T2-relaxometry for Myelin Water Fraction Estimation using a Mixture of Wald Distributions

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Purpose: Quantitative MRI assessment of myelin has been studied for over twenty years and advances in imaging speed and spatial resolution have led to the emergence of multi-echo T2 mapping as an important tool for studying neurological disorders including multiple sclerosis and schizophrenia [1]. The T2 spectrum of water in the brain has multiple components. The fastest decaying component is associated with myelin-bound water and has a T2 below 40 ms, the intra-cellular and extra-cellular water T2 values in the 80-120 ms range, and cerebrospinal fluid has a T2 greater than 2000 ms. The very rapid decay of myelin-bound water (MW) has made it challenging to measure. The most well established approach for extracting MW is with CPMG sequences that acquire multiple spin echo images for T2 decay curve analyses [2]. Conventionally, MW and free water fractions are identified by fitting a discrete mixture of impulse functions, each centered at pre-specified T2 values across the range of anticipated T2 values. A linear weight for each impulse function is fit to the multi-echo T2 data via non-negative least squares (NNLS) [3]. However, this approach of fitting a discrete mixture of impulse basis functions fails to exploit the continuity of the true distribution of T2. We have developed an alternative representation in which we use a finite mixture of continuous distributions to describe the complete T2 spectrum. The fraction of the myelin-bound water is the area under the fast component curve divided by the total area of each component curve. This representation has the specific advantage that the number of parameters that must be estimated from the data is much smaller. From 32 spin echoes, we estimate 3 parameters per component, for a total of nine parameters, where the NNLS approaches estimate more than 50 free parameters.
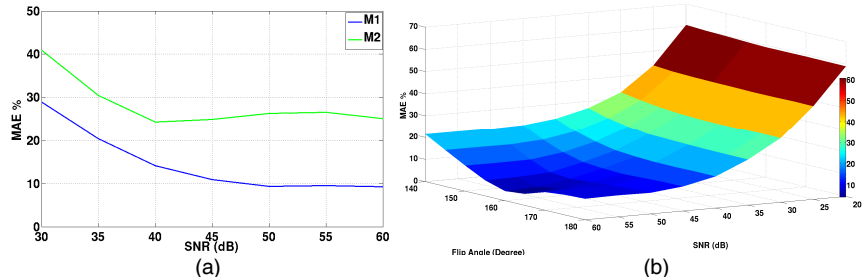
Methods & Materials: We use a model with small number of parameters to characterize the transverse relaxation rate spectrum at each voxel. We use a mixture of three Wald distributions with unknown mixture weights, mean and shape parameters to represent the distribution of myelin-bound water, tissue water, and cerebrospinal fluid [4]. The Wald distribution has a Gaussian-like distribution with positive support and a closed form Laplace transform which are exceptional and distinctive attributes for the representation of transverse relaxation rate distribution. The parameters of the model are estimated using the constrained variable projection method as a substantial number of unknown parameters are linear [5]. To compensate for the stimulated echo effect, we disregarded the first echo in the optimization process. Finally, the estimated parameters of our algorithm are used to estimate the MWF at each voxel. For validation of the algorithm, we generated a complex T2 spectrum with three components as the ground truth to present MW, the intra-cellular and extra-cellular water of the brain, and cerebrospinal fluid. We calculated 32 echoes equally spaced from 9ms to 288ms at different noise levels and estimated MWF using both NNLS and our method 1000 times at each noise level. We have used the extended phase graph (EPG) algorithm to synthesize CPMG data with different flip angles [6]. In addition, both methods were tested on an MS patient. T_2 relaxation measurements were performed on a 3T Siemens TRIO scanner with a single slice (4mm thick), multi-echo CPMG sequence acquiring 32 echoes with an echo spacing of 9 ms. A 21cm FOV was used with a matrix size of 192x192 (in plane resolution of 1.1mm) and the total scan time was 9 minutes and 41 seconds. Parameter initialization for each of the estimation procedures was the same as the simulation experiment.

Results: In Figure 1.a, we compared the relative mean absolute error (MAE) in the estimation of MWF using our approach and NNLS. It can be seen that our method has a smaller error compared to the conventional approach for the whole SNR range. When measuring the fraction of myelin water, our estimation approach is over 50% more accurate than the conventional approach at the practical SNR of 35 dB. Figure 1b shows the relative MAE of our method in the SNR range from 20 to 60 dB and flip angles larger than 140 degree. As can be seen for practical flip angles (>160°), our method could estimate the MWF with the accuracy comparable to the ideal scenario. These results show that the mixture of distributions can be used to estimate the MWF with an accuracy substantially superior to state-of-the-art methods described in the literature.
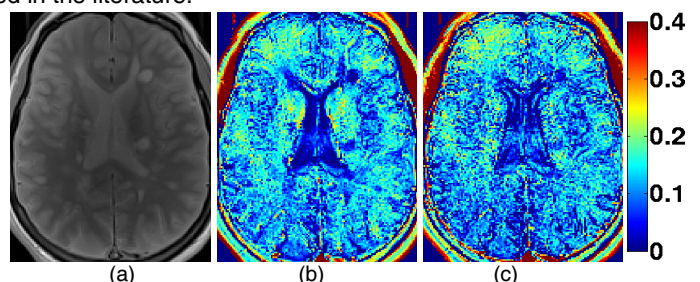

Figure 1. Quantitative comparaison of T2 spectrum estimation models for synthetic data. (a). Relative MAE of our method (M1) and NNLS(M2) for a range of SNRs. (b). The relative MAE of our method at different SNR and flip angles.

Figures 2 shows the MWF mapping of one slice of the patient using our and multi-exponential methods. For both models the components with T2 shorter than 40ms are used to estimate the MWF. The results show that our approach estimated the MWF more accurately compared to the NNLS method, since the MWF map has a sharper contrast between white matter and white matter lesion.

Conclusions: We have introduced a novel parametric model to represent the spectrum of the relaxation rate at each voxel. We have used both synthetic and real brain images to compare performance of our method with NNLS algorithm and showed the superiority of our method.

References: [1] Van der Knaap et al. Springer 2005. [2] Kolind et al. MRM 2009. [3] Whittall et al. MRM 1997. [4] Seshadri et al. Clarendon Press 1993. [5] Golub et al. Inverse problems 2003. [6] Hennig et al. JMR 1988.

Figures 2. Qualitative comparison of MWF maps for a MS patient. Mixture of Wald distribution (b) and NNLS (c) MWF map of an axial slice of a MS patient (a).