

Applications of Body Imaging Techniques in Clinical Practice and Biomedical Research: A Review

Abstract

Background: Applications of imaging technology modalities have accumulated evidence that individual components of body composition (BC) have significant influences on chronic disease onset, disease progression, treatment responses and health outcomes.

Objective: To analyse the currently available body imaging techniques and their applications in clinical practice and medical research.

Methods: To review the various body imaging techniques and their applications in clinical practice and medical research, Medline, PubMed, Google scholar, ResearchGate and other databases were searched. Furthermore, references of selected studies and documents available in different libraries were also searched.

Findings: Imaging modalities have provided a systematic method for differentiating phenotypes of BC that diverge from normal, i.e. having low bone mass (osteopenia/osteoporosis), low muscle mass (sarcopenia), high fat mass (obesity), or high fat with low muscle mass (sarcopenic obesity). Tremendous advances were made over the past decades in the sensitivity and quality of imaging techniques such as Dual-Energy X-Ray Absorptiometry (DXA), Computed Axial Tomography (CT), Ultrasound (US), Magnetic Resonance Imaging (MRI), Magnetic Resonance Spectroscopy (MRS), Positron Emission Tomography (PET), Bioelectrical Impedance Analysis (BIA) etc. These imaging techniques have been useful to differentiate layers or depots within tissues and cells enhancing our understanding of distinct mechanistic, metabolic and functional roles of BC within human phenotypes.

Conclusion: In the present overview, we focused on DXA, CT and US for the use in clinical practice and biomedical research relevant to future investigation of human BC and how they may be applied to remedy the pandemic of obesity, diabetes and metabolic syndrome.

Keywords: Imaging techniques, Bioelectrical impedance analysis, Computed axial tomography, Ultrasonogram

Introduction

The importance of understanding body composition (BC) in clinical practice and research has been increasingly recognised over the past decades, along with substantial progress in measuring body composition using sophisticated imaging methodologies. These advances have been partly driven by the increasing evidence that individual components of BC have significant influence on chronic disease onset, disease progression, treatment response and health outcomes. It has been

revealed that, even within a disease state, there is wide variability with regard to the role of BC.¹⁻⁴ Further, the BC response to treatment, whether dietary, pharmaceutical, or surgical, may vary owing to individual phenotype characteristics, including genetic traits, gender and race. Unfortunately, anthropometric methods, i.e. body mass index (BMI), waist circumference, or waist-hip ratio, and available clinical tools to assess body composition, i.e. girth tape measures, skin fold calipers, or bioelectrical impedance machines, are unable to precisely specify components of BC (e.g. visceral versus subcutaneous adipose tissue (SAT) or ectopic fat in tissues and organs) and thus, are limited in providing the information necessary to target preventative or treatment strategies to improve health or reduce risk that are phenotype specific.^{2,5,6}

Imaging modalities have advanced both clinical practice and research by providing a systematic method for differentiating phenotypes of human BC that diverge from what is considered normal, that is, having low bone mass (osteopaenia/osteoporosis), low muscle mass (sarcopenia/high fat mass, obesity), or high-fat with low muscle mass (sarcopenic obesity). Within the body, imaging methods can provide information about the spatial distribution of tissues and organs based on differences in their tissue and molecular properties that may be acquired as two-dimensional (2D) projections using a dual-energy X-ray absorptiometry (DXA) scanner or 2D or three-dimensional (3D) image volumes using computed axial tomography (CT) or magnetic resonance imaging (MRI) or positron emission tomographic (PET) scanners or bioelectric impedance analysis (BIA) or ultrasound (US). Magnetic resonance spectroscopy (MRS) provides detailed information about the actual composition of signals from metabolites within a volume of tissue. The accuracy for distinguishing tissue type and amount depends on the sensitivity of a particular imaging method with regard to contrasting tissues and the spatial resolution of the employed modality, as well as the speed and stability with which images are acquired.⁷⁻¹⁰

Many comprehensive reviews have been published on assessing BC using various imaging methods.^{4,10,11} An detailed review of the principles of each method, as well as their respective, strength and limitations, is beyond the scope of the present article. Here, we present an overview of advancements occurred in imaging technologies such as DXA, CT and US that show strong promise for future applications in the investigation of obesity and metabolic syndrome that impair health and nutritional status.

Dual-energy X-ray absorptiometry (DXA)

In organizing research on BC, it has been suggested that the human body comprises of more than thirty measurable components. As in vivo measurement of body components directly is not possible currently, indirect methods and models have been developed for the purpose.^{12,13} Although originally designed for determining bone mineral density and diagnosing osteoporosis and other bone diseases, DXA is also used to assess fat and fat-free soft tissue. DXA measures the absorption (attenuation) of two X-ray photon energies, typically near 40 and 70 keV which allows for the distinguishing of bone from soft tissue

After excluding pixels that represent bone tissue, DXA estimates fat from the proportion of fat to lean soft tissue in each pixel of a whole body image based on X-ray attenuation. It is assumed that, when estimating fat and lean soft tissue, the percentage of pixels that are excluded as bone do not differ from one area of the body to another. Additionally, DXA estimation of fat tissue may be influenced by conditions where the ratio of extracellular to intracellular water varies (e.g. due to edema, infancy or aging), as it is assumed that the hydration of lean soft tissue remains constant. However, in normal, healthy conditions, a change in hydration of 5% influenced fat estimation by only 11.5%. An additional consideration in obese persons is that body thickness (>25 cm) can result in underestimation of fat mass.^{14,15}

DXA is used in people of all ages owing to its relatively low ionizing radiation exposure (1 mSv per scan), although it is recommended that DXA not be performed during pregnancy. Comparison to the in vivo gold standard four-compartment model has

demonstrated the accuracy of DXA for assessing the percent of fat within the body ($\pm 5\%$) as well as changes in body fat over time. Within-individual test-retest coefficients of variation of <3% for fat and lean mass have demonstrated the reliability of DXA measures in obese children and adults. Hence, DXA has been utilized extensively, including for the development of body composition reference values from National Health and Nutrition Examination Survey data. In contrast to anthropometric measures (i.e. waist circumference or waist-hip ratio, which correlate well with progression of atherosclerosis and cardiometabolic risk), use of regional distribution of fat mass by DXA in obese individuals first provided recognition of the differential risk from excess fat accumulated in the android versus the gynecoid regions of the body. Even in children and adolescents, greater android fat was shown to be significantly and independently associated with elevated serum triglycerides, reduced HDL cholesterol levels, and higher systolic blood pressure. Another contribution from DXA has been identifying differences in body fat patterns by race and ethnicity.¹⁶⁻²⁰

In considering the importance of measuring visceral adipose tissue (VAT) volume or mass, it is remarkable that over half of US non-Hispanic males, 63% of US

non-Hispanic females, and 75% of Hispanic adults

PRELIMINARY REVIEW

have a level of abdominal obesity that is associated a fivefold increased risk for coronary heart disease. Several studies have demonstrated that ethnicity influences susceptibility to the adverse cardiometabolic effects of VAT. Although the prevalence of diabetes is 50% greater and coronary heart disease is 20% greater when comparing African Americans to non-Hispanic whites, African Americans seem to be more prone to accumulating SAT than VAT. In contrast, Asians—even those with BMI in the range of normal weight—accumulate larger amounts of VAT than whites who have similar waist circumference.²¹⁻²³

DXA measurement is becoming increasingly important due to its advantages in terms of accuracy, simplicity, availability, relatively low expense and low radiation exposure. DXA systems are practical, require no active subject involvement and impose minimal risk.²⁴⁻²⁷ Therefore, DXA is gaining international acceptance and emerging as the current reference method for the assessment of BC, mainly because it provides accurate estimates of bone mineral, fat and lean soft tissue, the so called three-component model. In addition, DXA is capable of supplying estimates of visceral fat using validated predictive algorithms and provides a measure of truncal fat mass, which was found to be predictive of disease risk.^{13,28-31} Although there are no contraindications reported to the use of DXA in clinical practice except pregnancy, it should not be performed no more than twice a year.^{13,32-34} However, uncertainty regarding the accuracy of DXA body composition measures, particularly in individuals at the lower and upper ranges of BMI, indicates that other imaging modalities may be more suitable choices depending on the research/clinical question or population group being addressed.^{13,21-23}

Computed Axial Tomography (CT)

Computed axial tomography (CT) maps X-ray attenuation characteristics of tissue, which are determined by the elemental composition (electron density) of the tissue through which X-rays pass. Using X-ray measurements from a large number of projection view angles, cross-sectional images (tomograms) are reconstructed, providing a 2D or 3D map of pixels that are given a numerical value (Hounsfield unit) where 0 is assigned to water and -1000 is assigned to air; lower numbers represent lower electron density. Thus, values of adipose tissue density typically fall in the range of -30 to -190 Hounsfield units. However, since whole body composition can be estimated from a

single cross-sectional image or slice, where radiation dose is close to 2.7 mSv for quantifying liver fat and as low as 1 mSv for quantifying abdominal fat, there is renewed interest in using CT scans for body composition research. In addition, advances in CT scanner technology and reconstruction algorithms, particularly with diagnostic cardiac CT, are not only improving image quality but also reducing radiation exposure in people of all body sizes by constraining image reconstruction to avoid artifacts and using sophisticated techniques that reduce radiation exposure throughout the scan.³⁵⁻³⁷

An important contribution of CT imaging has been elucidating relationships between VAT, insulin resistance, and cardiometabolic risk, both in persons who are obese and those who are normal weight but “metabolically obese.” Indeed, anthropometric measures such as waist circumference, waist-hip ratio, or even percent body fat are not as robust in predicting cardiometabolic dysfunction when BMI falls within the range of normal or underweight. The use of CT to measure adipose tissue distribution among individuals with obesity has also identified sex and race/ethnicity differences. Not only is the proportional amount of VAT to SAT different with regard to sex and race/ethnicity, but it appears that accumulation of VAT

is more robustly associated with insulin resistance in individuals of European and Asian descent, while insulin sensitivity in persons of African descent may be more greatly influenced by accumulation of excess SAT. Application of CT has also expanded our understanding of the strength of the relationship between the largest component of total body fat, SAT and insulin resistance.³⁸⁻⁴⁰ A major contribution of body composition research has been advancing our understanding of whether changes in adipose tissue depots from weight loss interventions have differential effects on components of cardiometabolic disease. It is understood that weight loss in overweight or obese persons, including those with metabolic syndrome, diabetes, or cardiovascular disease, can improve various risk factors including blood pressure, dyslipidemia, and insulin sensitivity. Improved insulin sensitivity after weight loss from consumption of very low-calorie diets and from gastric surgery has been strongly associated with reduced VAT measured by

CT. Moreover, when considering macronutrient composition (e.g. low fat versus high fat) of very low-calorie diets, CT measures show no difference by diet type for the amount of VAT loss, suggesting that the

Comment [IO1]: Macronutrient

relative amount of a particular macronutrient may not be the driving factor in achieving weight loss.^{41,42}

In addition to differentiating layers of adipose tissue depots, determining the quantity of fat deposition in the liver and skeletal muscle (ie ectopic lipid) has become of great interest, primarily due to its relationship with insulin resistance. Moreover, accumulation of hepatic lipid leads to inflammation, cirrhosis and, ultimately, liver failure as seen in the most common liver disease in the United States, nonalcoholic fatty liver disease (NAFLD). Being a noninvasive method, compared to liver biopsy, CT attenuation is used to evaluate the degree of hepatic steatosis. CT data from Framingham Heart Study subjects showed reproducibility of single-slice abdominal scans ($r=0.98$) for quantifying fatty liver. Greater awareness of the importance of maintaining muscle mass in health and disease has stimulated the use of scans that have been acquired in patient populations, typically as part of standard medical diagnosis and assessment of treatment response, to investigate the role of body composition in disease and treatment outcomes. Indeed, CT measurement of skeletal muscle attenuation, which reflects intramuscular adipose tissue (IMAT) accumulation, may be as robustly associated with insulin resistance as VAT. CT measurement of IMAT provides information on the effectiveness of interventions (diet, exercise, surgery) in various muscle groups, offering insight into the potential of such interventions for altering the physical and physiologic effects of obesity, disease and aging.⁴³⁻⁴⁵

Moreover, CT images acquired as part of routine clinical practice are being used to determine the relationships between loss of skeletal muscle mass (sarcopenia) and efficacy or toxicity of pharmacologic therapy, as well as the outcomes of surgical treatments. Skeletal muscle content from slices acquired at the anatomical region of the third lumbar (L3) vertebra is highly correlated with whole body muscle volume ($r = 0.71-0.92$). Further advancing the potential of exploiting single-slice CT images, both manual and automated software programs have been developed for segmentation of muscle, VAT and SAT. Cross-sectional area of VAT and SAT, quantified from a single CT slice, are strongly correlated with whole body measures in persons of various ages, race/ethnicities, and BMI ($r = 0.84-0.96$ for whole-body adipose tissue volume). This information is highly useful, as sarcopenic obesity (i.e. having the double burden of low skeletal muscle mass and high fat mass)

is increasing in the general population. Currently, the contribution of sarcopenic obesity to cardiometabolic disease risk is unclear, particularly due to the limitation of having no established criteria or cut points to classify individuals. Although some epidemiological investigations have not detected an association between sarcopenic obesity and cardiovascular risk, a low skeletal muscle to VAT ratio has been associated with metabolic syndrome and arterial stiffness (via pulse-wave velocity) in otherwise healthy adults.⁴⁶⁻⁴⁸

Recent advances in imaging modalities have been useful in early detection of severity and complications of metabolic syndrome thus reducing morbidity and mortality from it.^{34(a)} This early detection has been helpful in monitoring target organ injury and in turn developing novel therapeutic targets to alleviate and avert them. In particular, using CT to assess metabolic syndrome reported that accumulation of VAT is the best predictor of metabolic syndrome in women and a good predictor of metabolic syndrome in men.^{48,49}

Ultrasound (US)

Ultrasound (US) is likely the most convenient imaging method that has emerged for quantifying tissue amounts and types, due to widespread availability in clinical practice (where it is used for purposes of diagnosis and treatment response), portability, and relatively low cost. The US transducer produces sound waves that reflect off tissues, making echoes that are converted into signals for processing. The amount of sound reflected is determined by the acoustic impedance between tissues; while air has relatively no impedance, bone has a relatively high impedance (0.78 g/cm/s) and adipose and lean tissue have impedances of 0.138 and 0.170 g/cm/s, respectively. Measurement of mesenteric fat thickness by US is strongly associated with cardio-vascular risk factors in healthy young adults, but comparison of US measures for adipose tissue (VAT and SAT) to those acquired by CT suggest that, while there is strong correlation with VAT, there may be less accuracy and reliability with measurement of SAT. However, US-detected changes in total body fat after weight loss were comparable to DXA measures in obese adolescents.^{50,51}

Dysregulation of the human's energy balance, mediated by non-performing endocrine organs (liver, skeletal muscle, adipose tissue) can be related to human metabolic disorders characterized by an impaired BC such as obesity and sarcopenia. US, a fast, non-invasive, low-cost and widely available

Comment [IO2]: "a comparison" or "the comparison"

imaging technique, holds great potential in the study of BC. US can directly measure muscles, organs, visceral and subcutaneous fat tissue in different sections of the abdomen and body, overcoming some limits of anthropometric evaluation and other imaging techniques. US examination has the potential role in the context of BC characterization, investigating four pivotal topics: i.e. abdominal fat compartments, SAT, skeletal muscle and liver.^{51,52}

Conclusion

Advances in DXA, CT and US techniques have increased their applications in assessing adipose and lean tissue in various body deposits. DXA is gaining international acceptance and emerging as the current reference method for the assessment of BC. CT measurement of IMT provides information on the effectiveness of interventions (diet, exercise, surgery) offering insight into the potential of such interventions for altering the physical and physiological effects of obesity, disease and aging. US has become one of the most convenient imaging methods that has emerged for quantifying tissue amounts and types, due to wide spread availability in clinical practice. Measurement of mesenteric fat thickness by US is associated with cardio-vascular risk factors in healthy young adults and there may be less accuracy and reliability with measurement of SAT compared to VAT. However, US-detected changes in total body fat after weight loss were comparable to DXA measures in obese adolescents. Thus, biomedical imaging modalities have improved the ability to assess adipose and lean tissue in various body depots, have increased the availability of imaging modalities in clinical and research settings, have reduced scanning time and subject burden, and have lowered some of the cost of imaging. These advances have enhanced our understanding of the multifactorial and complex nature of obesity, metabolic syndrome, and the development of diabetes and cardiovascular disease. However, applications of other imaging modalities may be considered also depending on the research or clinical question or population group addressed.

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