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A rapid approach for quantitative magnetization transfer imaging in thigh muscles using the pulsed saturation method ☆

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ABSTRACT

Quantitative magnetization transfer (qMT) imaging in skeletal muscle may be confounded by intramuscular adipose components, low signal-to-noise ratios (SNRs), and voluntary and involuntary motion artifacts. Collectively, these issues could create bias and error in parameter fitting. In this study, technical considerations related to these factors were systematically investigated, and solutions were proposed. First, numerical simulations indicate that the presence of an additional fat component significantly underestimates the pool size ratio (F). Therefore, fat-signal suppression (or water-selective excitation) is recommended for qMT imaging of skeletal muscle. Second, to minimize the effect of motion and muscle contraction artifacts in datasets collected with a conventional 14-point sampling scheme, a rapid two-parameter model was adapted from previous studies in the brain and spinal cord. The consecutive pair of sampling points with highest accuracy and precision for estimating F was determined with numerical simulations. Its performance with respect to SNR and incorrect parameter assumptions was systematically evaluated. QMT data fitting was performed in healthy control subjects and polymyositis patients, using both the two- and five-parameter models. The experimental results were consistent with the predictions from the numerical simulations. These data support the use of the two-parameter modeling approach for qMT imaging of skeletal muscle as a means to reduce total imaging time and/or permit additional signal averaging.

1. Introduction

Quantitative magnetization transfer (qMT) MRI [1] has been developed to characterize the spatial distribution of the relative contents of the macromolecular and free water proton pools of biological tissues. Specifically, qMT MRI fits appropriately acquired MRI data to a two-pool model of magnetization exchange between macromolecules and protons, providing estimates of the relaxation and exchange rates of macromolecular and free water protons as well as the ratio of the sizes of these two pools (the pool size ratio, PSR). A number of different approaches have been developed for acquiring and analyzing qMT MRI data, including continuous-wave (CW) saturation [1], pulsed saturation [2–4], selective inversion recovery (SIR) [5–7], and stimulated echo [8] methods. Though there has been no quantitative comparison of all these methods, the pulsed saturation method is the most widely adopted method, and various strategies for rapid qMT imaging have been developed [9–11].

Several studies have demonstrated the potential clinical and translational value of qMT. For example, the PSR is correlated with myelin content in white matter [9,12]. QMT studies have also been performed in healthy skeletal muscles [13–15] and in a murine model of inflammation [16]. It was demonstrated that PSR may also serve as a biomarker of inflammation [16]. However, quantitative MRI studies in skeletal muscle are challenged by low signal-to-noise ratio (SNR), caused by the short T_2 values of water protons (~30 ms at 3.0 T), as well as static (B_0) and radiofrequency transmit (B_1^+) field inhomogeneities [15]. In a number of muscle diseases, fat infiltration is a major pathological component. It is possible that this third pool of protons, if unaccounted for quantitatively, would also confound qMT parameter estimations.

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Another potential confounding factor for qMT in muscle is related to the large number of data points required to fit a full model. As noted previously [15], voluntary and involuntary motion artifacts can occur during data collection (~10 min for a full dataset). These movements can result from gross subject movements, prolonged muscle contraction, and/or brief twitches. For translational and rotational bulk motions, image registration can be performed using a rigid-body registration algorithm. However, muscle contractions induce non-rigid deformations as well, making it challenging to register such images. More seriously, motion during the data collection process may introduce artifacts in the images that cannot be corrected using registration methods, and the parameter estimates may be biased as a result. To mitigate issues such as these, a two-point sampling approach was recently described for qMT studies of the brain and spinal cord [10,11]. In this approach, values are assumed for model parameters that do not undergo substantial biological variation or to which the model is relatively insensitive. By reducing the number of unknowns in the model, a reduced data sampling approach can be used and iterative curve-fitting is obviated.

The overall goals of this work were to 1) determine the quantitative effects of these sources of error and 2) propose and test strategies for reducing these errors. First, we investigated the effect of an additional fat component in pulsed-MT parameter fitting through numerical simulations. It was found that PSR would be underestimated in the presence of an additional fat component. For *in vivo* qMT image data collection in healthy controls and patients, a 1-3-3-1 binomial water selective excitation pulse was then used to minimize the fat signal contribution to the qMT data. Second, to minimize motion artifact-induced bias in parameter fitting, the two-point fitting approach [10,11] was adopted and applied to a set of data acquired with a conventional 14-point sampling scheme. Although this method has been previously applied in the central nervous system, muscle has significantly different MT and relaxation parameters compared to those in brain and spinal cord. A combination of numerical simulations and *in vivo* data indicated that the two-point scheme is more robust at low SNR levels, with the capability to minimize the occurrence and effects of motion artifacts and reduce total acquisition time.

2. Theory

2.1. Pulsed-MT model

All simulations and data processing are based on the model proposed by Ramani *et al.* [17]. For a two-pool exchange system, which includes the free water pool (A) and the macromolecular pool (B), the signal equation is written as [18]:

$$S_{qMT}(\omega_1,\Delta f)=\frac{S_0\left(R_B\left[\frac{RM_0^AF}{R_A}\right]+R_{RFB}+R_B+RM_0^A\right)}{\left[\frac{RM_0^AF}{R_A}\right](R_B+R_{RFB})+\left(1+\left[\frac{\omega_{1CWPE}}{2\pi\Delta f}\right]^2\left[\frac{1}{R_AT_2^A}\right]\right)(R_{RFB}+R_B+RM_0^A)} \tag{1}$$

where S_{qMT} is the observed MT-weighted signal; S_0 is the observed signal without the saturation pulse; RM_0^A is the exchange rate from the macromolecular pool to the free water pool; F is the PSR, defined as M_0^B/M_0^A; R_A is the longitudinal relaxation rate of the free water pool; T_2^B and T_2^A are the transverse relaxation time constants of the macromolecular and free water pools, respectively; R_B is the longitudinal relaxation rate constant of the macromolecular pool; and R_{RFB} is the rate constant for saturation of longitudinal magnetization of the macromolecular pool. It is noted that R_B is often assumed to be 1.0 s^{-1} due to the weak dependence of the measured signals on this parameter [1]. For *in vivo* tissue, a super-Lorentzian lineshape [19] is often adopted for calculating R_{RFB}:

$$R_{RFB}(\Delta f,\omega_1)=\omega_{CWPE}^2\sqrt{2\pi}\left[T_2^B\int_0^1\frac{1}{|3u^2-1|}\exp\left(-2\left(\frac{2\pi\Delta fT_2^B}{3u^2-1}\right)^2du\right)\right] \tag{2}$$

The average power, ω_{CWPE}, is calculated as:

$$\omega_{CWPE}=\sqrt{\frac{\int_0^\tau\omega_1^2dt}{TR}} \tag{3}$$

where τ is the saturation pulse width and TR is the repetition time of the pulse train. The fitted qMT parameters are: S_0, RM_0^A, F, T_2^B, and T_2^A. In addition, R_A is calculated from an independent estimate of the observed R_1 of the free water pool, noted as R_{AOBS} [17]:

$$R_A=\frac{R_{AOBS}}{1+\frac{RM_0^A\frac{F}{R_A}(R_B-R_{AOBS})}{R_B-R_{AOBS}+RM_0^A}} \tag{4}$$

A full pulsed-MT protocol thus includes four sets of measurements: T_1 mapping for R_{AOBS}, B_1^+ mapping to correct the irradiation power, B_0 mapping to correct the RF frequency offsets, and the pulsed saturation data collection.