T2 Measurements of Childhood Brain Tumours and Metabolite Concentration Correction

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Introduction: Magnetic resonance spectroscopy metabolite profiles have been shown to provide non-invasive diagnostic and prognostic biomarkers that can be used for classification and treatment stratification in childhood brain tumours, with recent studies identifying taurine (Tau) and the glutamate-glutamine complex (Glx) as being particularly important. However, the metabolite concentrations measured using single-voxel MRS may vary with acquisition protocol. In vivo, metabolite concentrations can be measured using the water signal as an internal reference, though these concentration measurements are affected by metabolite and water T2 relaxation times which can vary significantly in brain tumours as they are sensitive to tumour microenvironment. In this study, T2 relaxation times are measured in childhood brain tumours and normal brain for water and a range of metabolites to identify their variability and assess their importance in accurate metabolite quantification.

Methods: Twenty-nine childhood brain tumour patients (17 gliomas, 12 medulloblastomas) and sixteen children with normal brains were scanned on a Siemens 1.5T system using a single-voxel PRESS sequence at short TE (30ms) and long TE (135ms) with a TR of 1500 ms, 128 averages and voxel size 8cm^3. In-vivo spectra were retrospectively analysed using TARQUIN[1] to obtain metabolite concentrations. T2 relaxation times were calculated by fitting signal amplitudes to a monoexponential function. All data included had a water linewidth <15 Hz. Metabolites with CRLB <50% were excluded from this study and consequently a total of 26 NAA (5 glioma, 5 medulloblastoma, 16 normal), 37 Cr (10 glioma, 11 medulloblastoma, 16 normal), 39 Cho (11 glioma, 12 medulloblastoma, 16 normal), 23 Tau (4 glioma, 6 medulloblastoma, 13 normal) and 38 Glx (13 glioma, 9 medulloblastoma and 16 normal) were included in the analysis. The mean T2 relaxation times for both metabolites and water were compared between groups using two-tailed Student's t-tests. Metabolite concentrations were subsequently corrected for differences in T2 relaxation using $f_{TE} = e^{-\frac{TE}{T2_{water}}} / e^{-\frac{TE}{T2_{metabolite}}}$ Metabolite concentrations were corrected using the metabolite and water T2 relaxation times calculated for individual patients. These concentrations were then compared to concentrations corrected using various combinations of measured and literature T2 values to assess the importance of accurate T2 relaxation times (see Table 1 legend).

Results

	Medulloblastomas				Gliomas				Normal Brain			
	LM, LW	AM, AW	LM, IW	AM, IW	LM, LW	AM, AW	LM, IW	AM, IW	LM, LW	AM, AW	LM, IW	AM, IW
Short TE Singlets	11.6	5.1	4.6	3.9	22.0	11.1	9.2	9.0	6.6	3.8	3.9	3.3
Short TE Multiplets	18.8	9.5	12.8	13.7	30.2	14.1	18.1	11.6	19.3	13.0	16.9	12.5
Long TE Singlets	40.8	22.6	18.2	34.0	62.1	39.5	31.6	31.3	25.3	16.0	15.7	14.0
Long TE Multiplets	55.3	36.9	42.4	36.8	75.5	43.9	51.0	40.6	55.9	43.2	50.3	42.8

Table 1: The mean percentage difference between concentrations corrected using different combinations of T2 relaxation times compared to the corrected concentration using the patient's measured T2 values. Metabolite T2 from literature[2] (LM), water T2 from literature (LW), average metabolite T2 (AM), average water T2 (AW), and patient's individually calculated water T2 (IW).

From table 1, the mean percentage difference is consistently smaller when using individually measured water T2 relaxation times for concentration correction. At short-TE, an average of 5.6% and 14.3% difference from the fully-corrected concentrations were found when the water T2 values are known for singlets and multiplets respectively, while at long-TE differences of 24% and 44% were found. T2 relaxation times in children's brain tumours and in healthy childhood brain and their standard deviation are presented in tables 2 and 3 respectively. The T2 relaxation of water was significantly longer in gliomas than in medulloblastomas ($p<0.05$) and healthy brain ($p<0.01$). The T2 relaxation of water in medulloblastomas was in turn also significantly prolonged compared to healthy brain ($p<0.05$). Choline was significantly longer in medulloblastomas compared with gliomas ($p<0.01$). A large range of T2 values was observed in gliomas for NAA (1196 ms) and Cr (1314 ms).

	T2 (ms)				
	Gliomas		Medulloblastomas		
	Mean	SD	Mean	SD	p
Water	159	43	117	38	0.010
NAA	511	610	333	204	0.564
Cr	530	655	251	78	0.212
Cho	294	102	504	202	0.006
Tau	190	134	286	146	0.319
Glx	364	71	152	88	0.692

Table 2: T2 relaxation times in childhood brain tumours and their standard deviation.

	T2 (ms)				
	Basal Ganglia		White Matter		
	Mean	SD	Mean	SD	p
Water	86	8	90	9	0.130
NAA	318	168	373	101	0.208
Cr	272	239	320	138	0.498
Cho	381	168	384	246	0.971
Tau	201	113	221	186	0.834
Glx	163	137	151	72	0.760

Table 3: T2 relaxation times in basal ganglia and parietal white matter and their standard deviation.

Discussion: T2 is highly dependent on tissue type and may reflect differences in microenvironment. The smaller mean percentage difference when using a patient's individually measured water T2 relaxation time suggests that accurate water relaxation times are required for metabolite quantification. This is further supporter by the significant differences in water T2 times between both tumour types and between tumour and normal brain. A greater deviation from the concentrations individually corrected for both water and metabolite T2 relaxation was observed at long-TE compared with short-TE, indicating that accurate metabolite T2 values may be more important at long echo times than at short. A greater difference was also observed for multiplets compared with singlets. The smaller variation for medulloblastomas compared to gliomas may reflect their more cellular nature and the smaller range of T2 values measured.

Conclusions: There are significant differences in the T2 relaxation time of water between both brain tumours and healthy brain and between different tumour types and allowing for these differences are important for accurate metabolite quantification. Accurate metabolite T2 relaxation times are more important for obtaining concentrations from long-TE than for short-TE MRS.

References: 1. Wilson M, Reynolds G, Kauppinen RA, et al. A constrained least-squares approach to the automated quantitation of in vivo ^{1}H magnetic resonance spectroscopy data. Magn. Reson. Med., 2011; 65(1): 1-12. **2.** Isobe T, Matsumura A, Anno I, et al. Quantification of cerebral metabolites in glioma patients with proton MR spectroscopy using T2 relaxation time correction. Magn. Reson. Imaging, 2002; 20: 343-349

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