

## Review Article

# Imaging methods for the control and treatment of sarcopenia

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## Abstract

Sarcopenia is a progressive loss of skeletal muscle mass with advancing age. Both imaging and non-imaging methods are used for sarcopenia's diagnosis. The use of non-imaging techniques refer to the use of SARC-F scale questionnaires and the physical ability tests. On the other hand, from the group of imaging techniques used for sarcopenia's diagnosis the ones that assess the body mass composition (Body Composition) are: the ultrasound imaging (US), the Dual-energy X-ray absorptiometry (DXA), the computed tomography scan (CT) and the magnetic resonance imaging (MRI). In this review we refer more specific to Magnetic resonance imaging as the specialized imaging method as far as the identification of loss of muscle tissue quality. Sarcopenia is a common disease that has a negative impact on patients' health, as well as a heavy financial and social burden for the developed world. Today, imaging plays a crucial role in diagnosing patients with sarcopenia.

**Keywords:** Sarcopenia, Quality of life, Body mass composition, Magnetic resonance imaging, DXA

## Introduction

### Sarcopenia

The etymology of the word "sarcopenia" is derived from the ancient Greek lemmas *σαρξ* and *πενία*, meaning "flesh" and "poverty" respectively<sup>1</sup>. The term "sarcopenia" is constantly changing these last decades. The term was formed in 1989, meaning the gradual reduction of muscle mass in elderly people. Since then criteria in relation to muscle functioning, such as muscular strength, were added to the term<sup>2</sup>.

Sarcopenia's prevalence index is analogous to age. At the age of approximately 70 years of age, is in the range of 5-13% and up until the age of 80 it reaches 11-50%<sup>3</sup>. In addition, prevalence is of a wide range and it depends on the diagnostic methods used and the characteristics of the studied population<sup>4</sup>. Based on the average predictive models, it appears that in 2050 there will be more than 200 million people worldwide suffering from sarcopenia<sup>1,2</sup>.

The causal factors that lead to sarcopenia are various and numerous. They include the reduced use of the musculoskeletal system, due to co-morbidity (e.g. ischemic stroke, heart failure, osteoarthritis, poor and insufficient

nutrition), hormonal changes (including insulin, androgens and estrogens) muscular apoptosis, motor neuron disease, changes in the immune system, social circumstances and reduced mental function<sup>5</sup>.

Muscle mass reaches its highest value at approximately the age of 30 years. After that, it remains relatively stable and after the age of 50 it begins to decline steadily, at a rate of approximately 1% per year. This gradual loss of muscle mass as the age progresses is characterized by changes, both quantitative and qualitative (a 20% and 50% reduction of the size of Type II -fast twitch- muscle fibers and at a smaller rate the Type I -slow twitch- muscle fibers),

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which lead to the loss of muscle strength at a rate of 1-3% per aging year. Another qualitative change taking place with aging is the one relating to the fatty infiltration of the skeletal muscle, which appears to increase the likelihood of impaired mobility in elderly people. This phenomenon affects mainly elderly women, whose body composition has a high proportion of fatty tissue, and to lesser extent people that are obese (hence the use of the term "Sarcopenic Obesity")<sup>6</sup>.

The Foundation for the National Institutes of Health Sarcopenia Project recommends the use of specific cutoff points and criteria for the identification of people with limited functionality, relating to sarcopenia. This set of criteria includes the measurement of muscle strength (i.e. grip strength <26 kilos for men and <16 kilos for women) and the measurement of the body's muscle mass (i.e. the muscle mass of the limbs adjusted according to body mass index, in particular <0.789 for men and <0.512 for women)<sup>7</sup>.

The European Working Group on Sarcopenia in Older People (EWGSOP) argues that there are three stages to the disease, based on the above mentioned criteria with regard to sarcopenia's diagnosis:

- a. Pre-sarcopenia: the loss of only muscle mass.
- b. Sarcopenia: loss of muscle mass combined with either muscle weakness or reduced physical performance.
- c. Serious sarcopenia: loss of muscle mass, muscle weakness and reduced physical performance.

If sarcopenia is promptly diagnosed, the appropriate measures can be taken against the rapid rate of muscle mass loss and in this way achieve the delay or even the avoidance altogether of the beginning of physical disability with all its consequences<sup>1</sup>.

Due to the fact that sarcopenia has multifactorial etiopathogenesis, it is considered extremely difficult to develop a specialized treatment. As a result, there are different therapeutic approaches available which are divided in the following categories: a) medication, b) nutritional treatment and c) therapeutic exercise. As far as therapeutic exercise is concerned, it appears that a properly designed muscle strengthening program improves muscle mass, muscle strength and balance in people at risk of developing sarcopenia<sup>5,8</sup>.

### **Sarcopenia's diagnosis**

Both imaging and non-imaging methods are used for sarcopenia's diagnosis. The non-imaging techniques are used both in clinical practice and in research. A common and widespread method used is that of questionnaires, such as the SARC-F scale questionnaire for the probe of sarcopenia. This type of questionnaire does not require special measurements or equipment and it is used for the rapid probe of sarcopenia<sup>9</sup>. The credibility and validity of this questionnaire is considered to be comparable to more rigorous tests and has proven to possess good diagnostic abilities regarding physical limitations and mortality in the community's elderly population<sup>10</sup>.

The use of non-imaging techniques can also assess physical ability. A characteristic example is the physical ability test. It is a short test that requires approximately 15 minutes to be completed and it is used for the assessment of the function of lower limbs. As a technique it combines the values of walking speed and time required for repeated rise from a chair, as well as a series of balance tests. In addition, a dynamometer is often used for the assessment of muscle strength (measurement of grip strength or the strength of the quadriceps muscle)<sup>2</sup>.

From the group of imaging techniques used for sarcopenia's diagnosis the ones that assess the body mass composition (Body Composition) are: the ultrasound imaging (US), the Dual-energy X-ray absorptiometry (DXA), the computed tomography scan (CT) and the magnetic resonance imaging (MRI). As far as the assessment of muscle gain is concerned, the method considered to be the most accurate is that of the measurement of the muscle cross-sectional area (CSA). The measurement takes place through axial or magnetic resonance imaging and it measures the muscle mass of a particular area of the body. The best body location for the CSA measurement is the middle of the thigh, due to its great connection to the function level of the lower limb. Apart from that, other measurement locations are the psoas muscle, the lumbar paraspinal muscles and the rectus abdominis muscle<sup>2</sup>.

## **Imaging methods for the diagnosis of sarcopenia**

### ***Diagnosis through magnetic resonance imaging***

Magnetic Resonance Imaging (MRI), as a technique, has many advantages over the computed tomography scan (CT), due to the fact that ionizing radiation is not used in the process of imaging. The data are received by an induced magnetic field, which, in turn, causes the alignment of hydrogen nuclei. Then a radio frequency pulse is applied and these leads to the absorption of energy from the protons of hydrogen, which in turn emit energy, as the pulse is terminated and the protons return to their original position. Hereupon, the emitted energy is received by a sensor in the form of a radio pulse signal that is used in the creation of diagnostic imaging. The differences between the imaging of tissues and organs are related to the specific magnetic properties of every tissue, such as the protons' density and the time of longitudinal and transverse restoration<sup>11</sup>.

With the use of the magnetic resonance imaging method we have the ability to calculate the area and mass of the muscles; have an image of their morphological characteristics as well as their allocation, as is the case also with the ultrasound imaging and computed tomography scan. The Magnetic Resonance Imaging is now considered to be the most specialized imaging method as far as the identification of loss of muscle tissue quality is concerned<sup>2</sup>.

In the early stages of application of the magnetic

resonance imaging, the study of the body's composition started with the study of a small number of sections, which, however, had large spatial gaps between them. Just as with computed tomography scans, it was hard for reliable conclusions to be drawn from a single two-dimensional section with regard to the body's composition, especially for people with different body types, but, also, with regard to the allocation of tissues. These types of problems were overcome and significant progress was made with the coming of the three-dimensional scan of the whole body through the use of the magnetic resonance imaging.

By using special image analysis software, the gray scale images produced can be determined based on the information received through voxels and the surface. Through the use of anatomical knowledge and color codes that are pre-selected for specific areas, a calculation of both the total and the regional body mass can be achieved, according to a three-dimensional imaging equation, which results from the section's thickness, the tissue's surface, the distance between the successive images and the overall number of the initial images. The tissues' mass in kilograms can be calculated based on the assumed stable density values for the skeletal muscle (1.04 gr/cm<sup>3</sup>) and the adipose tissue (0.92 gr/cm<sup>3</sup>). Both the adipose tissue and the fibrous tissue are non-contractile tissues and their intramuscular deposition increases with age. The content of fat in the muscles could be responsible for up to one third of the total variations in muscle strength and constitutes a powerful predictive indicator for the loss of mobility in elderly people of good general health status. Similarly, muscle fibrosis is considered to be connected with reduced strength, reduced agility, reduced blood supply and increased muscular atrophy<sup>2</sup>.

It was proven recently that the multiparameter magnetic resonance imaging is valuable in the automatic quantification of the intramuscular adipose tissue storage areas, which could possibly cause toxicity to muscle cells via paracrine mechanisms<sup>12</sup>. The magnetic resonance imaging has been used mainly in the evaluation of adipose tissue (quantity and allocation), followed by the mass of skeletal muscles. Even though total body scan offers excellent information, the majority of the available studies up until today include one section protocols, especially at mid-thigh level. This technique has been proven to be useful in the evaluation of changes in body composition in cross-sectional studies or interventional studies in Sarcopenia<sup>13</sup>.

### ***Magnetic resonance imaging restrictions***

Both in research and clinical conditions, the magnetic resonance imaging restrictions are mainly connected to the significantly high cost of the examination, the high technical skills required for the careful analysis of the images produced, as well as the technical errors that may occur due to respiration movements during the examination. All of the above contribute towards making magnetic resonance imaging a difficult tool to use, not only in large-scale

epidemiological studies but also in everyday clinical practice. Hence, even though magnetic resonance imaging has proven to be very accurate, it is not the most common method used.

A significant issue concerning the imaging methods used in the diagnosis of the types of sarcopenia is radiation. The safest methods are those that do not use ionizing radiation, such as magnetic resonance imaging and ultrasound imaging, followed by the methods with a very small percentage of radiation, such as DXA. Finally, the computed tomography scan is the method with the greatest percentage of radiation, which makes it unsuitable for repeated measurements, regardless of the fact that it is easy to use and widely available. From the point of view of availability, the computed tomography scan and the ultrasound imaging are both widely available, followed by the Dual-energy X-ray absorptiometry X/DXA.

As far as the cost of the examination is concerned, the magnetic resonance imaging is the most expensive one, while the Dual-energy X-ray absorptiometry DXA and the ultrasound imaging are the least expensive costly ones. The CT and the DXA only need a couple of minutes to be completed, which makes them appealing to the patient, contrary to the MRI, which requires more time in order to be completed. Moreover, the MRI protocols require that the patient hold his/her breath for relatively long periods of time, while this method is deemed unsuitable for patients suffering from claustrophobia or carrying metallic foreign bodies. The cross-sectional methods, such as the computed tomography scan and the magnetic resonance imaging, are considered to be more accurate with regard to body composition study, since they possess the largest spatial resolution, their analysis is at body compartment level (and not at a molecular level, as is the case with DXA), while their results are not influenced by the patient's condition (i.e. their hydration degree), as is the case with the DXA and the ultrasound imaging. In addition, the accuracy of those methods is not affected by the person performing the examination, as is the case with the ultrasound imaging, where excessive pressure with the transducer could affect the measured muscle dimensions<sup>13</sup>.

### ***Diagnosis through Computer Tomography***

Computer Tomography is another imaging method that is able to provide information on muscle quantity and composition. Normal attenuation values for muscle density are variable ranging from 40 to 100 HU with fatty infiltration, muscle shows variable size areas of decreased HU values (between -200 and -35 HU). Two approaches are generally used for quantifying muscle CSA (squared centimeters) and density (Hounsfield units) on abdominal CT scans.

One method involves segmenting all of the muscle on an axial image at the L3 level, with image analysis software set to include tissue between -29 and 150 HU. L3 level is commonly used to estimate regional muscle mass, by calculating cross-section area (CSA) of all truncal muscles. This area is commonly normalized to patient's height (in centimeters), to yield skeletal muscle index (in centimeters

squared per meter squared).

Another method measures the psoas muscle CSA at the L3 or L4 level as well as to measure paraspinal musculature usually at T12 level<sup>14</sup>. High quality reconstruction images can be obtained with CT and may be helpful in increasing segmentation accuracy. The radiation exposure of CT represents a no-negligible limitation of this technique and limits its clinical application.

## Conclusions

Sarcopenia is a common disease that has a negative impact on patients' health, as well as a heavy financial and social burden for the developed world. Today imaging plays a crucial role in diagnosing patients with sarcopenia. It is used in:

- a. testing without the presence of symptoms,
- b. the diagnosis,
- c. the evaluation of the severity of a situation,
- d. the monitoring of the disease's progression and
- e. the evaluation of the effectiveness of its treatment.

Apart from that, through the use of imaging methods, the extraction of further useful information is possible, such as the evaluation of the adipose tissue of the central nervous system and of the bone-muscle functional unit.

The imaging methods that are used in the study of patients with sarcopenia, are the following: Dual-energy X-ray absorptiometry X/DXA, computed tomography scan/CT, magnetic resonance imaging/MRI, ultrasound imaging/US, peripheral Quantitative Computed Tomography (pQCT). Of all the above, DXA and CT are the methods more widely available and used in everyday clinical practice, with the first having an advantage in terms of radiation loads and the second having an advantage in terms of accuracy, due to data retrieval capability it offers from the previously performed CTs that exist in the patient's file.

The absence of commonly accepted quantitative criteria in the evaluation of sarcopenia through the use of imaging poses a problem. Special metabolic conditions that are connected with mixed forms of osteoporosis and sarcopenia are the Osteosarcopenic Obesity, the vulnerability syndrome and cachexia. The simultaneous existence of osteoporosis and sarcopenia is connected to a plethora of conditions, such as the long-term administration of glucocorticoids, chronic renal disease and chronic obstructive pulmonary disease, rheumatoid arthritis, neurological disorders, zero gravity conditions, as well as other endocrine, gastrointestinal, malignant or infectious diseases.

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