Test-Retest Reproducibility of MTR, T2 and 3-point Dixon Fat Quantification Methods in Muscle MRI

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Introduction

Recently there has been increasing interest in characterizing neuromuscular disease with quantitative MRI [1,2]. In particular, assessing the degree of fat infiltration in diseased muscles using the so-called multi-point 'Dixon' fat mapping methods is one promising approach [3]. Independent assessment of inflammation and hydration of muscle through changes in the T_2 relaxation time and the magnetization transfer ratio (MTR) are also of potential utility as quantitative markers [4,5]. In order to apply these methods with confidence in patient groups, where considerable variability is present, it is first necessary to evaluate the reproducibility and measurement precision of these techniques in a homogeneous healthy subject cohort. In this work we present normative values and test-retest reproducibility assessments of T_2, MTR and Dixon fat mapping histogram metrics by scanning 8 healthy individuals with the same quantitative MRI protocol on 2 separate occasions.

Methods

Eight subjects, age 28.9±4.5 (mean±sd) yrs, were scanned twice with a 14 day interval between sessions 1 and 2. Both limbs were imaged at the thigh and calf level using bony landmarks to ensure repositioning accuracy between the 2 scans. Imaging was performed at 3T (TIM Trio, Siemens, Erlangen, Germany) in a feet-first supine position, with signal reception from elements of a surface matrix array coil and an array coil in the scanner bed. MTR mapping was performed by acquiring 2 images (3D-FLASH, TR/TE=65/3ms, 10x10mm slices, 256x128matrix, 400mm FOV) with (M_1) and without (M_0) MT preparation (offset frequency 1200Hz) and MTR calculated in percentage units as MTR(p.u.)=100x(M_0-M_1)/M_0. To obtain pseudo-T_2 maps, axial turbo spin-echo images were acquired at 2 echo times (TR/TE1/TE2 5500/16/64ms) and maps calculated assuming a mono-exponential signal decay. A 3-point Dixon acquisition was used to generate water (W) and fat-only (F) images of the same volume using a 2D gradient echo sequence performed at 3 different echo times (TE=3.45, 4.6, 5.75ms, TR=100ms, α=10º, NEX=4, 512x256matrix, 400mm FOV) [6]. Fat fraction maps in % units were calculated using absolute values of F/(F+W). Absolute voxels per bin histograms for each parameter were generated without pre-segmentation from the central 5 slices of each limb in each subject for scans 1&2 with bin widths of 1p.u., 1ms and 1% for MTR, T_2 and fat-fraction respectively. The principle peak corresponding to the muscle signal was modeled with a single Gaussian function to determine the peak position, width and height of the T_2, MTR and fat-fraction histograms for scans 1&2. Intra-class correlation (ICC) coefficients, coefficients of reproducibility and Bland-Altman plots were produced for the pairs of fitted peak positions.

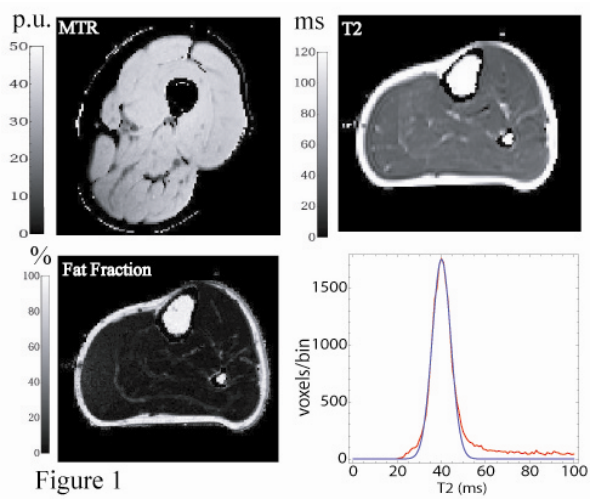

Figure 1

Results

An example MTR map (left thigh), T_2 map (left-calf) and fat-fraction map (left calf) from scan 1 of the same subject are shown in Fig. 1 with a accompanying T_2 histogram (red curve) showing the function fitted to the peak (blue curve). Mean peak positions (±sd) averaged over all subjects and scans were MTR: 37.1±2.0p.u., T_2: 39.9±0.9ms and fat-fraction: 3.5±0.4%. Paired sample t-tests on each of the peak position pairs were non-significant, indicating there was no systematic difference between scan 1 and scan 2 measurements (MTR: t=-1.1, p=0.27, T_2: t=0.1, p=0.92, fat-fraction: t=-0.92, p=0.37). ICC coefficients were 0.84 (MTR), 0.68 (T_2) and 0.33 (fat-fraction). Bland-Altman plots for the histogram peak-positions yielded by the 3 methods are shown in Fig.2 with horizontal lines denoting the mean difference and ±95% limits of agreement. The coefficients of repeatability were 2.5 p.u., 1.5 ms and 0.9% respectively.

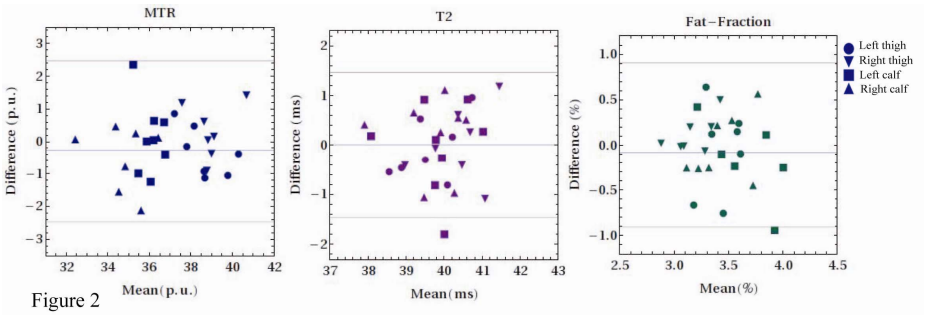

Figure 2

Discussion

The paired acquisitions from scan 1 and 2 were well matched and free from systematic variation, implying reproducible subject positioning and minimal physiological variation within the subjects over the 14 day scan interval. The subjects studied here were homogenous in terms of the distribution of the quantitative MRI measures in the volume histograms. The measured ICC coefficients indicate that the majority of the measured variability was due to differences between subjects rather than inter-scan measurement variation in the MTR and T_2 measurements, and to a lesser extent in the fat-fractions. Bland-Altman plots revealed no skew in the differences between paired measurements and satisfactory limits of agreement. MTR measurements were centered on a mean of around 37 p.u. with slightly higher MTR values in the thigh than in the calf. The absolute accuracy of the T_2 measurements are limited by systematic offset due to sampling at only 2 echo times and the assumption of mono-exponential decay. However, despite this limitation, the inter-scan reproducibility of the pseudo-T_2 values was very satisfactory with a repeatability coefficient of 1.5ms. The fat fractions in the healthy subjects were low and therefore prone to systematic positive bias due to noise. However, despite this, the measured fractions of around 3% were generally repeatable within subjects. Further investigation of fat-fraction reproducibility will be necessary in patient groups where fat-fraction is expected to cover the entire dynamic range up to nearly 100% fat [3].

Conclusion With careful experimental design at 3T the quantitative MRI methods examined showed good reproducibility between scans in a homogenous group of healthy subjects. These results will motivate further verification of reproducibility in more varied patient populations with neuromuscular diseases. Quantitative MRI measures show great promise as markers of neuromuscular disease onset and progression.

[1]Mercuri et. al. JMRI, 25,p433 (2007) [2] Koltzenburg and Yousry, Cur. Op. Neuro., 20, p595 (2007)[3] Wren et. al., AJR, 190, pW8 [4] McDaniel et. al. J. Comp. Ass. Tom. 23, p609 (1999) [5] Sinclair et. al. ISMRM 2009, p3958 [6] Glover and Schneider, MRM, **18**, 371 (1991)