Imaging muscle composition

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Objective of the lecture

Skeletal muscle is primarily composed of water, proteins and fat. Water and fat can be found within or outside the myocytes (i.e. the muscle cells). Therefore, skeletal muscle water can be further divided into intracellular and extracellular water and skeletal muscle fat can be further divided into intramyocellular and extramyocellular fat. Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS) techniques provide unique non-invasive capabilities to qualitatively probe or directly measure the relative composition of healthy and diseased skeletal muscle. The relative composition of water in intracellular and extracellular water can be indirectly probed using T_2 mapping techniques, whereas the relative composition of fat in intracellular and extracellular fat can be directly measured using ^{1}H MRS techniques. The water-fat composition of skeletal muscle can be also measured qualitatively using T_1-wighted imaging and quantitatively using fat selective imaging or chemical shift-based water-fat separation techniques. Finally, the presence of proteins and other macromolecules can be indirectly probed using magnetization transfer techniques.

It would be practically impossible for the present lecture to cover the aforementioned plethora of MRI and MRS techniques available to image muscle composition. The two most common patterns of muscle composition changes in diseased skeletal muscle are edema/inflammation and fat infiltration. Therefore, the present lecture aims to provide an overview of the most widely used MRI techniques in characterizing alternations in muscle composition associated with edema/inflammation (i.e. water T_2 measurements) and fat infiltration (i.e. fat content measurements). The first part of the lecture will briefly discuss T_2 mapping techniques. The second and main part of the lecture will focus on techniques studying water-fat composition (T_1-weighted imaging, fat selective imaging and chemical shift-based water-fat separation).

T_2 mapping

Skeletal muscle T_2 relaxation measurements have been performed using standard spin-echo sequences, multi-echo spin-echo sequences (i.e. the Carr-Purcell-Meiboom-Gill (CPMG) sequence) (1,2) and steady state free precession (SSFP) sequences (3). Skeletal muscle T_2 quantification using a multi-echo spin-echo sequence suffers from all the factors confounding T_2 mapping using this sequence in other body parts (4,5). These factors include diffusion effects during the inter-echo spacing, magnetization transfer effects in multi-slice acquisitions and the occurrence of stimulated echoes, induced by non-ideal slice profiles, B_0 and B_1 field inhomogeneities (6).

For a thorough analysis of the multiple T_2 relaxation components, acquisitions with a high number of echoes have been performed. In a study performed at 1.89 T and acquiring 1000 echo times, four T_2 components were observed with T_2 relaxation times < 5ms, 21 ms, 39 ms and 114 ms and relative fractions 11%, 28%, 46% and 11%, respectively (7). The shortest and longest components have been observed in ex vivo muscle studies, probably corresponding to

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water associated with macromolecules and extracellular water, respectively. The middle T_2 components were suggestive of an organization of in vivo intracellular water. In the same study, using a standard spin-echo acquisition of six echo times a single T_2 value of 30 ms was reported (7). Therefore, it is important to emphasize that the T_2 measured using a mono-exponential signal decay model in typical acquisitions with a low number of echoes is an apparent relaxation time including contributions from multiple T_2 components.

T_2 mapping has been widely used in different skeletal muscle disease states including muscular dystrophies (8,9) and muscle denervation (10). The observed increase of skeletal muscle mean T_2 value in these diseased states has been in general associated with an increase of relative fraction of free water in the presence of edema/inflammation. However, it should be pointed out that the reported T_2 values using multi-echo spin-echo sequences differ among different studies, as they are affected by the aforementioned confounding factors and therefore are highly dependent on the exact parameters of the employed imaging protocol.

Water-fat composition

T_1-weighted imaging

Muscle and fat have T_1 relaxation time values of 1400 ms and 360 ms respectively at 3 T. This large difference in the T_1 relaxation time between muscle and fat has established T_1-weighted imaging, combined with a fast spin-echo (FSE) or turbo spin-echo (TSE) sequence, as an efficient imaging technique for qualitative evaluation of fat infiltration in skeletal muscle. Different qualitative muscle grading scales have been proposed in the literature to assess the degree of muscle fat infiltration based on T_1-weighted images. Examples include the radiological grade proposed by Goutalier in the context of rotator cuff tendon injuries (11,12) and the neurological grade proposed by Mercuri in the context of neuromuscular disorders (13). However, the grading results remain qualitative and have been shown in certain cases to be highly observer-dependent (14).

Fat selective imaging

Given the limitations of T_1-weighted imaging, there has been a growing need for establishing a quantitative and efficient imaging technique for measuring fat content in skeletal muscle. Schick's proposal in 2002 to employ fat selective imaging constituted an important advancement towards quantitative assessment of skeletal muscle fat infiltration (15). The proposed technique relied on a fat-selective excitation and the use of appropriate reference signal for signal calibration in order to derive a quantitative fat fraction map (15). Fat selective imaging has been successfully used to measure fat content and characterize adipose tissue distribution in the skeletal muscle of diabetic and older patients (16,17). However, the technique remains inherently sensitive to B_0 field inhomogeneity effects and requires appropriate correction steps to account for coil profile effects in the required calibration process using a reference signal.

Chemical shift-based water-fat separation

Chemical shift-based water-fat separation techniques address the general issue of the sensitivity of chemical shift selective imaging to B_0 field inhomogeneity effects, also encountered in fat selective imaging. Chemical shift-based water-fat separation techniques excite both water and fat and acquire data at multiple echo times in a gradient-echo or an asymmetric spin-echo sequence. The separation of the total measured signal into water and fat components is based

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on the chemical shift difference between the two species. The two-point version of the technique has been traditionally used in diagnostic imaging for forming in-phase (addition of water and fat images) and out-of-phase (subtraction of water and fat images) images, by the selection of appropriate echo times in a two-echo gradient-echo sequence (18). The generalized multi-point version of the technique in a multi-echo gradient-echo sequence (19,20) has recently gained considerable interest in the MRI research community, leading to the further development of two-point and multi-point Dixon techniques (21-23) and the development of the IDEAL (iterative decomposition of water and fat with echo asymmetry and least-squares estimation) technique (24,25) .

Chemical shift-based water-fat separation has been emerging into becoming a quantitative tool for measuring proton-density weighted fat fraction maps in vivo (26,27). Specifically, quantitative water-fat imaging techniques have shown excellent agreement with single-voxel MRS in measuring fat content in different body parts (28-30), after consideration of multiple confounding factors, including main magnetic field inhomogeneity effects (31), the presence of multiple peaks in the fat spectrum (32,33), T_2^* effects (32,34), T_1-bias effects (32,35) and eddy current effects (36,37). In the context of quantitative water-fat imaging in skeletal muscle, previous works have addressed the need for noise efficient correction of T_1-bias effects (38) and have investigated the effect of susceptibility-induced extramyocellular fat resonance shift on the measured fat fraction (39). Quantitative water-fat imaging has been also combined with image-processing techniques, exploiting the inherent multi-modal imaging property of water-fat imaging, in order to segment different fat compartments and study adipose tissue distribution changes in the extremities (40).

On the application side, quantitative water-fat imaging has been recently applied to quantify fat infiltration in skeletal muscles affected by muscular dystrophies (6,41,42), in the rotator cuff muscles of patients with rotator cuff tendon injuries (43), in the spinal muscles of patients with back pain (44) and in the skeletal muscles of diabetic patients (45,46). Quantitative water-fat imaging has been also recently compared to qualitative fat infiltration grading schemes used to characterize skeletal muscle fat infiltration (41,43,45). The latter studies showed a strong correlation in the fat infiltration description results between the quantitative and qualitative approaches. In parallel, these comparison studies highlighted the benefits of a quantitative assessment of muscle fat infiltration using a continuous imaging marker (i.e. the fat fraction) measured at high spatial resolution. Finally, although most of the already reported results refer to cross-sectional studies, quantitative water-fat imaging shows great potential for longitudinal evaluation of muscle fat infiltration changes associated with disease progression, therapy and interventions.

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