Feasibility and reproducibility of MR fat-fraction measurements in muscle using iterative signal decomposition with a multifrequency fat signal model

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Purpose: Duchenne muscular dystrophy (DMD) is a debilitating muscle disease characterized by progressive fatty muscle infiltration, muscle weakness and eventually death. Several therapeutic approaches have been recently developed[1,2]. To accurately assess the effectiveness of these therapies at the tissue level, quantitative methods for patient follow up are essential because the standard method, biopsy, is invasive and provides only local information. A promising technique to assess fatty infiltration by MR is multiecho chemical shift-based water-fat separation[3,4]. However, in fat quantification the fat signal is commonly modeled as a single peak[5], whereas in reality the fat signal consists of multiple peaks[6]. Recently, Yu et al showed that accounting for the multiple peaks improved fat suppression considerably[4]. However, it is unknown how application of a multi peak fit would affect quantitative assessment of fat fraction. In this study we aim to validate the use of multiple frequency water-fat separation *in vitro*, and test the feasibility and reproducibility of this method *in vivo* in skeletal muscle in healthy volunteers.

Methods: For the in vitro fat fraction measurements a 3-point Dixon technique was implemented where the fat signal is modeled as a spectrum with components of amplitude A_p, at multiple frequencies f_p. The signals S_i at 3 echo times (TE_i) are modeled as,

$$S_i = \left(W + F \cdot 1 / \sum_{p=1}^{n} A_p \cdot \sum_{p=1}^{n} A_p \cdot e^{-j2\pi f_p TE_i} \right) \cdot e^{-j2\pi \phi TE_i}$$

Figure 1: Fat fraction measurements (solid line) in phantom based on a profile of an inclined imaging plane. Single peak (a) and a multifrequency (b) fat signal model. The red line indicates the reference value. Pixels were not averaged.

with W the water density, F the fat density and φ the field map estimate. Fat fraction is obtained as $cF/(W+cF)$, where the factor c corrects for the differences in both proton density and T2 values of fat and water[7]. All images were acquired on a 3T Philips Achieva scanner (Best, NL). In vitro experiments were performed on a bottle filled with vegetable oil and water. Correction factors for proton density (spin echo sequence, TR/TE 5000 ms/6 ms) and T2 (16 multiple spin-echos) were obtained. Scalar coupling effects were accounted for in the signal model. Finally, a 3-pt Dixon technique was used to acquire twenty-five 5 mm thick slices with an angulation of 8°, thus providing a gradual variation of fat fraction in the central slice: $TR/TE_1/\Delta TE$ were 400ms/4.41ms/0.76ms. The flip angle was set to 8°, to minimize the influence of T1 saturation. For signal decomposition a temperature compensated (20°C) version of the fat spectrum from Yu et al. was used: f_p = [72, -340, -442] Hz, A_p = [0.08, 0.15, 0.78]

In vivo scans were conducted in six healthy volunteers (age 29 ± 6 yr), using a 14 cm two-element coil for signal reception. The coil was placed directly below the patella. Dixon scans were conducted as described above without angulation. The centre of the field-of-view was positioned 10 cm below the knee joint space. In all volunteers, T1-weighted (TR 600ms, TE 16ms), proton density (TR 5000ms, TE 6.5ms) and two repeated sets of Dixon scans (TR 400ms, TE 4.41ms) were acquired. Data from the Dixon scans were fitted using both a regular fitting method with the fat signal modeled as one peak and the second using the multipeak method with f_p = [94, -318, -420] Hz, A_p = [0.08, 0.15, 0.78]. For an

Figure 2: Dixon water and fat image

assessment of reproducibility, volunteers were scanned twice on the same day, with a short interval and repositioning in between. The resulting Dixon images were analyzed using MIPAV[8] by drawing regions of interest in muscle and bone marrow in the five middle slices on the co-registered T1 weighted images. Fat fractions were obtained as described above. Reproducibility of the method was determined by calculating the coefficient of repeatability.

Results: In the phantom, the single peak fat model led to a consistently underestimated fat fraction (fig. 1a). The multi peak frequency spectrum shows a clearly improved correspondence to reference values (1b), albeit with an increased noise level for low fat fractions. In the in vivo experiment (fig. 2) the fat fraction was 4.1% (±0.7) in muscle and 93.3% (±0.3) in bone marrow for the single peak fitting method. Using the multi peak fitting method, the fat fraction was slightly higher, 5.1% (±1.0) in muscle and 93.7% (±0.6) in bone marrow. Values were borderline significant for muscle (p=0.09, paired t-test). Coefficient of repeatability (CR) for the two measurements in muscle was 0.73% in single peak and 0.79% in the multipeak method. For bone marrow CR was 0.59% in single and 0.90% in the multipeak method.

Figure 3: Histogram of fat percentage in muscle

Conclusions: In this study we show that the fat fraction in the phantom model is improved by multifrequency modeling of the fat signal. In vitro experiments demonstrated that the improvement is apparent not only in high fat fractions (top left of fig 1a), but also in the mid-range of 50% fat. This could be especially important in the measurements of muscle with increased fatty infiltration, like in DMD where fat percentages are estimated to lie between 5 and 80% in boys of 5 years and older[6]. The in vivo measurements showed that in muscle the fat percentage is slightly lower in the single peak model compared to the multiple peak model. In bone marrow, this difference is less apparent, possibly because of the T2 decay in trabecular bone. Finally, we have shown that the method is highly reproducible. Therefore, this method could be an important tool in the quantitative evaluation and follow up of fatty infiltration in patients with muscle disease.
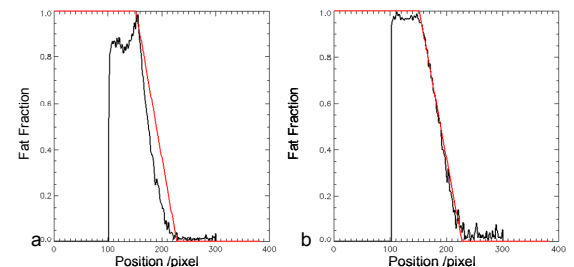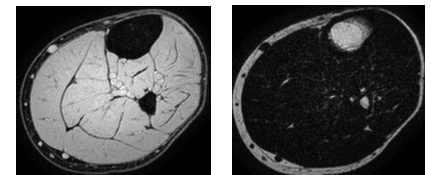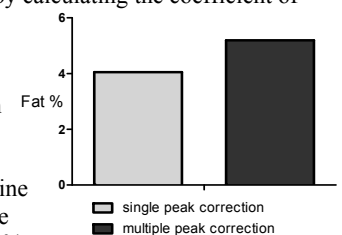
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