# Three-Dimensional Quantitative Magnetisation Transfer Imaging of the Human Brain

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### Synopsis

This work describes the implementation of a three-dimensional spoiled gradient echo (3D SPGR) acquisition for quantitative magnetisation transfer (qMT). The objective of qMT is the extraction of fundamental MT parameters, such as *f*, the bound proton fraction, and  $T_{2b}$ , the transverse relaxation time of bound protons. Starting from the initial work of Henkelmann<sup>1</sup>, various 2-pool (liquid and semi-solid protons) models have been developed in order to estimate these quantities *in vivo*<sup>2.3</sup>. In general, all models require the estimation of a number of parameters by non-linear fitting. As a consequence, a good signal-to-noise ratio (SNR) for the measured signal is essential, in order to reliably fit the parameters from a small number of samples, thus keeping the acquisition time to a minimum. A 3D acquisition has the advantage of providing higher signal-to-noise ratio than the commonly used 2D acquisition, also allowing a higher spatial resolution to be achieved. The purpose of this study was to evaluate the feasibility of 3D-qMT, and to optimise the acquisition.

### Methods

This work is based on the simplified model of the MT phenomenon developed by Ramani et al.<sup>2</sup>. All data were obtained on a 1.5 T SIGNA Horizon Echospeed scanner (General Electric, Milwaukee, USA). For this initial proof of concept study, a single healthy subject (male, 37 years) underwent the following scans: a) an MT-prepared 3D-SPGR (MTSPGR) (TR<sub>MT</sub>=30.7 ms, TE=5.3 ms) acquisition, with Gaussian MT pulses (pulse width = 14.7 ms); and b) a 3D SPGR (TR<sub>T1</sub>=13.1 ms, TE=4.2 ms) with three different flip angles (FAs) (25°, 15°, 5°) in order to independently estimate the longitudinal relaxation time of the system, T<sub>lobs</sub>. For sequence a) ten points, with different combinations of offset frequencies and amplitudes were used. The continuous wave power equivalent, i.e. the amplitude of a continuous wave giving the same mean power, was estimated as described by Ramani et al.<sup>2</sup>. In this case, since all slice-encoding locations were acquired in a single slab, the time between subsequent MT pulses (TR') is coincident with TR. During the first session, the acquisition matrix for both sequences was 256x128, over a field of view (FoV) of 32x16 cm, with twenty-eight 5 mm thick slices. In order to estimate the effects of T<sub>1</sub>-weighting on qMT parameters, the MT sequence was approximately 20 mins.

In Ramani & Henkelman's model, the signal depends on six independent parameters:  $gM_{0a}$ , (where g is a scaling factor, and  $M_{0a}$  is the native magnetisation of the free pool);  $RM_{0a}$  (where *R* is a measure of the coupling of the two pools);  $f/R_a(1-f)$  (where *f*, the bound proton fraction, is defined as the ratio between the magnetisation of the bound protons and the total magnetisation and  $R_a$  is the longitudinal relaxation rate of the free pool);  $R_b$  (the longitudinal relaxation rate of the semi-solid pool);  $1/R_a T_{2a}$ , (where  $T_{2a}$  is transverse relaxation time of the free pool); and  $T_{2b}$  (the transverse relaxation rate of the semi-solid pool).  $T_{2b}$  enters the model via  $R_{RFB}$ , a factor which represents the rate of RF absorption by the semi-solid pool. For this work, it was represented by a Gaussian lineshape as described by Ramani et al.<sup>2</sup>. Of these 6 independent parameters ( $gM_{0a}$ ,  $RM_{0a}$ ,  $R_b$ ,  $f/R_a(1-f)$ ,  $1/R_a T_{2a}$ ,  $T_{2b}$ ), only 5 ( $gM_{0a}$ ,  $R_b$ ,  $f/R_a(1-f)$ ,  $1/R_a T_{2a}$ ,  $T_{2b}$ ), were fitted using the Marquardt-Levenberg routine from the Numerical Recipes library<sup>4</sup>.  $T_{1obs}$  was estimated by linearly fitting the SPGR (sequence b) signal obtained from the 3 data points, divided by tan $\alpha$ , versus the SPGR signal divided by sin $\alpha$ , where  $\alpha$ , the true FA, is estimated according to the method of Barker et al.<sup>5</sup> and  $T_{1obs}$  is given by  $-TR_{TI}/ln(\text{grad})$ , where 'grad' is the gradient derived from the straight line fitting procedure.

 $R_a = 1/T_{1a}$  was calculated as described by Ramani et al.<sup>2</sup>, with  $R_{aobs} = 1/T_{1obs}$  and then used to extract f from the estimate of  $f/R_a(1-f)$ .

In order to show that the higher SNR provided by the 3D acquisition can be exploited to achieve a higher resolution, the same volunteer underwent a second scanning session consisting of the same scans (a and b) with higher resolution (acquisition matrix: 256x192 over a FoV of 24x18cm, sixty 3 mm thick slices). The MTSPGR was run only once with a FA of 10°. The total imaging time in this case was 45 minutes.

#### Results

A typical *f* map is shown in figure 1, for two different spatial resolutions. A reduction of the average *f* value was observed with increasing imaging FA, as shown by fig 2. In order to compromise between the SNR and the amount of  $T_1$ -weighting, the following measurements of *f* were assessed using the 5° dataset. Values of *f* were measured in regions of white matter located in the corona radiata, periventricular areas and corpus callosum, showing good agreement with previously published values<sup>6</sup>. The average *f* of white matter was 16.4% (range:14.0-18.3%), with higher values in the corpus callosum (mean=18.1, range=17.4-19.2). The SNR in the image with the highest saturation was measured in the 3D dataset obtained with FA of 5° and in a typical 2D dataset, with the same resolution, available from an independent acquisition, by positioning two square regions of interested: one within periventricular white matter and the other in the background. The SNR was then estimated as the ratio of the average values measured in these regions, divided by 0.655<sup>7</sup>. The average SNRs were, respectively, 17.4 for the 2D and 47.5 for the 3D acquisitions.

#### Discussion

We have implemented a 3D SPGR acquisition for qMT, providing a considerable increase in SNR in acquired data, despite the reduction in the FA. Due to the reduced TR, the use of small FAs is preferable for the 3D acquisition in order to reduce T1 weighting that might affect the estimate of f. Since by reducing the FAs, the SNR is also reduced, further investigations are ongoing to assess the effects of noise on parameter fitting.



**Fig1.** Typical f maps obtained with the 3D acquisition a)  $1.25 \times 1.25 \times 5$  mm resolution, 5° flip angle and b)  $0.976 \times 0.976 \times 3$  mm resolution, 10° flip angle.

## References

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**Fig2**. Variation of f with the imaging flip angle in a periventricular region of white matter (mean value  $\pm$  standard deviation).

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