

Lean Tissue Imaging: Present Concepts and Potential Impacts

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The human body is composed of fat, water, protein, glycogen, bone minerals, and non-bone minerals [1]. Two-component models divide the body into fat and fat-free components, whereas three-compartment models divide it into fat, lean soft tissue, and bone minerals. Hence, lean soft tissue is composed of water, protein, non-bone minerals, and glycogen. In clinical practice and research, accurate and precise measurement of body composition via imaging is essential for understanding the changes accompanying ageing, chronic disease, and the response to treatment [2].

Previous studies have shown that declines in physical activity are associated with increased total body fat and decreased fat-free mass [3]. Estrogen depletion may accelerate the decline in fat-free mass. The loss of muscle mass and muscle strength becomes pronounced at around the age of 50, progresses after 60, and accelerates after 75 [4]. In Taiwan, low muscle mass is present in 2.5% of community-dwelling women and 5.4% of men [5].

Both men and women lose strength, with the loss being almost twice as great in men than in women [6]. Annualized rates of decline in leg strength (3.4% in white men, 4.1% in black men, 2.6% in white women, and 3.0% in black women) are about three times the annualized rates of decline in leg lean mass (approximately 1%)[6].

Sarcopenia is an age-related decline in lean body mass primarily due to loss of skeletal muscle and muscle function (muscle strength and physical performance) and depletion of protein [7]. Sarcopenia results in frailty, low nutritional status, active catabolism, and systemic inflammation. Muscle protein synthesis declines with age, and ageing muscle fails to respond to anabolic stimuli. New evidence shows that older adults need more dietary protein than do younger adults to support age-related changes in protein metabolism [8].

The European Working Group on Sarcopenia in Older People (EWGSOP, 2010) has defined sarcopenia as the “progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality-of-life, and death” [9]. The Asian Working Group for Sarcopenia (AWGS, 2013) recommends using height-adjusted skeletal muscle mass measured via dual-energy X-ray absorptiometry (DXA) with cut-off values of 7.0 kg/m² in men and 5.4 kg/m² in women [4], handgrip strength (<26 kg for men and <18 kg for women), and usual gait speed (<0.8 m/s). The International Society for Clinical Densitometry’s Official Position (ISCD, 2013) defines “low lean mass” as appendicular lean mass divided by height squared, with Z-scores derived from a young adult-, race-, and gender-matched population [10].

Unlike sarcopenia, cachexia is a cytokine-driven loss of lean body mass commonly occurring in patients with rheumatoid arthritis, congestive heart failure, renal failure, and advanced cancer, and it is characterized by systemic inflammation, increased lipolysis, insulin resistance, and reduced physical activity. A loss of approximately 40% of lean body mass is fatal [7].

Muscle volume can be quantified by DXA and cross-sectional imaging techniques such as computed tomography (CT) and magnetic

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resonance imaging (MRI). The ability of DXA to assess body composition is well validated. In DXA, the exponential attenuation of high and low energy x-rays as they pass through the body is used to determine lean body mass (g). For a three-compartment DXA model of the total body and specific regions (e.g., the trunk and limbs), the precision of measurement was shown to be higher for the total body (coefficient of variation [CV, %] for the GE iDXA, GE Lunar Prodigy, Hologic QDR-1000W, and Hologic QDR 4500-A, 0.4–0.5%, 0.7–1.0%, 1.3%, and 0.6%, respectively [11]) than for body regions (arm, leg, trunk, pelvis, and spine; CVs from 1–3%) [10]. The accuracy of DXA in assessing body composition has not yet been tested in human cadavers. Thigh muscle area measured by DXA is well correlated with that measured by CT in normal adults ($r=0.77$) [11] and obese patients ($r=0.76$) [12] and with that measured by MRI in older patients ($r=0.91$) [13]. However, using CT images as a reference, DXA overestimates thigh muscle mass by 4.4–12% [12], yet it involves relatively low radiation exposure (i.e., 1–20 μ Sv for the adult spine and hip) [13].

Body composition can be analyzed from cross-sectional CT and MRI images using pre-established tissue electron density values (i.e., thresholds of radiation attenuation in Hounsfield units) and commercially available imaging analysis software. Cross-sectional areas (cm²) are computed automatically for each demarcated tissue area by summing the pixel values in those tissues and multiplying by the pixel surface area. In CT studies of thigh muscle volume, both intra- and inter-operator reanalysis precision errors were below 1% [15]. In MRI studies of quadriceps muscle volume, intra- and inter-operator reproducibility was excellent (CV 0.5% and 0.8%, respectively) [16].

Cross-sectional imaging is used to quantify muscle volume in both clinical research and follow-up. In most studies, the third lumbar vertebra (L3) is used as a landmark, and two consecutive slices are selected to measure the cross-sectional areas of the abdominal wall (transversus abdominus, external and internal obliques, and rectus abdominus) as well as the psoas and paravertebrae (erector spinae

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and quadratus lumborum) muscle groups. These areas were identified using Hounsfield unit thresholds of -29 to +150 [17,18].

The diagnosis of sarcopenia is based on the mean skeletal muscle index (SMI) (cm^2/m^2) (i.e., [the skeletal muscle cross-sectional area at L3]/ height²). This value is computed from two consecutive images using the program Image J 1.47 (National Institute of Health, Bethesda, MD, USA, <http://rsb.info.nih.gov/ij/>) or AZE Virtual Place (Virtual Place; AZE Inc., Tokyo, Japan).

Decade-wise percentiles for the total and regional distribution of appendicular lean mass have been well assessed by DXA in healthy individuals in various ethnic groups including Caucasians [19], Italians [20], Indians [21], and Chinese [22]. Such studies find that sarcopenia is not uniformly distributed; postural muscles are more affected than non-postural ones, and DXA-assessed limb body mass may be underestimated as much as 20% [23]. On MRI, cross-sectional areas of paraspinal and psoas muscles at the L5 level are significantly smaller in chronic low back pain patients [23,24] and patients with lumbar compression fractures than in control patients [25]. Muscle volume wasting from cancer can be quantified and monitored by CT or MRI and used to predict overall survival in patients with various advanced cancers including respiratory and gastrointestinal tract malignancies, hepatocellular carcinoma, breast cancers, urogenital cancers, and melanoma. A decline in muscle attenuation (i.e., decrease in Hounsfield units) due to increased intramuscular fat can also be used as an indicator of muscle mass loss.

Current imaging tools used to quantify lean muscle volume may allow early identification and follow-up of high-risk patients, thereby optimizing their treatment options. Future research should be aimed at increasing the accuracy of DXA in quantifying lean muscle mass, establishing lean mass thresholds that define sarcopenia in specific ethnic groups, improving quantification of intramuscular fat, and further revealing the relationship between imaging measurements and muscle strength.

Competing Interests

The authors have no competing interests with the work presented in this manuscript.

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