In Vivo Multislice Mapping of Myelin Water Content of the Brain with T2* Signal Decay

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Introduction: In recent years, substantial interests in quantitative assessment of myelin content in white matter (WM) have emerged for the study on the myelin-related diseases such as multiple sclerosis (MS). One commonly used approach for *in vivo* myelin quantification is based on the analysis of T_2 relaxation time. It has been reported that the T_2 spectrum of WM and several myelinated tissue samples consists of three components [1,2]. Since the water trapped in the myelin sheath has the shortest T_2 relaxation time among three components, myelin water fraction (MWF) which is the ratio of the amplitude of the shortest T_2 component to the total can represent the myelin content in WM. Histopathology studies showed a strong correlation between MWF and the myelin distribution. A single-slice technique based on the CPMG data acquisition has been successfully developed to study the pathology related to demyelination in patients with MS [3]. A new multi-slice technique to estimate MWF using T_2* relaxation has also been demonstrated for the *in vitro* studies [4]. In this abstract, we present the results of *in vivo* applications of the T_2* relaxation analysis technique for multi-slice and high-resolution MWF mapping.

Method: Two healthy subjects at the age of mid 30's were scanned with a multi-gradient-echo sequence on a GE 3T scanner to record the T_2* decay signals as known as free-induction decay (FID). Total 8 slices were acquired (up to 24 slices would be possible if gradient heating were not a limiting factor) in high resolution (256 x 256), a slice thickness of 4 mm, and a FOV of 24 cm. TR was 2 s, the first echo time was 2.1 ms, and echo spacing was 1.1 ms. The total number of echoes was 64. A three-pool model [5] was used for the multi-exponential fitting to estimate MWF from the decay measurements. The three-pool model consists of a myelin water pool (T_2* < τ_1), a myelinated axon water pool (τ_1 < T_2* < τ_2), and a mixed water pool (τ_2 < T_2*). Optimal set of (τ_1, τ_2) was selected from the T_2* distributions over the regions of interest (ROI) in WM.

Results: Figure 1 (a) shows the temporal noise level in the FID measurements from a single acquisition with a head volume coil. Our analysis indicated that this *in vivo* noise level was about 3 times higher than that of *in vitro* measurements. Consequently, the resulting MWF map contained high spatial noise as shown in Figure 1 (c). In order to increase the temporal SNR in the FID signals, we acquired 5 repeated measurements and averaged them (Figure 1 (b)). An adequate temporal SNR was obtained and an improved MWF map was estimated as shown in Figure 1 (d). However, 5 repeated scans required 43 minutes, which would be too long for a clinical application. Fortunately, an adequate SNR for the exponential fitting was able to be obtained with use of 8-channel phased-array coil in this study. For the selection of T_2* ranges for each of three pools, T_2* spectra were estimated over several ROIs in WM. FID signals with high SNR were obtained by averaging individual FID measurements over ROIs, and then fitted using the nonnegative least square algorithm to produce T_2* spectrum. Figure 2 shows the several T_2* spectra and the optimal τ_1 was found at 23 ms as indicated by an arrow. Figure 3 (a) shows two high-resolution MWF maps from a single acquisition (8.5 minutes) with the 8-channel phased-array coil. Higher MWF values (~0.12) were obtained on the myelin-rich areas (WM, especially corpus callosum) compared to other gray matter. The further improvements were made by averaging 4 repeated scans at the expense of the increased scan time (34 minutes) as shown in Figure 3 (b).

Discussion: These results demonstrated the feasibility of applying the multi-compartment analysis of T_2* decay to the *in vivo* multislice mapping of MWF. High resolution MWF maps (256x256) with detailed structures were successfully estimated from *in vivo* scans. The volumetric analysis with multislice and high resolution MWF maps has the potential to bring higher accuracy for the study of the myelin developments and the myelin-related diseases such as MS. An echo train of 64 echoes was used for the exponential fitting of the T_2* decay signals instead of using 126 echoes as in the *in vitro* studies. The later echoes in *in vivo* brain studies had low SNR and the measurements were distorted due to the field inhomogeneity. Therefore, the overall exponential fitting was degraded when the later echoes were included. In this study, the total number of echoes was reduced to 64 (~71.4 ms) for the exponential fitting. Some erroneous high MWF values (~0. 29) were observed at several regions such as the orbitofrontal area, veins, and Globus Pallidus. These abnormal MWF values are considered to be caused by T_2* shortening due to the presence of local field gradients, the increase of deoxyhemoglobin, and the increased level of iron concentration, respectively. Currently, these artifacts were not removed in this study and, therefore, any further analysis on MWF maps should be made with caution for these areas.

References: [1] MacKay A, et al. MRM 1994;31:673-7. [2] Does MD and Gore JC, MRM 2002;47:274-83. [3] Laule C, et al. J Neurol 2004:251:284-93. [4] Du YP, et al. MRM 2007;58:865-70. [5] Lancaster JL, et al. JMRI 2003;17:1-10.

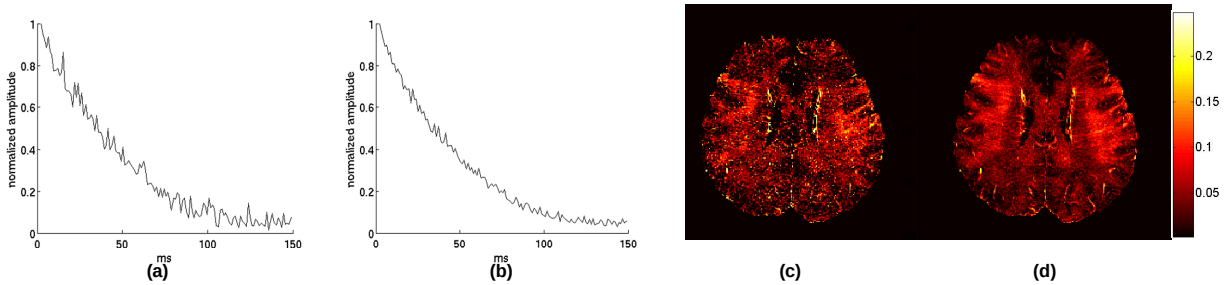

Figure 1. Typical FID signals from a single measurement (a) vs. an averaging of 5 repetitions (b), and their corresponding MWF maps (c, d), respectively (the data were acquired with a head volume coil).

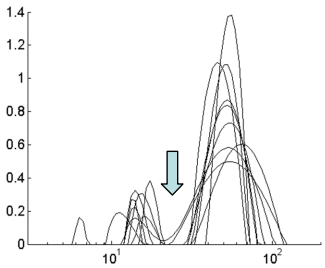

Figure 2. T_2* spectra over several regions of interest in WM. The arrow indicates the optimal τ_1 (23ms) for the myelin water content.

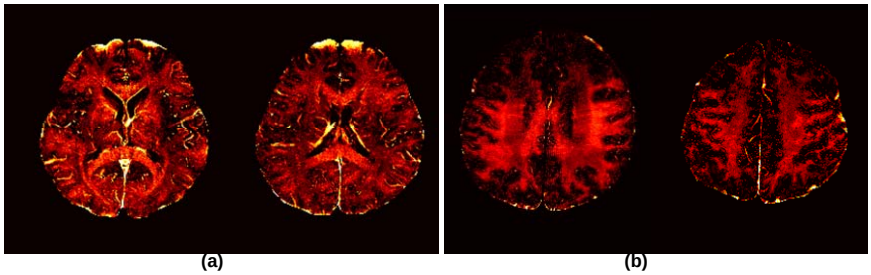

Figure 3. MWF maps from a single acquisition (a) and an averaging of 4 repetitions (b), with 8-channel phased-array coil. Even with a single acquisition (8.5 minutes scan), reasonable MWF maps with high resolution (256x256) were obtained. Further improvements were made by averaging 4 repeated scans (b).