Comparison of Linear Combination Filtering to DTI and MTR in whole brain myelin-water Imaging

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Introduction: Short T_2 imaging is commonly used to quantify myelin-water fraction (MWF) using a 32 echo Carr-Purcell-Meiboom-Gill (CPMG) acquisition sequence [1-3]. However, CPMG sequence requires a long scan time of 26 minutes for one slice [1-3]. Alternatively it has been proposed by Vidarsson *et al.* [4] to use a linear combination (LC) filtering method for short T_2 selective myelin-water imaging that only takes 5 minutes for 6 slices. Other methods, such as magnetization transfer (MT) and diffusion tensor imaging (DTI), have been used to characterize myelin content, with full brain coverage in under 5 minutes [5,6]. In this study, correlations between MWF using LC filtering T_2, magnetization transfer ratio (MTR) and DTI parameters such as fractional anisotropy (FA), mean diffusivity (MD), $\lambda_\perp$ (mean of the two smaller eigenvalues), $\lambda_{//}$) in healthy controls were measured.

Methods: Healthy volunteers (N=3) with a mean age of years 26.7 ± 1.5 years were studied using a 1.5T (GE Signa, GE Medical Systems, Milwaukee, WI). All MR studies were acquired with the same image geometry: FOV=240mm, slices=24, matrix=128x128, thickness=5mm. Images were acquired using a single-shot EPI DTI (25 directions; b=1000; 1 NEX; scan time≅4min) [7], 3D MT acquisition (with a 1600 Hz off-resonance sinc saturation pulse; TR/TE/α = 27ms/4ms/12; scan time≅5min), and a 3-echo LC filtered T_2 sequence (TR/TE = (698/8 723/33 800/110); α =90; scan time≅14min). The 3-echo LC filtered T_2 sequence was based on Vidarsson *et al.* [4], however we changed the acquisition from slices/gap = 6 /5 to 24 interleaved/0 which has given similar results [8]. Regions of interest (ROIs) were drawn on T_2-weighted images for minor forceps (MF), splenium (S), genu (G), internal capsules (IC), post central gyrus (PCG) and grey matter (GM) and transferred to all three imaging methods. FA, MD, $\lambda_\perp$, $\lambda_{//}$ were calculated for each region from DTI images. Magnetization transfer ratio (MTR) was calculated using MTR = $(1-M_s/M_o)x100\%$, where M_s and M_o are images with and without saturation pulse, respectively. MWF was calculated from the linear combination of the 3-echo T_2 sequence [4].

Results: Correlation coefficients between the various methods can be seen in Table 1 with and without GM ROI inclusion. The most significant correlations measured was FA vs MWF, $\lambda_\perp$ vs MWF, and MD vs MWF. Three example correlations are shown in Figure 1.

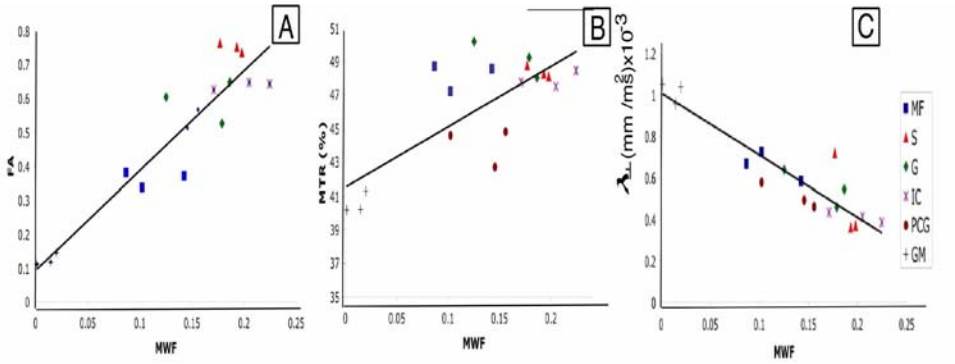

Figure 1: Correlations between (a) FA and MWF (b) MTR and MWF (c) $\lambda_\perp$ and MWF. In order of the legend ROIs MF (blue square), S (red triangle), G (green diamond), IC (purple x), PCG (brown circle) and GM (cross).

Table 1: Correlation coefficients (R^2) between different MR measurements

Correlations	(R^2) without GM	(R^2) with GM
MTR vs MWF	0.03	0.57
FA vs MWF	0.59	0.86
MD vs MWF	0.36	0.60
$\lambda_\perp$ vs MWF	0.54	0.85
$\lambda_{//}$ vs MWF	0.03	0.05

Discussion/Conclusion: The MWF measured in this study was consistent with literature values of 10-16% using the LC filtering method [5] or quantitative T_2 (qT_2) method acquired using CPMG [1-3,9]. It has been demonstrated that both MWF and MTR characterize myelin content, however the correlation between the two methods have been demonstrated to be very weak [8, 10] or absent [11,12] within normal appearing WM as confirmed in this study. However, it has been shown that MTR is sensitive to structural changes (i.e. changes in extra-cellular water content) seen in WM diseases [11,13]. This is demonstrated by a significant correlation of MTR vs MWF when a GM ROI is included. The water-fraction of GM gives a longer T_2 component as in pathological cases [14]. This study showed a high correlation between MWF and diffusion parameters. This demonstrates, that for healthy volunteers, FA and $\lambda_\perp$ measurements characterize myelin content ($\lambda_\perp$ is characterized by diffusion along the myelin direction). However, in pathological cases the correlation between FA and myelin water content appears to breakdown [15]. This could be due to the different proton pools each method probes. Where as diffusion probes the intra/extra-cellular water pools, MWF probes the proton pools of myelin-water and tissue water. Also, it has been shown that qT_2 can characterize differences in WM hyperintensities between different pathologies [16]. While, this has not been demonstrated with MWF measurements with LC filtering method it can be assumed that this result should also be seen. This whole brain technique can be used in future work to distinguish MF hyperintensities in diseased populations in a reasonable scan time.

References: **[1]**Mackay *et al.* (1994) MRM. 31:673**[2]**Jones *et al.* (2004). MRM 51:495**[3]**Henkelman *et al.* (1994) MRM. 32:592**[4]**Vidarsson *et al.* (2005) 53:398**[5]**Dousset Am J Neuroradiol (1995) 16: 225**[6]**Mädler B (2002) Proc ISMRM: 1188**[7]**Reese *et al.* (2003). *MRM.* 49: 177**[8]**Morris *et al.* (2007) ISMRM submission.**[9]**Whittall *et al* (1997) MRM. 37:34 **[10]**Vavasour *et al* (2006) Proc International Workshop on Myelin Imaging: 78**[11]**Gareau (2000) JMRI, 11:586 **[12]**Mackay *et al.* (2006) MRI 24:515**[13]** Laule *et al.* (2003). J Neurol. 250:924**[14]**Vavasour *et al.* (2000) MRM. 44:860**[15]**Kolind *et al.* (2006) Proc International Workshop on Myelin Imaging: 75**[16]**Oakden et al. (2006) Proc International Workshop on Myelin Imaging: 76