

## Fully automated unsupervised multi-parametric classification of adipose tissue depots in skeletal muscle

Alexander Valentinitisch<sup>1</sup>, Dimitrios C. Karampinos<sup>1</sup>, Hamza Alizai<sup>1</sup>, Karupppasamy Subburaj<sup>1</sup>, Thomas M. Link<sup>1</sup>, and Sharmila Majumdar<sup>1</sup>

<sup>1</sup>Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, United States

**Introduction:** Metabolic abnormalities including obesity and type 2 diabetes have been associated with alterations in the amount and the regional distribution of adipose tissue in the lower extremities, including changes in intermuscular adipose tissue (IMAT) and subcutaneous adipose tissue (SAT) volumes [1, 2]. Chemical shift-based water/fat separation approaches, like Dixon methods and the iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) method, have been recently applied to measure a quantitative proton density fat fraction map in skeletal muscle, enabling an accurate and reliable determination of fat amount in the muscle cross-section [3]. However, a study of fat distribution would require a reproducible extraction of SAT and muscle regions to determine the amounts of SAT and IMAT respectively. A fully automated, accurate and reproducible segmentation technique for identifying the SAT and the muscle region still remains challenging due to severe fatty infiltration of certain muscles in numerous pathologic conditions. The inherent multi-modal imaging (MMI) property of chemical shift-based water/fat separation makes it an ideal candidate for multi-parametric segmentation. Therefore, the purpose of the present study is to introduce and validate a fully automated unsupervised multi-parametric segmentation method of the SAT and muscle region to determine SAT and IMAT volumes based on the images from a quantitative chemical shift-based water/fat separation approach.

**Methods:** MRI measurements: The right middle-calf muscle region of 28 post-menopausal women were scanned on a 3.0 T whole-body GE scanner using an 8-channel low extremity coil with an investigational version of a 3D six-echo flyback SPGR sequence (TR/TE/ΔTE=12/1.4/0.7 ms, flip angle=3°, ETL=2, bandwidth=83.33 kHz, 180x180 matrix size, FOV=18 cm, 30 slices with 4 mm thickness). The computation of water, fat and fat fraction images was based on the IDEAL algorithm [4] with multi-peak spectral modeling of fat and single  $T_2^*$  correction [5]. The patients were grouped according to the presence of fatty infiltration in the medial gastrocnemius muscle based on a 5-point semi quantitative scale described by Goutallier [6]: G0 (normal), G1 (some fatty streaks), G2 (less fat than muscle), G3 (fatty degeneration), G4 (fatty infiltration).

Segmentation method: The segmentation method has 3 phases as shown in Fig. 1: (1) calf extraction – an unsupervised k-means clustering was performed on the intensity distribution of three different diagnostic volumes (IDEAL – in-phase, water fat); (2) muscle extraction – on the masked calf clustering was performed using water/fat images; (3a) bone marrow extraction - the same features are used for clustering on a masked calf as in phase 1; (3b) cortical bone extraction – using a threshold (local minimum between the smallest and highest peak of the histogram). The combination of each phase results in a muscle mask, where we can extract the SAT and muscle region.

Validation: A single operator manually segmented the SAT and the muscle region on the IDEAL images, which served as a ground truth (GT) for validation. To assess the accuracy, we compared the SAT and muscle masks from manual segmentation by dice coefficient (DC of 1 – perfect agreement) [7]. As a complementary local measure we evaluated the local contouring error (LCE). The LCE was defined as the mean distance between the closest corresponding pairs of contouring points of the manual mask and mask resulting from the multi-parametric segmentation. We compared the performance for the different muscle fat infiltration grades. Additionally, we calculated the IMAT and SAT area and plotted the agreement using Bland-Altman plots (GT vs. multi-parametric method).

**Results:** Figure 2 shows examples of the different Goutallier grades, and the performance of our multi-parametric segmentation algorithm. The overall agreement of the SAT and muscle region between our method and the GT, as expressed by the DC, was 0.965 and 0.974. The accuracy was stable across the different muscle infiltration patterns with grade from G0 – G3. This trend was also observed in the LCE graph (Fig. 3). The G4 group showed the lowest overlap and had highest local contouring error. All contours were less than the 1-pixel error mark, except the muscle contour for subjects with the highest fat infiltration grade.

**Discussion & Conclusion:** The proposed method using unsupervised multi-parametric k-means clustering can achieve a robust and consistent separation of the SAT and muscle region across different degrees of muscle fat infiltration. The accuracy in the subjects with the highest grade of fatty infiltration was reduced relative to those with lower grades, due to lack of image information – too few parameters- in separating the SAT from IMAT correctly. To overcome this issue of misclassification, texture features and edge information can be additionally extracted from the IDEAL images. Possible improvements to the automated segmentation algorithm would be the extension from an unsupervised classification model to a supervised method. In conclusion, the presented multi-parametric segmentation method based on water/fat separated images can give a reproducible and reliable fully automated calculation of the SAT and IMAT volumes, considerably reducing the post-processing time in the study of skeletal muscle fat distribution in large scale patient studies.

**References:** [1] Gallagher et al, AJCN 89:807, 2009, [2] Boettcher et al, JMRI 29:1340, 2009, [3] Karampinos et al, MRM 66:1312, 2011, [4] Reeder et al, MRM 54:636, 2005, [5] Yu et al, MRM 60:1122, 2008, [6] Goutallier et al, CORR 1994; [7] Dice, Ecology, 1945

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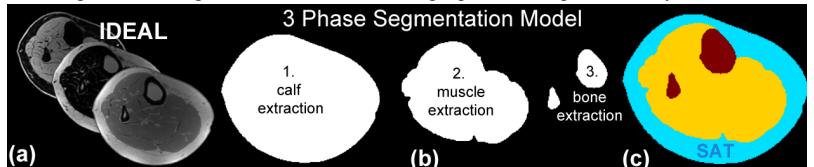


Fig. 1: 3 Phase Segmentation model: (a) IDEAL images (in-phase, fat, water) used as multi-modal imaging (MMI) volumes, (b) Phase 1. calf extraction: separates the background from the calf, Phase 2. muscle extraction: separates the SAT region from the calf region, Phase 3 bone extraction: getting rid of the bones in the muscle region (c) final muscle mask: SAT region and muscle region without the bones.

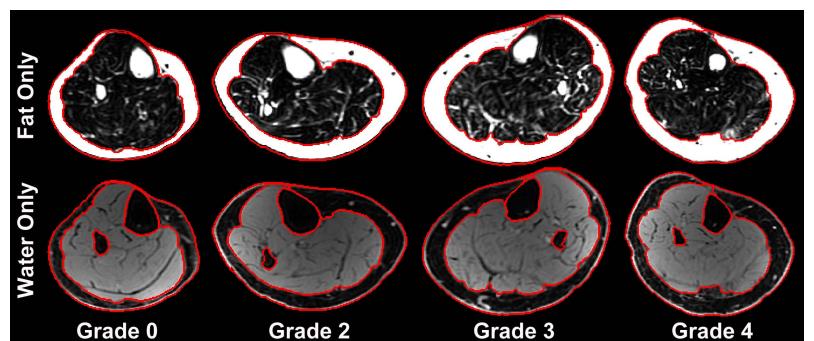


Fig. 2: Representatives of the multi-parametric segmentation of the SAT and muscle region for different muscle infiltration grades (Semi-quantitative Goutallier scoring method).

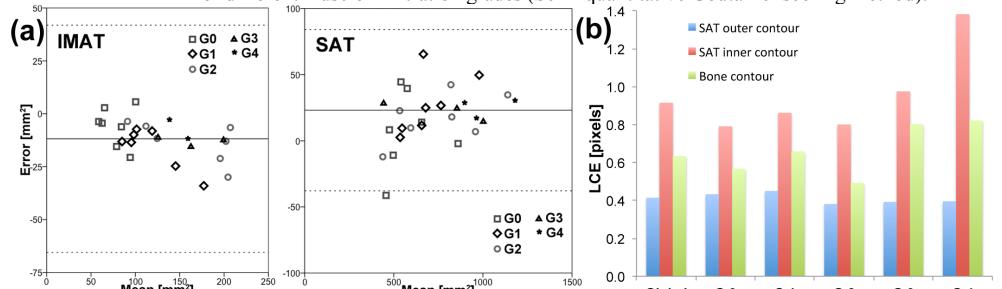


Fig. 3: Validation of the multi-parametric segmentation method: (a) Bland-Altman plot of the IMAT and SAT area - dotted lines on plots represent 95% confidence intervals for agreement between GT and our method (b) the local contouring error (LCE) in pixels for the SAT outer and inner contour and bone contour compared to the GT. Both validation methods are shown for different muscle infiltration grades (G0 – G4).