

Regarding our article entitled “Quantitative Magnetization Transfer Mapping of Bound Protons in Multiple Sclerosis,” which appeared in *Magnetic Resonance in Medicine* 2003; 50(1): 83–91:

Some of us have published several papers(1–3) on a technique for quantitative magnetization transfer (qMT) in the brain. A range of MT pulse amplitudes and offset frequencies is used, and the resulting image intensities are used to fit a binary spin bath model, hence giving estimates of fundamental MT parameters such as the bound proton pool fraction (f) and T_2 (T_{2b}). We have recently discovered an error in the pulse sequence used to collect these data; fortunately a retrospective correction to the raw image data was possible, and here we give corrected normal values for f and T_{2b} . In addition we correct some minor errors in our previous papers.

In the continuous wave power equivalent (CWPE) model, the effect of the MT pulse is replaced by a continuous RF field of amplitude equal to the root mean square value of the MT pulse amplitude, averaged over the repetition time for the pulses TR' . This can be calculated(1,4) from

$$\omega_{1\text{cwpe}} = \sqrt{\frac{p_2}{\tau_{\text{sat}} TR'} \frac{\theta_{\text{sat}} \pi}{p_1 180}} \quad [1]$$

where $\omega_{1\text{cwpe}}$ is the CWPE field (rad sec^{-1}), θ_{sat} is the flip angle of the MT saturating pulse (degrees), τ_{sat} is the duration of the MT pulse, and TR' is the repetition time of the MT pulses. (Our previous version of this equation (2) had a typographical error). The parameters p_1 and p_2 describe the pulse shape (4): p_1 is the area under the pulse, relative to a rectangular pulse of the same amplitude and duration; p_2 is the area under the square of the pulse B_1 value, relative to a rectangular pulse. For the Gaussian pulse used, $p_1 = 0.4819$, $p_2 = 0.3441$. In this context, we report that our textual definition of the parameter p_2 has been given incorrectly (1,2); it should have read “ p_2 is the ratio of the mean square amplitude of the saturation pulse to that of a rectangular pulse of the same amplitude and duration” (4). For our sequence, $TR' = 40.71$ msec, $\tau_{\text{sat}} = 14.59$ msec, and hence using Eq. [1] we find that $\omega_{1\text{cwpe}} = 0.8684 \theta_{\text{sat}}$.

The pulse amplitude scaling procedure in the 5x software from General Electric Medical Systems is complex. RF pulses within a subsequence are played out at full amplitude wherever possible, giving the maximum digital resolution, with all the necessary scaling happening via physical (analogue) attenuators. If the maximum B_1 amplitude for a particular subsequence requires greater attenuation than the maximum available from the physical attenuators in the transmit chain, then additional scaling is introduced by reducing the amplitude of the RF waveforms themselves, by multiplication of the digital representation. However, adjustment of the attenuators requires the auto prescan procedure to be repeated, which was not carried out in our 2D qMT sequence.

Consequently, at the highest MT power all RF pulses were erroneously scaled down (by a factor of 0.5918). Thus, the signal from the imaging pulse was reduced (even in the absence of an MT effect), and less MT saturation was applied than intended. This error was found during the development of a 3D qMT sequence (5) by an independent physicist (MC), and confirmed using a search coil and oscilloscope to directly monitor the MT pulse amplitudes.

Fortunately the reduction of the imaging and MT pulses can be corrected for in the analysis and the qMT image data were reanalyzed. The image intensity values for the highest power were multiplied by the factor ($\sin 25.0^\circ / \sin 14.8^\circ$), since the programmed 25° pulse was in fact $0.5918 \times 25^\circ = 14.8^\circ$, and at the TR we used (1140 msec) T_1 -weighting is minimal. In the model fit, instead of the programmed value of 735 rad sec^{-1} , the saturating field ω_1 was set to 435 rad sec^{-1} ($0.5918 \times 735 \text{ rad sec}^{-1}$). As a result, our confidence in our new set of fitted parameters has increased for three reasons:

- (i) the residual errors after fitting are now very low (root-mean-square value about 1.2% of the unattenuated signal; see Fig. 1a), there are no signs of systematic deviation of the model from the data, and the resulting parameter maps are of higher quality;
- (ii) a super-Lorentzian lineshape now fits much better than a Gaussian line shape, contrary to our previous experience, and as reported by others;
- (iii) the good fit between the model and the data suggest that our CWPE approximation (1) is very good for this sequence (see Fig. 1a and b).

Our normal values for f and T_{2b} are now greatly altered. In frontal white matter, mean values (6) are now as follows: f , 9.0% (SD = 0.7); T_{2b} , 10.6 μsec (SD = 0.7).

The preliminary clinical conclusions we have drawn (3), namely that f is sensitive to multiple sclerosis (MS) pathology in lesions and normal-appearing brain tissue, while T_{2b} appears specific for lesion pathology, are not altered

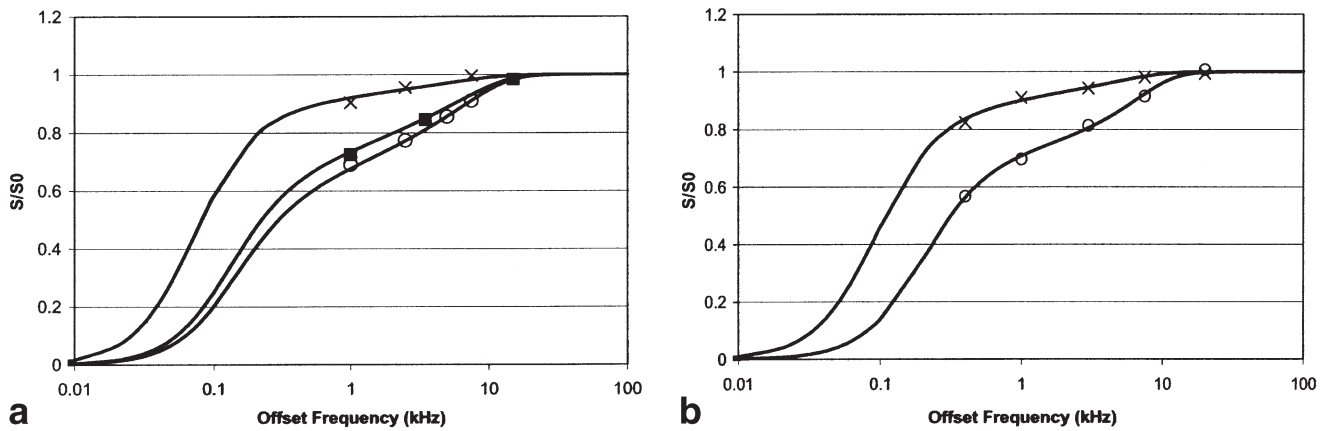


FIG. 1. Greatly improved model fits in normal frontal white matter, using the corrected sequence and super-Lorentzian line shape. S/S_0 is the measured signal divided by the fitted value of the maximum (unsaturated) signal. (a) MT pulse FA $\theta_{\text{sat}} = 212^\circ, 434^\circ, 499^\circ$, (corresponding to CWPE values of $\omega_{1\text{CWPE}} = 185, 378, \text{ and } 435 \text{ rad sec}^{-1}$). (b) Extended offset frequencies (400 Hz to 20 kHz) and two MT fields only (185 and 435 rad sec^{-1}), showing the quality of the CW model approximation.

upon reanalysis of the data. A subsequent study in a larger group of patients has revealed that f is a clinically relevant parameter in that better correlation is seen between f and MS disability than between T_1 and disability (6).

We apologize to the readers for the confusion these mistakes might have caused.

REFERENCES

1. Ramani A, Dalton C, Miller DH, Tofts PS, Barker GJ. Precise estimate of fundamental in-vivo MT parameters in human brain in clinically feasible times. *Magn Reson Imaging* 2002; 20(10):721–731.
2. Tozer D, Ramani A, Barker GJ, Davies GR, Miller DH, Tofts PS. Quantitative magnetization transfer mapping of bound protons in multiple sclerosis. *Magn Reson Med* 2003; 50(1):83–91.
3. Davies GR, Ramani A, Dalton CM, Tozer DJ, Wheeler-Kingshott CA, Barker GJ, Thompson AJ, Miller DH, Tofts PS. Preliminary magnetic resonance study of the macromolecular proton fraction in white matter: a potential marker of myelin? *Mult Scler* 2003; 9(3):246–249.
4. Berry I, Barker GJ, Barkhof F, Campi A, Dousset V, Franconi JM, Gass A, Schreiber W, Miller DH, Tofts PS. A multicenter measurement of magnetization transfer ratio in normal white matter. *J Magn Reson Imaging* 1999; 9(3):441–446.
5. Cercignani M, Symms MR, Boulby PA, Tozer DJ, Tofts PS, Barker GJ. Three-dimensional quantitative magnetization transfer imaging of the human brain. In: *Proceedings of the 12th Annual Meeting of ISMRM, Kyoto, Japan, 2004*.
6. Davies GR, Tozer D, Cercignani M, Ramani A, Dalton C, Thompson AJ, Barker GJ, Tofts PS, Miller DH. Estimation of the macromolecular proton fraction and bound pool T2 in multiple sclerosis. *Mult Scler* 2004; in press.

P.S. Tofts,
M. Cercignani,
D.J. Tozer,
M.R. Symms,
G.R. Davies
A. Ramani¹
G.J. Barker²
Institute of Neurology
University College London
Queen Square
London WC1N 3BG, UK

¹Current address: New York University School of Medicine, 650 First Avenue, 6th Floor, Room 600F, New York, NY 10016.

²Current address: Centre for Neuroimaging Sciences, Box 089, Institute of Psychiatry, Kings College London, London SE5 8AF, UK.