Optimization of Multi-Compartment Analysis of T2* Decay in Myelin Water Fraction Mapping with Fixed Brains

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Introduction: Myelin water fraction (MWF) in the brain can indicate the integrity of myelin sheath of neurons, which is critical for the communication and coordination among different regions of the brain. Therefore, MWF map of the brain can provide diagnostic information on brain diseases such as multiple sclerosis (MS). However, the quantitative mapping of MWF is very challenging due to its short T_2 relaxation time. Several researchers acquired T_2 decay measurements and successfully estimated MWF from them. MacKay et al. [1] used a nonnegative least squares (NNLS) algorithm to estimate MWF from 32-echo T_2 decay measurements. Jones et al. [2] used a linear combination method to select short T_2 components and suppress long T_2 components. Lancaster et al. [3] used a three-pool white matter model to fit multi-exponential decay curve to the measurements. We have presented MWF mapping technique using T_2* relaxation, which makes the acquisition much faster with finer temporal resolution than the previous approaches with T_2 relaxation [4]. In this abstract, we present an approach to optimize the fitting algorithm with a three-pool model and analysis of MWF map will be described.

Method: Multi-gradient-echo sequence was used to record the T_2* decay curve. We used the three-pool model to analyze the decay measurements for quantitative mapping since the linear combination approaches cannot give clear cut-off at the desired T_2* values and NNLS algorithms are often unable to find the correct number of components [5]. Post mortem brains were scanned with a 128-echo multi-gradient-echo sequence on a GE 3T scanner. Images with 256 x 256 matrix were acquired with a slice thickness of 5 mm and a FOV of 20 cm. TR was 2s and flip angle was 90 degrees. The three-pool model consists of a myelin water pool (T_2* < τ_1), a myelinated axon water pool ($\tau_1 < T_2* < \tau_2$), and a mixed water pool ($\tau_2 < T_2$*). The proper selection of (τ_1, τ_2) is important for reliable fitting results. If τ_1 is set too small, a large portion of myelin water signals would leak into the myelinated axon pool, resulting in underestimation of MWF and a higher fitting error. If τ_1 is set too high, some portion of myelinated axon water signals would leak into the myelin pool, resulting in overestimation of MWF and a higher fitting error due to the misfitting of the myelinated axon pool. We found the optimal (τ_1, τ_2) where the rate of change of the measured MWF (i.e., the derivative d(MWF)/dτ) as well as the fitting errors were minimized. Based on these optimal T_2* ranges, MWF were estimated and their characteristics were analyzed.

Results: Figure 1 shows the average MWF measurement at a white matter region, its variation over τ_1, and the fitting error for different τ_1 values. The optimal τ_1 is found be to at 16-20 ms. We repeated the same procedure to find the optimal τ_2, which was 36 ms. Figure 2 shows the anatomical image of the fixed brain (top) and its MWF (bottom) obtained with the optimal τ_1 and τ_2. Figure 3 shows the T_2* distribution over the regions of interest in white matter that are depicted in Figure 2 (top). It clearly shows the three distinct peaks which correspond to the myelin pool (3~16 ms), the myelinated axon pool (16~34 ms), and the mixed pool (34~45 ms), respectively. Figure 4 shows the detected MWF histogram. It has two separate lobes, denoted by 'A' and 'B'. Figure 5 left and right show pixels corresponding to 'A' and 'B' lobes in red color, respectively. It can be observed that MWF for most white matter ranges from 9~14 % (lobe B). MWF of the edges between white and gray matter ranges from 4~8 % (lobe A). Figure 6 shows the estimated MWF for other fixed brains.

Discussion: This study shows that the three-pool model analysis with T_2* relaxation can produce myelin maps based on MWF in human brain. Optimal selection of T_2* ranges for the fitting of three pools has been made and T_2* distribution of the estimated myelin maps shows three distinct peaks corresponding to each of the three pools. T_2* relaxation time in a pixel is related to T_2 relaxation time by: $1/T_2* = 1/T_2 + 1/T_2'$, where $1/T_2'$ is determined by mesoscopic field inhomogeneities . We can estimate that T_2' in WM at 3 Tesla is approximately at 100ms, based on the documented T_2 (79.6ms) and T_2* (44.8ms) of WM [6]. Assuming that T_2' is the same in all these 3 pools, the estimated T_2* value would be 9.1ms, 28.8ms, and 57.3ms in myelin, myelinated axon, and mixed pools, respectively. Considering the T_2* shortening by the fixation of tissue, T_2* distribution obtained in our experiments is consistent with these expectations. Preliminary studies on living brain show a longer T_2* distribution. Further investigations are needed for *in vivo* application to minimize the effects of inhomogeneous B_o field and noise on FID decay measurements.

References: [1] MacKay A, et al. MRM 1994; 31:673-7. [2] Jones CK, et al. MRM 2004; 51:495-502. [3] Lancaster JL, et al. JMRI 2003; 17:1-10. [4] Du YP, et al. ISMRM 2006, p.2104. [5] Andrews T, et al. MRM 2005; 54:449-54. [6] Wansapura JP, et al. JMRI 1999; 9:531-8.

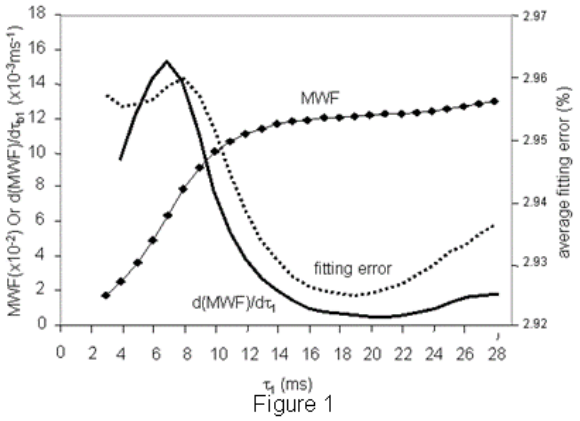

Figure 1

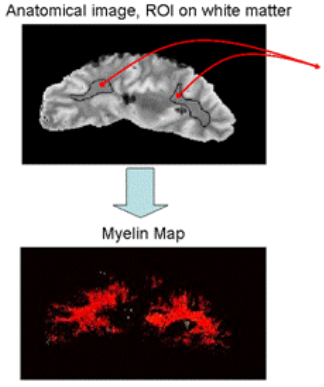

Figure 2

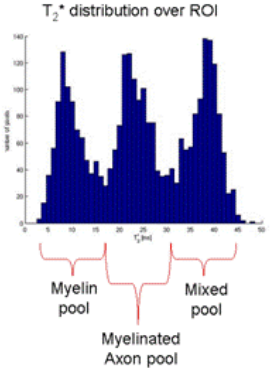

Figure 3

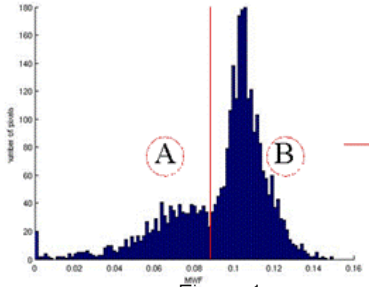

Figure 4

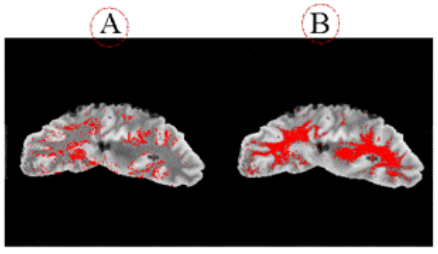

Figure 5

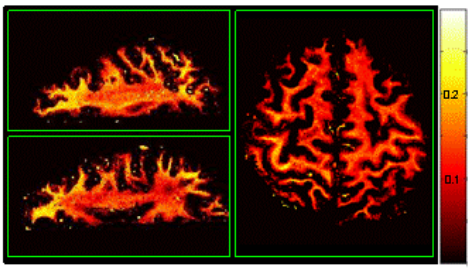

Figure 6