Quantitative *in-vivo* brain water contents measurements at 3.0T

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Introduction: Many neurological diseases are accompanied by global or focal increases in water content. While several MRI techniques have been shown to measure water content quantitatively [1,2,3], additional challenges (such as increased B_1 inhomogeneity) arise at higher field strength. In addition, it is desirable to have a technique which also provides information about the environment in which the water resides. From T_2 decay curves obtained using a multi-echo imaging sequence, the relative contributions from water in different compartments can be resolved. In white matter, the shortest T_2 component is attributed to water trapped between the myelin bilayers and an intermediate T_2 component arises from intra/extracellular water. In certain neurological diseases, longer T_2 components are sometimes detected. However, despite these very promising results, this technique is not in common usage due to limitations of the multi-compartmental T_2 relaxation experiment, particularly the long measurement time and restriction to single slice acquisition. Recently, Mädler et al [4] developed an exciting new technique enabling the acquisition of multi-echo T_2 relaxation data over a large volume of the brain in clinically feasible times. The goal of this study was to use this new multi-echo T_2 relaxation sequence, capable of resolving individual water compartments (including myelin water), to derive a precise measure of absolute water content *in-vivo* at 3.0T.

Methods:

MRI Experiments: MRI measurements were performed on five healthy volunteers (1 male, 4 females; mean age 44.2 years; range 21-59 years) using a six-element phased array coil on a Philips Achieva 3.0T system. One of the five volunteers was scanned on two separate days. Two $MnCl_2$-doped water reference phantoms (one with T_1=650ms and T_2=92ms, the other with T_1=1700ms and T_2=110ms) were placed within the volume of interest.

T_2 relaxation: 3D 32 echo turbo spin echo modified Carr-Purcell-Meiboom-Gill sequence for T_2 relaxation measurement: 256x128 matrix, echo spacing=10ms, TR=1200ms, 7 slices, FOV=240x205mm [4].

T_1 relaxation: Inversion recovery 3D fast gradient echo for T_1 relaxation measurement: 256x256 matrix, TE=2.6ms, TR=3000ms, 5 inversion times (150ms, 400ms, 750ms, 1500ms and 3500ms), 11 slices, FOV=240x205mm [5].

B_1 mapping: Two spin echo segmented EPI acquisitions with nominal excitation/refocusing flip angles of 60˚/120˚ and 120˚/240˚, 128x96 matrix, TE=31ms, TR=2500ms, 7 slices, FOV=240x240mm [6].

Data Analysis: Regions of interest (ROIs) were drawn around five grey matter (GM) and five white matter (WM) structures, as well as around the water references. The T_1 was calculated from the inversion recovery experiment using $M_z(t)=M_0(1-f*\exp(-t/T_1))$. T_1 distributions were estimated for a range of values of f; that which yielded the minimum χ^2 was selected as optimal. Water content (WC) for each tissue ROI was calculated as follows:

(1) The average proton density for each ROI was found by integrating the T_2 distribution obtained using a regularized non-negative least squares method with 120 input relaxation times spaced logarithmically from 15ms to 2s [7]. Both χ^2 and solution roughness were minimized such that χ^2 fell between 1.02 and 1.025 times the minimum χ^2 from the non-regularized least-squares solution. (2) The density was then corrected for B_1 inhomogeneity using the method of Wang et al [6].

(3) Because the results were collected at a finite TR of 1200ms, a correction was required to account for the different T_1 times of water in each ROI, as well as in the reference phantoms. The correction for T_1 losses is given by $PD_0=PD_{B1}/(1-\exp(-TR_{eff}/T_1))$ where PD_{B1} is the B_1 corrected proton density, PD_0 is the integral of the T_2 distribution with no T_1 weighting, and TR_{eff} is the effective TR equal to the time from the last refocusing pulse to the next excitation, in this case 1200ms-320ms = 880ms. (4) Next, the spin densities of the two water reference phantoms were temperature corrected to 37ºC and averaged (PD_{WR}) [8]. (5) Finally, water content was defined as $WC_{ROI}= PD_0/PD_{WR}$.

Results and Discussion: Figure 1 illustrates a WC map for one volunteer. Table 1 shows the average WC for each ROI across the 5 volunteers along with values obtained using a similar method at 1.5T[1]. Compared to the literature values, WC values in WM were systematically lower and in GM were generally higher, resulting in a larger ratio between WM and GM WC than expected. However, values for each ROI were within 5% of literature values. Rescanning the same volunteer on two separate days resulted in WC values for each ROI that were within 3% between scans. WM and GM averages were within 1% between scans.

The discrepancy between values obtained here and literature values may be due to the large T_1 dependence of the T_2 relaxation sequence, since a small misfit in T_1 results in a large change in calculated WC. In order to verify this, one volunteer was scanned with a TR of 3000ms, with all other parameters remaining the same. The resulting WC values were all within 2% of the literature values, and the ratio between white and grey matter contents was within 2%. Unfortunately the resulting scan time for such a long TR is not practical, but future work will include developing methods for reducing scan time as well as improving the accuracy of T_1 mapping.

Conclusion: Obtaining absolute water contents at 3.0T using a spin echo sequence is feasible, with the benefit of providing information about the water environments.

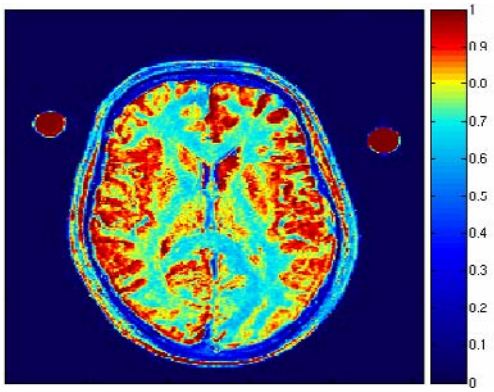

Figure 1: Water Content map for one volunteer.

Structure	Water Content (g/ml) 3.0T	Water Content (g/ml) 1.5T [1]
Minor Forceps	0.662 (0.011)	0.702 (0.007)
Major Forceps	0.658 (0.012)	0.698 (0.007)
Genu	0.668 (0.015)	0.715 (0.009)
Splenium	0.666 (0.008)	0.717 (0.010)
Internal Capsules	0.686 (0.012)	0.708 (0.009)
Putamen	0.850 (0.015)	0.831 (0.009)
Thalamus	0.794 (0.011)	0.798 (0.010)
Caudate nucleus, head	0.877 (0.018)	0.874 (0.010)
Cingulate Gyrus	0.883 (0.021)	0.849 (0.008)
Insular cortex	0.894 (0.037)	0.846 (0.009)
Average, white matter	0.668	0.708
Average, grey matter	0.860	0.840

Table 1: Water content (standard deviation) for 5 white and 5 grey matter structures averaged over 5 volunteers, compared to results from a previous study [1].

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