The effect of noise on quantitative MT imaging: 3D vs 2D acquisition

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Introduction: The objective of quantitative magnetization transfer (qMT) is the extraction of fundamental MT parameters that may be more specific for distinct pathological features than conventional MR techniques[1]. In general, qMT imaging requires the collection of a series of MT-weighted images and the estimation of a number of parameters by fitting a non-linear model to the measured signal. The first goal of this study was to investigate the sensitivity of MT parameters to background noise using synthetic data, and simulating the effects of different levels of noise on the fit. This analysis showed that a good signal-to-noise ratio (SNR) for the measured signal is essential in order to reliably estimate the parameters from a small number of samples, thus prompting the use of a sequence with high SNR per unit time. In principle, data acquisition can use any pulse sequence, but due to their short scan times and low contrast on unsaturated images, mainly 2D gradient echo sequences have been investigated to date, and these have both been validated in phantoms[2] and applied in vivo[1,3,4]. On the other hand, 3D imaging provides higher SNR per unit time, making it an interesting candidate for qMT acquisition[5]. The second aim of this work was, therefore, to validate a 3D acquisition for qMT in *ex vivo* brain tissue by comparing the estimated parameters with those obtained using a 2D acquisition.

Methods: This work is based on a modified version of the Henkelman model[4]. Simulations of the effect of noise were obtained by creating a synthetic data set starting from published MT parameters measured *ex-vivo*[6], and assuming a T1 of approximately 350 ms in fixed normal appearing white matter[7] (NAWM). By using two RF amplitudes and 5 offset frequencies (matching those used to acquire the 2D data, see below), we generated a noise-free synthetic set of 10 MT-weighted signal intensities. We then added complex noise with Gaussian real and imaginary parts (mean=0, SD=desired level of noise, corresponding to SNR ranging from 180 to 30). Noisy datasets were then obtained by taking the magnitude of this complex number. For each level of noise 1000 independent samples were generated, and the MT model was fitted to every synthetic dataset. A coronal post-mortem brain slice (thickness: 1cm) of one hemisphere of a patient with primary progressive multiple sclerosis was provided by the UK Multiple Sclerosis Tissue Bank, based at Charing Cross Hospital, Imperial College, London, UK. Age at death and disease duration were 44 and 18 years, respectively. The sample was fixed for 133 days in 10% Formalin solution. MRI was performed on a 1.5 T GE Signa system. The following scans were collected during a single session: a) a MT-prepared 3D spoiled gradient recalled echo (SPGR) sequence (TE/TR=5.3/30.7 ms, imaging flip angle=5º, matrix=256x192x32, FOV=240x180x160); b) a MT prepared 2D SPGR sequence (TE/TR=12/1040 ms, imaging flip angle=25º, matrix = 256x192, in plane FOV= 240x180, 28 5 mm thick slices). For both acquisitions, Gaussian MT pulses were used (duration=14.6 ms), whose flip angle and offset frequency (Δ) were varied. The RF power corresponding to each MT flip angle was estimated as the continuous wave power equivalent[4,8] (CWPE). The flip angles of the MT pulses were chosen to be similar in the two protocols, within the constraints of their different interval between subsequent pulses (although this match was not perfect due both to differences in the CPWE, and to the different handling of pulse scaling[8]). Pulse powers ranged between 190 and 845 rad/sec. Five values of Δ per flip angle, ranging from 0.4 to 20 kHz, homogeneously spaced on a logarithmic scale, were used for both 2D and 3D acquisitions. Protocol b) was repeated 3 times. A 17.6 mm^2 region of interest was placed in the NAWM. Five of the six independent parameters of the model (gM_0^A, $1/R_AT_2^A$ $f/R_A(1\text{-}f)$, RM_0^A and T_{2B}) were extracted by Levenberg-Marquardt non linear fitting[5] using the ROI signal measured from 1) the 3D data sets, 2) a single 2D data set, 3) the (magnitude) average of two 2D data sets and 4) the (magnitude) average of three 2D datasets. R_B was kept fixed, and set equal to 1 sec^{-1} [2,4].

Results: Fig 1 shows the results of simulations for RM_0^A, $f/R_A(1\text{-}f)$, T_{2B}, and $1/R_AT_2^A$. $1/R_AT_2^A$ is the most robust parameter, with average deviations from its asymptotic value < 2%. The other parameters appear biased towards higher values at lower SNR (<50). In particular, RM_0^A tends to vary widely. The SNR of experimental *ex vivo* data was measured according to (9) on the images with less saturation giving, respectively, SNR2D≈43 and SNR3D≈71. Although the relative SNR of the remaining images differed between protocols[7], for simplicity this number has been used as index of SNR for each of them. The values of RM_0^A, $f/R_A(1\text{-}f)$,$1/R_AT_2^A$ and T_{2B} obtained by fitting the model to the 4 datasets are shown in Fig 2 (gM_0^A depends on an arbitrary multiplicative gain factor and therefore was not compared). Consistent with what was observed experimentally, RM_0^A appears to be the most sensitive to background noise. All estimates obtained from 2D datasets approach the values obtained from the 3D datasets when increasing the number of averages and thus the SNR.

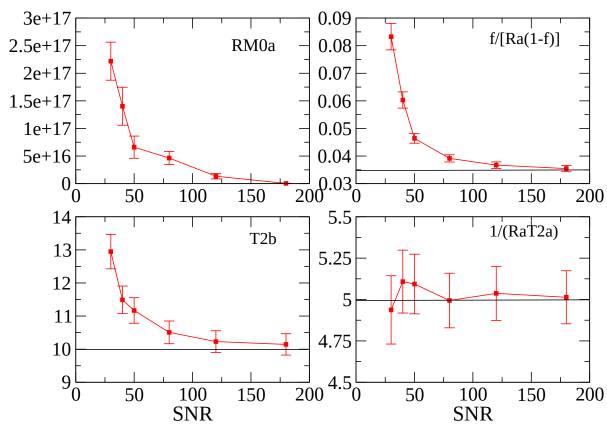

Fig 1. Mean estimated MT parameters from synthetic data at different SNR levels. Error bars represent the standard error over 1000 randomizations. The black line represents the value used to generate the noise-free dataset.

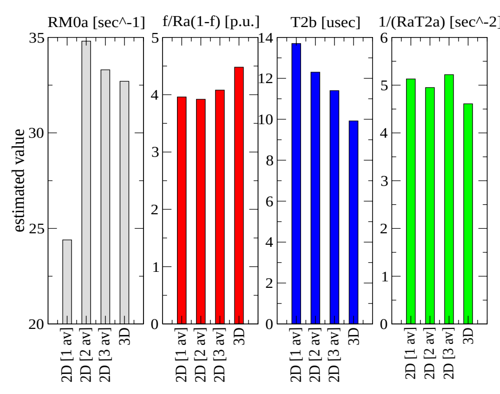

Fig 2. MT parameters resulting from fitting the model to a 2D dataset, the average of two 2D datasets, the average of three 2D datasets, and a 3D dataset in a ROI positioned in the NAWM. See text for details.

Discussion: To our knowledge, this is the first attempt to characterize the effects of background noise on qMT parameters. The results of simulations suggest that both f and T_{2B} could be overestimated at low SNR. Nevertheless, over the range of SNR normally available for clinical MT-weighted scans their variance is within acceptable limits. The analysis of experimental data showed that 2D and 3D acquisitions for qMT produce consistent results in terms of estimated MT parameters, particularly when several 2D datasets are averaged to reach a SNR comparable to the 3D data. The residual difference can be explained by the different amount of partial volume effect due to different slice profiles in the two cases, and by slightly different values of CWPE in the two protocols. Both experimental data and simulations demonstrated that RM_0^A is the least robust parameter, which is to be expected as the measured signal is quite insensitive to variation in RM_0^A. Unexpectedly, while the simulations predict an increase in $f/R_A(1\text{-}f)$ at lower SNR, our experimental data seem to follow an opposite trend.

References

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