ΔB_0 Correction for Myelin Water Fraction Imaging Based on Multi-Slice MGRE Acquisitions

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INTRODUCTION: Quantitative MRI can achieve greater pathological specificity in diseases affecting the myelin of white matter (WM). One approach, based on multicomponent (MC) relaxation using non-negative least squares (NNLS) analysis identifies two components attributed to myelin water (MW) and intra/extracellular water (IEW)[1]. The myelin water fraction (MWF) is the ratio of MW to total water. While MWF imaging has traditionally been done using multi-echo spin-echo (MESE) imaging, multi-gradient echo (MGRE) sequences have been proposed for T_2^*-based MWF mapping[2], providing fast, whole-brain or multi-slice imaging capability, low specific absorption rate (SAR) and short echo spacing (ES). However, MGRE imaging suffers signal loss caused by magnetic field inhomogeneities (ΔB_0) (*e.g.* at air-tissue boundaries), making ΔB_0 correction necessary to obtain accurate MWF maps. In 2D multi-slice acquisitions, voxels are typically larger in the slice (z) direction, making magnetic field gradients in this direction (G_z) the dominant source of signal loss and T_2^* bias. The effect of G_z on estimates of single-component T_2^* from 2D MGRE has been described[3], and several approaches have been proposed for correcting single component T_2^*[4,5,6] data. The approach presented here is based on a combined method (B_0 mapping from MGRE phase data and joint estimation of G_z and a single T_2^*)[6] that has been adapted to multi-component T_2^* relaxation. The G_z calculated using our method were used to correct our MGRE data, and NNLS fitting was used for MC T_2^* analysis. Simulations were performed to assess the method and the technique was evaluated *in vivo* in 5 healthy volunteers.

THEORY: Assuming negligible in-plane field gradient effects, the additional signal decay in 2D MGRE caused by G_z can be modeled as a sinc function with a first order approximation of $\boldsymbol{G_z}$[3]: $S(t) = S_0(t)sinc(\gamma G_z(\Delta z/2)t)$ [Eq. 1]. $S(t)$ is the measured signal, $S_0(t)$ is the signal without the effect of ΔB_0, γ is the gyromagnetic ratio, and Δz is the slice thickness. The proposed ΔB_0 correction for 2D multi-slice MGRE data for MWF mapping can be broken down into a three-step process:

1. A B_0 field map is calculated using the four-quadrant arctangent function and the phase images acquired at TE_1 and TE_3 of the MGRE sequence. This field is fit to a sixth-degree polynomial in the *z*-direction, and the derivative in the z-direction (G_z) is calculated at each voxel.
2. The time taken for a short MW component of 5 ms to decay to 1.9% of its initial amplitude is calculated (t_{MW_end}). The signal after $t = t_{MW\_end}$ is approximated as mono-exponential, since the remaining signal is dominated by a single IEW component. Eq. 1 is fit to the signal from $t = t_{MW\_end}$ onward, with $S_0(t) = S_0(t = t_{MW\_end})e^{-t/T_2^*}$ using non-linear least squares to yield $G_{z,fit}$. The value of G_z obtained from the field map (step 1) is used as a starting point in this fit.
3. The $G_{z,fit}$ values at each voxel are then used to calculate the MGRE signal in the absence of ΔB_0, by dividing the measured signal, $S(t)$, by the sinc modulation factor (Eq. 1). To account for singularities, which can occur when the sinc modulation factor displays zero-crossings, data points in the vicinity of the zeros are excluded from subsequent MC T_2^* analysis.

METHODS & RESULTS - *Simulations*: *Ad hoc* discrete T_2^* distributions were generated, with a mean and standard deviation (std) T_2^* of 5(3) ms and 50(10) ms for MW and IEW, respectively, and the MWF was set to 12%. The corresponding MGRE signal consisted of 64 echoes with TE_1 = 2.4 ms and ES = 1.2 ms. Next, the MC T_2^* decay signal was multiplied by the sinc modulation factor (Eq. 1) to simulate ΔB_0, for various G_z values from 0 – 4.5 mG/cm (in steps of 0.5 mG/cm), and 600 realizations of Rician distributed noise ($SNR(TE_1)$ = 150) were added for each G_z. $G_{z,fit}$ estimation was performed as described above, and the simulated signal was corrected for ΔB_0 (using $G_{z,fit}$). MC T_2^* analysis of the corrected signal was performed using regularized NNLS and a 25 ms cutoff time for MW (Fig. 1).

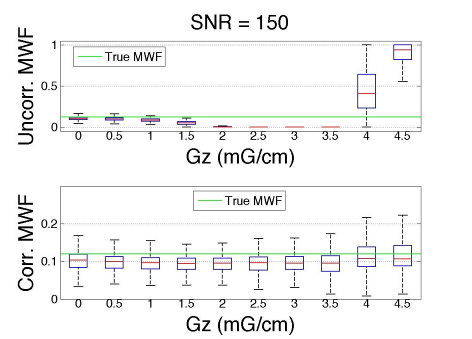

Figure 1: Pre (top) and post (bottom) B_0 correction median (± inter-quartile range) MWFs

***In vivo*:** Measurements were performed on a Siemens 3 T scanner with a 32-channel head coil. 5 healthy volunteers were scanned with approval of the local ethics committee, after giving informed consent. High-order shimming was performed to minimize ΔB_0, and a 64-echo MGRE sequence with bipolar readout gradients was acquired: 19 axial 2.5-mm slices (no slice gap), FOV = 338×222 mm^2, TR/TE_1/ES= 2000/2.4/1.2 ms, BW = 1090 Hz/Px, matrix = 256×168, flip angle = 85^0, 3 averages, scan time ~ 15 min, and $SNR(TE_1)$ = 120. A high-resolution 3D T_1-weighted scan was acquired for anatomical reference and for WM segmentation using FSL FAST[7]. WM masks were used to guide manual drawing of regions of interest (ROIs) for each subject in 5 WM structures (genu and splenium of the corpus callosum, minor and major forceps, and posterior internal capsules). The average MWF across 5 volunteers for the 5 WM ROIs is shown in Fig. 2, as well as the average over all 5 WM ROIs (labeled as WM ROIs). All the corrected MWFs were found to be significantly greater ($p < 0.05$) than the uncorrected MWFs.

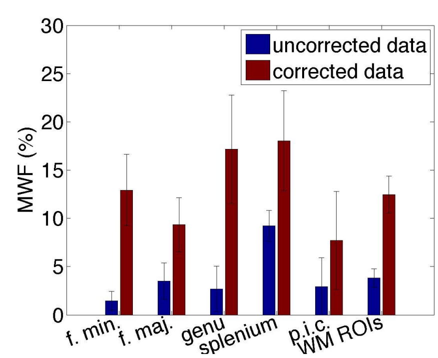

Figure 2: Uncorr. MWFs (blue), corr. MWFs (red).

DISCUSSION & CONCLUSIONS: A ΔB_0 correction method was presented for 2D MGRE data acquired for MWF imaging. The approach does not necessitate additional data acquisition for field mapping. Simulations demonstrated that MWF values are significantly biased in the presence of G_z (Fig. 1, top), and that our ΔB_0 correction method recovers the MWF for all G_z values investigated (Fig. 1, bottom). The corrected MWF values appear to slightly underestimate the true MWF, a previously documented consequence of the NNLS approach[8]. Despite this, post-correction MWFs are close to the true MWF for all G_z. Experimentally (Fig. 2), pre-correction MWFs were found to be similar to those observed by Lenz *et al.*[2] at 1.5 T using NNLS for MC T_2^*-based MWF imaging with no prior ΔB_0 correction, with the exception of ROIs with high ΔB_0 (forceps minor, genu). The disparity between MWFs in these regions is attributed to the difference in field strength. Most importantly, all post-correction values are in agreement with literature values found using MESE[1]. These results highlight the importance of proper ΔB_0 correction when imaging MW using MGRE sequences and provide a solution for achieving this.

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