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Effect of Gd-DOTA on fat quantification in skeletal muscle using two-point Dixon technique – preliminary data

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ABSTRACT

Purpose: To assess differences in fat signal fraction (FSF) in skeletal muscle as determined by two-point Dixon technique at 3T before and after application of intravenous gadoterate meglumide (Gd-DOTA).
Materials and methods: Eight patients (mean age, 50.8 years; range, 41–72 years) underwent clinical whole-body MRI at 3T for myopathic symptoms. Two-point Dixon technique based T1-weighted turbo spin-echo images were acquired before and after the administration of intravenous Gd-DOTA. On both image sets, the FSF was calculated in the gluteus medius, gluteus maximus, and quadriceps muscles bilaterally. Pre- and post-contrast FSF values were compared by linear regression, Bland–Altman plot as well as paired Student *t*-tests with Bonferroni correction.
Results: The mean pre- and post-contrast FSF of included muscles were 28.7% ± 14.9% and 27.8% ± 15.1%, respectively. Linear regression indicated almost equivalent FSF estimation between pre- and post-contrast measurements (sum of squared residuals R^2, 0.92 ± 0.04; slope, 0.97; *X*-intercept, −0.05; *Y*-intercept, +0.05). The Bland–Altman plot revealed a minimal systematical bias of the post-contrast FSF measurements of −0.87%. Paired Student *t*-tests did not reveal significant differences (overall *p*-value, 0.168).
Conclusion: Gd-DOTA does not significantly influence FSF quantification in skeletal muscle based on the two-point Dixon technique at 3T.

1. Introduction

Magnetic resonance imaging (MRI) is an accurate modality not only for morphological evaluation of skeletal muscle but also for non-invasive quantification of muscular fat content in vivo [1–3]. This is of growing clinical interest as a biomarker for muscular insufficiency and for progression of neurodegenerative and metabolic diseases [4–9].

A method widely used for estimating the muscular fat content is the two-point Dixon technique [10], which has been validated and found highly accurate and reproducible in numerous studies [3,4,8,11–13]. This technique uses the chemical shift between water and fat signal resulting from the slightly lower precession frequency of protons in fat molecules. By using two different echo times, in-phase and opposed-phase images are acquired. From these, water-only and fat-only images are subsequently calculated by simple signal addition and subtraction, respectively, and the fat signal fraction (FSF) can be measured in any region of interest.

The standard clinical imaging protocol at our institution for evaluating muscular disease includes a short-tau inversion recovery (STIR) sequence for depiction of muscle oedema as well as pre- and post-contrast two-point Dixon based sequences for FSF quantification and for detecting pathological contrast enhancement.We prefer the Dixon technique over conventional fat suppression methods, as it typically provides better fat suppression in areas of magnetic field inhomogeneities compared to conventional fat saturation techniques.

Gadolinium-based MRI contrast agents, such as gadoterate meglumide (Gd-DOTA), shorten the T1 and T2 relaxation time of nearby

Abbreviations: FSF, fat signal fraction; Gd-DOTA, gadoterate meglumide; GRAPPA, generalized autocalibrating partially parallel acquisition; MRI, magnetic resonance imaging; ROI, region of interest; STIR, short-tau inversion recovery; TE, echo time; TR, repetition time; TSE, turbo spin-echo.

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tissue. In phantom studies, gadolinium increased the water signal relative to the fat signal and led to underestimation of the FSF [14]. In contrary, there is evidence that the presence of gadolinium-based agents may not significantly bias the FSF quantification (in the liver) [15,16]. Regarding skeletal muscle, the influence of gadolinium on fat quantification is still unknown. This is however of clinical importance, because substantial scanning time could be saved and patient comfort increased if fat quantification could be based on post-contrast sequences only. Therefore, the purpose of the present study was to assess whether FSF quantification in skeletal muscle is significantly affected by intravenous administration of Gd-DOTA at 3T.

2. Materials and methods

2.1. Study subjects

This was a retrospective study on anonymized imaging data only. According to local and federal laws, no ethics board approval was necessary. MR imaging data from eight consecutive patients (4 males, 4 females; mean age, 50.8 years; range, 41–72 years) who underwent clinical MRI for myopathic symptoms were included. The patients had the following underlying diseases: polymyositis ($n = 2$), dermatomyositis ($n = 1$), overlap syndrome (anti-synthetase/scleroderma, $n = 1$), muscle dystrophy ($n = 1$), and myopathic symptoms of unclear etiology ($n = 3$).

2.2. Image acquisition

All MRI examinations were performed on a 3T system (MAGNETOM Skyra, Siemens, Erlangen, Germany). Axial pre-contrast in-phase and opposed-phase T1-weighted turbo spin-echo (TSE) images using a two-point Dixon technique of the pelvis and upper legs were acquired (TR, 702 ms; TE, 8.7 and 11.0 ms; slice thickness, 4 mm; in-plane resolution, $1.4 \times 1.4\,mm^2$; matrix, 320×182; number of signal averages, 2; Generalized Autocalibrating Partially Parallel Acquisition GRAPPA acceleration factor, 2; flip angle, 90°; refocusing pulse, 135°; scanning duration, 5:48 min). This sequence was optimized for the triglyceride peak at 1.3 ppm, which represents the clinically most relevant fat peak. Subsequently, post-contrast images were acquired with equal imaging parameters 10 min following intravenous administration of Gd-DOTA (Dotarem®, Guerbet, Paris, France) at a dose of 0.2 mL/kg of body weight and at a rate of 3 mL/s, followed by a 20 mL 0.9% saline bolus.

2.3. Quantitative analysis

From the in-phase (IP) and opposed-phase (OP) images, water-only and fat-only images were calculated based on simple signal addition and subtraction (IP + OP = water-only image, IP − OP = fat-only image). On the pre-contrast water-only image, standardized regions of interest (ROIs) were drawn by one experienced, fellowship-trained musculoskeletal radiologist blinded to clinical data (E.J.U., 9 years of experience) by using commercially available software (Myrian®, Intrasense, Paris, FR). Separate ROIs were drawn in different representative muscles, i.e., in the gluteus maximus and medius bilaterally at the level of the center of the sacroiliac joint as well as in the quadriceps muscle bilaterally at the middle of the femoral shaft. The same ROIs were automatically assigned to the pre-contrast fat-only and the post-contrast water-only and fat-only images. Correct assignment by the software was visually verified by the radiologist.

From the mean signal intensities within the ROIs on the water-only (SI_{WATER}) and fat-only (SI_{FAT}) images, the fat signal fraction (FSF) was calculated [1]:

$$FSF = \frac{SI_{FAT}}{SI_{FAT} + SI_{WATER}} \tag{1}$$

For better illustration of the FSF distribution within the muscles, we calculated a voxel-wise FSF map (part of Fig. 1).

2.4. Statistical analysis

The reproducibility of FSF measurements was evaluated by using a Bland–Altman plot of pre- and post-contrast mean FSF values [17,18]. Furthermore, pre- and post-contrast mean FSF values were compared in the six different muscles using paired Student t-tests with Bonferroni correction for multiple comparisons; a p-value < 0.0083 (0.05/6) was considered statistically significant.

FSF values measured on pre-contrast (x-axis) and post-contrast images (y-axis) were plotted on a scatter diagram in order to calculate the slope and intercept of a linear regression curve. By means of a two-sided t-test at a significance level of $p = 0.05$, it was determined whether the slope and intercept of the least-square fit were significantly different from 1.0 and 0.0, respectively (representing the hypothesis that Gd-DOTA does not significantly influence FSF

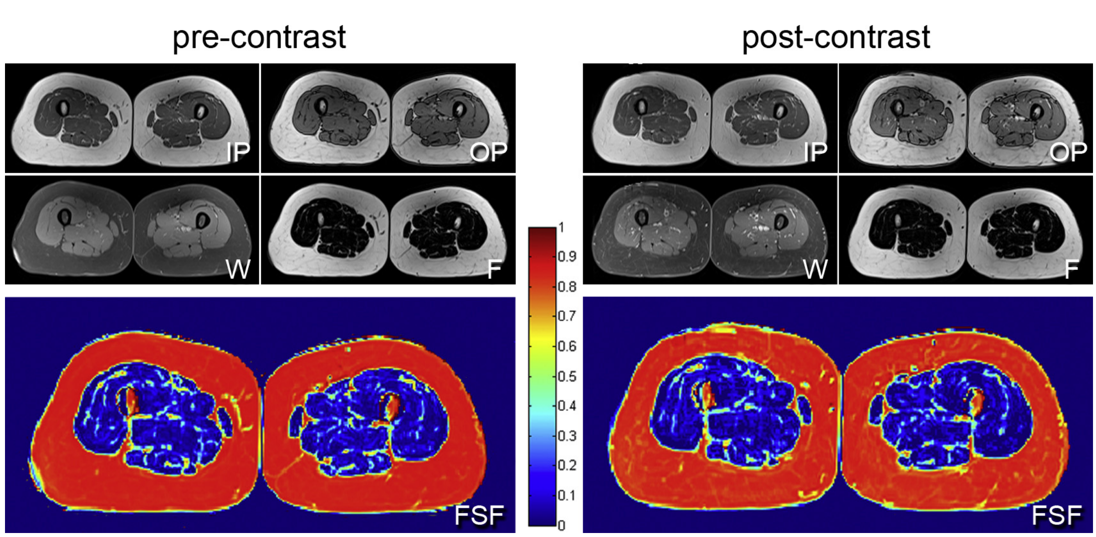

Fig. 1. Axial pre- and post-contrast in-phase (IP) and opposed-phase (OP) images, resulting water-only (W) and fat-only (F) images as well as color maps of the calculated fat signal fraction (FSF) in the quadriceps muscles of a 44-year-old female patient with myopathy of unknown etiology.