Correcting RF Inhomogeneities in Skeletal Muscle Magnetization Transfer Maps

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Introduction Quantitative MR methods such as magnetization transfer (MT) ratio (MTR) mapping may provide valuable measures of disease severity and activity in neuromuscular conditions such as the muscular dystrophies. Pathologies affecting skeletal muscle have been shown to reduce muscle MTR significantly [1] and in a manner which is strongly associated with clinical severity [2]. There is an indication that MTR reductions in so-called 'normal-appearing muscle' can occur before these changes become apparent on conventional MRI [2]. However, the MT signal is strongly dependent on the local rf transmit-field (B1) homogeneity, which can be variable, particularly at 3T. In order to increase the sensitivity of muscle MTR maps to pathological changes, B1 variation should ideally be measured and taken into account. In this work we demonstrate a simple correction scheme for muscle MTR maps using the double-angle B1 mapping method (DAM) [3].

Theory Using a 2-pool quantitative model of MT (qMT) it can be shown that the error on the measured MTR (MTR_M) scales approximately linearly with the underlying B1 error [4,5]. Using a qMT model and previously measured MT properties of skeletal muscle [6], we have established that the relationship $MTR_{True} = MTR_M / (k \times B1_{Err} + 1)$ (Eq. 1) holds true for the entire MTR map where k=m/c is a scaling factor determined from the gradient m and intercept c of a linear fit to MTR_M vs. $B1_{Err}$ in a region containing only skeletal muscle.

Methods Both lower limbs of 28 healthy subjects were scanned at 3T (Siemens TIM Trio) operated with the body transmit coil and a surface matrix coil for signal reception. An MT weighted image (M_1) was acquired with a 3D-FLASH sequence (TR/TE=65/3ms, FA=10°, 256x120x40 matrix, 400x190x400mm FOV) preceded by a 10ms Gaussian pulse of nominal flip angle 500° and 1200Hz frequency offset. The sequence was repeated without MT saturation (M_0) and the MTR (p.u.) calculated as $100x(M_0-M_1)/M_0$. Maps of the actual flip angle α were acquired using the double angle method [6] (turbo-spin echo readout (TSE), TR/TE=7000/11ms, α_N=60°, 128x60 matrix) and maps of the B1 error were calculated as $100x(\alpha-\alpha_N)/\alpha_N$. T1-maps were acquired using the Despot-1 method for the purposes of segmentation [7]. All volumes were registered with the FSL software (FSL, FMRIB, Oxford) and analysed with the Python language and Mathematica software. In each subject, normal muscle only regions were created with a fully automated process using a binary mask generated by thresholding the T1 map in the range 1200<T1<1600ms and subsequent erosion with a 2D 3x3 kernel. MTR was plotted vs. B1 error for each voxel in the segmented region and the scaling parameter k determined from a linear fit. The scaling factor k was applied to the whole MTR map using Eq. 1 and individual and group parameters calculated. 12 patients with inclusion body myositis (IBM) and 11 patients with Charcot-Marie disease type 1A (CMT1A) were also imaged as representative neuromuscular conditions.

Results A map of B1 error using the DAM method in the lower-leg of a single subject is shown in Fig. 1a) and the accompanying raw MTR map in Fig 1b). The MTR in each voxel is plotted against B1error for a region containing only muscle in Fig 1c) and a linear fit to the data is overlaid. The gradient and intercept yield a correction factor of $k=7.0x10^{-3}$ for this data set. The corrected MTR map is shown in Fig. 1d). The mean(±sd) k for the 28 healthy subjects was k = $7.1±0.7x10^{-3}$. Correction of the MTR maps reduced the inter-subject coefficient of variation (CoV) of the mean segmented muscle MTRs by 52%. Inter-subject CoVs were reduced by 67.3% and 59.3% in the IBM and CMT1A patients respectively. The muscle MTR mode values were reduced from 35.4 to 33.9 p.u. in IBM and from 34.9 to 32.9 p.u. in CMT1A respectively.
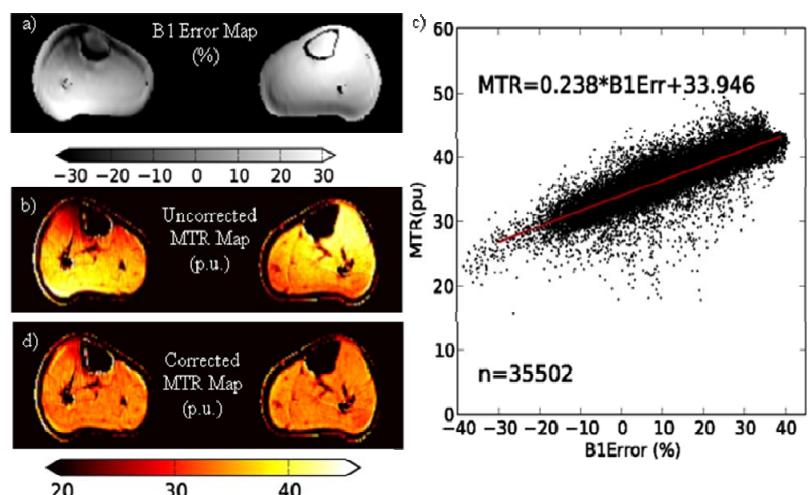
Discussion The B1 maps showed considerable variation in amplitude across the calf, corresponding closely to regions of inhomogeneity in the MTR maps. By performing a linear fit to the muscle voxels, a correction factor was derived which compensated for these variations, resulting in MTR maps with a smooth profile (Fig1b)&d)). The correction process, which was validated using a quantitative 2-pool model of skeletal muscle MT and shown to be independent of the particular MT properties of the tissue, substantially reduced the inter-subject variation in measured MTR parameters of healthy and diseased skeletal muscle. Given this reduction in variability, correction of MTR maps in this manner is likely to further increase the measurement sensitivity of muscle MTR, a quantity demonstrated to be sensitive to subtle processes in diseased muscle. Such a correction scheme is also likely to further strengthen established correlations between MTR and muscle strength [2], enhancing the potential benefits of MTR as an imaging marker in neuromuscular diseases.

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