Brain Metabolites Proton T2 Mapping at 3 Tesla in Relapsing-Remitting Multiple Sclerosis

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INTRODUCTION: MRI-occult pathology in Multiple Sclerosis (MS) is detectable with proton MR spectroscopy (^{1}H-MRS), but unlike conventional (qualitative) MRI, ^{1}H-MRS needs to account for parameters that affect its quantitative assessment. At intermediate- and long-echo times (*TE*) the molecular environment factors require knowledge of the local transverse, T_2, relaxation time. To our knowledge, brain metabolites T_2s have not been thoroughly characterized in MS patients, forcing two implicit assumptions on ^{1}H-MRS: that the same global T_2s can be used (*i*) anywhere in the brain (*ii*) for all MS subjects. While recently substantiated in healthy individuals (1-2), these assumptions require validation in MS, given its well documented focal and diffuse pathology and different clinical course. Specifically, three scenarios can be envisioned (from best to worst): (*i*) regional inter- and intra-patient T_2s are indistinguishable from controls, incurring no bias; (*ii*) similar inter- and intra-patient T_2s differ significantly from controls', requiring one set of T_2 corrections; (*iii*) significant regional intra- and inter-patient variations, requiring individual regional T_2 correction. Our aim, therefore, was to obtain the T_2 distributions of *N*-acetylaspartate (NAA), choline (Cho) and creatine (Cr) at 3 T in the most common (85%) relapsing-remitting (RR) phenotype of MS and assess any bias incurred by differences in inter- and intra-patient T_2s. This was done using 1 cm^3 spatial resolution three-dimensional ^{1}H-MRS in a two-point protocol optimized for T_2-precision per unit time (3).

METHODS: Seven patients (42±13 years old, 3 women, 4 men) with clinically definite RR MS (mean disease duration 3 years, range 1-7) and mean EDSS of 3 (range 0.0-5.0) were scanned at 3 Tesla. MPRAGE and T_2-weighted FLAIR MRI guided a PRESS $10_{AP}\times8_{LR}\times4_{IS}$ cm^3 volume of interest (VOI) with *TR*=1.26 s. The two-point T_2 estimation paradigm (3) optimized the two *TE*s, and the number of averages (N_1 and N_2) to TE_1=35 ms (N=1) and TE_2= 260 ms (N=3). The VOI was encoded with Hadamard spectroscopic imaging into 4 (IS) slices, each partitioned with 16×16 CSI over a 16×16 cm^2 (AP×LR) FOV, yielding 320 voxels, each $1.0_{AP}\times1.0_{LR}\times 1.0_{IS}$ cm^3. Metabolite peak areas at the short (S_1) and long *TE* (S_2) were fitted (SITools software (4)) and T_2s estimated using $T_2 = (TE_2 - TE_1) / \ln (S_1 / S_2)$ in all 320 voxels in the VOI, within 10 manually transcribed gray matter (GM) and white matter (WM) structures, and within T_2-weighted MRI hyperintense lesions (Fig. 1). All T_2s were corrected for the T_1-weighting incurred by our use of the 1.26 s *TR*, assuming an average T_1 value of ~1.2 s for each of the three metabolites reported in the literature (5).

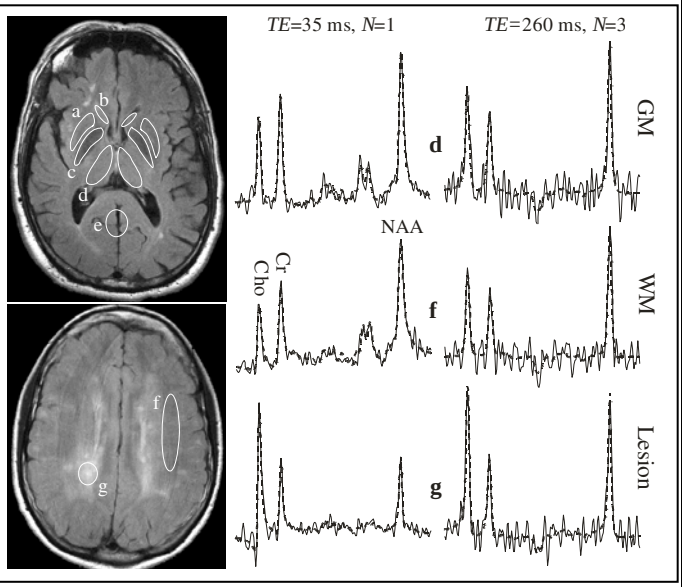

Figure 1: Left: Axial T_2-weighted FLAIR images showing the manually outlined ROIs in the putamen (a), caudate (b), globus pallidus (c), thalamus (d), posterior cingulate gyrus (e), centrum semiovale (f) and T_2-hyperintense lesion (g).
Right: GM, WM and lesion spectra from the ROIs at both *TE*s (solid lines), superimposed with their model functions (dashed lines) fit (4) for NAA, Cr and Cho. Note the excellent SNR and fit in both *TE*s.

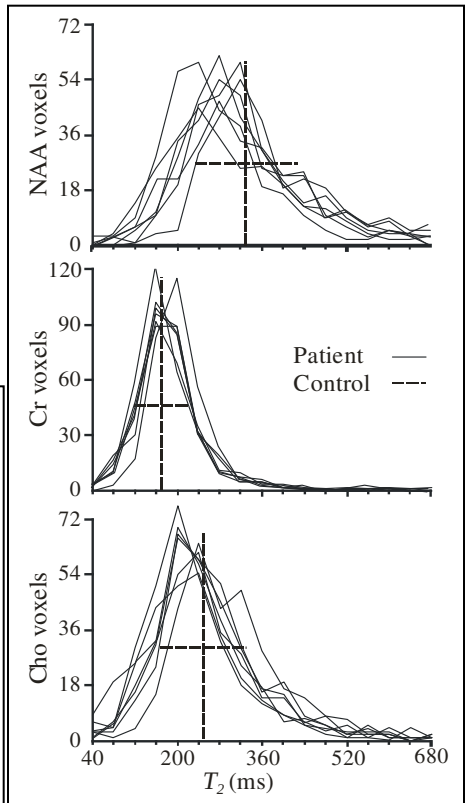

Figure 2: NAA, Cr and Cho T_2 histograms from all 320 voxels of each patient (solid lines) superimposed on the age-adjusted mean and full-width-at-half maximum of normal controls (dashed lines) from ref (1). Note the overlapping histograms, reflecting the inter- and intra-subject T_2-similarity among patients.

RESULTS: Histograms of T_2s from all voxels of each patient revealed inter- and intra-subject similarity similar to age-matched controls' (Fig. 2). The T_2s (average±standard error) in GM, WM and lesions were: NAA: 307±21, 354±16 and 358±72 ms; Cr: 174±2, 181±15 and 184±18 ms; and Cho: 252±19, 259±10 and 226±124 ms. Compared to average T_2s of controls, this amounted to differences of only 4% for NAA, and 3% for Cr and Cho.

CONCLUSION: Based on these results we can conjecture that for metabolic quantification in MS: (*i*) obtaining T_2 values for each patient is unnecessary; and (*ii*) for *TE*s under 100 ms a global average T_2 value per metabolite suffices, therefore, (*iii*) obtaining regional brain and lesion T_2s is also not needed.

REFERENCES: 1. Kirov *et al.* MRM 2008 2. Tsai *et al.* MRM 2007 3. Fleysher *et al.* MRM 2007 4. Soher *et al.* MRM 1998 5. Traber *et al.* J Magn Reson Imaging 2004