Faster myelin imaging in vivo; validation of 3D multi-echo T_2-relaxation measurements

S. H. Kolind[1], B. Mädler[2], and A. L. MacKay[1,3]

[1]Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada, [2]Philips Medical Systems, Vancouver, BC, Canada, [3]Radiology, University of British Columbia, Vancouver, BC, Canada

Introduction: Development of sensitive, clinically relevant biomarkers for diagnosis, prognosis and treatment monitoring of neurological disease is a significant challenge in MRI research. A technique that yields several quantities that have been shown to be sensitive to changes in human brain is multi-echo T_2 relaxation, which allows different reservoirs to be resolved based on T_2 relaxation times. In normal human white matter, the shortest T_2 component (~20ms) is attributed to water trapped between the myelin bilayers and an intermediate T_2 component (~80ms) is thought to arise from intra/extracellular (IE) water [1, 2]. The ratio of the short T_2 signal to the total signal in the T_2 distribution gives the myelin water fraction (MWF), which has been shown to be very highly correlated with histological measures of myelin in formalin-fixed human brain [3, 4]. Increases in the geometric mean T_2 (GMT_2, analogous to the amplitude-weighted mean on a logarithmic scale) as well as broadening of the IE peak are believed to indicate inflammation [5, 6]. Unfortunately, the most commonly used technique for acquiring multi-echo T_2 relaxation data, which consists of a single slice multi-echo pulse sequence utilizing large gradient crushers and composite radiofrequency pulses [7], is difficult to implement and has a very long acquisition time (on the order of 25min per slice). A rapid 3D multi-echo T_2 relaxation sequence was recently introduced by Mädler et al [8], which is capable of acquiring 7 slices in less than the time required to scan one slice using the 2D pulse sequence and is less problematic to implement. While other multi-slice or 3D multi-echo T_2 techniques have been proposed [9, 10], to our knowledge none have been quantitatively compared to standard 2D multi-echo T_2 results. The goal of this study was to validate the new 3D multi-echo T_2 relaxation imaging technique against the 2D technique which is the current standard.

Methods: *MRI Experiments:* MRI measurements were performed on 10 healthy volunteers (mean age: 33 years; range: 21-59 years) on a Philips Achieva 3.0T system. The 2D multi-echo T_2 relaxation measurements were acquired for a single transverse slice through the base of the genu and splenium of the corpus callosum (32 echoes, BW=±32kHz, TR=3000ms, 4 NSA, scan duration=25.6min)[1]. The 2D sequence used a slice–selective 90° pulse, composite (90_x-180_y-90_x) hard-refocusing pulses and a series of slice–select crusher gradient pulses of alternating sign with descending amplitude flanking the refocusing pulse to eliminate contributions from stimulated echoes[1, 7]. The 3D T_2 relaxation sequence had the centre slice aligned with the 2D T_2 measurement (7 slices, 32 echoes, BW=±42kHz, TR=1200ms, 1 NSA, scan duration=19.8min)[8]. Differences between the 3D and 2D measurements included the replacement of the initial slice-selective 90° pulse with a 90°slab-selective pulse, and replacing the composite rectangular refocusing pulses by slice-selective pulses. The following parameters applied to both scans: slice thickness=5cm, FOV=22cm, 256x128 matrix, 10ms echo spacing. Six of the subjects had both the 2D and 3D scans in the same session, while 4 of them had the two scans on separate days. In all cases, the 3D T_2 data set was registered to the 2D T_2 data using in-house registration software based on the maximization of mutual information.

Data Analysis: T_2 decay curves were analyzed with a regularized non-negative least squares (NNLS) method using 120 input relaxation times spaced logarithmically from 15ms to 2s [11]. 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. The peak assigned to myelin water was defined as having $15ms<T_2<40ms$, and the intra/extracellular (IE) water peak was defined as having $40ms<T_2<200ms$. Maps of MWF, GMT_2 for the IE peak, and SNR_{NNLS} (the signal-to-noise ratio for the NNLS fit, defined as the theoretical amplitude at TE=0ms divided by the standard deviation of the residuals of the fit) were created by calculating values for each pixel in the image. Averages of each metric were taken within 22 regions of interest (ROIs) in white and gray matter (WM and GM). Linear regression and Pearson correlations were calculated using all of the ROI results, and a two-tailed paired Student's t-test was used to compare results for each brain structure between the two methods. Statistical significance was taken as $p \leq 0.05$.

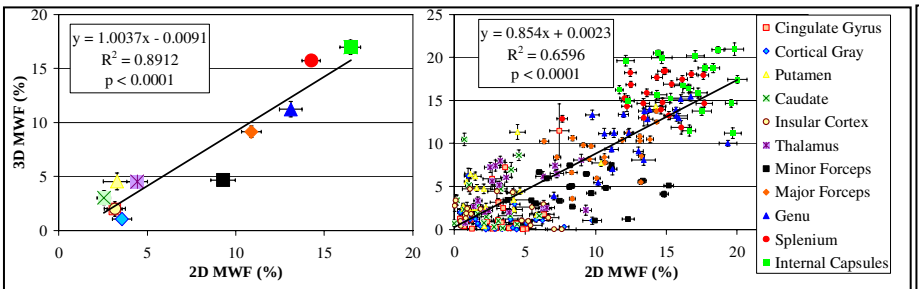

Fig 1. Correlation between 3D and 2D MWF measurements using (left) mean MWF for all 10 volunteers for each brain structure and (right) all ROIs for each subject. Error bars indicate standard error (s.e.).

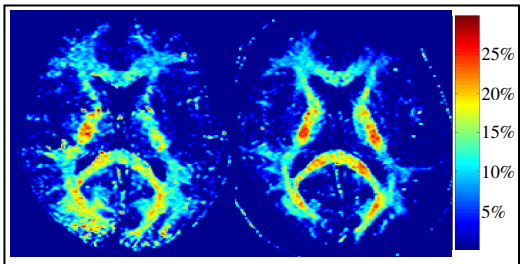

Fig 2. MWF maps for (left) 2D and (right) 3D T_2 decay data. They are qualitatively in good agreement, except for signal loss in the outer brain regions for the 3D technique.

Results: Plots of the correlation between MWF using 2D and 3D multi-echo T_2 relaxation for the average values in each brain structure and for all ROIs (22 per subject) are shown in Fig 1. Table 1 gives the average values of MWF, GMT_2 and SNR_{NNLS} for each brain structure examined, with structures that showed significant differences between the 2D and 3D techniques indicated in bold. Fig 2 depicts a MWF map for one volunteer using both 2D and 3D techniques.

Discussion: The relationship between MWF using the 2D and 3D techniques was linear and highly significant with a slope close to unity and intercept near zero (Fig 1). The brain structure that deviated most from the relationship was the minor forceps, which is also apparent in Fig 2; most of the brain appears the same on both maps except in peripheral brain regions (particularly frontal WM) where signal drop-out using the 3D technique caused lower MWF values compared to the 2D technique. The other structures that showed significant difference in MWF (major forceps and cortical gray) were also outer brain structures. Differences are likely due to the different refocusing pulses. GMT_2 was consistent between the two techniques (only minor forceps showed a significant difference), and the SNR_{NNLS} was better for the 3D technique in 64% of all 220 ROIs, though only significantly so for 3 brain structures (no structures were significantly higher for the 2D technique).

	MWF (%)		GMT_2 (ms)		SNR_{NNLS}	
	2D	3D	2D	3D	2D	3D
Cingulate Gyrus	3.2 (0.4)	2.0 (0.7)	88 (02)	84 (02)	292 (19)	277 (21)
Cortical Gray	**3.6 (0.5)**	**1.0 (0.3)**	86 (03)	85 (02)	258 (16)	221 (13)
Putamen	3.3 (0.8)	4.5 (0.8)	72 (03)	74 (02)	**216 (16)**	**301 (16)**
Caudate	2.5 (0.4)	3.0 (0.6)	74 (01)	73 (01)	229 (16)	254 (19)
Insular Cortex	3.2 (0.6)	2.0 (0.3)	94 (03)	89 (02)	**192 (16)**	**270 (16)**
Thalamus	4.4 (0.6)	4.5 (0.5)	77 (01)	76 (02)	261 (12)	251 (11)
Minor Forceps	**9.3 (0.7)**	**4.7 (0.4)**	**87 (02)**	**78 (01)**	298 (15)	319 (25)
Major Forceps	**10.9 (0.6)**	**9.1 (0.5)**	102 (02)	97 (02)	302 (15)	322 (14)
Genu	13.1 (0.6)	11.2 (0.7)	95 (02)	94 (02)	**301 (14)**	**366 (17)**
Splenium	14.3 (0.5)	15.7 (0.5)	116 (02)	117 (02)	278 (14)	264 (12)
Internal Capsules	16.5 (0.6)	17.0 (0.7)	133 (02)	130 (03)	254 (13)	278 (17)

Table 1. MWF, GMT_2 and SNR_{NNLS} (s.e.) for both 2D and 3D T_2 relaxation imaging techniques. MWF was only significantly different in outer brain regions where signal drop-out occurred for the 3D technique. GMT_2 values were consistent for nearly all structures. SNR_{NNLS} was usually greater for 3D imaging.

Conclusion: Using 3D multi-echo T_2 relaxation allows for greatly improved brain coverage in clinically feasible times. SNR_{NNLS} was usually higher than for the standard 2D technique and GMT_2 and MWF were consistent with 2D results for nearly all brain structures examined.

References: [1] MacKay. MRM. 1994;31:673-7. [2] Whittall. MRM. 1997;37:34-43. [3] Laule. Mult Scler. 2006;12:747-53. [4] Moore. Neurology. 2000;55:1506-10. [5] Stanisz. MRM. 2004;51:473-9. [6] Stanisz. MRM. 1999;42:1128-36. [7] Poon. JMRI. 1992;2:541-53. [8] Mädler. Proc. ISMRM. 2006:2112. [9] Vidarsson. MRM. 2005;53:398-407. [10] Oh. MRI. 2006;24:33-43. [11] Whittall. JMR. 1989;84:64-71.

Acknowledgments: Volunteers, technologists, Eugene Yip, Irene Vavasour, Philips Medical Systems (particularly Stefan Fischer for assistance in developing pulse sequences), MS Society of Canada and Killam Trusts.