

# Behind an image: Advanced quantitative methods of clinical imaging for sarcopenic muscle

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## Abstract

Sarcopenia has been identified as a serious risk factor for morbidity and mortality in late aging and early aging related to neurological disorders, in particular SCI. In the presented paper, the quantitative potential of computed tomography (CT) image analysis is used to describe skeletal muscle quality changes of anatomically defined human skeletal muscles. Current literature reports average Hounsfield unit (HU) values and/or segmented soft tissue cross-sectional areas to investigate muscle quality and quantity. Standardized methods for CT analyses and their utility as comorbidity indexes remain undefined, and no existing studies compare these methods to the assessment of entire radio densitometric distributions. The primary aim of this study is to present a comparison of material content of entire radio densitometric muscle distributions. The results highlight the specificities of each muscle quality metric between an able-bodied subject, an elderly subject and and SCI subject, and particularly highlight the value of the connective tissue regime in this regard.

## Introduction

The progressive decay of aging muscle, known as Sarcopenia, has been consistently identified as a risk factor for morbidity and mortality [1-7]. Its prevalence in older persons and neurological patients, in particular Spinal Cord Injury (SCI) is characterized by serious decreases in both physical activity and muscle masses, but a quantitative definition for its diagnosis remains debated [8-11]. Clinical literature correlates decay of physiological function (loss of muscle strength) to sarcopenia [12-14]. However, the degree to which this loss of muscle strength may be attributed to the loss of muscle mass remains uncertain, if quality of skeletal muscle is not clearly defined and quantitate [15-18]. Nonetheless, methodological comparisons for the precise, non-invasive quantification of the progressive reduction of muscle quality remain disparately described in literature. Standardizing a quantitative methodology for muscle assessment in this regard would allow sarcopenia concept research to become a useful indicator, in particular of compensatory targets for clinical intervention. Aging skeletal muscle has a significantly reduced proportion of glycolytic type II muscle fibers compared to young muscle, that may explain at least in part its decreased speed, force and, thus, power [19-21]. Additionally, aged tissues significantly lack the ability to process triglycerides, resulting in increased lipid droplet storage in and along muscle fibers [22]. This increased adiposity and decreased contractility has been linked to mitochondrial dysfunction and impaired oxidative metabolism, which has been shown to relate to metabolic insulin resistance and Type 2 diabetes mellitus in patients [23, 24]. In general, increased percentage of non-contractile tissues (adipocytes and fibrous connective tissues), aggravates the size loss (and eventually, number) of muscle fibers, conferring an increased risk for reduced mobility, frailty, disability, and eventual hospitalization [25 - 27]. Studying how these changes affect mobility is the prime motive for lower extremity function (LEF) research, which cites LEF as the main indicator for mobility as a clinical screening tool [28]. LEF is generally assessed by measuring walking capacity (gait speed) and leg strength [29]. Altogether, the association of sarcopenic muscle degeneration with decreasing LEF illustrates how

aging induces mobility impairment, incident disability, and eventual mortality [30-34].

Muscle biopsy is the standard clinical procedure used for the assessment of muscle, but the procedure is invasive and occasionally limited in relevance by the small size of excised tissue. However, recent investigations have realized the potential of X-ray computed Tomography (CT) and Magnetic Resonance Imaging (MRI) to describe muscle quality and composition. This is often performed either quasiquantitatively, via the visual grading of muscle structure morphologies [35-38], or quantitatively via the computation of muscle cross-sectional areas and radiodensitometric absorption values in CT, measured in Hounsfield units (HU) [39-44]. Despite the superior soft tissue contrast in MRI and non-dependence on the use of ionizing radiation, CT has higher spatial resolution and is comparatively less obfuscated by technical variations in machine preparation and acquisition protocols [45]. These notions are critical when attempting to discern diagnostically-relevant information from cross-sectional images of soft tissue.

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### Special Issue: Assisted Exercise

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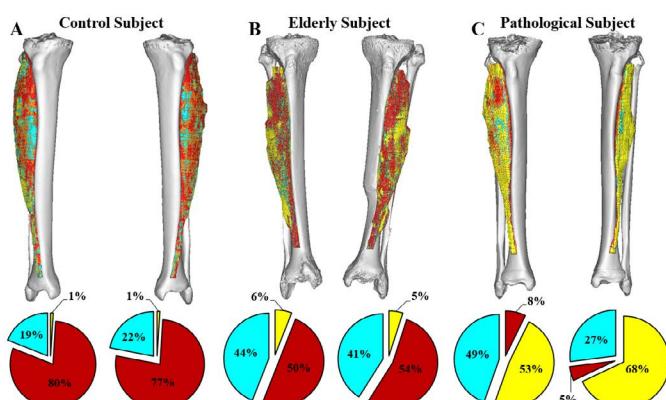
Recent studies have demonstrated the utilization of CT image analysis to quantify muscle composition and quality [46]. Analyzing muscle degeneration in particular has been of great focus in research and many studies have been focused how changes in skeletal muscle density correlate with changes in muscular volume and function in patients suffering from a variety of conditions or diseases. [47]. Further research is therefore essential to associate how muscle composition can give indications about the overall physical condition of the patient.

## Methods

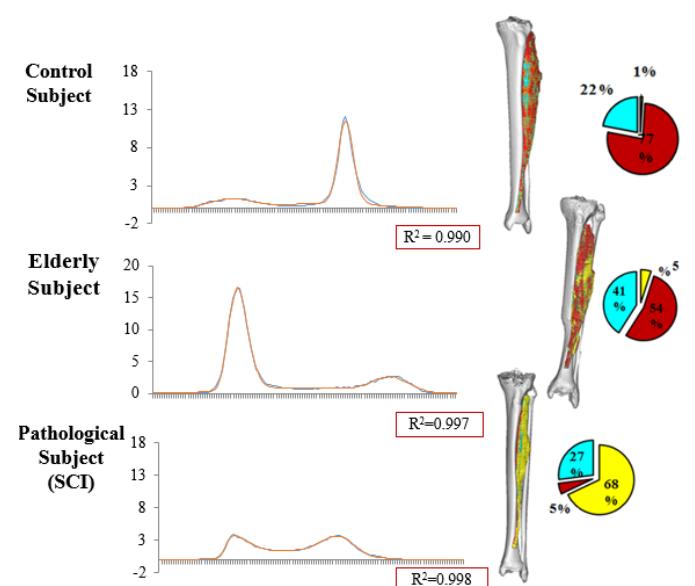
Patients were CT scanned using a phantom that calibrated against the density changes within each tissue. The muscle that was identified was the Tibialis Anterior. The scans ranged from the proximal tibia to the lateral malleolus. Three subjects were recruited, a young able-bodied control subject, an elderly subject and a spinal cord injury patient. The scans were segmented using Mimics (Materialize) using masking technique to identify the Tibialis Anterior, the tibia and the fibula in each slice. Three dimensional models were created from the masks. Depending on the Hounsfield values for the muscle, the pixel was determined to belong to fat (HU<-10), connective tissue (-10<HU<41) and muscle tissue (HU>41). By examining the density distributions in the three-dimensional model, the material composition of the muscle was quantified.

## Results

The linear relationship between the Hounsfield units and the material density was used to map all voxels belonging to the Tibialis Anterior muscle. A three-dimensional image of the muscle and the density values was created for all the subjects and can be seen in Figure 1. The figure shows the three-dimensional model of the muscle along with the representation of the three different tissue types: fat, connective tissue and muscle fibres. The material distributions were quantified for both legs which gives information about the symmetrical aspects between the muscles. From the figure, it can be seen how the elderly subject and pathological subject, who suffered from asymmetrical lower body paralysis from a pelvic mass infiltration of the sciatic nerve, exhibited increasing amounts of fat and loose connective tissue, compared to the control subject. Likewise, the left leg of the pathological subject contains higher amount of fat than the right leg, thus quantifying the asymmetric nature of the subject's condition and be able to quantify the severity of the muscle degeneration. Figure 2 shows the histogram analysis of the soft material content of the entire leg for the same individuals. The graphs show the volume as a



**Figure 1.** Shows the material composition within the *Tibialis anterior* from each subject. The tissue types are: fat (yellow), connective tissue (cyan), and muscle (red).



**Figure 2.** Material histogram distribution of the right leg between all the subjects

function of Hounsfield units. The height of the peak and the location give indication about amount of each tissue present in the thigh. From the figure, it can be seen the two peaks accounting fat and muscle and how their distribution is dramatically different in three cases. The comparison between figure 1 and 2 shows the different composition of a single muscle (Figure 1) in respect of the overall thigh (histograms in Figure 2). Muscle and fat are inverted in terms of volumes for young healthy and aged individual while the distribution in the pathological subject has a completely different profile.

## Discussion

This work shows the possibility to characterize graphically the muscle based on computer tomographic image and to create a subject specific profile that could be used to assess sarcopenia. The results show how the material changes in the muscle. Understanding of how the distribution between muscle tissue, fat and connective tissue can underline how sarcopenia occurs in patients. Connection with the biomechanical output of the muscle has been established [47], where a higher muscle tissue peak and a lower fat tissue peak were associated with increased kinetic performance of the muscle. This is in agreement with the findings presented in the study where a reduction of muscle tissue was found in the elderly subject and the SCI patient compared to the able-bodied subject [48-59]. Using the analysis presented in the paper to quantify the material composition of any anatomically defined skeletal muscle is the first step to standardize when discussing how to address skeletal muscle quality and rehabilitation by Assisted Exercise.

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