

## Original Article

# Thigh tissue composition exhibits a curvilinear relationship with aging: A cross-sectional study

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## Abstract

**Objectives:** To explore whether quadratic model will better estimate the relationship between aging and thigh tissue composition in a cohort that range in age from young to older adults. **Methods:** 51 healthy subjects participated in this investigation. All subjects underwent CT imaging for the thigh. Cross-sectional area of the fat and muscular tissues in the thigh were quantified. Hierarchical regression models were created. Age was entered first into the models to estimate its linear relationship with the thigh tissues. Then the squared value of the age variable was entered second to identify whether a quadratic model would better estimate the relationship between the variables. **Results:** The linear model was significant for thigh muscular tissue. Quadratic models were able to account for additional significant prediction of the cross-sectional area of thigh tissues. Muscular area decreased with aging until 60 years after that it didn't change. Fat areas increased with aging until 45-50 years and then it decreased. **Conclusions:** The cross-sectional area of different thigh tissues exhibit a curvilinear pattern with aging. Muscular tissue area may not change after 60 years; this could be explained by the reduction in fat that may infiltrate inside the muscles and offset the muscular reduction.

**Keywords:** Aging, Fat, Intermuscular Adipose Tissue, Muscle, Subcutaneous Adipose Tissue

## Introduction

The Thigh region in our bodies is composed of different tissues including adipose and muscular tissues. The adipose tissue is considered a large and dynamic structure that can adjust to different changes in healthy individuals<sup>1</sup>. Adipose tissue can be divided into subcutaneous, visceral, intermuscular, intramuscular and bone adipose tissues<sup>2</sup>. The adipose tissue of interest in the thigh region includes subcutaneous (SAT) and intermuscular adipose tissues (IMAT)<sup>3,4</sup>. Another tissue in the thigh region is the muscular one which can be categorized into normal density muscular tissue that is fat-free and low density fatty muscular tissue<sup>3</sup>.

Computed tomography (CT) is a precise imaging system

that could separately measure the fat tissue, muscle tissue, and other soft tissues within the body, therefore, it is considered the gold standard method for estimating muscle mass in research<sup>5</sup>.

Advancing in age is associated with structural changes in body composition. Reduction in muscle mass and performance, which is referred to as "sarcopenia", is one of these age-related changes<sup>5</sup>. Several studies reported that muscle cross-sectional area (CSA) decreases with aging<sup>6-8</sup>.

Older adults not only have lower muscle cross-sectional area but also they have lower muscle quality due to lower attenuation values of muscles as expressed by lower Hounsfield units (HU) on CT images which indicates a fatty infiltration in muscular tissue<sup>4,9,10</sup>.

Several studies reported that changes in thigh tissue composition are associated with different health conditions. Age-related decrease in muscular tissue CSA was associated with loss of muscle strength<sup>11</sup>. A study by Lang et al revealed that decreased thigh muscle HU is associated with increased risk of hip fracture in older adults<sup>12</sup>. Moreover, IMAT was linked to increased insulin resistance which is associated with diabetes<sup>13,14</sup>.

Although many studies have examined the age-related changes in thigh composition, the relationship between age

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and thigh composition in the Jordanian population has not been examined before. Furthermore, most of the evidence on the relationship between aging and thigh tissue composition was studied on older adult cohorts<sup>3,4,6,7,9-11</sup>. In those studies, linearity was assumed for these relationships. Therefore, we might be overlooking the nature of these relationships as we advance in age throughout the life span. Accordingly, the purpose of the current study is to re-examine the relationship between aging and thigh tissue composition in a cohort that range in age from young to older adults in Jordanian individuals using CT imaging technique. The current research hypothesis is that different tissues composing the thigh region don't exhibit linear changes with aging but curvilinear ones.

## Methods and methods

### Subjects

A convenient sample of 51 healthy subjects was recruited to participate in this cross-sectional investigation. Participants were recruited if they were 20 years old or older and could walk independently without using assistive devices. Subjects were excluded from participation if they had any cardiovascular, respiratory, neuromuscular diseases, inflammatory arthritis, muscular disorders or were participating in a regular exercise program.

All testing procedures were executed at the University of Jordan Hospital.

All study procedures were approved by the University of Jordan Hospital Institutional Review Board, and all subjects provided informed consent before participation.

### Demographic and anthropometric measures

Age, height, weight, and sex were recorded, and body mass index (BMI) was calculated for each subject.

### Thigh tissue composition

All subjects underwent CT imaging for the thigh region. The cross-sectional areas (CSA) of different tissues composing the thigh region were calculated on CT images of the midthigh region as previously described<sup>3</sup>. Scout images were obtained for subjects' femurs, then the mid-distance between the most lateral part of the greater trochanter and the most lateral part of the lateral femoral condyle was identified to determine the mid-thigh region. A 10 mm thick axial CT image of the mid-thigh region was captured. A commercial software (Slice-O-Matic, Tomovision, Montreal, Canada) was used to quantify the cross-sectional area of the adipose and muscular tissues in the thigh region. Different tissues of the thigh region were identified by the attenuation coefficients measured in Hounsfield units. The adipose and muscular tissues have Hounsfield units that range from -190 to -30 and from 0 to 100 respectively. CSA of Subcutaneous adipose tissue (SAT) and intermuscular adipose tissue (IMAT) were separately measured by manually tracing fascia

covering the thigh muscles. Average CSA from both sides for each tissue was calculated and used in the analysis. Evaluating the CSA and attenuation of thigh muscles using CT-imaging has been shown to have excellent inter- and intra-reliability<sup>15</sup>.

### Statistical Analysis

Descriptive analysis (means, ranges, and SD) were calculated for anthropometric and thigh tissues variables (CSA of muscular tissue, subcutaneous and intermuscular adipose tissues).

To explore the nature of the relationship between aging and the tissues composing the thigh region, a hierarchical regression model was created for each dependent variable. The dependent variables were the CSA of thigh region muscular, subcutaneous and intermuscular adipose tissues. The independent variable (age) was entered first into the regression models to estimate its linear relationship with the thigh tissues. Then the squared value of the age variable was entered second to identify whether a quadratic model would better estimate the relationship between the variables. Since different body tissues could be associated with body weight, Pearson product-moment correlation coefficients were estimated between body weight and the dependent variables. If the correlation coefficients were significant, the dependent variables were normalized to the body weight and used in the regression models.

## Results

The cohort in the current study included 37.3% females, and their average age was 51.24 years. Anthropometric information for the study sample along with different tissues composing the thigh region are presented in Table 1. Our results found that estimated total muscle CSA (123.32 cm<sup>2</sup>) constitutes the largest portion amongst the tissues composing the thigh region, followed by SAT CSA (106.19 cm<sup>2</sup>), then by IMAT CSA (11.23 cm<sup>2</sup>) (Table 1).

Pearson correlation revealed that there were significant positive associations between body weight and the different thigh tissues ( $r=0.376-0.684$ ,  $p<0.001-0.007$ ). However, there was no relationship between age and body weight ( $r=0.046$ ,  $p=0.748$ ) (Table 2).

The hierarchical regression models for predicting the CSA of the thigh tissues with both age and age squared were statistically significant. Table 3 presents the ANOVA statistics for all the regression models. Linear prediction of the muscular tissue CSA, by entering the age in the first step, was statistically significant ( $\Delta R^2=.154$ ,  $p=.004$ ). However, the quadratic model, by adding squared age in the second step, was able to account significantly for additional 12.1% of the variance in the prediction of the muscular CSA by age ( $\Delta R^2=.121$ ,  $p=.007$ ). For the prediction of the SAT, the linear model was not able to predict the relationship between SAT and age ( $\Delta R^2=.041$ ,  $p=.152$ ). However, the quadratic model was able to explain significantly additional 9.8% of

**Table 1.** Subject characteristics.

	Mean	Range	Standard deviation
Weight (kg)	85.04	55.5-148	16.80
Height (cm)	167	152-186.5	8.78
BMI ( $\text{kg}/\text{m}^2$ )	30.53	21.53-55.7	5.90
Age (years)	51.24	21-82	15.77
Muscle CSA ( $\text{cm}^2$ )	123.32	78.65-192.9	28.39
SAT CSA ( $\text{cm}^2$ )	106.19	24.67-296.85	61.56
IMAT CSA ( $\text{cm}^2$ )	11.23	3.07-45.25	6.98

BMI: Body mass index. SAT: Subcutaneous adipose tissue. IMAT: Intermuscular adipose tissue. CSA: Cross Sectional Area.

**Table 2.** Pearson correlation coefficients between body weight, age and CSA of the thigh tissues.

	CSA Muscle	CSA SAT	CSA IMAT	Age
Body weight (kg)	0.379	0.376	0.684	0.046
P value	0.006	0.007	<0.001	0.748

CSA: Cross-sectional area. SAT: Subcutaneous adipose tissue. IMAT: Inter-muscular adipose tissue.

**Table 3.** Hierarchical regression models for predicting the CSA of the thigh tissues with both age and age squared entered in the model.

Regression model	Total R Square	F test	P value
Normalized muscular tissue CSA	0.275	9.13	<0.001
Normalized SAT CSA	0.139	3.87	0.028
Normalized IMAT CSA	0.156	4.42	0.017

CSA: Cross sectional area. SAT: Subcutaneous tissue. IMAT: Intermuscular adipose tissue.

the variability between SAT and age ( $\Delta R^2=0.098$ ,  $p=.024$ ). similarly, for the prediction of IMAT by age, the linear model did not predict the relationship between variables ( $\Delta R^2=0.029$ ,  $p=.235$ ).

However, the quadratic model was able to account significantly for an additional 12.7% of the variability of IMAT by age variable ( $\Delta R^2=.127$ ,  $p=.010$ ).

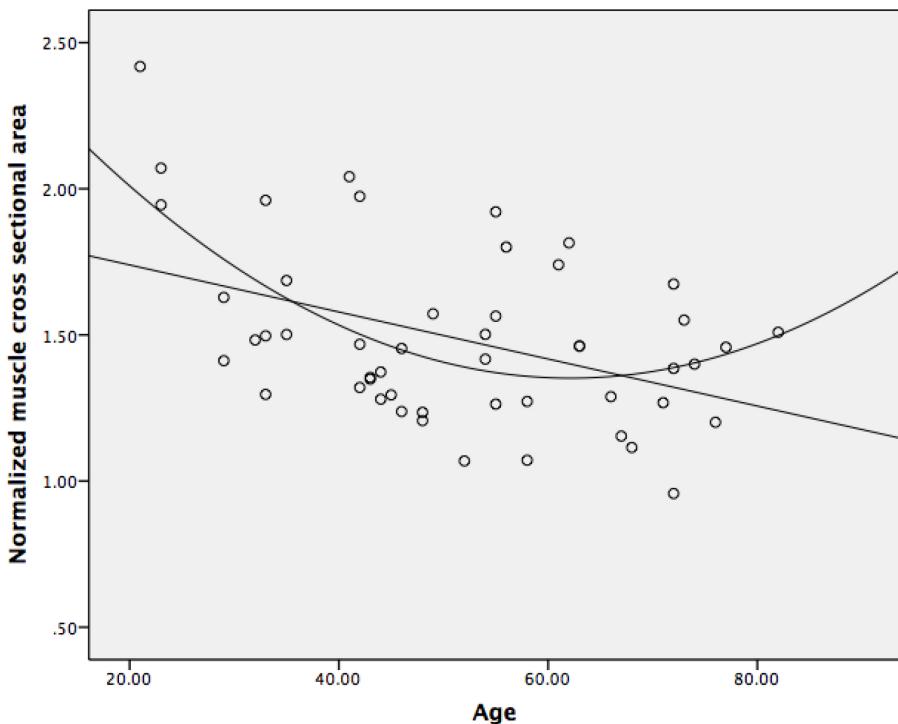
## Discussion

The current study aims to re-examine the relationship between aging and the different tissues composing the thigh region in a cohort that range in age from young to older adults. We hypothesized that the quadratic model would better estimate these relationships than the linear model.

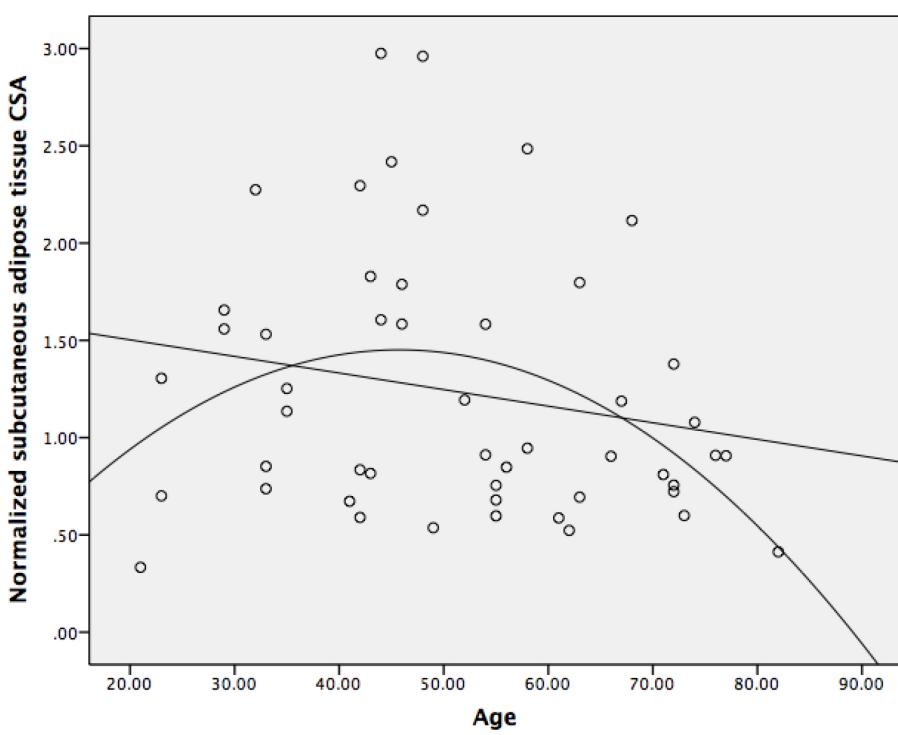
The linear model was able to estimate the relationship between age and muscular tissue. According to this model,

the cross-sectional area of the muscular tissue of the thigh region decreased with aging and this is in accordance with findings from several studies<sup>6-8</sup>. However, the quadratic model was able to better estimate the relationship between age and muscular tissue. The quadratic model added a significant prediction of the variability of the muscular tissue by age. The curvilinear model showed that the CSA of the muscular tissue decreased with age until about 60 years then the curve became flat suggesting that the muscular tissue CSA may not change after 60 years of age (Figure 1).

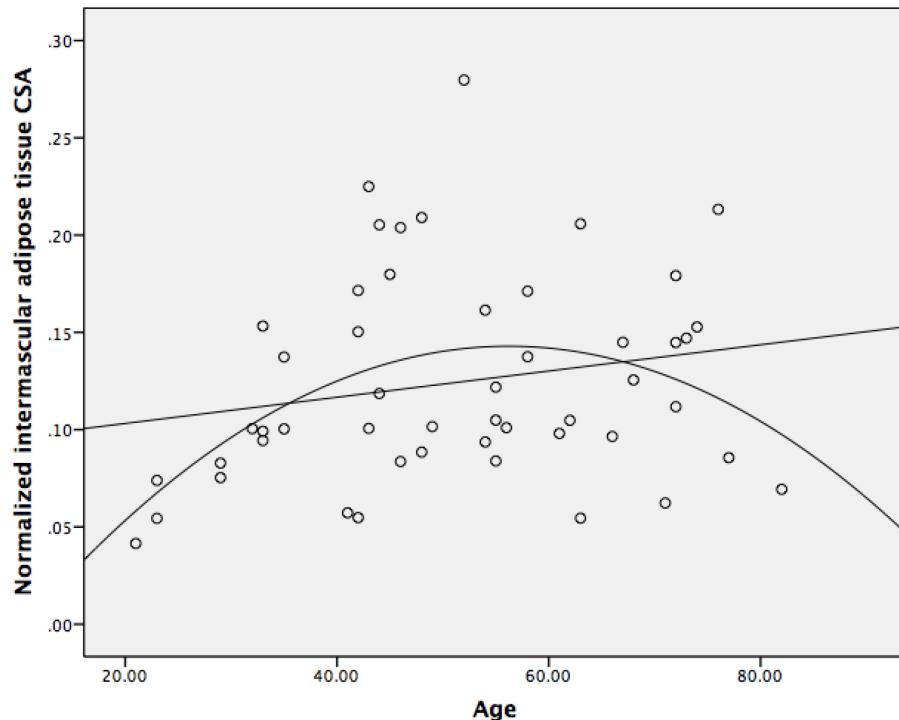
The linear model did not show a relationship between age and the CSA of both SAT and IMAT. Which is in contrast to the results revealed by Delmonico et al<sup>9</sup> who reported an increase in the intermuscular adipose tissue with aging. However, the quadratic model demonstrated a significant prediction of the variability of both adipose tissues with age. The CSA of the SAT increased with aging until about 45 years then it decreased (Figure 2). The same pattern was revealed



**Figure 1.** Linear and curvilinear relationships between age and normalized muscle CSA.



**Figure 2.** Linear and curvilinear relationships between age and normalized SAT CSA.



**Figure 3.** Linear and curvilinear relationships between age and normalized IMAT CSA.

for the CSA of the IMAT in the quadratic model however the turning point was about 50 years of age (Figure 3). Part of our results (i.e. the decrease in fat CSA in Quadratic models) is in accordance with findings from Kasai et al study, which was conducted on individuals 40 years old and above, in which fat CSA decreased with advancing age and especially in women<sup>8</sup>. However, we can't compare our results pertaining to the increase in fat CSA in younger participants as shown in the quadratic models to Kasai et al study since the participants in the latter study were at least 40 years old.

The curvilinear relationship between age and the thigh tissues revealed that the rate of change peaked at variant ages for the different tissues of the thigh in diverse directions. The CSA of the SAT was the fastest to reach the top of the change then the IMAT then the muscular tissue CSA. However, the change in the muscular tissue CSA with age was in the opposite direction to that in both adipose tissues. When examining the curves of the thigh tissues and their relationship with age, we hypothesized that after both adipose tissues' CSA reached its maximum level, fat started to get infiltrated inside the muscular tissue. That could explain why the adipose tissues' CSA decreased and muscular tissue' CSA became flattened after 60 years of age. As explained earlier in the introduction, the muscular tissue is composed of both fatty and fat-free muscular tissues. Therefore, if the fat got infiltrated inside the muscular tissue, the fatty muscular tissue' CSA will increase which then will

result in offsetting the decrease in the whole muscular tissue' CSA with age. To confirm this statement, we ran a regression model to examine the relationship between the CSA of the fatty macular tissue and age. To identify the CSA of the fatty muscular tissue we used a Hounsfield Units that range from 0-35<sup>16</sup>. The linear model for predicting fatty muscular tissue CSA by age was statistically significant ( $R^2=.149$ ,  $F=8.55$ ,  $p=.005$ ). The slope of the curve (standardized  $\beta=.385$ ) was positive indicating an increase in the fatty muscular tissue CSA with increased age. Furthermore, the quadratic model for the relationship between the fatty muscular tissue CSA and age was not significant ( $\Delta R^2=.015$ ,  $p=.354$ ). This finding was in support to our hypothesis that fat got infiltrated inside the muscular tissue with aging. Accordingly, the increase in the CSA of the fatty muscular tissue might offset the decrease in the whole muscular tissue CSA which explain the curvilinear relationship between the whole muscular tissue CSA and age.

Additionally, there is another probable explanation for the curvilinear relationship between aging and the thigh muscular tissue. The muscular tissue in the thigh region is composed of different muscle groups; the extensors, the hamstrings and the adductors groups. Each muscle group might have different rate of reduction in its cross-sectional area with aging. Consequently, the whole thigh muscular tissue might show the curvilinear pattern with aging. Furthermore, if the thigh muscle groups have different rates of change in their

CSA with aging; the performance of different functional tasks might be affected differently according to the task executed and the muscle group been activated. Therefore, future study is warranted to explore the relationship between different thigh muscle groups and the performance of functional activities with aging to identify activities that reflect on the status of the different thigh muscle groups.

To our knowledge, it is the first time to investigate the age-tissue composition relationship using a quadratic analysis which it could be considered as a strong point for this study, therefore the comparisons between our results with those reported in previous studies could be limited for two reasons; the linear analysis or age-groups comparisons were applied in previous studies, and participants in those studies were limited to middle-aged and older adults' cohort.

This study is not without limitations. First, the sample size may be considered small. Second, although the results of this study indicate that age is a contributor to the changes in thigh tissues; it only accounts for 14-27.5% of variances as seen in the quadratic models. Therefore, other factors may influence such a relationship, for instance: gender, race, physical activity level, and diet style.

Therefore, further research with a larger sample size is warranted to confirm the results of the current study. Additionally, future studies are needed to investigate the contributions of other potential underlying factors to the age-tissues relationship. The design of the current study did not permit us to explore the impact of this age-tissues relationship on the performance of a physical function, thus future work is needed to investigate such effect.

In conclusion, the cross-sectional area of different thigh tissues exhibits a curvilinear pattern with aging. The thigh muscular tissue CSA decreased until 60 years of age then it might not change after that; this could be explained by the infiltration of fat inside the muscles which might increase the fatty muscular tissue's CSA and offset the reduction of the whole muscular tissue's CSA.

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#### Authors' contributions

*IA and SA both contributed significantly in designing the study, analysis and interpretation of the data, drafting and approval of the final version of the manuscript. IA was responsible for the integrity of the data analysis.*

#### References

- Palmer AK, Kirkland JL. Aging and adipose tissue: potential interventions for diabetes and regenerative medicine. *Exp. Gerontol* 2016;86:97-105.
- Hausman GJ, Basu U, Du M, Fernyhough-Culver M, Dodson M V. Intermuscular and intramuscular adipose tissues: Bad vs. good adipose tissues. *Adipocyte* 2014;3(4):242-55.
- Altubasi I. Physical performance of elderly adults in association with thigh tissue composition: A cross-sectional study. *J Phys Ther Sci* 2017;29(12):2194-8.
- Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The health ABC study. *J Appl Physiol* 2001;90(6):2157-65.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis. *Age Ageing* 2010;39(4):412-23.
- Altubasi IM. Is quadriceps muscle strength a determinant of the physical function of the elderly? *J Phys Ther Sci* 2015;27(10):3035-8.
- Fragala MS, Kenny AM, Kuchel GA. Muscle Quality in Aging: a Multi-Dimensional Approach to Muscle Functioning with Applications for Treatment. *Sport Med* 2015;45(5):641-58.
- Kasai T, Ishiguro N, Matsui Y, et al. Sex- and age-related differences in mid-thigh composition and muscle quality determined by computed tomography in middle-aged and elderly Japanese. *Geriatr Gerontol Int* 2015;15(6):700-6.
- Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr* 2009;90(6):1579-85.
- Forsberg a M, Nilsson E, Werneman J, Bergström J, Hultman E. Muscle composition in relation to age and sex. *Clin Sci [Internet]* 1991;81(2):249-56.
- Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: The Health, Aging and Body Composition Study. *Journals Gerontol - Ser A Biol Sci Med Sci* 2006;61(10):1059-64.
- Lang T, Cauley JA, Tylavsky F, Bauer D, Cummings S, Harris TB. Computed tomographic measurements of thigh muscle cross-sectional area and attenuation coefficient predict hip fracture: The health, aging, and body composition study. *J Bone Miner Res [Internet]* 2010;25(3):513-9.
- Boettcher M, Machann J, Stefan N, et al. Intermuscular adipose tissue (IMAT): Association with other adipose tissue compartments and insulin sensitivity. *J Magn Reson Imaging* 2009;29(6):1340-5.
- Goodpaster BH, Thaete FL, Simoneau JA, Kelley DE. Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. *Diabetes* 1997;46(10):1579-85.
- Strandberg S, Wretling ML, Wredmark T, Shalabi A. Reliability of computed tomography measurements in assessment of thigh muscle cross-sectional area and attenuation. *BMC Med Imaging* 2010;10.
- Goodpaster BH, Kelley DE, Thaete FL, He J, Ross R. Skeletal muscle attenuation determined by computed tomography is associated with skeletal muscle lipid content. *J Appl Physiol* 2000;89(1):104-110