Pulsed Magnetization Transfer Spin-Echo MR Imaging

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Cross relaxation between macromolecular protons and water protons is known to be important in biologic tissue. In magnetic resonance (MR) imaging sequences, selective saturation of the characteristically short T2 macromolecular proton pool can produce contrast called magnetization transfer contrast, based on the cross-relaxation process.

Selective saturation can be achieved with continuous wave irradiation several kilohertz off resonance or short, intense 90° pulses on resonance. The authors analyze 90° binomial pulses for T2 selective saturation. Present design guidelines, and demonstrate the use of these pulses in spin-echo imaging sequences in healthy volunteers and patients.

Using the phenomenologic Bloch equations modified for two-site exchange, the authors derive the analytic expressions for water proton relaxation under periodic pulsed saturation of the macromolecular protons. This relaxation is shown to be monoexponential, with a rate constant dependent on the saturation pulse repetition rate and the individual and cross-relaxation rates.

The exchange of magnetization between protons in distinct environments constitutes an important relaxation mechanism in biologic tissues (1–3). In a two-pool model of tissue, protons may exist in a highly mobile liquid state associated with “free” water (1Hf) or in semisolid “restricted” motion sites (1Hr) such as macromolecular protein matrices or cell membranes (4). Assuming that each magnetization pool is at a uniform spin temperature and that cross relaxation is first order, the longitudinal magnetization evolution of the system can be modeled by a pair of coupled differential equations that, in general, describe biexponential relaxation (5–8). The difference in proton mobility results in the 1Hf pool having a relatively long T2 (> 10 msec) and the 1Hr pool having a very short T2 (< 200 μsec). Therefore, the pools are characterized by narrow and broad resonances, respectively. In imaging experiments, the 1Hr pool is not directly observed because the minimum TEs are at least an order of magnitude longer than the 1Hf T2. However, exchange between the pools affects the observed 1Hf bulk T1.

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The magnetization transfer (MT) phenomenon has been widely studied in spectrometers with the method of continuous wave (CW) saturation transfer (9). In this technique, the 1Hf pool is continuously saturated and the observed 1Hr T1 (T1cw) and steady-state magnetization (M0,cw) are measured. These parameters, along with steady-state magnetization without 1Hf saturation (M0,0), allow calculation of the 1Hr pool T1 in the absence of exchange (T1,0) and the 1Hr to 1Hf exchange time constant (τf) with the equations

\[
T1 = \frac{M_{0,0}}{M_{0,cw}}T1_{cw}. \quad (1)
\]

\[
\tau_f = \frac{M_{0,cw} - M_{0,0}}{T1_{cw}}. \quad (2)
\]

In these experiments, the broad line shape of the 1Hr pool is exploited for selective saturation by using a CW irradiation several kilohertz off resonance. On most spectrometers, this is easily achieved by using the decoupler channel.
MT imaging was first demonstrated by Wolff and Balaban (4), who used the CW saturation transfer technique. In addition to demonstrating contrast due to cross relaxation, which they termed "magnetization transfer contrast" (MTC), they performed quantitative $\tau_1$ and $T_1$ experiments and calculated $M_{0,\text{cw}}/M_{0,t}$ images (10). However, since most clinical imagers do not have a decoupler channel, hardware modifications involving the addition of a second radio-frequency (RF) amplifier must be performed to allow CW imaging experiments. In addition, the power deposition in a true CW experiment can be prohibitive for in vivo imaging.

Hu et al (11,12) introduced an alternate approach to selective $^1$H saturation by using short, intense on-resonance RF pulses. Specifically, a 121 binomial pulse was used to produce a net 0° rotation of long $T_2$ components while saturating a range of short $T_2$ species. They demonstrated substantial in vivo MTC and $T_1$ and $T_2$ experiments and calculated $M_{0,\text{cw}}/M_{0,t}$ images (10). However, since most clinical imagers do not have a decoupler channel, hardware modifications involving the addition of a second radio-frequency (RF) amplifier must be performed to allow CW imaging experiments. In addition, the power deposition in a true CW experiment can be prohibitive for in vivo imaging.

The purpose of this work is twofold: optimization of the binomial saturation pulse for MT imaging and derivation of the signal behavior in spin-echo imaging sequences with periodic pulsed $^1$H saturation. Binomial pulses up to the fourth order are examined in terms of their ability to saturate the $^1$H component while leaving the $^1$H$_r$ pool unaffected over a reasonable passband. Analytic expressions for the signal response in pulsed MT spin-echo imaging are derived from the Bloch equations modified for two-site exchange. The technique is demonstrated in vivo in healthy volunteers and patients.

**METHODS**

$^1$H Saturation

While off-resonance CW $^1$H selective saturation is easily understood from a frequency domain perspective, pulsed on-resonance $^1$H saturation is best examined in the time domain. Because the pulse durations (~1–2 msec) are typically two to three orders of magnitude shorter than the exchange time constants found in tissue (4,19), cross-relaxation effects during the pulse may be neglected, as can $T_1$ relaxation. With these assumptions, the Bloch equation solution for a constant amplitude $B_1$ directed along the x axis, with the initial condition $M_0(0)=0$, can be written (20):

$$M_y(t) = M_y(0)e^{-\alpha t}(\cosh \beta t - \frac{\alpha}{\beta} \sinh \beta t),$$

(5)

where $\alpha = \frac{1}{2} T_2$ and $\beta = \alpha \sqrt{1 - 4 \omega_1^2 T_2^2}$. From these expressions, it is clear that when $\omega_1 \gg \frac{1}{2} T_2$, angular rotation of the net magnetization vector is the dominant behavior, whereas magnetization decay dominates when $\omega_1 < \frac{1}{2} T_2$ (the system is critically damped at $\omega_1 = \frac{1}{2} T_2$). As first demonstrated by Edzes and Samulski in their "selective hydration inversion technique" (1), careful selection of the $B_1$ amplitude can result in simultaneous $^1$H$_s$ rotation and $^1$H$_r$ decay. This situation is illustrated in Figure 1, which shows the magnetization evolution during a 1.25-msec $2\pi$ rectangular pulse for materials with $T_2$ values of 100 msec and 100 $\mu$sec ($B_1 = 18.7 \mu T = B_{1\text{cd}}$ for $T_2$ of 100 $\mu$sec). To overcome the high $B_1$ homogeneity requirement of a $2\pi$ (or any integer multiple thereof) pulse, Hu et al (12) suggested 0° binomial pulses (ie, constant-magnitude rectangular pulses whose sign, and hence the subpulse areas, are modulated by the coefficients in the binomial expansion [1 - $x^n$]) and demonstrated the use of a 121 binomial pulse. In the present study, we examine binomial pulses up to the fourth order ($n=4$).

The design goals for a 0° $^1$H$_s$ selective saturation pulse for use in an MT imaging sequence are (a) complete saturation of the $^1$H$_s$ pool, (b) minimal saturation of the $^1$H$_r$ pool over an acceptable passband (ie, reasonably insensitive to $B_0$ inhomogeneity), and (c) a minimal specific absorption rate (SAR). Because the SAR of a pulse is minimized when $|B_1|$, is constant, only duration (as opposed to amplitude) modulation of the subpulses is considered.

While Equations (3)–(5) describe magnetization evolution during a constant-amplitude RF pulse, the sign reversals during a binomial pulse violate the initial condition $M_y(0)=0$. Therefore, we calculated magnetization responses numerically, including $T_2$ effects. Figure 2a shows $^1$H$_s$ saturation as a function of $T_2$ (normalized to the pulse duration) for the four binomial pulses. All pulses had equal total duration (1 msec) and were scaled to be critically damped at $T_2 = 100 \mu$sec ($|B_1| = 18.7 \mu T$). Figure 2b shows the...
From these data, a number of important observations can be made. First, from Figure 2a, we see that for this |B1|, the greatest saturation is achieved with the 11 pulse and that the saturation efficiency decreases with the order of the binomial. Note that all these pulses can produce complete saturation if their amplitudes are increased. However, the minimum |B1| required to achieve complete saturation of a selected T2 increases with the order of the binomial. This is illustrated in Figure 2c, which shows Mf/Mo as a function of |B1| for T2 = 100 μsec and each binomial pulse. Of note in this figure is the dramatic increase in the B1 required for saturation beyond approximately 90% (Mf/Mo < 0.1). These are particularly important points for clinical applications, since the SAR is proportional to B1². Therefore, for example, achieving 90% saturation with a 1464 pulse requires approximately twice the power of an equal duration 11 pulse. Similarly, increasing the saturation from 90% to 99% with a 121 pulse requires a power increase of about 75%. From Figure 2a, we also note that the greatest saturation is achieved for materials with T2 approximately 10%–15% of the pulse duration. Again, increasing the pulse amplitude will result in the saturation of a larger range of T2 values but at the expense of higher SAR. Greater saturation may also be achieved by increasing the pulse duration. However, this results in both decreased Hf bandwidth and increased on-resonance Hf saturation. Therefore, to avoid direct Hf saturation, which can mimic true cross relaxation, it is desirable to keep the pulse duration as short as possible.

The Hf frequency response shown in Figure 2b illustrates the expected increase in bandwidth with binomial pulse order. Note that the greatest bandwidth gain is obtained when going from a 11 to a 121 pulse. Although these frequency responses obviously change with effective pulse angle (β/|B1|), this general behavior holds for the range of B1 values and pulse widths (τ) considered here. For substantially larger effective pulse angles, the frequency responses may change dramatically. For example, increasing the effective pulse angle of a 11 pulse from 2π to 4π increases the pulse duration × Hf passband (calculated at 0.9 Mf/Mo) product from 0.2 to 2.4. However, to achieve an effective 4π rotation on a typical whole-body imager (maximum B1 < ~25 μT) requires a relatively long pulse and hence substantial direct Hf saturation. For example, a 4-msec 11 pulse (|B1| = 25 μT) would produce approximately 4% saturation for on-resonance materials with T2 = 50 μsec.

While a T2-selective pulse design technique is not, to our knowledge, currently available, the above observations can be used as a guide in designing 0° binomial Hf saturation pulses for MT imaging. The important specification parameters for pulse design are the Hf pool T2 (T2p) and required Hf passband. First, the pulse duration can be chosen to be about 10 T2. The binomial pulse order required to meet the Hf bandwidth specification can then be selected on the basis of Figure 2b. Finally, the pulse amplitude needed to achieve a given Hf saturation can be determined from numerical simulations such as those presented in Figure 2c. If, for example, at least 90% saturation is desired for a T2, of 100 μsec, with a
maximum 5% $^1$H$_f$ saturation over a 500-Hz bandwidth, a 1-msec 121 pulse with an amplitude of ~23 $\mu$T would be indicated by this procedure.

**Spin-Echo Imaging**

In an ideal CW saturation transfer experiment, the $^1$H$_r$ longitudinal magnetization is held at zero. To approximate this condition in a pulsed MT imaging sequence, and thereby maximize MTC, saturation pulses should be applied at regular intervals with a period that is short relative to the cross-relaxation rate. This was achieved in a single-section spin-echo imaging sequence by adding 0° binomial pulses at constant intervals ($TR_{ps} = \text{pulsed saturation}$) throughout the recovery portion of TR. Because the binomial pulses are not completely transparent to the longer T2 and off-resonance spins, a strong spoiler gradient was added to dephase any residual transverse magnetization created by them.

In a multisection sequence, the saturation pulses should be distributed over the TR so as to ensure that each section experiences the same pulse timings and therefore equal MTC. We accomplished this by adding a single $^1$H$_f$ saturation pulse before each section-select excitation in a standard multisection spin-echo sequence (Fig 3). An important characteristic of this sequence is that the time between successive excitation pulses—and hence saturation pulses—is constant. This is ensured by uniformly distributing section-select pulses over the sequence TR. With this implementation, the effective $TR_{ps}$ is TR divided by the number of interleaved sections.

**Signal Behavior**

In the absence of a $B_1$ driving field, the Bloch equations modified for two-site MT (5) are

$$\frac{dM_{2,1}}{dt} = R_{1,1}(M_{0,1} - M_{2,1}) - k_2 M_{2,1} + k_2 M_{2,r},$$

$$\frac{dM_{2,r}}{dt} = R_{1,1}(M_{0,1} - M_{2,r}) - k_2 M_{2,r} + k_2 M_{2,1},$$

where $R_{1,1}$ and $R_{1,2}$ are the relaxation rate constants (1/1$\tau$1) of the $^1$H$_r$ and $^1$H$_f$ pools, respectively, $k_2$ and $k_1$ are the forward ($^1$H$_f$ $\rightarrow$ $^1$H$_r$) and reverse ($^1$H$_r$ $\rightarrow$ $^1$H$_f$) exchange rate constants (1/1$\tau$2 and 1/1$\tau$3, respectively), and by definition in this model, $M_{0,1}/M_{0,2} = k_2/k_1$.

The solutions to these equations are biexponentials and in their general form may be written as

$$M_{2,1}(t) = M_{0,1} + C_1 e^{-\lambda_1 t} + C_2 e^{-\lambda_2 t},$$

$$M_{2,r}(t) = M_{0,r} + C_1 \frac{(R_{1,1} + k_2 - \lambda_1)}{k_2} e^{-\lambda_1 t} + C_2 \frac{(R_{1,1} + k_2 - \lambda_2)}{k_2} e^{-\lambda_2 t},$$

where

$$C_1 = \frac{R_{1,1} + k_2 - \lambda_2}{\lambda_1 - \lambda_2} [M_{2,1}(0) - M_{0,1}],$$

$$C_2 = \frac{k_1}{\lambda_1 - \lambda_2} [M_{2,r}(0) - M_{0,r}].$$

From these solutions, we can derive an expression for the signal response in the pulsed MT spin-echo experiment. Let us first make the following assumptions: (a) All RF pulses are instantaneous and therefore cross relaxation during each pulse may be neglected; (b) the $^1$H$_f$ saturation pulses are applied with a repetition time $TR_{ps}$, starting at the 90° excitation pulse; (c) TE is short relative to the observed T1 (ie, negligible $M_r$ recovery occurs between the 90° and 180° pulses, and therefore the sequence may be modeled as a simple saturation recovery); (d) each binomial pulse completely saturates $^1$H$_f$ and partially saturates $^1$H$_r$ by a factor $S_f$ (ie, $M_{2,r} = S_f M_{2,1}$ where $M_r$ and $M^*$ are the magnetizations immediately before and after the pulse, respectively). In this case, the magnetization state immediately after a 90° excitation is $^1$H$_r$, and partially saturates $^1$H$_r$ by a factor $S_f$ (ie, $M_{2,r}(0) = M_{2,r}(0) = 0$). By using Equation (8) and these boundary conditions, $M_{2,1}$ at the end of the first $TR_{ps}$ may be written

$$M_{2,1}(TR_{ps}) = \frac{[(R_{1,1} - \lambda_1)E_2 - (R_{1,1} - \lambda_2)E_1]}{\lambda_1 - \lambda_2} + \frac{\lambda_1 - \lambda_2}{(\lambda_1 - \lambda_2)} M_{0,1}.$$  

Figure 3. Pulsed MT multisection spin-echo imaging sequence. A single binomial pulse (a 121 pulse is shown here), followed by a strong dephasing gradient, precedes each 90° excitation pulse. Sat = saturation.

$$C_2 = -\frac{R_{1,1} + k_1 - \lambda_1}{\lambda_1 - \lambda_2} [M_{2,1}(0) - M_{0,1}]$$

$$+ \frac{k_1}{\lambda_1 - \lambda_2} [M_{2,r}(0) - M_{0,r}].$$  

and

$$\lambda_{1,2} = [(R_{1,1} + k_1 + R_{1,1} + k_2) + [(R_{1,1} + k_1 + R_{1,1} + k_2)]^2$$

$$- 4(R_{1,1}R_{1,1} + R_{1,1}k_2 + R_{1,1}k_1)]^{1/2}/2.$$

The magnetization state immediately after the next 90° saturation pulse is now $M_{2,1}(TR_{ps})$ and $M_{2,1}(TR_{ps})$ is $M_{2,1}(TR_{ps})$ with these new boundary conditions, the evolution of the system during the sec-
Figure 4. Plots of (a) steady-state $^1$H$_f$ magnetization ($M_{0,ps}$) and (b) observed $T_{1,ps}$ under periodic pulsed $^1$H$_f$ saturation as a function of $TR_{ps}$. These plots were generated by using Equations (18) and (19), assuming $R_1 = R_1 = 1$ sec$^{-1}$, $S_f = 1$, and $M_{0,fs}/M_{0,fs} = 10$. The fast, moderate, and slow designations correspond to $k_f$ exchange rates of 10, 1, and 0.1 sec$^{-1}$, respectively. The open circles on the vertical axes are the steady-state $^1$H$_f$ magnetization ($M_{0,fs}$) and observed $T_{1,fs}$ under CW $^1$H$_f$ saturation for the same parameters calculated by using Equations (21) and (22).

and $TR_{ps}$ is again given by Equation (8). Continuing in this fashion, we can propagate the magnetization state forward and write the general expression for the steady-state $^1$H$_f$ magnetization just before the $n$th saturation pulse as

$$M_{0,fs}(nTR_{ps}) = AM_{0,fs} \sum_{i=0}^{n-1} (S_f B)^i. \quad (14)$$

where

$$A = \frac{(R_1 - \lambda_1)E_2 - (R_1 - \lambda_2)E_1 + \lambda_1 - \lambda_2}{\lambda_1 - \lambda_2}, \quad (15)$$

$$B = \frac{(R_1 + k_f - \lambda_2)E_1 - (R_1 + k_f - \lambda_1)E_2}{\lambda_1 - \lambda_2}. \quad (16)$$

Rewriting Equation (14) as

$$M_{0,fs}(nTR_{ps}) = \frac{AM_{0,fs}}{1 - S_f B} (1 - S_f B^n), \quad (17)$$

and noting that $|S_f B| < 1$, we see that in the limit ($n \to \infty$) the steady-state $^1$H$_f$ magnetization observed just before each saturation pulse is

$$M_{0,ps} = \left[\frac{(R_1 - \lambda_1)E_2 - (R_1 - \lambda_2)E_1 + \lambda_1 - \lambda_2}{\lambda_1 - \lambda_2} \right] + \left[\frac{(R_1 + k_f - \lambda_2)E_1 - (R_1 + k_f - \lambda_1)E_2}{\lambda_1 - \lambda_2}\right] M_{0,fs}. \quad (18)$$

By using Equation (17), the magnetization evolution observed at $t = nTR_{ps}$ may now be written as a monoexponential recovery to $M_{0,ps}$:

$$M_{0,ps}(t) = M_{0,ps}(1 - e^{-t/T_{1,ps}}), \quad (19)$$

with the effective relaxation time

$$T_{1,ps} = \frac{\ln \left[\frac{S_f (R_1 + k_f - \lambda_2)E_1 - (R_1 + k_f - \lambda_1)E_2}{\lambda_1 - \lambda_2}\right]}{(R_1 + k_f - \lambda_2)E_1 - (R_1 + k_f - \lambda_1)E_2}. \quad (20)$$

The signal intensity ($I$) in our pulsed MT spin-echo sequence is therefore

$$I = K_p \frac{M_{0,ps} M_{0,fs}}{M_{0,fs}} (1 - e^{-T_{2,ps}/T_{2,fs}}) e^{-TE/T_{1,fs}}, \quad (21)$$

where $p$ is the proton density and $K$ a system constant.

As expected, the steady-state $^1$H$_f$ magnetization and the recovery time constant depend on the $^1$H$_f$ saturation period. This is illustrated in Figure 4, which shows $M_{0,ps}$ and $T_{1,ps}$ as a function of $TR_{ps}$ for various relaxation and exchange parameters, with $S_f = 0 (M_{0,fs}/M_{0,fs})$ and $S_f = 1$. Note that as $TR_{ps}$ approaches zero, $M_{0,ps}$ and $T_{1,ps}$ approach their CW $^1$H$_f$ saturation equivalents (9):

$$M_{0,ps} = \frac{R_1}{R_1 + k_f} M_{0,fs}, \quad (22)$$

$$T_{1,ps} = \frac{1}{R_1 + k_f}. \quad (23)$$

Recall that the above derivations assume that each $0^\circ$ pulse completely saturates the $^1$H$_f$ pool. If only partial saturation were achieved (ie, $M_{0,ps} = S_f M_{0,fs}$ with $0 < S_f \leq 1$), the magnetization evolution would in general follow a biexponential recovery. However, for the relaxation and exchange parameters expected in biologic tissues and an $S_f$ of approximately zero, the monoexponential response of Equation (19) gives an excellent approximation. For example, with $R_1 = R_1 = k_f = 1$ sec$^{-1}$, $M_{0,fs}/M_{0,fs} = 10$, $TR_{ps} = 50$ msec, and $S_f = 0.2$, $M_{0,ps}$ determined from numerical simulations—including partial $^1$H$_f$ saturation effects—differs by 4.5% from that given by Equation (19). However, direct saturation of the $^1$H$_f$ pool can be substantial, and $S_f$ was therefore included in the above derivations. Using the same parameters as for the previous example, but with $S_f = 0$, we note that 2%
Figure 5. Images of normal brain (a–c) and lower legs (d–f) acquired with the multisection MT spin-echo sequence shown in Figure 3 (1,000/20, TR\textsubscript{p} = 50 msec, 1-msec 121 binomial pulses, and |B\textsubscript{1}| = 18 μT) without (a, d) and with (b, e) \textsuperscript{1}H\textsubscript{s} saturation. e and f are the percent difference images. Higher signal intensities on the percent difference images represent greater MT.

\textsuperscript{1}H\textsubscript{s} saturation per pulse (ie, S\textsubscript{f} = 0.98) results in an 18% M\textsubscript{0,ps} attenuation. This underscores the importance of minimal-duration binomial pulses. Consider again the example of the 4-msec, 4π, 11 pulse presented in the \textsuperscript{1}H\textsubscript{s} Saturation section. With this pulse, materials having T\textsubscript{1}/T\textsubscript{2} of 1,000/50 msec and no cross relaxation would have S\textsubscript{f} = 0.96 and show approximately 25% attenuation with a TR of 1,000 msec and TR\textsubscript{p} of 50 msec. For the same material, a 1-msec, 2π, 121 pulse would produce S\textsubscript{f} = 0.99 and about 7% attenuation.

\textbf{RESULTS}

We have implemented single- and multisection pulsed saturation spin-echo sequences on a 1.5-T whole-body imaging system (Signa; GE Medical Systems, Milwaukee, Wis) and performed MT imaging in phantoms, healthy volunteers, and patients. Typically, a dual acquisition was performed, one with and one without \textsuperscript{1}H\textsubscript{s} saturation. A ratio image (M\textsubscript{L,ps}/M\textsubscript{L,fs}) may then be calculated to isolate signal variations resulting from the \textsuperscript{1}H\textsubscript{s} saturation pulses. We have preferred to calculate percent difference images (100 × [1 − M\textsubscript{L,ps}/M\textsubscript{L,fs}]), which provide the same information but show MT with positive contrast. To avoid singularities in these calculations, a threshold is selected below which the result is set to zero. Therefore, in these images, regions undergoing substantial MT appear bright and those lacking MT appear dark. Example images without and with \textsuperscript{1}H\textsubscript{s} saturation and percent difference images of the head and legs of a healthy volunteer are shown in Figure 5. In these examples, 20 5-mm-thick sections were acquired with a TR msec/TE msec of 1,000/20, TR\textsubscript{p} of 50 msec, and 1-msec 121 binomial saturation pulses with |B\textsubscript{1}| = 18 μT. The average and peak SAR for this sequence were 0.18 W/kg and 7.5 W/kg, respectively. Normal white and gray matter showed approximately 45% and 30% signal loss, respectively, while cerebrospinal fluid signal decreased by less than 5%. Skeletal muscle showed about 35% attenuation and fat about 11%.

Two vials of manganese chloride solutions with T\textsubscript{1}/T\textsubscript{2} of 600/60 msec (left vial in Fig 5) and 1,090/120 msec (right vial) were also imaged to measure the \textsuperscript{1}H\textsubscript{s} signal loss in the absence of exchange (direct saturation). The 60- and 120-msec T\textsubscript{2} solutions showed 6% and 4% signal loss, respectively, results that are in good agreement with the theoretical predictions of 5.5% and 3.2% based on Equation (20) and on-resonance direct saturation factors S\textsubscript{f} of 0.992 and 0.996 per pulse, determined from numerical simulations.

Using the single-section MT spin-echo sequence, we collected images of the head and lower legs of a healthy volunteer with a range of TR values, and calculated observed T\textsubscript{1} and M\textsubscript{0} with and without \textsuperscript{1}H\textsubscript{s} saturation. Again, 1-msec 121 pulses were used with a TR\textsubscript{p} of 50 msec. However, since only one 90°–180° pulse pair was used for each TR, the saturation pulse |B\textsubscript{1}| was increased to 23 μT, remaining within SAR guidelines. For this pulse, materials with a T\textsubscript{2} of 50 msec – 300 μsec experience an S\textsubscript{f} less than or equal to 0.2. In addition to the manganese chloride-doped water samples described above, freshly drawn venous blood was heparinized and transferred into 2-cm-di-
DISCUSSION

In a clinical imaging setting, pulsed on-resonance \(^1\)H saturation is a simple and efficient means of generating MTC. Analysis of binomial pulses up to the fourth order indicates that the 121 pulse represents the best compromise between \(^1\)H saturation efficiency, \(^1\)H bandwidth, and acceptable SAR for in vivo human imaging at 1.5 T. While the 91 pulse is more efficient at \(^1\)H saturation, its poor spectral response results in substantial direct \(^1\)H saturation, even in regions of relatively high Bo homogeneity, such as the brain. In especially inhomogeneous regions, such as the lung, a higher-order binomial may be required. However, either the pulse amplitude (and hence SAR) must be increased or a decrease in \(^1\)H saturation must be accepted.

The derivation of observed \(^1\)H relaxation under periodic pulsed \(^1\)H saturation presented in the Methods section showed that a monoexponential response is obtained if complete \(^1\)H and partial \(^1\)H saturation is achieved per pulse. As expected, \(T1_{fps}\) and \(M0_{fps}\) depend on the frequency of \(^1\)H saturation (1/TRps) and approach the CW limit as this frequency is increased. Although the derivation presented here is for a saturation recovery experiment, the expressions for \(M0_{fps}\) and \(T1_{fps}\) (Eqq [18], [20]) are also valid for other experiments. For example, the signal in an inversion recovery sequence with periodic pulsed \(^1\)H saturation and inversion time \(T1\) is

\[
I = Kp(M0_{fps}/M_{0,f}) \left(1 - 2e^{-T1/T_{1fps}}\right) e^{-TR/T_{2fps}}.
\]

Similarly, starting from a fully relaxed state, the \(M0_{fps}\) evolution in the absence of excitation pulses is

\[
M0_{fps}(t) = M0_{fps} + (M_{0,f} - M_{0,0}) e^{-TR/T_{1fps}}.
\]

Both of these techniques could be used to prepare the magnetization prior to a rapid gradient echo (24,25) or echo-planar (26,27) acquisition. For a single-shot inversion recovery from a fully relaxed state, \(I = Kp(M0_{fps}/M_{0,f} - (1 + M0_{fps}/M_{0,f}) e^{-T1/T_{1fps}}) e^{-TR/T_{2fps}}.\) Multiple acquisitions with a range of delay or inversion times could then be used to rapidly measure \(T1_{fps}, M0_{fps},\) and \(M0_{fps}.

Unlike ideal CW saturation transfer experiments, the relaxation rates and steady-state magnetizations measured in pulsed MT experiments cannot be used to directly compute exchange rate constants or \(^1\)H pool relaxation rates in the absence of exchange. This is because the observed \(T1_{fps}\) and \(M0_{fps}\) are dependent on the additional parameters \(M0_{f}, R1,\) and \(S1,\) as shown in Equations (18) and (20), thus making the problem underdetermined. However, the parameters measured in pulsed saturation experiments do provide some insight into the underlying cross-relaxation processes. Also, they allow modeling of signal behavior in other pulsed MT experiments and can therefore

![Figure 6](image-url)
<table>
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<th>Parameter</th>
<th>White Matter</th>
<th>Gray Matter</th>
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<th>Muscle</th>
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<td>1.218 ± 8.26</td>
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<td>T₁₅₀₂ (msec)</td>
<td>379 ± 12.91</td>
<td>697 ± 28.73</td>
<td>901 ± 21.17</td>
<td>468 ± 23.63</td>
<td>960 ± 20.20</td>
</tr>
</tbody>
</table>

M₀₅₀₆

M₀₅₀₂

Note.—The single-section MT spin-echo sequence was used with a TRₚₙ of 50 msec and 1-msec 121 binomial pulses with a |B₁| of 23 μT. T₁ values are given as mean ± standard error.

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**Figure 7.** (a) T₁-weighted (800/20), (b) proton density (3,500/30), and (c) T₂-weighted (3,500/80) images of a patient with multiple sclerosis. The same section was acquired without (d) and with (e) T₁₁₂ saturation (1,000/20, TR₀ = 50 msec, 1-msec 121 pulse, and |B₁| = 18 μT). The percent difference image is shown in f.

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be used to optimize contrast in specific applications. For example, from the data presented in the Table, it is clear that the contrast between blood and various tissues (white matter, gray matter, and muscle) may be considerably improved by pulsed T₁₁₂ saturation. We have exploited this simple observation to improve the contrast in three-dimensional time-of-flight angiography (15). Therefore, measurement of T₁₅₀₆ and M₀₅₀₆ in various diseases provides a direct means of evaluating the potential of pulsed MT imaging in improving contrast and, hence, disease detection.

Percent difference or ratio images calculated from acquisitions with and without T₁₁₂ saturation isolate signal variations resulting from the T₁₁₂ saturation pulses. However, as with any dual-acquisition technique, motion between measurements can cause substantial artifacts. Unfortunately, the time constants of exchange and T₁ relaxation in biologic tissues preclude interleaved acquisitions. In addition, care must be taken in interpreting these images because values depend on sequence timing parameters and relaxation and exchange rates. For example, note that the percent difference images in Figures 5 and 7 are based on measurements made with a TR of 1,000 msec and are not equivalent to images calculated from steady-state magnetizations (TR = ∞). TR may, of course, be selected to optimize contrast in such images. For example, from the data presented in the Table and Equation (20), we can see that the contrast between white and gray matter in a percent difference, or ratio, image is maximized at a TR of about 750 msec.
Direct saturation of the $^1H_2$ pool by the $0^0$ pulses is another potential problem with this technique. Assuming the binomial pulse has been designed to accommodate the expected range of $B_0$ and chemical shift within the region of interest, minimal direct $^1H_1$ saturation would be expected. However, since pulse transparency is dependent on not only frequency offset but also $T2$, both possibilities should be considered before interpreting signal attenuation as evidence of MT. For example, the approximately 11% attenuation of fat in Figure 5e can be attributed to direct saturation and does not indicate MT. Other potential regions of difficulty are tissue-air interfaces, such as the sinuses, and regions surrounding metallic implants, such as dental work. Note that direct saturation effects may also be substantial in CW MT experiments, as recently demonstrated by Henkelman et al (28).

In conclusion, on-resonance $0^0$ binomial pulses permit $^1H_2$ selective saturation and can produce considerable MTC in conventional, whole-body MR imaging systems. Design of these pulses involves trade-offs between $^1H_1$ saturation efficiency, $^1H_2$ passband characteristics, and SAR. Under periodic saturation, the observed $^1H_1$ relaxation is monoexponential and dependent on the pulse TR. The clinical value of pulsed MT imaging remains to be established. However, the analytic expressions presented here, along with measured relaxation times ($T1_{ps}$) and steady-state magnetizations ($M_{0,ps}$) in normal and pathologic tissues, provide a means of assessing the utility of MT imaging. In cases in which MT can improve lesion detection, these expressions allow contrast optimization.

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References