Optimisation of quantitative Magnetisation Transfer (qMT) sequence acquisition parameters

R. S. Samson[1,2], M. R. Symms[1], M. Cercignani[2], D. J. Tozer[2], P. S. Tofts[2]

[1]Department of Clinical and Experimental Epilepsy, Institute of Neurology, London, United Kingdom, [2]Department of Neuroinflammation, Institute of Neurology, London, United Kingdom

INTRODUCTION:

We optimise quantitative Magnetisation Transfer (qMT) acquisition to minimise uncertainty of parameter estimates, using the Cramer-Rao Minimum Variance Bound (CRMVB) (1). Two parameters are of interest: $f/R_A(1-f)$, a measure of the fraction of protons that are bound to macromolecules, and T_{2B}, their T_2 value.

Figure 1: SD's from Monte Carlo simulations compared with theoretical CRMVB SD's: f/RA(1-f) white matter

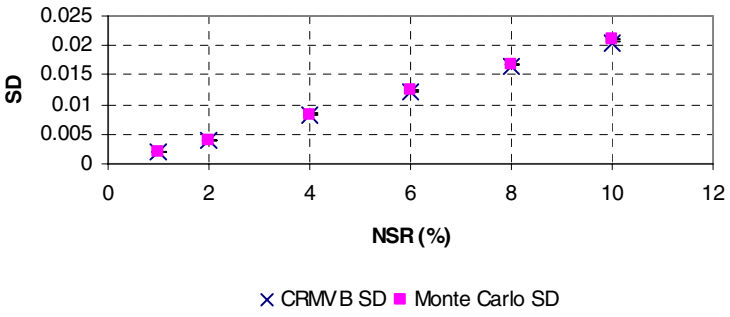

Table 1: qMT Acquisition Scheme Parameters		
Acquisition Scheme	**MT pulse Flip Angle (°)**	**Offset frequency (kHz)**
Existing scheme (2)	212	1.0, 2.5, 7.5
	434	1.0, 3.5, 15.0
	843	1.0, 2.5, 5.0, 7.5
Proposed Scheme 1	0	2.75, 2.80, 2.85, 2.90, 2.95
	900	2.75, 2.80, 2.85, 2.90, 2.95
Proposed Scheme 2	500	1.0, 1.25, 1.5, 12.5, 15.0
	900	1.5, 1.75, 2.0, 12.5, 15.0
Proposed Scheme 3	0	1.0, 2.0, 10.0
	500	1.0, 1.5, 2.0
	900	2.5, 7.5, 10.0, 12.5

METHODS:

Noise-free model signal data were generated using previously measured control white (WM) and grey matter (GM) parameter values and an existing data acquisition scheme (2). Random computer-generated Gaussian noise was superimposed, giving 10,000 synthetic data sets (Monte Carlo (MC) 'realisations'), which were fitted to yield 10,000 parameter sets. CRMVB SDs were calculated for the same parameters and Noise-to-Signal-Ratio (NSR) values, and compared with SDs from MC simulations.

The estimation of different combinations of qMT parameters ($f/R_A(1-f)$, T_{2B}, or both, with remaining parameters fixed) was investigated. Acquisition schemes were optimised, and CRMVB SDs were compared with those calculated for an existing scheme (2).

qMT data were acquired for three healthy volunteers using optimal acquisition parameters for estimation of each combination of parameters, and also using an existing scheme (2) for comparison. The qMT model was then fitted to all data sets using a Marquardt-Levenberg algorithm, implemented using Numerical Recipes (3) to obtain sets of parameter estimates. Coefficients of variation (CVs) were calculated in regions of interest (ROIs) in GM and WM and compared with theoretical values.

RESULTS:

Theoretical (CRMVB) and numerical simulation (MC) SDs agreed well (Figure 1). At higher NSR values, linear CRMVB theory slightly underestimates SDs.

Optimal sampling strategies for different combinations of estimated parameters are given in Table 1, and CRMVB CVs for WM and GM (for NSR=2.2%) are compared with those for an existing protocol in Table 2. This NSR value is the average measured NSR using uniform regions of WM and GM in an image with no signal attenuation due to MT (i.e. zero power, high offset frequency data point), and uniform ROIs in the absence of any signal (i.e. in air) for the noise SD measurement (4).

Table 2: Theoretical (CRMVB) and measured (using data from three control subjects) CVs for optimal sampling schemes are compared with those for an existing protocol (2)

Parameters to be estimated	Acquisition Scheme	Theoretical CV (%)				Measured CV (%)			
		White Matter		Grey Matter		White Matter		Grey Matter	
		f/RA(1-f)	T2B	f/RA(1-f)	T2B	f/RA(1-f)	T2B	f/RA(1-f)	T2B
f/RA(1-f)	**Proposed Scheme 1**	**4.8**	**-**	**5.1**	**-**	**5.7**	**-**	**5.5**	**-**
	Existing Scheme	6.8	-	7.3	-	7.2	-	8.1	-
T2B	**Proposed Scheme 2**	**-**	**6.2**	**-**	**6.8**	**-**	**8.9**	**-**	**7.5**
	Existing Scheme	-	12.3	-	13.5	-	11.7	-	13.7
f/RA(1-f), T2B	**Proposed Scheme 3**	**6.2**	**6.9**	**7.2**	**8.3**	**6.9**	**10.4**	**8.4**	**9.4**
	Existing Scheme	7.5	13.5	8.0	15.0	9.1	16.9	10.0	17.0

Measured CVs from regions of WM (frontal) and GM (cerebellar) were compared with theoretical (CRMVB) values (Table 2). These were found to be larger than those predicted theoretically, which may be a result of underestimating the NSR value used for simulations. Tissue heterogeneity was demonstrated not to be a limiting factor for the particular ROIs selected, by varying the ROI size and observing the change in SD. It was shown that experimentally measured CVs for parameters estimated using the new proposed schemes were reduced in comparison to those estimated using the existing scheme (2) for GM and WM regions, verifying theoretical calculations.

DISCUSSION AND CONCLUSIONS:

- Measured CVs are consistently higher than theoretical predictions, by ~1-35%, for yet unknown reasons (which may include underestimation of the NSR value for qMT images used in simulations (95% confidence limits for NSR measurements were large), large uncertainties in measurements of SDs in ROIs (due to the ROI size or small number of samples), and possibly by B_0 and B_1 field errors, which were not corrected for in this study).
- We have produced a set of optimal qMT data collection schemes which substantially reduce uncertainties in parameter estimates, and are applicable to a range of brain tissues.
- This increase in precision could alternatively be traded off to reduce qMT acquisition time, by acquiring less 'MT-weighted' data points.
- Scheme 1, using no power and a single high power, at a restricted range of frequencies, reduces the theoretical $f/R_A(1-f)$ CV by 29%. Experimental data shows a 21% reduction in the WM $f/R_A(1-f)$ CV, and a 32% reduction in the GM $f/R_A(1-f)$ CV.
- In scheme 2, using two powers to map the restricted proton line shape reduces the theoretical T_{2B} CV by 50%, however a smaller improvement was observed experimentally, with the GM T_{2B} CV reduced by 45%, but the WM T_{2B} CV only reduced by 23%.
- Scheme 3 was optimised for T_{2B} estimation, to observe small changes in normal-appearing WM, whilst retaining good performance for $f/R_A(1-f)$. This gave a theoretical improvement of 45% in T_{2B} CV and a 11% (GM) or 18% (WM) improvement in $f/R_A(1-f)$ CV. Experimentally, however, a 39% (WM) or 45% (GM) improvement on the precision of T_{2B}, and a 17% (GM) or 24% (WM) improvement on the precision of $f/R_A(1-f)$ estimation were observed.
- This approach could also be applied to the estimation of other quantitative MR parameters.

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