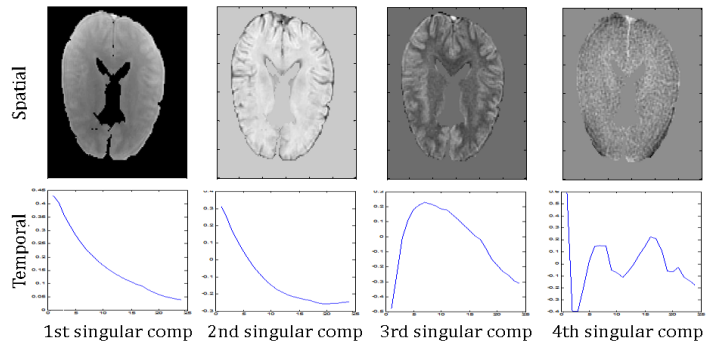
Fig1. Principal components of data matrix Y. The 1st component captures overall decay of brain, 2nd and 3rd components are more specific to myelin pool. But higher components (e.g. 4th shown here) simply appear to capture noise.
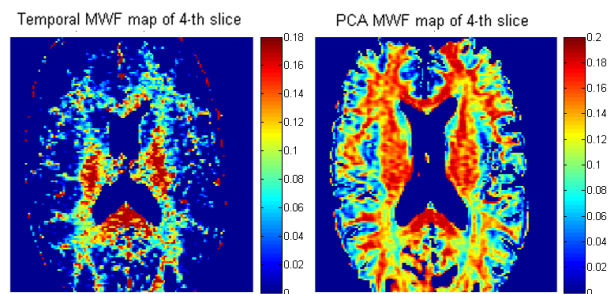

Fig2. Conventional MWF map (left) and proposed spatial map (right). Note improved detection of myelin pool and reduced spatial variability.
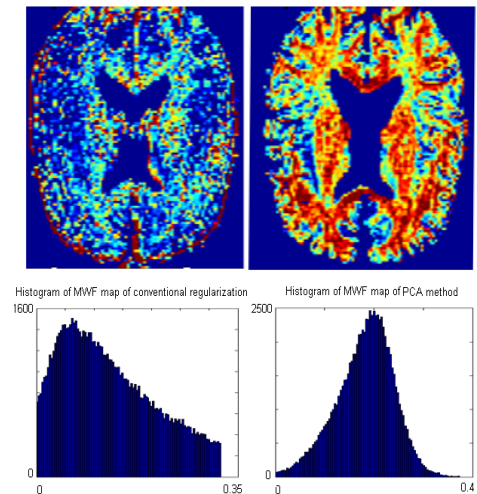

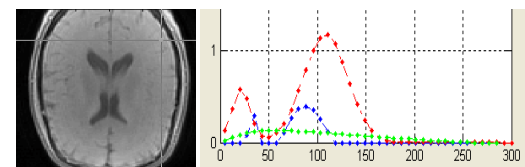
Fig4. MWF map and histogram from T2prep spiral

Fig3. Axial PD-weighted slice and T2 distributions of selected voxel obtained from conventional (blue) and PCA (green) algorithms. For comparison a spatial method (red) is also shown. The distributions are not to the same scale.