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Fast Magnetization Transfer and Apparent T_1 Imaging with a Short Saturation Pulse using with and without Inversion Preparation

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Abstract

Purpose—Measurements of magnetization transfer (MT) metrics, such as the steady-state (SS) MT ratio (MTR_{ss}) and apparent longitudinal relaxation rate (R_{1sat}) require multiple MT irradiation durations and a long experimental time. To overcome these problems, we propose a novel method with a short MT off-resonance pulse by using with and without on-resonance inversion preparation pulse.

Theory and Methods—Computer simulations were performed to examine the accuracy of the proposed method and to find the optimal off-resonance irradiation pulse duration (T_{irad}) and power level (ω_1). Our approach, with EPI data acquisition, was applied to animals at 9.4 T and humans at 3 T with $\omega_1/2\pi = 100$ Hz and 177 Hz, respectively. MTR_{ss} and R_{1sat} were obtained from a pair of MT images at a T_{irad} , with and without inversion.

Results—For $T_{irad} = 0.4$ s, MTR_{ss} and R_{1sat} measured at any single T_{irad} agreed well with those of the conventional fitting method that use multiple T_{irad} . Our simulation indicates that shorter T_{irad} values can be used at higher ω_1 .

Conclusion— MTR_{ss} and R_{1sat} can be determined from MT data with only one, short T_{irad} by incorporation of an inversion pre-pulse. This MT imaging approach is simple, fast, and easily implementable.

Keywords

magnetization transfer; Specific Absorption Rate; Magnetization Transfer Rate; apparent longitudinal relaxation rate

Introduction

Magnetization transfer (MT) contrast is generated from signal attenuation induced by magnetization exchange between free water protons and the restricted semi-solid macromolecular protons following selective irradiation of the semi-solid pool (1). This

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technique is useful to enhance tissue contrast for angiography, brain, body, and cardiac imaging (2,3). The magnitude of the MT effect is usually measured with and without MT irradiation pulses and is calculated by the ratio of the differences, which is referred to as the magnetization transfer ratio (MTR). This metric was previously shown to reflect the degree of neuron myelination, and can be used to characterize white matter degeneration in multiple sclerosis and other neuropsychiatric diseases, such as Alzheimer's disease and bipolar disorder (4–10). MTR value is also sensitive to edema and inflammation (11,12). MTR requires a long, off-resonance irradiation pulse to enhance the contrast between tissues, generally to reach steady state (SS), because sufficiently saturated immobile protons in macromolecules are the most sensitive to inherent MT properties.

The apparent longitudinal relaxation rate (R_{1sat}), the rate constant for two pools to reach equilibrium during irradiation, is also an important metric of MT effects. R_{1sat} is measured in many studies as an index of acute blood brain barrier damage in ischemia (13,14), estimation of ischemia infarction (15), prediction of hemorrhagic transformation (16), assessment of ischemia treatment (17), and evaluation of multiple sclerosis (18). Traditionally, R_{1sat} is obtained by fitting a mono-exponential function to multiple measurements in the presence of MT saturation (1,18), leading to a relatively long experimental running time to obtain sufficient data points for accurate curve fitting. The combination of MTR and R_{1sat} can provide a more detailed description of tissue characteristics for a variety of pathological tissues (13,15,17). The long duration of MT saturation pulses to maximize MTR and accurately measure R_{1sat} may exceed specific absorption rate (SAR) in a clinical setting, especially at high magnetic fields. It should be noted that in conventional MT studies, a short MT pulse is repeated every TR until a sufficient number of pulses are applied to reach SS and, thus, MTR in the *steady state* condition (MTR_{ss}), but not R_{1sat} , is easily obtainable (19,20).

In this study, we propose a fast method to obtain MTR in the steady state condition and T_{1sat} ($=1/R_{1sat}$) from a pair of *transient* MT data at a single off-resonance saturation duration, with and without an on-resonance inversion pre-pulse. This approach, in conjunction with echo planar imaging (EPI), reduces off-resonance irradiation duration and experimental time. To validate our approach, computer simulations were performed, and MT images with and without an inversion pre-pulse were acquired with multiple saturation durations at two MT pulse power levels in human brains at 3 T and rat brains at 9.4 T. Then, MTR_{ss} and T_{1sat} were measured with our method using a single MT saturation duration and compared with those determined by the conventional fitting approach.

Theory

A two-pool model, consisting of the free water proton and the restricted macromolecular proton pools, can describe MT behavior (21). A quantitative model of this coupled system describing magnetization behavior by off-resonance irradiation with a continuous wave mode was proposed by Henkelman et al. (22). When the restricted pool is assumed to be selectively and completely saturated by an off-resonance RF irradiation, the time-dependent change in longitudinal magnetization of the free water pool, $M_{sat}(T_{irad})$, is

$$M_{sat}(T_{irad}) = (M_0 - M_{ss}) \cdot \exp(R_{1sat} \cdot T_{irad}) + M_{ss}, \quad [1]$$

where T_{irad} is the duration of the MT-inducing off-resonance pulse irradiation; M_0 is the fully relaxed longitudinal magnetization; and R_{1sat} is the longitudinal relaxation rate of tissue water in the presence of MT. When MT pulses are sufficiently long ($T_{irad} \gg 1/R_{1sat}$, i.e., steady-state), $M_{sat}(\infty) = M_{ss}$, which is commonly used for the calculation of MTR = $(1 - M_{ss}/M_0)$. R_{1sat} approximates to $(R_1 + Ck_f)$, where C is a constant dependent on the irradiation pulse power (B_1) and offset frequency, and k_f is the MT exchange rate from macromolecules to water protons (23). At higher B_1 , a larger R_{1sat} and a smaller M_{ss} are expected. Commonly, R_{1sat} and M_{ss} are determined by single exponential fitting of time-dependent MT data, which is referred to as a steady-state (SS) method. The SS method has been used for MT imaging, but requires multiple time-dependent data points for accurate fitting.

When the on-resonance inversion pre-pulse is applied prior to application of the MT pulses, the time-dependent magnetization is

$$M_{sat+IR}(T_{irad}) = (-\alpha \cdot M_0 - M_{ss}) \cdot \exp(-R_{1sat} \cdot T_{irad}) + M_{ss}, \quad [2]$$

where α is the inversion efficiency of water protons. With the usage of the on-resonance inversion pre-pulse, the dynamic range also increases from $(M_0 - M_{ss})$ to $(-\alpha M_0 - M_{ss})$, leading to improvement of the time-dependent MT data fitting (24).

Using Eqs. [1] and [2] (by subtracting and adding), R_{1sat} and M_{ss} can be calculated from M_{sat} and M_{sat+IR} at each T_{irad} as:

$$R_{1sat} = -\frac{1}{T_{irad}} \ln \left(\frac{M_{sat} - M_{sat+IR}}{M_0 + \alpha M_0} \right) \approx -\frac{1}{T_{irad}} \ln \left(\frac{M_{sat} - M_{sat+IR}}{2M_0} \right), \text{ and} \quad [3]$$

$$M_{ss} = \frac{(M_{sat} + M_{sat+IR}) - (M_0 - \alpha \cdot M_0) \cdot \exp(-R_{1sat} \cdot T_{irad})}{2 \cdot (1 - \exp(-R_{1sat} \cdot T_{irad}))} \approx \frac{M_{sat} + M_{sat+IR}}{2 - (M_{sat} - M_{sat+IR})/M_0} \quad [4]$$

This approach is referred to as an intermediate state (IS) method, which requires data without MT irradiation (M_0) and only two MT measurements, one with an IR pre-pulse (M_{sat+IR}) and the other without IR (M_{sat}), at a single T_{irad} value.

Methods

Computer simulations

The accuracy of our proposed IS method is dependent on T_{irad} and the off-resonance saturation RF power level, ω_1 . In order to determine T_{irad} and ω_1 (radian/s) for *in vivo* studies, computer simulations were performed with Henkelman's modified Bloch equations (Eqs. [1]–[6] in ref. (22)). Irradiation duration-dependent $M_{sat}(t)$ and $M_{sat+IR}(t)$ were simulated at different off-resonance RF powers, ranging from $\omega_1/2\pi = 50$ to 490 Hz with an

offset frequency for MT = 4000 Hz. Simulation parameters were: MT-inducing macromolecular fraction = 0.06; the apparent rate constant for magnetization transfer from free water to restricted macromolecular pool (RM_0^b in ref (22)) = 1.7 s^{-1} ($K_{mf}(P_m/P_r)$ in (25)); water T_1 of gray matter at 9.4 T = 2 s (26,27); macromolecule T_1 = 1.7 s (25); tissue water T_2 at 9.4 T = 42 ms (27); and macromolecule T_2 = 10 μs (19). The on-resonance IR pulse does not fully invert the macromolecular magnetization due to the much shorter T_2 compared to pulse length (28), so, we assumed the IR pulse reduces the macromolecular proton signal to 88% of its pre-pulse value (i.e., $0.88M_{m0}$) (29). Then, $R_{1\text{sat}}$ and M_{ss} were calculated at each T_{irad} using Eqs. [3] and [4], respectively, and compared with those determined from the SS method by single exponential fitting with all irradiation duration-dependent data (Eq. [1]). If the difference between values, determined by the SS and IS methods, was less than 10%, then we considered the T_{irad} and $\omega_1/2\pi$ conditions to be acceptable for *in vivo* IS measurements. In addition, to determine the effect of offset frequency to MT effects, simulations were performed with T_{irad} = 400 ms for a 500 to 8000 Hz range.

Animal and human MRI data collection

Animal and human experiments were performed, with approvals by the University of Pittsburgh Animal Care and Use Committee and the University of Pittsburgh Institutional Review Board, respectively. All images were acquired by single-shot, spin-echo (SE) EPI. Experiments were performed without and with on-resonance inversion prior to MT pulses for MT studies. Inversion recovery without off-resonance saturation was measured to calculate T_1 of tissue water (logarithmic scale of 20–22 inversion times ranging 70 ms – 7 s and 90 ms – 9 s, with an inter-image delay = 10 s and 14 s for 3T and 9.4T, respectively). Inversion was achieved by an adiabatic full passage RF pulse (with hyperbolic secant amplitude and hyperbolic tangent frequency modulations); 16 ms duration and 22 μT amplitude for humans, and 6 ms duration and 16.6 μT amplitude for animals. To generate MT effect, a train of off-resonance RF pulses was applied (30); each Gaussian pulse with duration (τ_p), was followed by a spoiler gradient during the inter-pulse delay (τ_d) to suppress residual transverse magnetization. For dependency of $T_{1\text{sat}}$ and M_{ss} on the MT irradiation power level, two different power levels of MT pulses ($\omega_1/2\pi$ = 99–100 and 177 Hz) were used with an off-resonance frequency of 4 kHz away from water resonance frequency where a direct irradiation of water molecules is minimal (31). It should be noted that if a lower offset frequency is used, a lower pulse power is needed to achieve the same MT effect, but direct water saturation is occurring. Twenty to twenty-two different MT durations (T_{irad}) were applied within the range of 0–7 s to test the dependency of T_{irad} on MT metrics obtained with the IS method.

Animal MR experiment—Four male Sprague-Dawley rats weighing 350–450 g were studied on a 9.4-T/31-cm Varian system with a 12-cm actively shielded gradient insert operating at maximum gradient strength of 400 mT/m and a slew rate of 3,333 mT/m/ms. Actively decoupled coils (Nova Medical, INC, MA) were used; a volume coil (inner diameter (ID) = 6.3 cm) for RF transmission and a single loop surface coil (ID = 2.2 cm) for reception. All animals were initially anesthetized with 5% isoflurane and maintained under ~1.2 % in air supplemented with O_2 to attain a total O_2 level of ~30% for the remainder of

the experiment. The animal's rectal temperature was maintained at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$. One coronal image was acquired with parameters: $\tau_p = 198$ ms, $\tau_d = 2$ ms, slice thickness = 2 mm, matrix size = 64 (readout) $\times$ 32 (phase-encode), FOV = 3.0×1.5 cm², TE = 18 ms, and number of averages = 10. We fixed inter-preparation delay (including data acquisition and delay before next spin preparation) as 14 s to ensure full relaxation of magnetization. The total experimental time for one MT power level was $[34$ s (the summation of all 22 different MT spin preparation periods) + 22 saturation data points $\times$ 14 s] $\times$ 2 (with and without inversion) $\times$ 10 averages = 6840 s; the imaging time was 3420 s for the SS method and ~430 s for the IS method.

Human MRI experiment—Four healthy male subjects (age: 27–45) were scanned on a 3-T Siemens Allegra scanner with a gradient coil operating with a maximum gradient strength of 40 mT/m and a slew rate of 400 mT/m/ms. A CP volume head coil (ID = 25 cm) was used for RF excitation and receive. Two image slices were acquired with imaging parameters: $\tau_p = 65$ ms, $\tau_d = 5$ ms, slice thickness = 5 mm, matrix size = 64×64 , FOV = 24×24 cm², inter-preparation delay = 10 s, TE = 40 ms, and number of averages = 1. Total experimental time for one MT power level was $[32$ s (the summation of all 20 different MT spin preparation periods) + $(20$ saturation times $\times$ 10 s)] $\times$ 2 (with and without inversion) = 464 s; the imaging time was 232 s for the SS method and ~31 s for the IS method.

Data processing

T_1 and inversion efficiency were determined by fitting data to $S(TI) = 1 - 2a \cdot \exp(-TI/T_1)$. $T_{1\text{sat}}$ and M_{ss}/M_0 values were calculated on a pixel-by-pixel basis and analyzed in gray matter (GM) and white matter (WM) regions-of-interest (ROIs). For rats, cortical and white matter regions were defined based on a rat brain atlas (32). For humans, tissue segmentation was performed on an inversion recovery images (TI = 1400 s) by probability maps (probability > 0.8) available in Statistical Parametric Mapping software (33).

M_{ss}/M_0 and $R_{1\text{sat}}$ were obtained by two separate methods.

- i. Curve fitting of time-dependent MT data without inversion was performed using Eq. [1] as a reference (SS method).
- ii. MT metrics were determined with Eqs. [3] and [4] from data sets with and without an inversion pulse at each T_{irad} (IS method).

Then, values determined by the SS and the IS approaches were compared. Voxel-wise comparisons were performed with Pearson's linear correlation analysis, and correlation coefficients were reported for all subjects.

Results

Figure 1 shows simulation results with various off-resonance frequencies, irradiation power levels, and durations. The offset frequency of MT pulses can influence MT effects significantly. Fig. 1A shows M_{ss} for various MT offset frequencies. When a lower offset frequency is used, a lower pulse power is sufficient for achieving the same M_{ss} and, consequently, the same MT effect. However, reducing the offset frequency can cause the

direct saturation of water. In our simulation and experimental studies, we chose an offset frequency of 4 kHz. R_{1sat} and M_{ss} determined at each T_{irad} with the IS method were compared to those obtained with the SS method, and marked with filled symbols when the error was within 10% of the fitted value (see Fig. 1B and C). The shortest T_{irad} for achieving <10% measurement errors with the IS method is plotted as a function of $\omega_1/2\pi$ in Fig. 1D. At the higher MT irradiation power, the shorter T_{irad} is sufficient for reaching the steady state condition and can be used for R_{1sat} determination; T_{irad} needs to be 400 ms for $\omega_1/2\pi$ of 170 Hz, and 600 ms for $\omega_1/2\pi$ of 130 Hz. However, M_{ss} was within 10% of error for all $\omega_1/2\pi$ values when T_{irad} 300 ms. R_{1sat} and M_{ss} determined using the IS method from simulated data with $\omega_1/2\pi = 170$ Hz at $T_{irad} = 400$ ms were 9.0 % and 8.1% different from the corresponding values determined with the SS method. Thus, these imaging parameters were selected for *in vivo* experiments.

Experimental MT saturation data (M_{sat}/M_0 signals) in the ROI of GM (solid lines in Fig. 2A and 2B) and WM (dotted lines in Fig. 2A and 2B) were acquired with and without on-resonance inversion prior to MT off-resonance irradiation at two different power levels. The inversion efficiency (α) was measured to be 0.96 ± 0.001 and 0.95 ± 0.01 at 9.4T and 3T, respectively. T_1 of gray matter and white matter without MT effects were 2.06 ± 0.01 s and 1.66 ± 0.04 s at 9.4 T, and 1.65 ± 0.07 s and 0.98 ± 0.06 s at 3 T, respectively. Note that MT irradiation duration in human 3T studies was limited to ~ 2 s at $\omega_1/2\pi = 177$ Hz (red color symbols in Fig. 2B) due to the SAR limitation. At each T_{irad} before the zero-crossing point, R_{1sat} and M_{ss} values were calculated using Eqs. [3] and [4], respectively, and compared with those determined by fitting with Eq. [1] (see Fig. 2C–2F). In both rat and human studies, R_{1sat} and M_{ss} values agree between SS (fit) and IS methods at an off-resonance irradiation duration of >350 ms (green shadowed regions), except human $\omega_1/2\pi = 177$ Hz data. It is also noted that due to insufficient human data points for $\omega_1/2\pi = 177$ Hz, R_{1sat} and M_{ss} values determined by the SS method (closed red squares) contain errors. Our experimental finding is also consistent with simulation data.

Better agreements between SS and IS approaches were observed at the higher power irradiation condition (177 Hz), because the saturation of macromolecules is more effective. Thus, pixel-wise T_{1sat} and M_{ss}/M_0 values were calculated at $\omega_1/2\pi = 177$ Hz with the IS method at each T_{irad} value of 0.35 s to 0.75 s, and were compared with those obtained by the SS method (Fig. 3 for rat and Fig. 4 for human). In both animal and human maps, similar GM and WM contrasts were observed for SS and IS (Figs. 3A and 4A). Based on pixel-wise correlations between IS and SS values in one subject (Figs. 3B–3C and 4B–4C) and in all subjects (Figs. 3D and 4D), T_{1sat} and M_{ss}/M_0 values agree well between SS and IS at T_{irad} of 0.35 to 0.75 s. A slight mismatch was observed between IS and SS in human data due to fitting errors in calculating the SS maps, but values measured with the IS method agreed well with each other for different T_{irad} (see Fig. 4A). Overall, these data show that the IS method at short T_{irad} can measure M_{ss} and T_{1sat} accurately.

Discussion

This study shows a simple method for the fast measurement of T_{1sat} and M_{ss} using a single T_{irad} MT method with and without the on-resonance inversion pulse prior to off-resonance

MT irradiation. Our new approach, in conjunction with EPI data collection, reduces off-resonance irradiation duration significantly, and, consequently, alleviates the SAR concern associated with long off-resonance irradiation pulses, especially at ultra-high magnetic fields. This technique also reduces imaging time significantly; if 10 points are needed for fitting of multi- T_{irad} data, then the imaging time shortens by ~ 5 times when our new approach is used. In our 3 T studies, only ~ 31 s (= with 3 measurements; M_0 , MT saturation with and without inversion preparation, single $T_{\text{irad}} = 350\text{--}500$ ms) is needed for MTR and T_{1sat} imaging.

Our EPI approach has advantages over conventional MT gradient-echo imaging, which uses a short off-resonance pulse for each TR and reaches the steady-state condition over multiple TR periods (19,20). First, although the implementation of the conventional technique is easy on clinical scanners, the image contrast is contributed by the MT effect induced by off-resonance pulses and the longitudinal saturation of free water during TR. Therefore, the desired MTR level is reached by adjusting multiple MT pulse parameters (including TR and flip angle), and by higher RF deposition compared to our approach. Second, this conventional method cannot obtain T_{1sat} , which is also an important parameter.

In our experimental data, T_{1sat} and M_{ss} obtained with the IS method agree well with the values determined by the SS method in animal studies at 9.4 T, but less well with those in human studies at 3 T. The 9.4 T animal scanner allows a shorter delay (τ_d) to pulse duration (τ_p) ratio for MT (delays are only 1% of the total pulse train duration), resulting in less magnetization recovery during delays; since tissue T_1 is relatively long at 9.4 T, this condition approaches a continuous wave. On the other hand, the 3T human scanner requires a longer delay between MT RF segments and the T_1 of tissue is relatively shorter, thus, MT data are affected by longitudinal magnetization recovery during delays, and, consequently, the measured T_{1sat} is longer than the actual T_{1sat} obtained with continuous MT saturation. M_{ss}/M_0 ratio (consequently MTR_{ss}) is also affected by this phenomenon, and it induces a discrepancy between SS and IS methods. Especially at $\omega_1/2\pi = 177$ Hz, we could not obtain data points with sufficiently long T_{irad} for the SS method due to the SAR limit, so the difference between IS and SS methods is even larger. In our specific application, a relatively long inter-pulse delay time was employed to achieve long T_{irad} within the SAR limit for comparing SS vs. IS methods. However, a shorter delay between off-resonance saturation pulses can be used for the IS approach when a short duration of T_{irad} is applied.

Our studies have a few concerns. (i) The complete selective saturation of macromolecule is assumed. This condition may not be satisfied in the equilibrium state, especially at lower MT power. However, our experimental data from the SS method agree well with those from the IS method regardless of irradiation power levels (Fig. 2C and 2E), and our 9.4-T data (Fig. 2C and E) are also consistent with theoretical simulation data (Fig. 1A and B). This indicates that this assumption is valid or does not significantly affect our approach. (ii) Only 1 to 2 slices were used for our studies. In terms of multi-slice imaging studies, different slices are acquired sequentially after MT preparation, similar to any magnetization-prepared EPI study. Thus, MT-prepared signals recover during the imaging acquisition period and reduces MT effects in later-acquired slices. (iii) It is unknown whether CSF with no MT effect causes an error in our approach with inversion. If only CSF is considered in our

approach, R_{1sat} calculated with Eq. [3] = R_1 of CSF and M_{sat} with Eq. [4] = M_0 . Thus, any CSF contribution to the partial volume effect for MT will be same with conventional MT techniques and SS method. (iv) We assumed the same T_{1sat} values for the with and without on-resonance inversion pulse conditions of the IS method. However, the inversion pulse is typically longer than T_2 of immobile macromolecules ($\sim 10 \mu s$), but is much shorter than T_2 of free water protons ($\sim$ tens of millisecond), thus selectively inverting the free water proton pool while having a limited effect on the immobile macromolecular proton pool. The resulting recovery function is biexponential due to coupling between the free water and immobile macromolecular proton pools, which influences the fast relaxation (34). Gochberg and Gore applied this phenomenon to quantify MT metrics for phantoms and animals (25,29). Since our model did not consider this cross-relaxation between the two pools, error could be produced in estimating the MT metrics by the IS method. However, it is not easy to measure how much of the macromolecular pool is partially inverted by a long on-resonance inversion pulse. Based on our simulation with Henkelman's modified Bloch equations, the mismatch of MT metrics calculated between SS and IS methods increases when the macromolecules are inverted less by the on-resonance inversion pulse. For example, when $\omega_1/2\pi = 170$ Hz, the differences of T_{1sat} and M_{ss} between the IS and SS methods are 6.7% and 5.2%, respectively, if the macromolecular magnetization = 0.88 (i.e., $0.88M_{m0}$) following inversion; and 5.5% and 4.4%, respectively, if the macromolecular magnetization = 0.50. However, the mismatch between SS and IS methods is insignificant, regardless of the spin status of macromolecules, when the power level of off-resonance RF irradiation is sufficiently high (less than 10% difference when $\omega_1/2\pi > 130$ Hz at $0.88M_{m0}$). This indicates that small differences in T_{1sat} values with and without inversion does not significantly influence the estimation of MT metrics using the IS method when relatively high MT saturation power is applied.

In summary, both T_{1sat} and steady-state M_{ss} may provide better information on pathological brain changes (13,15,17) and can be simultaneously determined from transient MT data obtained at a single off-resonance saturation duration with and without an inversion preparation. This simple approach needs relatively short MT saturation duration, consequently reducing experimental time. The shortest T_{irad} at the highest power level within the SAR limitation is expected to be the ideal condition; $T_{irad} = \sim 400$ ms and $\omega_1/2\pi = \sim 200$ Hz would be optimal for a 3 T scanner. This method can be highly useful in high magnetic field human studies, because a long duration of high RF power is usually very difficult within the SAR limits.

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Fig. 1. Simulation results of MT effects with various offset frequencies, power levels and durations

The influence of MT offset frequency to M_{ss}/M_0 (A) was simulated with $T_{irad} = 400$ ms. When a lower offset frequency is used, a lower pulse power is sufficient for achieving the same MT effect. However, reducing offset frequency can cause the direct saturation of water. Thus, we chose an offset frequency of 4 kHz for further simulations. R_{1sat} (B) and M_{ss} (C) determined with the IS method at different MT pulse durations vs. the SS method were compared. Twenty-three different off-resonance RF powers ranging from $\omega_1/2\pi = 50$ to 490 Hz were simulated for gray matter at 9.4 T. Only five MT power levels were selected for display purposes. SS values (marked as “Fit”) were obtained with Eq. [1] from multiple T_{irad} MT data, while R_{1sat} and M_{ss} were determined at each T_{irad} with Eqs. [3] and [4], respectively. Filled symbols: IS results less than 10% difference from SS results. (D) The shortest MT duration was determined at each MT power for achieving <10% errors of M_{ss} and T_{1sat} with the IS method. At higher $\omega_1/2\pi$, a shorter MT pulse duration can be used for obtaining accurate R_{1sat} and M_{ss} with the IS method.

Fig. 2. Averaged experimental M_{sat}/M_0 , $R_{1\text{sat}}$, and M_{ss}/M_0 of rat(left column) and human brains (right column)

(A–B) Averaged MT saturation curves (M_{sat}/M_0 signals) in GM (solid lines) and WM (dotted lines) with (filled symbols) and without (open symbols) on-resonance inversion pulse prior to MT irradiation at two different power levels (green circles: $\omega_1/2\pi = 99\text{--}100$ Hz, red squares: 177 Hz). The MT irradiation duration was limited to ~ 2 s at $\omega_1/2\pi = 177$ Hz (red squares) for humans at 3T. The averaged values of $R_{1\text{sat}}$ (C and D) and M_{ss}/M_0 (E and F) from GM (red rectangles) and WM (blue diamonds) of rat and human brains. SS values (marked as “Fit”) were obtained with Eq. [1] from multiple T_{irad} MT data, while $R_{1\text{sat}}$ and M_{ss} were determined at T_{irad} with Eqs. [3] and [4], respectively. Two different power levels of off-resonance MT irradiation were applied; $\omega_1/2\pi = 99$ or 100 Hz (open symbols) and $= 177$ Hz (closed symbols). Data determined by the IS method at T_{irad} of 350 ms (green shadowed regions) agree well with those by the SS method. *: significantly different between IS and SS values ($p < 0.01$, paired t-test). Our data indicate that MT

metrics can be obtained by MT measurements with and without inversion pre-pulse, but with significantly reduced off-resonance irradiation duration.

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Fig. 3. Pixel-wise M_{ss}/M_0 and T_{1sat} of rat brain obtained with SS and IS methods

Only data with $\omega_1/2\pi = 177$ Hz were used. To show the robustness of our approach, M_{ss}/M_0 and T_{1sat} maps were calculated using Eqs. [3] and [4] at each T_{1rad} between 0.35 and 0.75 s, and compared with maps obtained from fitting using Eq. [1]. (A) Maps obtained using three T_{1rad} values (0.45 s, 0.55 s and 0.65 s) were chosen in a representative rat for display purposes. Similar contrasts between SS and IS maps were observed. Pixel-by-pixel comparisons of M_{ss}/M_0 (B) and T_{1sat} (C) maps between IS and SS methods are shown for two off-resonance irradiation durations in one animal. Coefficient of correlation (CC) values were 0.77 and 0.70 for M_{ss}/M_0 , and 0.59 and 0.62 for T_{1sat} , at T_{1rad} of 0.45 s and 0.65 s, respectively. (D) All animals' data were used in the correlation analysis of M_{ss}/M_0 (red bars) and T_{1sat} (green bars), determined by the SS method vs. the IS method at each T_{1rad} .

Fig. 4. Pixel-wise M_{ss}/M_0 and T_{1sat} of human brain obtained with SS and IS methods

Only data with $\omega_1/2\pi = 177$ Hz were used. To show the robustness of our approach, M_{ss}/M_0 and T_{1sat} maps were calculated using Eqs. [3] and [4] at each T_{1rad} between 0.35 and 0.63 s, and compared with maps obtained using Eq. [1]. (A) Maps obtained using T_{1rad} values (0.35 s, 0.49 s and 0.63 s) were chosen in one human subject for display purposes. Maps from the IS method at different T_{1rad} agree well with each other, showing its robustness. However, a slight mismatched contrast was observed between IS and SS, which is caused by insufficient data points for the SS method. (B–C) M_{ss}/M_0 and T_{1sat} values at two T_{1rad} were correlated with those measured by the SS method in one subject. Coefficient correlation values were 0.73 and 0.84 for M_{ss} , and 0.77 and 0.75 for T_{1sat} , at T_{1rad} of 0.35 s and 0.63 s, respectively. (D) All subjects' data were used in the correlation analysis of M_{ss} (red bars) and T_{1sat} (green bars), determined by the SS method vs. the IS method at each T_{1rad} . Pixel-wise M_{ss}/M_0 values from IS and SS methods are highly correlated (B and D), but T_{1sat} values are less correlated (C and D).