Simultaneous measurement of total water content and myelin water fraction at 3T: validation in phantoms and results from in vivo human brain

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INTRODUCTION:

Myelin water imaging based on multi-component T_2 relaxation is valuable for investigating neurological diseases such as multiple sclerosis, schizophrenia and phenylketonuria[1]. The myelin water fraction (MWF), defined as the ratio of the myelin water signal (15ms<T_2<40ms) to the total water signal[2], correlates strongly with histological staining for myelin[3]. However, it is also affected by changes in the total water content (TWC), which can occur with edema or inflammation. In order to isolate changes in MWF due to myelin alone, it is therefore also necessary to measure TWC. Simultaneous measurement of MWF and TWC could be a very valuable tool when studying brain disease, as one could more effectively observe and differentiate between processes such as edema, inflammation, demyelination, remyelination, resolution of inflammation, etc. **Here we present a T_2 relaxation based technique in which MWF and TWC are measured simultaneously at 3T.**

METHODS:

MRI Experiment: The method was first validated by scanning a phantom consisting of 9 tubes with known mixtures of H_2O/D_2O (with TWC ranging from 60-100%). A Philips Achieva 3.0T MR scanner with an 8 channel phased-array head coil was used for reception and the internal quadrature bird-cage body coil for transmission. The MRI protocol consisted of a 32 echo 3D GRASE sequence[4] (TR=1s, 10ms echo spacing, acquired voxel size=1x1x5mm, 40 reconstructed slices at 2.5mm thickness, 232x192 matrix, SENSE=2) and an inversion recovery (IR) prepared MPRAGE to measure T_1 (5 TIs (150 -3500ms), TR/TE=6.5/3.2ms, TFE=120, shot interval=5s, FA = 10°, 13 slices)[5]. Total imaging time was 22 minutes. The phantom was measured twice, rotated by 180° in between in order to see the effects of position on TWC measurements. 5 healthy volunteers (4F/1M, mean age 27y, range 21-35y) were scanned with the same protocol.

Post-Processing and Analysis: IR and GRASE data were registered using FSL's FLIRT tool[6]. Voxel-wise T2 distributions were calculated using a modified Extended Phase Graph algorithm combined with regularized non-negative least squares[7] and flip angle optimization[8] (effectively a B_1^+ correction). Signal amplitudes were T_1 corrected by dividing by $(1-\exp(-TR_{eff}/T_1))$, where TR_{eff} is the time from the last echo to the next excitation (680ms); the CSF portion of the T_2 distribution was corrected for T_1 relaxation using a T_1 of 4s, while the rest of the distribution was corrected using the T_1 obtained from the IR experiment, which was fit with a single exponential. TWC was calculated from the sum of signal amplitudes in the T_2 distribution, normalized to the mean proton density of CSF located within the ventricles, using the method outlined by Whittall and MacKay[9], which includes a correction for CSF contribution. MWF was calculated as the ratio of signal in the short T_2 peak to the total signal[2]. FSL's FAST tool was used to create white matter (WM) and grey matter (GM) masks from the IR.

RESULTS:

Phantom: MR measurements of TWC correlated strongly with actual TWC in phantom (Fig. 1), although MR TWC was generally high, with discrepancies from expected values ranging from -0.6 to 3.9% (mean discrepancy=1.7%). The small error bars indicate that position had little effect on TWC accuracy.

In vivo: Example TWC and MWF maps for one subject are displayed in Fig. 2, and WM and GM means for TWC and MWF in Table 1.

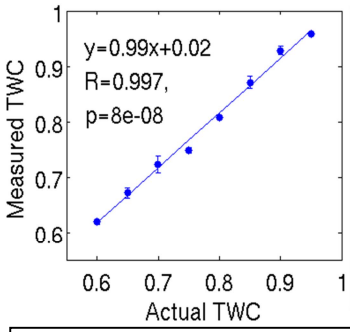

Figure 1. TWC measured in phantom tubes relative to actual values. Error bars indicate standard error over the 2 scans.

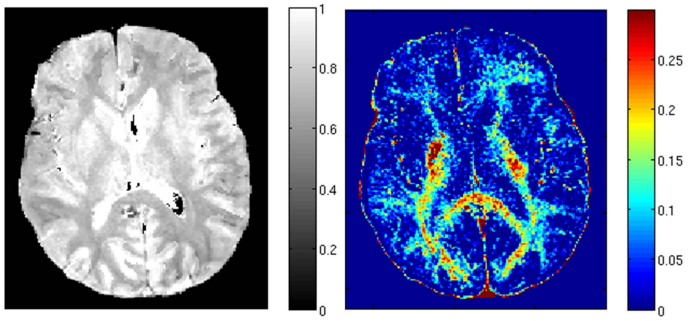

Figure 2. Water content map (left) and myelin water fraction map (right) for one subject. Holes in water content map in CSF are due to CSF correction[9].

DISCUSSION:

Phantom validation revealed excellent agreement between MR-measured and actual water content. TWC WM and GM means (0.70 and 0.82, respectively) were in close agreement to literature (on average 0.71 in WM and 0.82 in GM)[9,10], as were MWF values[6]. TWCs in internal GM were slightly high, which could be the result of imperfect B_1 homogeneity correction or the CSF correction. Further correction of the effects of B_1 inhomogeneity is currently being explored.

Table 1. WM and GM means for TWC and MWF, with standard error over subjects in brackets.

	WM	GM
TWC	0.702 (0.003)	0.821 (0.004)
MWF	0.121 (0.004)	0.042 (0.002)

CONCLUSION:

Simultaneous measurement of TWC and MWF with T_2 relaxation imaging is feasible, as shown by excellent consistency and accuracy in phantom results and *in vivo* values consistent with literature. This approach could provide valuable pathological insight.

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