Note

Quantification of Magnetization Transfer by Sampling the Transient Signal Using MT-Prepared Single-Shot EPI

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ABSTRACT: We describe the standard model for magnetization transfer (MT): a two-pool system with pseudo-linear exchange kinetics; under the influence of repetitive "MT-pulses" that create arbitrary instantaneous saturation. The influence of the pulse repetition period on the steady state (Part I) and the transient behavior of the system (Part II) provides similar but not equivalent information about relaxation, exchange and saturation. A quantification of all six parameters was possible by sampling the transitions and steady state at pulse repetition times between 8 ms and 200 ms by means of single-shot echo-planar imaging of the human brain in vivo. Concepts Magn Reson Part A 19A: 149–152, 2003

KEY WORDS: magnetization transfer; pulsed saturation; quantification; human brain

INTRODUCTION

Magnetization transfer (MT) contrast of biological tissues (*1*) is created by selectively saturating the "invisible" magnetization of macromolecules and can be observed as an attenuation of the "free" water signal. On clinical MR-systems, selective saturation can be achieved by periodic irradiation of radio-frequency pulses in order to limit the specific absorption rate. Repetitive pulsed saturation introduces a time dependence of the MT-experiment that depends on the pulse repetition period (PR). It also depends on how much each pool is saturated by a each single MT-pulse. In a series of papers (two full papers and the present research note) we will describe the PR dependence of the standard MT-model, i.e., a two-

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pool system with pseudo-linear exchange kinetics. In order to investigate the transition behavior of the system and to achieve short pulse repetition periods, we choose to use single-shot detection by echo-planar imaging (EPI). We show that, by means of appropriate approximations, all four rate constants that describe the two-pool model as well as the saturation of each MT-pulse can be determined by sampling the transition to the steady state for various PR-values. This method of quantification, that represents an alternative to current steady state techniques, was applied to MT experiments of the human brain in vivo.

THEORY

The standard kinetic model for MT considers a linear exchange kinetic between the "free" bulk water, M_f^0, and motion-restricted "macromolecules," M_m^0, described by the pseudo first-order rate constants k_{fm} and k_{mf}. The modified Bloch equations describe transfer and relaxation (by R_{1f} and R_{1m}) assuming the kinetic equilibrium of M_f^0 and M_m^0. For their general solution, we suggest a simple parameterization using the apparent rates (λ_+, λ_-), the "transfer term,"

$$T = \frac{k_{fm} + R_{1f} - \lambda_-}{\lambda_+ - \lambda_-}, \qquad [1]$$

and the "difference term,"

$$D = \frac{R_{1f} - \lambda_-}{\lambda_+ - \lambda_-}. \qquad [2]$$

Assuming "fast-transfer" in tissue ($\delta R_1 = R_{1m} - R_{1f} \ll k_{mf} + k_{fm}$), the rapid apparent rate,

$$\lambda_+ = k_{mf} + k_{fm} + R_{1f} + \frac{k_{mf}}{k_{mf} + k_{fm}}\,\delta R_1 = k_{mf} + k_{fm} + \frac{k_{fm}}{k_{mf} + k_{fm}}\,R_{1f} + \frac{k_{mf}}{k_{mf} + k_{fm}}\,R_{1m} \qquad [3]$$

corresponds to a rapid transfer equilibrating the individual saturations of the two pools. This takes place in early phase of PR before the critical delay time defined by the maximum saturation transfer in the idealized case (*2*). A pre-equilibrium state is established, which then relaxes with the weighted average of the pools' relaxation rates

$$\lambda_- = R_{1f} + \frac{k_{fm}}{k_{mf} + k_{fm}}\,\delta R_1 = \frac{k_{mf}}{k_{mf} + k_{fm}}\,R_{1f} + \frac{k_{fm}}{k_{mf} + k_{fm}}\,R_{1m}. \qquad [4]$$

Inversion of Eqs. [1]–[4] yields the kinetic and relaxation parameters. We describe the MT-pulses by instantaneous saturation of each pool, expressed by two saturation factors, σ_f and σ_m. The iteration of MT-pulse and free evolution are then solved in closed form. The bases to the number of pulses, or "transients," can be approximated by:

$$\mu_- \cong \mu_{-\mathrm{app}} = \sigma_m E_+ \qquad [5]$$

$$\mu_+ \cong \mu_{+\mathrm{app}} = \sigma_f E_- - T\,\frac{(\sigma_f - \sigma_m)(E_- - E_+)}{1 - \sigma_m E_+}. \qquad [6]$$

E_+ and E_- abbreviate the decaying exponentials of the two apparent rates, $\exp(-\lambda_{+/-}PR)$. The minor transient, μ_-, can only be observed for weak MT-pulses (large σ_m) and short PR as a delay in the transition to steady state governed by the major transient, μ_+. For strong MT-pulses and/or long PR, the transition to steady state is mono-exponential. The steady state magnetization is

$$\frac{M_f^\infty}{M_f^0} = \frac{1 - E_-}{1 - \mu_{+\mathrm{app}}}\left[1 + D\,\frac{(1 - \sigma_m)(E_- - E_+)}{(1 - \sigma_m E_+)(1 - E_-)}\right]. \qquad [7]$$

The main term appears like progressive saturation of a homogeneous system. The correction term accounts for the mismatch due to the difference between R_{1f} and R_{1m} (Eqs. [2], [4]). It may be set to zero for a more robust evaluation.

METHODS

MT-experiments were performed on a 1.5 T clinical MR-system (Magnetom Vision, Siemens Medizintechnik, Erlangen, Germany) using a "single-shot" spin-echo echo-planar imaging (EPI) sequence (TE = 50 ms, 10 s recovery time, single axial slice of 5 mm thickness, FOV 192 mm, 64 × 64 matrix). An equidistant train of band-selective Gaussian-shaped pulses was used for saturation. 720° pulses of 6.4 ms duration were applied at a frequency offset of 1 kHz to achieve both strong saturation and short PR. The transition to steady state was sampled at short PR of 8 ms, 16 ms, 24 ms and long PR of 100 ms and 200 ms. The steady state was

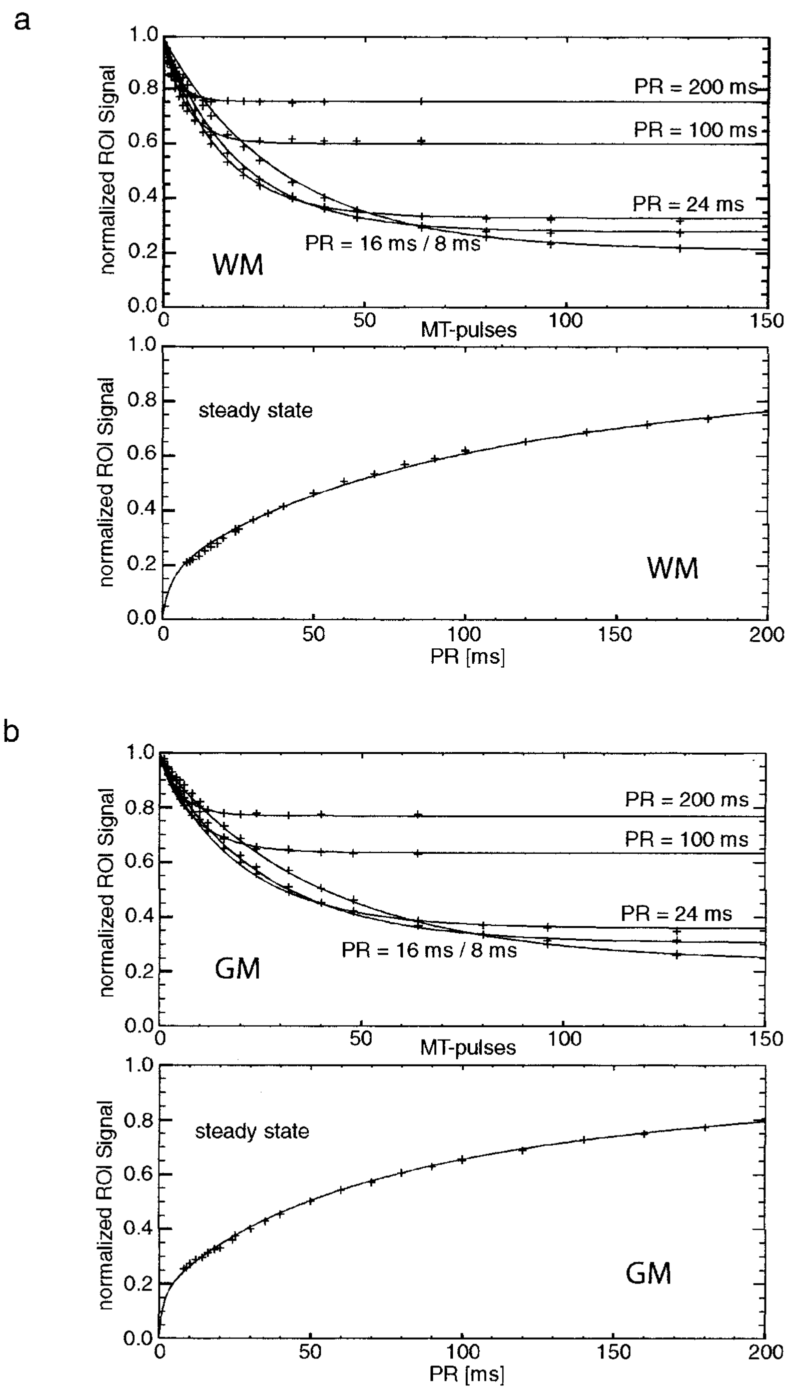

Figure 1 Global fit of a monoexponential transient μ_{app+} in WM and GM.

measured in the *PR* range between 8 ms and 200 ms. Transfer and difference term, apparent rates, and saturation factors were estimated by a global fit to the signal from manually selected regions of central white matter and cortical gray matter. We applied a modified Levenberg–Marquardt routine without constraints as implemented in IDL 4.0.1 (Research Systems Inc., Boulder, CO). To simplify the partial derivations, we assumed a monoexponential transition by μ_{+app} (Eq. [6]) towards the steady state (Eq. [7]). The approximations were tested by simulation using the parameters for bovine gray and white matter as determined ex vivo at 37°C (*3*).

Table 1 Parameters Determined from a Global Fit of a Monoexponential Transient μ_{app+}

	WM	WM	GM	GM
λ_- [s^{-1}]	1.31 ± 0.01	0.96 ± 0.02	0.74 ± 0.05	0.70 ± 0.05
λ_+ [s^{-1}]	20.2 ± 0.6	30.1 ± 0.7	23.7 ± 2.7	23.4 ± 2.8
σ_f [%]	99.1 ± 0.1	99.6 ± 0.01	99.2 ± 0.1	99.3 ± 0.1
σ_m [%]	49.6 ± 0.1	62.8 ± 0.1	54.2 ± 3.8	60.0 ± 3.2
T [%]	10.6 ± 0.05	15.6 ± 0.6	7.9 ± 0.5	9.5 ± 0.6
D [%]	−3.2 ± 0.1	0[a]	−0.3 ± 0.3	0[a]

[a] Assuming $R_{1f} = R_{1m}$.

RESULTS AND DISCUSSION

Figure 1 shows the normalized data points sampling the transitions and the steady state. The curves are calculated from the parameters estimated by the global least-squares fit. The fitted parameters with free D and $D = 0$ are given in Table 1. The latter corresponds roughly to the common assumption of $R_{1m} \cong 1\ s^{-1}$ (*2–7*). So far, quantitative in vivo studies of the kinetic and relaxation properties have been performed in the steady state, by varying the frequency offset and power of the radio-frequency irradiation (*4–6*). The backward rate, k_{mf}, was smaller than found by others (*3–6*) corresponding to a larger content of macromolecules, especially in GM. The large negative D in WM corresponds to $R_{1m} = 4.5\ s^{-1}$, which is consistent with the influence of myelin water at times <200 ms (*7, 8*). A tentative explanation for the deviating findings in GM is the influence of signal instabilities, probably due to subject motion causing varying contributions from adjacent CSF. The difference term exerts a strong influence when inverting Eqs. [1]–[4]. Hence, it should be set to zero if it cannot be reliably determined, like in GM. The technique is limited to single-slice detection. The protocol should be optimized with regard to measuring time and adequate sampling of *PR* shorter and longer than the critical delay.

SUMMARY

The evolution of two pools of magnetization undergoing periodic pulsed saturation for magnetization transfer experiments can be analytically solved. The *PR* dependence of the transition to steady state can be used to estimate the kinetic and relaxation rates together with the arbitrary saturation of each pool.

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