A comparison between quantitative models of pulsed-MT

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Introduction

As continuous wave (CW) saturation is impractical for *in vivo* imaging experiments, MT-weighted MRI is generally obtained using pulsed MT acquisition, for which Henkelman's model [1] must be modified to include saturation pulses of short duration [2]. A number of simplified models for pulsed MT have been developed [2-5], and this paper is concerned with the comparison between two of them. In Ramani's model [3], the effect of the excitation pulses is neglected and the MT pulse is replaced by CW irradiation with the same mean square amplitude, thus making the implicit assumption that the relative signal intensity in data obtained with different MT-weightings only depends on the characteristics on the MT pulse (i.e. that T_1 and T_2 relaxations equally affect all measurements), and therefore it is appropriate to describe the MT weighted signal only when the amount of T_1-weighting in the acquisition sequence is minimal. Sled and Pike propose an alternative equation [4] which can be fitted directly to the measured signal, and has the advantage of incorporating the effect of the excitation RF pulses and therefore to make it possible to account for T_1-weighting. This model, however, requires the numerical evaluation of ordinary differential equations at least for the estimation of the effect of the MT pulse on the free pool, and is therefore computationally more intensive. Here we investigate the effects of T_1-weighting and noise on the MT parameters fitted by either model using numerical simulations.

Methods

The magnetization of the liquid (A) and macromolecular (B) pools can be described by their longitudinal (M_z^A, M_z^B) and transverse (M_x^A, M_y^A, M_x^B, M_y^B) components, and the signal behaviour can be predicted as a function of the acquisition parameters by solving the coupled Bloch Equations for the system [1,2]. We consider here the case of an MT-weighted spoiled gradient echo acquisition, where off-resonance saturation is achieved using 15 ms long Gaussian pulses applied once every TR prior to RF excitation, while on resonance excitation is obtained using short sinc pulses. In order to investigate the effects of T_1-weighting on the estimated parameters we simulate the outcome of 6 MT experiments using 6 regularly spaced excitation flip angles ranging from 5° to 20° and *TR*=30 ms, and fit either model to the simulated data. The set of MT parameters (R_A, F, T_2^A, T_2^B, and RM_0^B, where R is the exchange rate, and $F = M_0^B/M_0^A$, with M_0^A and M_0^B being the fully relaxed values of longitudinal magnetization for the two pools) used to generate the synthetic data is based on values measured in white matter [6,7], and is shown in Table 1. We fix $R_B = 1\text{s}^{-1}$ [1]. Each simulated set consists of 60 points, generated using the Bloch Equations with two MT equivalent flip angles (250° and 850°) and 30 values of offset frequency (Δ) per flip angle. Δ ranges from 400 to 30000 Hz, sampled at regular interval on a logarithmic scale. The simulated signal is computed by using a Runge-Kutta ordinary differential equation integrator. Ramani's and Sled&Pike's models are fitted to the six synthetic datasets using the Levenberg–Marquardt method, using the true values as starting points. In order to investigate the sensitivity to noise, we add complex noise with zero-mean Gaussian real and imaginary parts to the dataset obtained for θ=5°, varying the SNR level over [50, 300]. For each level of noise, we generate 10000 sets of noisy independent samples and fit both models to each set.

Results

Results of noise-free 5°-excitation simulations are shown in Table 1. As the flip angle increases, the estimates of all parameters obtained based on Ramani's model (with the exception of T_2^B) increasingly deviate from the original value. The estimates obtained using Sled and Pike's model are more stable, with the exception of T_2^A. RM_0^B increases slightly, with no corresponding change in *F*. The magnitude of the error is nevertheless small compared to Ramani's model for large excitation flip angles. The estimates of *F* against flip angle are shown in Fig 1A as an example. Fig 1B compares the estimates of *F* as a function of SNR using 5° excitation. For all four parameters (*F*, RM_0^B, T_2^A, and T_2^B), the estimates obtained from the noisy dataset using Ramani's model are more precise (although not necessarily more accurate) than those obtained with Sled and Pike's model, with standard deviations smaller by a factor of at least 2/3 (for T_2^B), and up to 1/10 (for RM_0^B), particularly at low SNR (≤100).

	RM_0^B [s^{-1}]	**F**	**T_2^B [μs]**	**T_2^A [ms]**	**R_A [s^{-1}]**
ORIGINAL	3.1	0.107	10.0	66.0	1.45
RAMANI	2.9	0.105	10.0	64.1	1.44
SLEd&PIKE	3.2	0.111	10.0	81.9	1.45

Table 1. *MT parameter values used to create synthetic data and results of noise-free simulation with excitation flip angle = 5°.*

Discussion

We have shown that 1) Ramani's and Sled and Pike's models yield consistent estimates of RM_0^B, *F*, and T_2^B, providing that T_1-weighting of the imaging sequence is minimal, and that SNR in the raw data and/or the number of MT points are sufficient; 2) Ramani's model is inadequate to fit T_1-weighted data, leading to underestimate *F* and RM_0^B by factors up to 30%; 3) Sled and Pike's model is less robust than Ramani's model in the presence of noise. These observations should be accounted for when designing a quantitative MT experiment. The effect of other factors, such as the duty cycle, remain to be investigated.

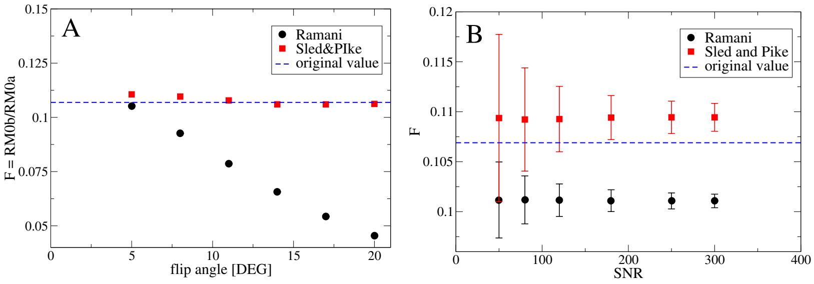

Fig 1. *Plot of estimated F from noise-free simulated data against excitation flip angle* (A); *plot of mean (± SD) estimated F from noisy datasets against SNR in the unweighted image* (B)**.**

References

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