

Age-associated Changes in Triceps Surae Muscle Composition and Plantarflexor Strength – an MR imaging based Study with Ultra-short Echo-time (UTE) and Fat-Water Quantification of Connective, Adipose and Contractile Tissues.

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Target Audience: Researchers of Sarcopenia, Musculoskeletal Radiologists, Muscle Physiologists, Imaging Physicists.

PURPOSE: The aging process is accompanied by a progressive loss of muscle mass and strength, with the declines in force significantly exceeding those in muscle mass [1]. The disproportionately larger losses in muscle force reflect a deterioration of the intrinsic capacity of the neuromuscular system to generate force. One potential explanation for this deterioration is a change of muscle composition, characterized by an increasing infiltration with intramuscular adipose (IMAT) and fibro-collagenous connective (IMCT) tissues[2]. The aims of this study were to (i) use Ultra-short Echo-time (UTE) and Fat-Water Quantification sequences and image analysis routines to quantify IMCT and IMAT, (ii) apply these techniques to study muscle composition in young and senior subjects, and (iii) investigate their roles in determining age-associated changes in muscle strength.

METHODS: Five young (YW: age: 31.6 ± 7.0 yrs) and 5 senior (SW: age: 83.4 ± 3.2 yrs) Japanese women were scanned on a 3T, GE scanner using a custom-made (Millennial MRI Co., NY), 8-channel phased-array lower-leg coil. For measurements of intramuscular connective tissue, two sets of interleaved ultra-short echo time (UTE) sequences were used with a short 40 to 80 μ sec hard RF pulse for excitation followed by dual echo radial ramp sampling, FAST Gradient-echo acquisition (with FOV: 20 cm, TR = 200 ms, TE1 = 8 μ s, TE2 = 2.6 ms, FA = 30°, BW = ± 62.5 kHz, NEX = 2, 512 x 512 matrix, slice thickness of 5 mm with 5 mm gap, scan time = 14 min. Subsequently, T_2^* maps of each voxel were calculated [4]. A value of 8 ms was empirically determined to include all full and most partial volume non-muscle voxels. In a second step, the IMAT voxels identified from the water-saturated images (described below) were removed from the segmented T_2^* maps (sum of non-muscle voxels) to obtain fat-free IMCT maps. In the 2nd part, to determine the amount of IMAT in the Triceps Surae complex, two FGRE sequences with fat- and water-suppression (TE/TR::

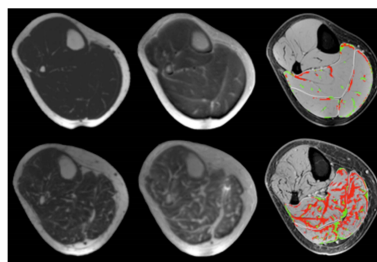


Figure 1. Left: water-sat FGRE (IMAT), Middle: UTE (IMCT), Right: fat-sat FGRE with superimposed results of automated tissue segmentation. Top and bottom row representing a typical young and senior subject, respectively.

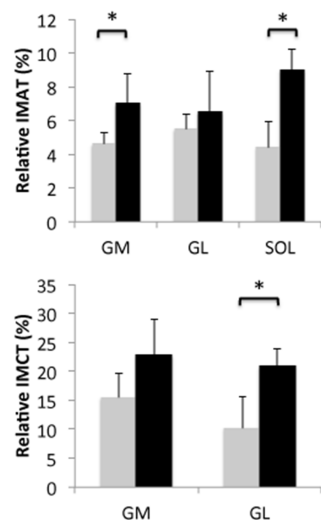


Figure 2. Relative amount of Intramuscular Adipose (left) and Intramuscular Connective Tissue (right). YW and SW shown in grey and black, respectively.

2.1/~450ms, , 20 cm FOV, 5 cm thick contiguous typically 75 slices covering from the origin of Gastrocnemius muscle to the calcaneus) were obtained. The contours of the Gastrocnemius Medialis (GM), Gastrocnemius Lateralis (GL) and Soleus (SOL) muscles were manually identified using the fat-saturated FGRE series. Subsequently, the water-saturated FGRE images from the above protocol were cropped to remove subcutaneous fat, and 3D bias-field corrected. The muscle contours were then superimposed on the pre-processed water-saturated FGRE images to create masked image stacks of GM, GL and SOL, respectively. A MALAB Fuzzy C-means clustering algorithm was used to separate 3 sets of clusters, one corresponding to muscle and fat each and an intermediate cluster with voxels including a combination of both tissues. The output of the Fuzzy clustering was threshold-segmented at an intensity value in the valley between the second and third cluster of intensity ranges. To validate this approach, fat fractions were additionally determined by iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) imaging [3] in 4 subjects with excellent agreement between results ($r = 0.94$, SEM $1.38 \text{ cm}^3 \pm 0.96 \text{ cm}^3$). Plantarflexor muscle strength was measured under isometric conditions using a custom-made foot pedal device [5]. Muscular forces were estimated by dividing the resulting measures of torque by Achilles tendon moment arms, determined from sagittal-plane localizers.

RESULTS: In SW, Triceps Surae muscle volumes were smaller by 17.5%. Representative cross-sectional water-saturated FGRE (used for the segmentation of IMAT), UTE (for IMCT) and fat-saturated FGRE images with the superimposed results of the segmentation process (showing the amount and spatial distribution of IMAT and IMCT within the Triceps Surae complex) are displayed in Figure 1. Relative IMAT contents were larger in SW in all heads of the Triceps Surae complex, with differences observed in the GM and SOL muscles reaching statistical significance. For IMCT, statistical differences were found for the GL (see Figure 2). Jointly, the **total amounts of non-contractile tissues**, calculated as the sum of Triceps Surae IMAT and IMCT in both heads of the Gastrocnemius muscle, did not differ statistically in absolute terms (young: $56.96 \text{ cm}^3 \pm 14.62 \text{ cm}^3$ vs. senior: $79.21 \text{ cm}^3 \pm 26.08 \text{ cm}^3$, $p = 0.107$, $r = 0.54$) but were significantly **larger by 48.9% in the elderly cohort** after normalization to Triceps Surae muscle volumes (young: $10.5\% \pm 2.1\%$ vs. senior: $17.3\% \pm 2.9\%$, $p = 0.003$, $r = 0.83$). The measurements of muscle force demonstrated a 38.6% difference in plantarflexor muscle force. **Specific force**, representing muscle quality, was **lower by 18.4% in the senior cohort**. Differences in specific force decreased to 10.3% when forces were normalized to the amount of contractile muscular tissue only, i.e., after subtraction of IMAT and IMCT from total muscle volume

CONCLUSIONS: The present study represents the first attempt to non-invasively determine the total amount of intramuscular content of non-contractile tissues *in vivo* using UTE's. Our comparison of young and senior women suggests that during aging the total amount of Triceps Surae IMAT and the IMCT content within the GM and GL muscles increase by ~55% and ~49%, respectively. Subtraction of these non-contractile tissues from total muscle volume substantially reduced the differences in specific force between age groups, suggesting that the accumulation of IMAT and IMCT is an important determinant of decrease in muscle quality observed in aging muscles. **REFERENCES:** [1] Delmonico, MJ et al. (2009). Am J Clin Nutr; [2] Miljkovic, I et al. (2010). Curr Opin Clin Nutr Metab Care; [3] Reeder, SB et al. (2007). JMRI; [4] Williams, A et al. (2010). Osteoarthritis Cartilage; [5] Sinha, S et al. (2012). JMRI.