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Magnetization transfer using inversion recovery during off-resonance irradiation

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Abstract

Estimation of magnetization transfer (MT) parameters in vivo can be compromised by an inability to drive the magnetization to a steady state using allowable levels of radiofrequency (RF) irradiation, due to safety concerns (tissue heating and specific absorption rate (SAR)). Rather than increasing the RF duration or amplitude, here we propose to circumvent the SAR limitation by sampling the formation of the steady state in separate measurements made with the magnetization initially along the -z and +z axis of the laboratory frame, i.e. with or without an on-resonance inversion pulse prior to the off-resonance irradiation. Results from human brain imaging demonstrate that this choice provides a tremendous benefit in the fitting procedure used to estimate MT parameters. The resulting parametric maps are characterized by notably increased tissue specificity as compared to those obtained with the standard MT acquisition in which magnetization is initially along the +z axis only.

Keywords: Exchange; Solid pool; Brain imaging; Parametric mapping

1. Introduction

The exchange of bulk water protons with the protons contained in the macromolecules generates the so-called magnetization transfer (MT) effect when the "solid" pool is saturated by placing a continuous-wave (CW) radiofrequency (RF) pulse several kHz off resonance from water [1]. By progressively incrementing the duration of the off-resonance pulse, the T_1 of water in the presence of saturation (T_{1sat}) and the steady-state (SS) magnetization (M_{ss}) can be estimated. In addition, the forward exchange rate from the solid to the free pool, k_f, can be calculated as $(1-M_{ss}/M_0)/T_{1sat}$. This expression for k_f is valid when complete saturation of the solid pool is achieved, and in the absence of off-resonance artifacts. Attempts to provide a quantitative description of the MT effect in the case of incomplete saturation and in the presence of off-resonance artifacts led to the introduction of an analytical description of the two-pool model (for review, see [2]), whereas more extended and realistic models can even involve more than two pools of exchanging spins [3,4].

The MT effect is an attractive MR imaging modality for clinical applications, because the interaction of bulk water protons with the protons contained in the macromolecules can ultimately provide information about tissue integrity. However, the detection of the MT effect in clinical practice is usually limited to the measurement of a qualitative MT ratio (MTR), which is the result of the combination of several fundamental quantities, and is dependent on the acquisition parameters [5]. Likely due to this limitation, controversial results about MTR differences have been reported in literature, for instance in the brains of schizophrenic patients as compared to control subjects [6–9]. In multiple sclerosis, weak correlations of MTR with disability parameters have also been found [10]. On the other hand, the acquisition and processing MT protocols for obtaining quantitative MT parametric maps, which are based on the two-site exchange

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model [11], are generally not straightforward in clinical MRI practice, and provide parametric maps with limited tissue contrast and specificity.

The basic source of instability in the fitting procedure of T_{1sat} and M_{ss} originates from the impossibility of using MT pulses that are long enough to achieve the steady state, due to safety limitations imposed by the specific absorption rate (SAR) of RF power deposition. To circumvent this limitation, here we suggest a novel protocol for the acquisition of MT in vivo. The method is easy to implement, as it relies on classical CW MT measurements, with the difference that two consecutive sets of measurements are acquired with the magnetization initially along the -z or +z axis, i.e. with or without an on-resonance inversion prior to the off-resonance irradiation (Fig. 1). Whereas the usage of inversion recovery approaches have been suggested to measure MT effects ([12,13] and reference therein), the implementation of an on-resonance inversion pulse prior to the off-resonance irradiation has not been exploited so far. In vivo results from the human brain are reported to demonstrate the efficacy of the proposed approach.

2. Methods

Five healthy subjects (35 average years old) were investigated on a 90-cm-bore 4 T magnet (OMT, Inc., Oxon, UK) with Varian INOVA^{UNITY} console (Varian Inc./Agilent, Palo Alto, CA). A transverse electromagnetic design (TEM) volume coil [14] was used for signal transmission and reception from the human brain. Images were acquired using fast spin-echo readout, TR=9-10 s (depending on the coil loading), number of echoes=16, TE=0.073 s, matrix 256×256, FOV=25.6×25.6 cm^2 and slice thickness=4 mm. The MT experiment used a 6 kHz off-resonance CW-pulse with incremental duration (0.0, 0.3, 0.6, 0.9, 1.2 s) and $\omega_1^{max}/(2\pi)$=0.15 kHz, applied prior to the imaging readout. Separate measurements were performed with the magnetization initially along the +z or –z axis, i.e. without or with initial global inversion achieved by an adiabatic full passage pulse of the hyperbolic secant family (pulse length=6ms, $\omega_1^{max}/(2\pi)$= 1.2 kHz, bandwidth ~3.3 kHz). With this choice of parameters, the duration of the MT protocol was ~25 min. First order shim terms were manually adjusted using the global, unlocalized water signal, typically reaching a water line-width ~20-30 Hz. Data were collected from an axial (transverse) section at the level of the corpus callosum, for optimal visualization of grey and white matter structures. The RF power delivered to the coil was limited to a safe operating range using the hardware monitoring module of the Varian console. In addition, the RF power output over the full range of settings used in these experiments was measured with an oscilloscope connected to the coil port. From these measured values, the average RF power delivered to the coil was computed by integration of all RF pulses in the sequence, and SAR was estimated assuming a tissue load of 3 kg in the volume coil. When using the longest pulse, the estimated SAR was always below the Food and Drug Administration limit of 3 W/kg averaged over the head for 10 min http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072686.htm).

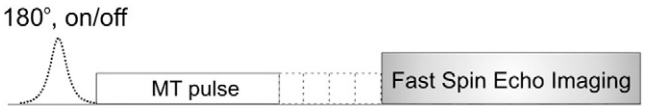

Fig. 1. Pulse sequence for the described MT protocol. The frequency of the MT pulse is 6 kHz off-resonance, and the peak amplitude ($\gamma B_1/2\pi$) is 150 Hz for human studies. The dashed squares indicate incremental durations of the MT pulse, which is applied immediately prior to the excitation pulse of the imaging module. The MT measurement is performed twice, with and without an on-resonance inversion pulse prior to the off-resonance irradiation, with no time delay. The time between the inversion pulse and the excitation pulse of the imaging module is determined by the duration of the MT pulse, thus leading to inversion recovery that occurs entirely in presence of the off-resonance irradiation. In this study, the imaging module consisted of a fast SE readout with 90° excitation, while the MT pulse consisted of CW irradiation. However, other types of imaging readout are possible, as well as other pulsed approaches can be implemented instead of CW irradiation to achieve the off-resonance saturation.

2.1. Estimation of MT parameters

The parameters T_{1sat} and M_{ss} were calculated on a pixel-by-pixel basis from the time-course of signal intensity (SI) using a non-linear regression algorithm with the following functions:

$$SI(t) = M_0 e^{-t/T_{1sat}} + M_{ss}\left(1 - e^{-t/T_{1sat}}\right) \quad (1)$$

$$SI(t) = -M_0 e^{-t/T_{1sat}} + M_{ss}\left(1 - e^{-t/T_{1sat}}\right) \quad (2)$$

where M_0 is the fully relaxed magnetization in the absence of RF, and t is duration of the CW pulse. Eqs. (1) and (2) apply when magnetization is first placed in the positive or negative hemispheres of the laboratory frame, respectively. Note that the in vivo system is generally characterized by multiple pools of protons (for instance, characterizing white and grey matter), which could invalidate the simple description based on mono-exponential functions provided by Eqs. 1 and 2. However, the mono-exponential approximation seems a reasonable choice for parametric maps which are generated on a pixel-by-pixel basis. In addition, the presence of the on-resonance inversion pulse prior to the CW irradiation might slightly modify the conditions of saturation of the solid pool as compared to the case of Eq. 1, especially at short saturation times. Only when the effect of the inversion pulse is inconsequential as compared to the effect of the subsequent off-resonance irradiation for saturating the solid pool, there is no conceptual difference between Eq. 1 and 2. If this is the case, then the magnetization of the observed free water pool either decays or recovers in presence of the off-