An Improved Gradient Echo Myelin Water Imaging using a Frequency Offset Model and Early Echoes

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Purpose Myelin water imaging (MWI) has been proposed as a potential biomarker for demyelinating diseases. The method is based on the T_2 or T_2^* differences among water compartments (myelin water vs. axonal/extracellular water) and utilizes multi-echo SE or GRE sequences. Compared to the SE approach,[1] the GRE-based MWI has the advantages of a lower SAR and larger volume coverage.[2] In several recent studies at 7T, the multiple T_2^* components have been demonstrated to have frequency offsets.[3-5] This finding may allow us to generate a more accurate and reliable myelin water fraction (MWF) in GRE-MWI. In this study, we demonstrate that the multi-component model with frequency offsets offers substantially reliable MWF results that are less affected by the number of echoes used in the analysis. Additionally, we reveal that the MWF map generated from early echoes (~12 echoes) is less sensitive to B_0 field inhomogeneity and, hence, provides wider brain coverage. Lastly, we perform a test-retest scan and demonstrate that the frequency offset model with early echoes provides more reproducible results.

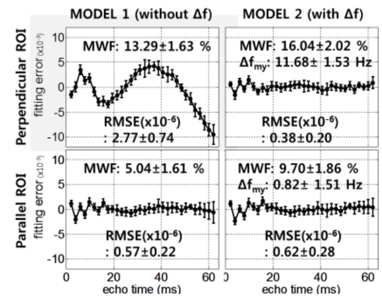

Figure 1: Residuals errors in the ROIs. Model 1 (left) and Model 2(right)

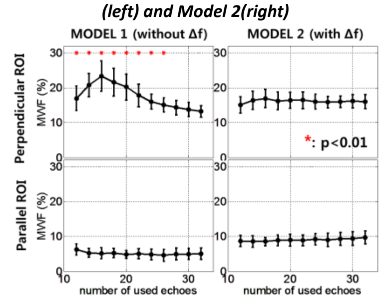

Figure 2: MWF estimated by various number of echoes used in the fitting.

Methods Eleven volunteers (IRB approved) were scanned at 3T (Siemens, Tim Trio). For MWI, 3D multi-echo GRE was acquired with the following parameters: TR=120 ms, TE=2.1:1.93:61.93 ms (32 echoes), flip angle=30°, bandwidth=1502 Hz/px, voxel size=2x2x2 mm^3, matrix size=128x128x64, scan time=16 min. For reference, DTI and MPRAGE images were also acquired. ***Signal Model:*** To investigate the effects of the frequency offsets (Δf) in MWF, the following two signal models were examined: Model 1 (without Δf): $S(t) = |A_{my} \exp(-t/T_{2\ my}^*) + A_{ma} \exp(-t/T_{2\ ma}^*) + A_{mx} \exp(-t/T_{2\ mx}^*)|$, and Model 2 (with Δf): $S(t) = |A_{my} \exp(-t/T_{2\ my}^* - i2\pi\, \Delta f_{my}\, t) + A_{ma} \exp(-t/T_{2\ ma}^* - i2\pi\, \Delta f_{ma}\, t) + A_{mx} \exp(-t/T_{2\ mx}^*)|$ where A_{my}, A_{ma} and A_{mx} represent the amplitude of the myelin (my), axonal (ma) and mixed (mx) water pools, and Δf_{my}, and Δf_{ma} represent the relative frequency offsets of my and ma pools with respect to mx pool respectively. An iterative curve fitting algorithm was used to estimate the parameters. The initial values for A_{my}, A_{ma}, A_{mx}, $T_{2\ my}^*$, $T_{2\ ma}^*$, $T_{2\ mx}^*$, Δf_{my}, and Δf_{ma} were 0.1, 0.3, 0.6, 10 ms, 48 ms, 72 ms, 5 Hz, and -0.5 Hz, respectively. ***ROI analysis:*** Two ROIs whose fiber orientations were approximately parallel (spinal-cortical tract) and perpendicular (optic radiation) to B_0 were manually drawn guided by DTI. The two models were then fitted to ROI-averaged signals for varying number of echoes (12 to 32 echoes). A t-test was performed with respect to the 32 echo MWF. ***Voxel-by-voxel analysis:*** To compare the MWF maps from the two models, the fitting was performed for every voxel. Before the fitting, a 3D anisotropic diffusion filter was applied to increase the SNR.[2] Lastly, the MWF in five ROIs (genu, splenium, internal capsule, minor forcep, and major forcep) were estimated in the MWF map generated using Model 2 with 12 echoes in all subjects. ***Reproducibility:*** Two subjects were scanned twice using the same protocol one hour apart, with slightly different head positions. The two multi-echo GRE images were registered using the image registration information from the MPRAGE images (FSL). Then the multi-echo GRE data were processed to generate MWF maps using the two models and three different numbers of echoes (12, 22, and 32 echoes). Pearson correlation coefficients of the MWF values of the two scans were calculated in the entire white matter for each model and echo.

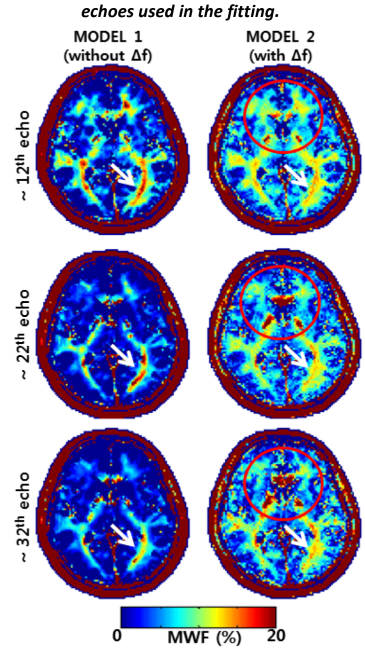

Figure 3: The MWF maps estimated from the first 12 (top), 22 (middle), and 32 (bottom) echoes using the two models

Results When Model 1 is used, the perpendicular ROI has a larger root mean squared error than the parallel ROI (Fig. 1, left). When Model 2 is used, the root mean squared error in the perpendicular ROI is reduced and similar to the error in the parallel ROI (Fig. 1, right). When each model was fitted with different number of echoes (Fig. 2), the estimated MWF shows large variation in the perpendicular ROI of Model 1. However, the results were stable in Model 2, demonstrating the reliability in the MWF estimation. These results are further confirmed when the MWF maps from the two models at the three different echoes (12, 22, and 32 echoes) are compared (Fig. 3). The perpendicular fibers (optic radiation; white arrow) are less variable across multiple TEs in Model 2. In both models, the errors in the frontal lobe increase as the number of echoes increases (red circle). This may originate from B_0 inhomogeneity, which affects later echoes more significantly. Hence, limiting the number of echoes can be an effective approach to reduce such artifacts. Figure 4 shows a whole brain MWF map using Model 2 with 12 echoes. The MWF map reveals most of white matter regions. The mean MWF and Δf_{my} values from five ROIs (N = 11) are summarized in Table 1. The test-retest results are shown in Table 2, demonstrating the best reproducibility when Model 2 with 12 echoes was used.

Discussion & Conclusion In this study, we demonstrated that the multi-component frequency offset model (Model 2) with early echoes (~12 echoes) provides the most reliable and reproducible MWF map in GRE-based MWI at 3 T. The resulting 3D MWF map shows a wide coverage of white matter, demonstrating potential for clinical applications. **References** [1] Mackay, MRM 33:673,1994. [2] Hwang, NI 52:198, 2010. [3] Lee, PNAS 107:5130, 2010. [4] Wharton, PNAS 109:18559, 2012. [5] Sati, NI 77:268, 2013.

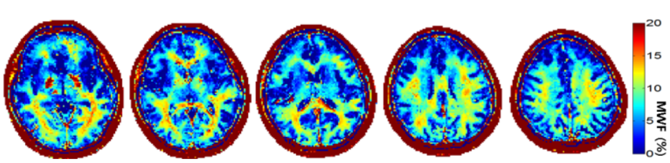

Figure 4: A MWF map showing 5 slices out of 64

ROI	MWF (%)	Δf_{my} (Hz)
Genu	12.0 ± 2.4	9.0 ± 4.0
Splenium	14.5 ± 1.2	10.2 ± 2.7
Internal capsule	9.0 ± 1.2	1.4 ± 1.5
Minor forcep	8.1 ± 1.5	4.4 ± 3.1
Major forcep	11.8 ± 0.8	6.8 ± 3.0

Table 1: Average MWF and Δf_{my} in ROIs

# of echoes used:		12	22	32
Subject 1	Model1	.74	.68	.68
	Model2	**.85**	.82	.78
Subject 2	Model1	.61	.70	.73
	Model2	**.83**	.79	.74

Table 2: Correlation coefficients of the test-retest scan