Accepted Manuscript

Title: IMAGING OF SARCOPENIA

Author: Giuseppe Sergi Caterina Trevisan Nicola Veronese Paola Lucato Enzo Manzato

PII: S0720-048X(16)30120-6
DOI: http://dx.doi.org/doi:10.1016/j.ejrad.2016.04.009
Reference: EURR 7458

To appear in: *European Journal of Radiology*

Received date: 24-11-2015
Revised date: 13-3-2016
Accepted date: 13-4-2016

Please cite this article as: Sergi Giuseppe, Trevisan Caterina, Veronese Nicola, Lucato Paola, Manzato Enzo.IMAGING OF SARCOPENIA.*European Journal of Radiology* http://dx.doi.org/10.1016/j.ejrad.2016.04.009

IMAGING OF SARCOPENIA

Giuseppe Sergi, MD[1]; Caterina Trevisan, MD[1]; Nicola Veronese, MD[1]; Paola Lucato, MD[1]; Enzo Manzato, MD[1,2].

[1] Department of Medicine (DIMED), Geriatrics Division, University of Padova, Via Giustiniani 2, Padova, Italy.

[2] National Research Council, Institute of Neuroscience, Aging Branch, Via Giustiniani 2, Padova, Italy.

Address for correspondence and reprints:

Giuseppe Sergi

Department of Medicine - DIMED, Geriatrics Division, University of Padova, Padova, Italy

Via Giustiniani 2, 35128 Padova, Italy

Phone: +390498218492; Fax: +390498211218

Email: giuseppe.sergi@unipd.it

IMAGING OF SARCOPENIA

Running head: Imaging of sarcopenia

Word count: 2519.

HIGHLIGHTS

- Sarcopenia involves quantitative and qualitative changes of muscle mass with aging.

- Computed Tomography and Magnetic Resonance are the gold standard for the study of sarcopenia.

- Sonography' reliability has not been fully evaluated compared with other methods, yet.

- Dual X-ray Absorptiometry is the most used method to estimate the loss of muscle mass.

ABSTRACT

Sarcopenia is currently considered a geriatric syndrome increasing in older people. The consequences of sarcopenia - in terms of impaired mobility, limited self-sufficiency and disability - have been amply demonstrated, increasing the need to develop methods to identify muscle mass loss as early as possible. Although sarcopenia involves a reduction in both muscle mass and function, loss of muscle mass remains the essential criterion for diagnosing this condition in daily practice. Computed tomography and magnetic resonance imaging represent the gold standard for studying body composition, and can identify quantitative and qualitative changes in muscle mass. These techniques are costly, time-consuming and complex, however, so their applicability is limited to the research field. Sonography, on the other hand, has the advantage of being a relatively quick and inexpensive method for detecting loss of muscle fibers and fat infiltration by analyzing muscle thickness and echo intensity. To the best of our knowledge, however, only few studies have compared the results of ultrasound with those obtained by other methods in order to establish its reliability in this setting. Dual X-ray absorptiometry thus remains the most often used technology for studying body composition, detecting quantitative changes in muscle mass with the advantages of a low radiation dose, a simple technology and a rapid assessment.

Keywords: sarcopenia; dual X-ray absorptiometry; magnetic resonance; computed tomography; ultrasound.

1. Introduction

1.1. Sarcopenia: a geriatric syndrome

The term *sarcopenia* (from the Greek *sarx*, flesh, and *penia*, loss) was coined by Rosenberg in 1989 to define the age-related loss of skeletal muscle mass and strength [1,2]. Nowadays, sarcopenia is rightly considered a geriatric syndrome, with a prevalence that ranges between 10% and 50% among individuals over 65 years of age, as demonstrated by means of anthropometrics, bioelectrical impedance or dual X-ray absorptiometry (DXA) analyses [3]. The negative effects of sarcopenia have been amply demonstrated and include physical impairment, a greater risk of falls and fractures, disability, limited self-sufficiency in activities of daily living, and higher mortality[4]. As a result of these effects and of the increasing prevalence of sarcopenia in the elderly, 1.5% of the total healthcare expenditure in the United States has been attributed to sarcopenia [5].

The diagnostic criteria for sarcopenia proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) concern a low muscle mass combined with a documented muscle weakness or poor physical performance [6]. Considering these criteria and the progressive nature of the condition, three stages of sarcopenia have been defined: pre-sarcopenia, sarcopenia and severe sarcopenia (Table 1). Pre-sarcopenia is defined as loss of skeletal muscle mass alone; sarcopenia involves loss of muscle mass associated with either muscle weakness or poor physical performance; and severe sarcopenia identifies cases meeting all three criteria (low muscle mass, muscle weakness, and poor physical performance) [6]. Detecting sarcopenia at an early stage can prompt measures to delay the loss of muscle mass, thereby avoiding or postponing the onset of functional impairment and its consequences. Since loss of muscle mass is the *condicio sine qua non* of sarcopenia, muscle mass imaging has become more important in recent years. The aim of the present study was therefore to review the currently-used imaging technologies capable of detecting the loss of skeletal muscle mass and serving as fundamental tools in the diagnosis of sarcopenia.

1.2. Changes in muscle mass with aging

The progressive loss of muscle mass occurring with advanced age is characterized by qualitative and quantitative changes that lead to a loss of strength at an estimated rate of 1-3% a year [7–10]. The main determinant of this age-related decline in muscle function seems to be the loss of skeletal muscle mass. In an autoptic study on whole vastus lateralis muscles, older people had a total muscle cross-sectional area (CSA) that was about 40% smaller than in young adults [11]. The atrophic phenomenon responsible for this muscle loss seems to begin from 25 years of age onwards, speeding up after the fifth decade and affecting men more than women [10–12]. The loss of muscle mass is accompanied by qualitative changes in muscle fibers, particularly involving a reduction in the size of type II (fast twitch) fibers and, to a lesser degree, of type I (slow twitch) fibers. The demonstrated reduction in type II fiber size differs depending on the sampling procedures used, ranging between 20% and 50% [10]. The process is associated with a progressive atrophy and a stronger expression of the two myosin heavy chain isoforms [10,11,13]. A fiber type grouping has also been reported in the muscles of older people, probably due to a motor neuron impairment that may be the primary culprit responsible for the loss of muscle mass [11]. Another qualitative change occurring in muscle mass with aging involves fat infiltration within the muscle [14], which seems to increase the risk of mobility impairment in older people [15]. This phenomenon mainly affects older women with a rising proportion of fat mass in their body composition [16], and individuals who are obese - hence the term “sarcopenic obesity” used to define the combination of sarcopenia and obesity in the elderly [17].

1.3. Imaging in sarcopenia

The imaging technologies used to detect loss of skeletal muscle mass in sarcopenia include: dual X-ray absorptiometry (DXA), magnetic resonance imaging (MRI), computed tomography (CT), peripheral quantitative computed tomography (pQCT), and ultrasound (US). These methods differ considerably in terms of reliability, exposure to radiation, time taken to complete the examination and analyze the results, the availability and complexity of the equipment involved, costs and applications. The characteristics of DXA, CT, MRI, and US are compared in **Table 2** [18-20]. On the other hand, qualitative changes in muscle fibers can be investigated only by means of histochemical analyses and microscopy imaging. The following sections describe the main features of the imaging techniques used to assess loss of skeletal muscle mass.

2. Dual X-ray Absorptiometry (DXA)

DXA is the technology most frequently used to study body composition. Based on the attenuation of two X-ray beams with different energy levels, DXA estimates bone mineral density, fat mass and fat-free mass of the whole body, or of specific anatomical regions (e.g. arms, legs, trunk and head) (Figure 1) [21,22]. Although the lean mass measured by DXA includes the skin, connective tissues, parenchyma and skeletal muscle mass, the method has demonstrated a strong correlation with the results obtained by means of anthropometric measures and models based on total body potassium and nitrogen in fat-free mass [23]. Appendicular skeletal muscle mass (ASMM) is currently the measure most often considered for the purpose of assessing sarcopenia; it is calculated from the sum of the muscle mass of the arms and legs, as shown in **Figure 1**. The ratio between ASMM and height squared defines the appendicular skeletal muscle mass index (ASMMI). Several ASMMI cut-offs have been proposed for the diagnosis of sarcopenia, adopting values below the 15th percentile (for a young population's ASMMI) or less than 20th percentile (for an old population's ASMMI), or below 1 or 2 standard deviations from the average ASMMI of a young population [24–27]. The cut-offs most often applied are shown in **Table 3**. DXA thus emerges as a valid tool for diagnosing sarcopenia, giving an accurate quantitative estimate of skeletal muscle mass. Low costs and a low radiation dose (less than 1 mrem) justify the widespread use of DXA in clinical practice [22], although it can provide no information on qualitative changes in muscle mass (unlike CT and MRI). The instrument used for DXA is not portable, however, and must be used by a skilled operator, both aspects that may limit its use.

3. Computed Tomography (CT) and peripheral Quantitative Computed Tomography (pQCT)

Like MRI, CT is considered one of the most suitable methods for analyzing quantitative and qualitative changes in body composition, investigating skeletal muscle mass and distinguishing adipose tissue in different body compartments [22,28]. Based on the average attenuation of the X-ray beam through different body substrates, CT produces cross-sectional scans enabling segmental and total measures of fat and fat-free mass. Bearing in mind that normal attenuation values for muscle density range between 40 and 100 Hounsfield units (HU), CT imaging can reveal fat infiltration within muscle by identifying areas in the range of -190 to -30 HU [29] or, as Ross suggested, by finding muscle attenuation values of 0-30 HU [30]. The reliability of CT for the purpose of studying quantitative and qualitative changes in fat and fat-free mass with aging has been well documented in the last 25 years [22]. Like the known drawbacks of MRI, the high radiation levels used in CT have led to its use mainly in the field of research [28].

In recent years, *Peripheral Quantitative Computed Tomography* has been proposed for use in studying musculoskeletal changes since it sidesteps the limitations of CT: pQCT uses a smaller scanner and lower radiation doses to analyze the volumetric density and structure of peripheral tissue slices (Figure 2). The cross-sectional area of the tibia two-thirds along its length (starting from the tibiotarsal joint) is analyzed to identify quantitative muscle mass changes, since this region coincides with the largest outer calf diameter with a small inter-individual variability [31].

Lauretani *et al.* suggested adopting values lower than 2 standard deviations of the mean for a young reference group to define sarcopenia, which corresponded to cut-offs of 83.3 cm^2 (95%CI 78.9-87.8) for men, and 62.6 cm^2 (95%CI 58.5-66.7) for women [32]. Another work by Cesari *et al.* defined sarcopenia on the grounds of fat-adjusted muscle mass, calculated as the lowest gender-specific tertile of the residuals of a linear regression model that predicted muscle mass area (in cm^2) from height (in cm) and fat mass area (log value of cm^2) [33]; this was similar to the method used by Newman et *al*. to identify sarcopenia in older people [24]. The reliability of pQCT for analyzing muscle mass has been examined in several works, which found errors of 1-3% for the CSA of the lower leg muscle [31,34–36]. Swinford and Warden confirmed an overall error of less than 1.5% for muscle and 3% for fat mass [37]. These accuracy values proved to be negatively influenced by the time elapsing between scans and by anthropometric characteristics, due to both device- and operator-related factors [37].

High-resolution pQCT (HR-pQCT) is the latest technology to be applied to the study of bone micro-architecture with a high SNR (Signal-to-Noise Ratio) and spatial resolution. HR-pQCT focuses on peripheral sites (generally the distal radius or tibia) and quickly obtains tomographic scans, using a lower radiation dose than whole-body CT and sparing radiosensitive organs [38]. Both pQCT and HR-pQCT have been used to seek potential associations between the muscle criteria for diagnosing sarcopenia and the structure of cortical and trabecular bone [28,36–38]. The results of these investigations demonstrate that muscle size is strongly associated with bone size and strength [31,39–41]. Total cortical and trabecular BMD, and cortical bone area have also revealed a significant relationship with physical performance, probably due to genetic, endocrine and lifestyle factors (e.g. physical activity according to the mechanostat hypothesis, dynamic loading, and so on) influencing both muscle and bone mass [39,42,43].

4. Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging, like CT, is among the recommended methods for diagnosing sarcopenia, since it can evaluate skeletal muscle mass and distinguish it from fat. By analyzing variations in the radio frequency pulse sequence, MRI can estimate fat mass or fat-free mass and generate cross-sectional images [22,44]. As shown in Figure 3 comparing cross-sectional images of the thigh of a young and an old man, MRI reveals the reduction in muscle mass and the infiltration of fat in lean mass that occurs with aging. MRI is used to assess adipose tissue distribution in subcutaneous and visceral compartments, demonstrating a satisfactory agreement with the findings of dissection and chemical analysis [45]. MRI is also a non-invasive solution for studying muscle fiber composition based on T1 and T2 relaxation times, since these parameters are longer for fast-twitch than for slow-twitch fibers [46,47]. As for its accuracy, MRI is associated with an error in quantifying muscle that ranges between 1.1% and 4.4%, as shown by Nordez *et al.*, who compared axial MRI with four methods for estimating quadriceps volume [48]. Unlike indirect methods for assessing body composition (anthropometry, bio-impedance, body water dilution, underwater weighing), MRI minimizes potential errors of individual variability thanks to its absolute calibration for volume measurements [49]. MRI also escapes additional sources of bias in other techniques due to the adoption of constant density values for fat and lean mass [22]. These factors contribute to increase the accuracy of MRI, particularly in estimating fat-free mass, the water, protein and bone mineral content of which can change with aging [49]. Finally, in contrast with CT and DXA, MRI involves no ionizing radiation. MRI is one of the most reliable techniques for studying body composition, but its high cost and complexity, and availability issues limit its use in clinical practice, so it is still used mainly in the field of research [21,28].

5. Ultrasound (US)

Ultrasound scanning is a low-cost, non-invasive imaging technique used to study muscle damage or wasting diseases like sarcopenia [50]. International guidelines on sarcopenia generally recommend using other approaches to identify loss of muscle mass, but US can be a good initial choice for assessing qualitative or quantitative changes in muscle mass. Measuring muscle thickness can provide an estimate of the reduction in lean body mass, and grayscale analysis to assess echo intensity can provide a measure of qualitative changes such as adipose infiltration within the muscle [50,51]. Quantitative US has been compared with MRI and demonstrated a satisfactory consistency in estimating lean and fat body mass [52,53]. On the other hand, examiner-dependent factors such as the orientation of the sound transducer relative to the body surface, or the compressive stress brought to bear by the operator on the tissue, can give rise to measurement errors and interfere with the test's reproducibility [52,54]. Using an augmented force-feedback, calibration phantoms, standardized procedures, and echo intensity correction factors when comparing different US measures could improve the consistency of the technique [55].

6. Conclusions

For a diagnosis of sarcopenia we need to assess loss of skeletal muscle mass, muscle weakening, and declining physical performance. A reduction in muscle mass is nonetheless the main diagnostic criterion for sarcopenia, especially in the early stage, so it has become increasingly important to be able to study muscle changes in order to identify this geriatric syndrome. MRI and CT are the most reliable methods for this purpose because they can reveal both quantitative and qualitative changes in muscle mass, but they are only used for research purposes because they are costly, time-consuming and complex technologies. Although DXA can only provide a quantitative estimate of muscle loss, it is currently the method most often used to detect sarcopenia because the method requires a few time and only a low radiation dose. To date, US represents a valid potential alternative for identifying changes in muscle such as loss of fibers or fat infiltration, although comparative studies have yet to be conducted to demonstrate its reliability vis-à-vis the other techniques.

REFERENCES

[1] I. Rosenberg, Summary comments: epidemiological and methodological problems in determining nutritional status of older persons., Am J Clin Nutr. 50 (1989) 1231–3.

[2] I.H. Rosenberg, Sarcopenia: origins and clinical relevance., J. Nutr. 127 (1997) 990S–991S. http://www.ncbi.nlm.nih.gov/pubmed/9164280 (accessed November 9, 2015).

[3] R.A. Fielding, B. Vellas, W.J. Evans, S. Bhasin, J.E. Morley, A.B. Newman, et al., Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia., J. Am. Med. Dir. Assoc. 12 (2011) 249–56. doi:10.1016/j.jamda.2011.01.003.

[4] R. Roubenoff, Sarcopenia and its implications for the elderly., Eur. J. Clin. Nutr. 54 Suppl 3 (2000) S40–7. http://www.ncbi.nlm.nih.gov/pubmed/11041074 (accessed February 5, 2016).

[5] I. Janssen, D.S. Shepard, P.T. Katzmarzyk, R. Roubenoff, The healthcare costs of sarcopenia in the United States., J. Am. Geriatr. Soc. 52 (2004) 80–5. http://www.ncbi.nlm.nih.gov/pubmed/14687319 (accessed January 22, 2016).

[6] A.J. Cruz-Jentoft, J.P. Baeyens, J.M. Bauer, Y. Boirie, T. Cederholm, F. Landi, et al., Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People., Age Ageing. 39 (2010) 412–23. doi:10.1093/ageing/afq034.

[7] E.J. Bassey, U.J. Harries, Normal values for handgrip strength in 920 men and women aged over 65 years, and longitudinal changes over 4 years in 620 survivors., Clin. Sci. (Lond). 84 (1993) 331–7. http://www.ncbi.nlm.nih.gov/pubmed/8384956 (accessed February 7, 2016).

[8] T. Rantanen, K. Masaki, D. Foley, G. Izmirlian, L. White, J.M. Guralnik, Grip strength changes over 27 yr in Japanese-American men., J. Appl. Physiol. 85 (1998) 2047–53. http://www.ncbi.nlm.nih.gov/pubmed/9843525 (accessed February 7, 2016).

[9] M.M. Porter, A.A. Vandervoort, J. Lexell, Aging of human muscle: structure, function and adaptability., Scand. J. Med. Sci. Sports. 5 (1995) 129–42. http://www.ncbi.nlm.nih.gov/pubmed/7552755 (accessed February 7, 2016).

[10] T.J. Doherty, Invited review: Aging and sarcopenia., J. Appl. Physiol. 95 (2003) 1717–27. doi:10.1152/japplphysiol.00347.2003.

[11] J. Lexell, C.C. Taylor, M. Sjöström, What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men., J. Neurol. Sci. 84 (1988) 275–94. http://www.ncbi.nlm.nih.gov/pubmed/3379447 (accessed February 3, 2016).

[12] I. Janssen, S.B. Heymsfield, Z.M. Wang, R. Ross, Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr., J. Appl. Physiol. 89 (2000) 81–8. http://www.ncbi.nlm.nih.gov/pubmed/10904038 (accessed August 25, 2015).

[13] J.L. Andersen, G. Terzis, A. Kryger, Increase in the degree of coexpression of myosin heavy chain isoforms in skeletal muscle fibers of the very old., Muscle Nerve. 22 (1999) 449–54. http://www.ncbi.nlm.nih.gov/pubmed/10204778 (accessed February 7, 2016).

[14] B.H. Goodpaster, C.L. Carlson, M. Visser, D.E. Kelley, A. Scherzinger, T.B. Harris, et al., Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study., J. Appl. Physiol. 90 (2001) 2157–65. http://www.ncbi.nlm.nih.gov/pubmed/11356778 (accessed February 7, 2016).

[15] M. Visser, B.H. Goodpaster, S.B. Kritchevsky, A.B. Newman, M. Nevitt, S.M. Rubin, et al., Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons., J. Gerontol. A. Biol. Sci. Med. Sci. 60 (2005) 324–33. http://www.ncbi.nlm.nih.gov/pubmed/15860469 (accessed December 21, 2015).

[16] A. Coin, G. Sergi, N. Minicuci, S. Giannini, E. Barbiero, E. Manzato, et al., Fat-free mass and fat mass reference values by dual-energy X-ray absorptiometry (DEXA) in a 20-80 year-old Italian population., Clin. Nutr. 27 (2008) 87–94. doi:10.1016/j.clnu.2007.10.008.

[17] S. Stenholm, T.B. Harris, T. Rantanen, M. Visser, S.B. Kritchevsky, L. Ferrucci, Sarcopenic obesity: definition, cause and consequences., Curr. Opin. Clin. Nutr. Metab. Care. 11 (2008) 693–700. doi:10.1097/MCO.0b013e328312c37d.

[18] J.P. Despres, R. Ross, S. Lemieux, Imaging techniques applied to the measurement of human body composition. In Human Body Composition, eds Roche A. F., Heymsfield S. B., Lohman T. G. (Human Kinetics, Champaign, IL), (1996), pp 149–166.

[19] K.J. Ellis, Human body composition: in vivo methods. Physiol Rev. 80(2) (2000) 649-80.

[20] Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol (1985). 1998 Jul;85(1):115-22.

[21] G. Rubbieri, E. Mossello, M. Di Bari, Techniques for the diagnosis of sarcopenia., Clin. Cases Miner. Bone Metab. 11 (2014) 181–4.

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4269140&tool=pmcentrez&rendertype=abstract (accessed February 7, 2016).

[22] M.S. Lustgarten, R.A. Fielding, Assessment of analytical methods used to measure changes in body composition in the elderly and recommendations for their use in phase II clinical trials., J. Nutr. Health Aging. 15 (2011) 368–75. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3376910&tool=pmcentrez&rendertype=abstract (accessed February 7, 2016).

[23] S.B. Heymsfield, R. Smith, M. Aulet, B. Bensen, S. Lichtman, J. Wang, et al., Appendicular skeletal muscle mass: measurement by dual-photon absorptiometry., Am. J. Clin. Nutr. 52 (1990) 214–8. http://www.ncbi.nlm.nih.gov/pubmed/2375286 (accessed November 19, 2015).

[24] A.B. Newman, V. Kupelian, M. Visser, E. Simonsick, B. Goodpaster, M. Nevitt, et al., Sarcopenia: alternative definitions and associations with lower extremity function., J. Am. Geriatr. Soc. 51 (2003) 1602–9. http://www.ncbi.nlm.nih.gov/pubmed/14687390 (accessed November 20, 2015).

[25] M.J. Delmonico, T.B. Harris, J.-S. Lee, M. Visser, M. Nevitt, S.B. Kritchevsky, et al., Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women., J. Am. Geriatr. Soc. 55 (2007) 769–74. doi:10.1111/j.1532-5415.2007.01140.x.

[26] R.N. Baumgartner, K.M. Koehler, D. Gallagher, L. Romero, S.B. Heymsfield, R.R. Ross, et al., Epidemiology of sarcopenia among the elderly in New Mexico., Am. J. Epidemiol. 147 (1998) 755–63. http://www.ncbi.nlm.nih.gov/pubmed/9554417 (accessed August 20, 2015).

[27] A. Coin, S. Sarti, E. Ruggiero, S. Giannini, M. Pedrazzoni, S. Minisola, et al., Prevalence of sarcopenia based on different diagnostic criteria using DEXA and appendicular skeletal muscle mass reference values in an Italian population aged 20 to 80., J. Am. Med. Dir. Assoc. 14 (2013) 507–12. doi:10.1016/j.jamda.2013.02.010.

[28] G. Woodrow, Body composition analysis techniques in the aged adult: indications and limitations., Curr. Opin. Clin. Nutr. Metab. Care. 12 (2009) 8–14. doi:10.1097/MCO.0b013e32831b9c5b.

[29] L. Sjöström, H. Kvist, A. Cederblad, U. Tylén, Determination of total adipose tissue and body fat in women by computed tomography, 40K, and tritium., Am. J. Physiol. 250 (1986) E736–45. http://www.ncbi.nlm.nih.gov/pubmed/3717334 (accessed February 7, 2016).

[30] R. Ross, Advances in the application of imaging methods in applied and clinical physiology., Acta Diabetol. 40 Suppl 1 (2003) S45–50. doi:10.1007/s00592-003-0025-y.

[31] J. Rittweger, G. Beller, J. Ehrig, C. Jung, U. Koch, J. Ramolla, et al., Bone-muscle strength indices for the human lower leg., Bone. 27 (2000) 319–26. http://www.ncbi.nlm.nih.gov/pubmed/10913929 (accessed February 7, 2016).

[32] F. Lauretani, C.R. Russo, S. Bandinelli, B. Bartali, C. Cavazzini, A. Di Iorio, et al., Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia., J. Appl. Physiol. 95 (2003) 1851–60. doi:10.1152/japplphysiol.00246.2003.

[33] M. Cesari, M. Pahor, F. Lauretani, V. Zamboni, S. Bandinelli, R. Bernabei, et al., Skeletal muscle and mortality results from the InCHIANTI Study., J. Gerontol. A. Biol. Sci. Med. Sci. 64 (2009) 377–84. doi:10.1093/gerona/gln031.

[34] M. Burrows, D.M.L. Cooper, D. Liu, H.A. McKay, Bone and muscle parameters of the tibia: agreement between the XCT 2000 and XCT 3000 instruments., J. Clin. Densitom. 12 186–94. doi:10.1016/j.jocd.2008.09.005.

[35] K.W. Creamer, K.L. Butner, W.G. Herbert, Short-Term Precision of Peripheral Quantitative Computed Tomography for Hard and Soft Tissue Measurements at Mid-Shaft and Distal Regions of the Tibia, J. Clin. Densitom. 11 (2008) 466. doi:10.1016/j.jocd.2008.05.080.

[36] B.L. Gordon CL, Webber CE, Accuracy and precision error of muscle cross-sectional area measured using peripheral quantitative computed tomography in adults [abstract], J Bone Min. Res. 18 (2003).

[37] R.R. Swinford, S.J. Warden, Factors affecting short-term precision of musculoskeletal measures using peripheral quantitative computed tomography (pQCT)., Osteoporos. Int. 21 (2010) 1863–70. doi:10.1007/s00198-009-1151-3.

[38] R. Krug, A.J. Burghardt, S. Majumdar, T.M. Link, High-resolution imaging techniques for the assessment of osteoporosis., Radiol. Clin. North Am. 48 (2010) 601–21. doi:10.1016/j.rcl.2010.02.015.

[39] M.H. Edwards, C.L. Gregson, H.P. Patel, K.A. Jameson, N.C. Harvey, A.A. Sayer, et al., Muscle size, strength, and physical performance and their associations with bone structure in the Hertfordshire Cohort Study., J. Bone Miner. Res. 28 (2013) 2295–304. doi:10.1002/jbmr.1972.

[40] Y. Hasegawa, P. Schneider, C. Reiners, Age, sex, and grip strength determine architectural bone parameters assessed by peripheral quantitative computed tomography (pQCT) at the human radius., J. Biomech. 34 (2001) 497–503. http://www.ncbi.nlm.nih.gov/pubmed/11266673 (accessed February 7, 2016).

[41] A.W. Frank, A.L. Lorbergs, P.D. Chilibeck, J.P. Farthing, S.A. Kontulainen, Muscle cross sectional area and grip torque contraction types are similarly related to pQCT derived bone strength indices in the radii of older healthy adults., J. Musculoskelet. Neuronal Interact. 10 (2010) 136–41. http://www.ncbi.nlm.nih.gov/pubmed/20516630 (accessed February 7, 2016).

[42] N.A. Tritos, B.M.K. Biller, Growth hormone and bone., Curr. Opin. Endocrinol. Diabetes. Obes. 16 (2009) 415–22. doi:10.1097/MED.0b013e3283319e6d.

[43] A. Gómez-Cabello, I. Ara, A. González-Agüero, J.A. Casajús, G. Vicente-Rodríguez, Effects of training on bone mass in older adults: a systematic review., Sports Med. 42 (2012) 301–25. doi:10.2165/11597670-000000000-00000.

[44] O. Selberg, W. Burchert, G. Graubner, C. Wenner, C. Ehrenheim, M.J. Müller, Determination of anatomical skeletal muscle mass by whole body nuclear magnetic resonance., Basic Life Sci. 60 (1993) 95–7. http://www.ncbi.nlm.nih.gov/pubmed/8110175 (accessed February 7, 2016).

[45] N. Abate, D. Burns, R.M. Peshock, A. Garg, S.M. Grundy, Estimation of adipose tissue mass by magnetic resonance imaging: validation against dissection in human cadavers., J. Lipid Res. 35 (1994) 1490–6. http://www.ncbi.nlm.nih.gov/pubmed/7989873 (accessed January 23, 2016).

[46] S. Kuno, S. Katsuta, T. Inouye, I. Anno, K. Matsumoto, M. Akisada, Relationship between MR relaxation time and muscle fiber composition., Radiology. 169 (1988) 567–8. doi:10.1148/radiology.169.2.3175009.

[47] S. Kuno, S. Katsuta, M. Akisada, I. Anno, K. Matsumoto, Effect of strength training on the relationship between magnetic resonance relaxation time and muscle fibre composition., Eur. J. Appl. Physiol. Occup. Physiol. 61 (1990) 33–6. http://www.ncbi.nlm.nih.gov/pubmed/2289496 (accessed February 7, 2016).

[48] A. Nordez, E. Jolivet, I. Südhoff, D. Bonneau, J.A. de Guise, W. Skalli, Comparison of methods to assess quadriceps muscle volume using magnetic resonance imaging., J. Magn. Reson. Imaging. 30 (2009) 1116–23. doi:10.1002/jmri.21867.

[49] E.L. Thomas, N. Saeed, J. V Hajnal, A. Brynes, A.P. Goldstone, G. Frost, et al., Magnetic resonance imaging of total body fat., J. Appl. Physiol. 85 (1998) 1778–85. http://www.ncbi.nlm.nih.gov/pubmed/9804581 (accessed January 5, 2016).

[50] S. Pillen, N. van Alfen, Skeletal muscle ultrasound., Neurol. Res. 33 (2011) 1016–24. doi:10.1179/1743132811Y.0000000010.

[51] Y. Watanabe, Y. Yamada, Y. Fukumoto, T. Ishihara, K. Yokoyama, T. Yoshida, et al., Echo intensity obtained from ultrasonography images reflecting muscle strength in elderly men., Clin. Interv. Aging. 8 (2013) 993–8. doi:10.2147/CIA.S47263.

[52] A.C. Dupont, E.E. Sauerbrei, P. V Fenton, P.C. Shragge, G.E. Loeb, F.J. Richmond, Real-time sonography to estimate muscle thickness: comparison with MRI and CT., J. Clin. Ultrasound. 29 (2001) 230–6. doi:10.1002/jcu.1025.

[53] T. Abe, M. Kondo, Y. Kawakami, T. Fukunaga, Prediction equations for body composition of Japanese adults by B-mode ultrasound, Am. J. Hum. Biol. 6 (1994) 161–170. doi:10.1002/ajhb.1310060204.

[54] H. Ishida, S. Watanabe, Influence of inward pressure of the transducer on lateral abdominal muscle thickness during ultrasound imaging., J. Orthop. Sports Phys. Ther. 42 (2012) 815–8. doi:10.2519/jospt.2012.4064.

[55] M.O. Harris-Love, R. Monfaredi, C. Ismail, M.R. Blackman, K. Cleary, Quantitative ultrasound: measurement considerations for the assessment of muscular dystrophy and sarcopenia., Front. Aging Neurosci. 6 (2014) 172. doi:10.3389/fnagi.2014.00172.

Table 1. Classification of sarcopenia

Diagnostic criteria for sarcopenia	Pre-sarcopenia	Sarcopenia		Severe sarcopenia
Low muscle mass	+	+		+
Muscle weakness	-	+	-	+
Poor physical performance	-	-	+	+

Table 2. Imaging technologies for diagnosing sarcopenia

Technologies	Dual X-ray Absorptiometry	Computed Tomography	Magnetic Resonance Imaging	Ultrasound
Reliability	++	+++	+++	+
Rapidity	+++	+	+	+++
Complexity	+	+++	+++	++
Expenditure	++	+++	+++	+
X-ray exposure	+	+++	-	-
Error of lean mass	<5%	<8.5%	6-8.5%	-

estimate [18-20]				
Field of application	Clinical/ Research	Research	Research	Clinical

Table 3. ASMMI (appendicular skeletal muscle mass index) cut-offs for diagnosing sarcopenia in men and women

	ASMMI cut-offs (kg/m^2)	
	Men	**Women**
Baumgartner *et al.*, 1998 [26]	< 7.26	< 5.45
Delmonico *et al.*, 2007 [25]	< 7.25	< 5.67

Newman *et al.*, 2003 [24]	< 7.23	< 5.67
Coin *et al.*, 2013 [27]	< 7.59	< 5.47

Abbreviations: ASMMI, appendicular skeletal muscle mass index.

Figure 1. Total-body DXA for assessing body composition. Left: 84-year-old woman with sarcopenia, ASMMI 5.05 kg/m^2. Right: 72-year-old woman without sarcopenia, ASMMI 6.48 kg/m^2.

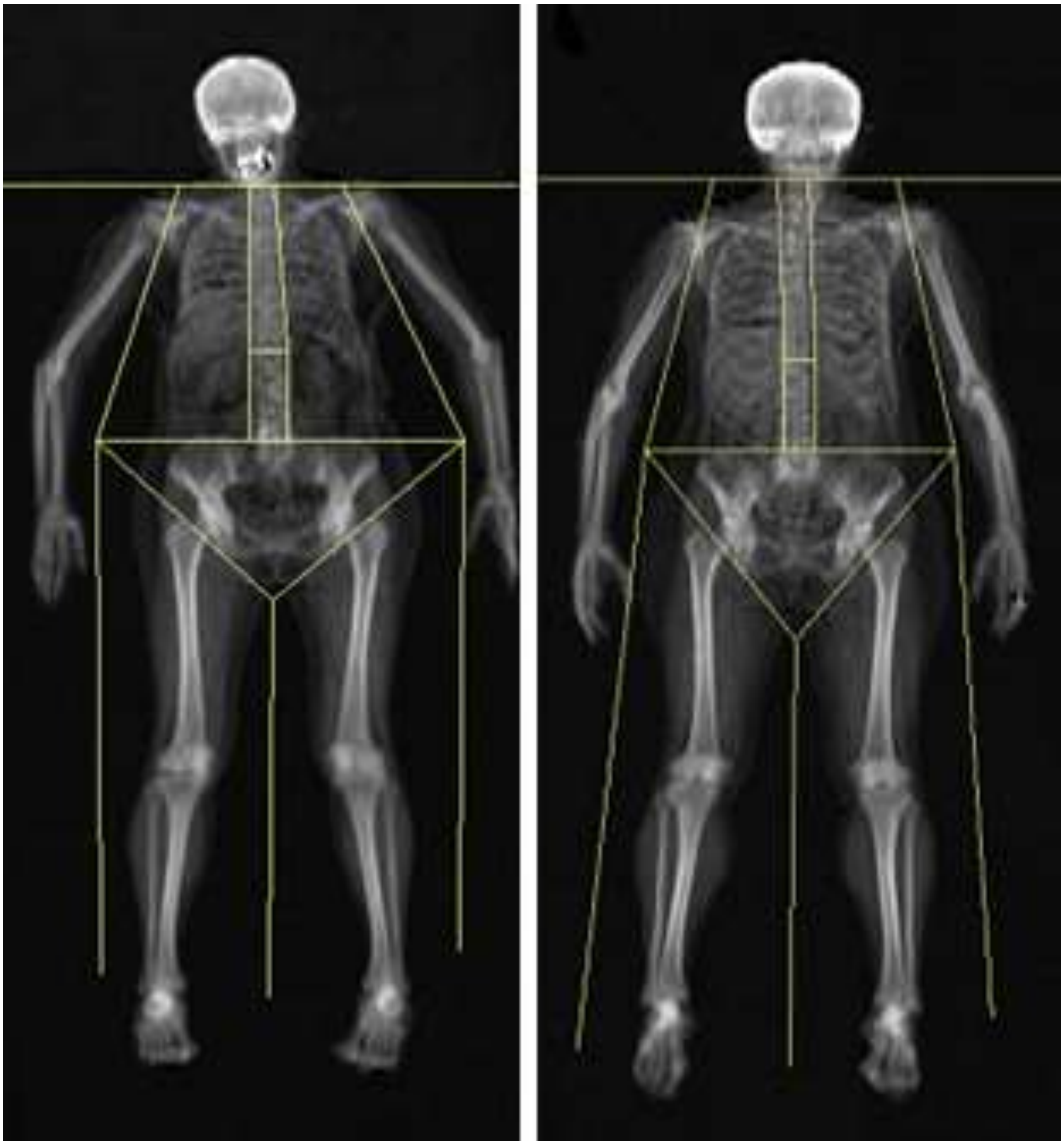

Figure 2. Cross-sectional area at 66% along the length of the tibia in subjects with (right) and without (left) sarcopenia: the pQCT scan shows loss of muscle mass and significant adipose tissue infiltration in the sarcopenic muscle (right).

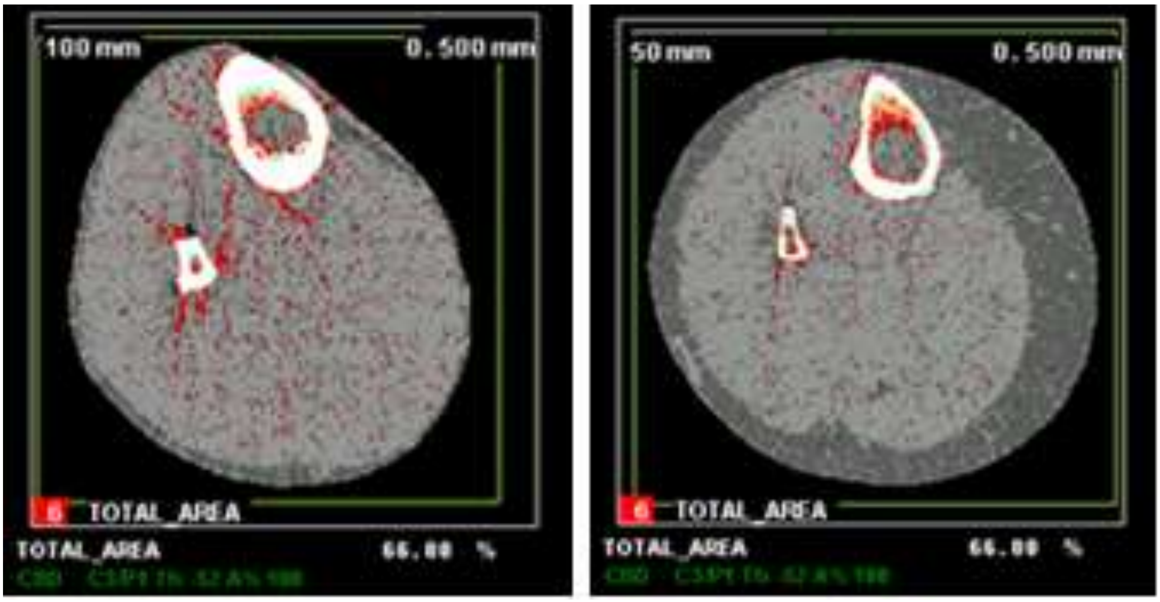

Figure 3. Cross-sectional images of a thigh in a 25-year-old (left) and a 65-year-old (right) man. MRI shows significant loss of muscle fibers and fat infiltration in the older, sarcopenic muscle (right).