"Imaging of metabolism": the role of imaging in the study of body composition

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Learning objectives

The analysis of body composition (BC) is essential in the study of many physiological, para-physiological and pathological conditions (Fig. 1 on page 3).

Despite the origin of Radiology, the "radiological" sensibility to what is not directly visualized on images is poor. As a consequence, diseases like diabetes as well as many other metabolic disorders are not very considered among radiologists, unless the study of their complications is demanded.

In the eyes of radiologists the "metabolism" is somewhat mainly linked to nuclear medicine, or magnetic resonance imaging. However, more and more papers and researches are turning to and demonstrating BC as a key factor in the study of human biology. In the radiological world, many authors are addressing their attention to topics directly related to human metabolism (e.g. diffuse liver diseases, epicardial fat etc.), to the whole human metabolism, although this happens more often unconsciousness. The attention of clinicians for BC has recently driven to Imaging, because of the great advantages offered by imaging tools in the research and clinical setting of this field.

The aim of this education exhibit is to illustrate potentials and limits of imaging in the research and clinical assessment of BC.

We would like to focus on applications of dual-energy X-ray absorptiometry (DXA) and ultrasonography (US), from so called "metabolic diseases" to a "constellation" of other disorders or conditions with the support of our large record of cases. Moreover, a full description and clinical-technical comments on methods are provided as well as keynotes for all investigated parameters and BC hot topics.
Images for this section:

Fig. 1: Fat mass, lean mass and bone mineral content. Designed by Guido Mariani, Faenza, Italy.

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Background

The aim of BC analysis is the quantification and characterization of elements composing the human (and animal, in pre-clinical research) organism.

Evidence of the importance in studying BC has grown rapidly in the last few years. BC is crucial for the comprehension and decoding of a multitude of pathogenetic processes involving various diseases (e.g. obesity, diabetes, and endocrine diseases but also gastrointestinal, renal, nervous, infectious diseases etc.), as well as physiological and para-physiological conditions such as in athletes or in growth and aging processes [1-3].

BC study is a branch of human biology based on three interconnected areas.

The first one is depicted by the systematic organization of BC. The most shared way to investigate BC include a five-level model, that allows to organize the human body according to five levels with increasing complexity: I, atomic; II, molecular; III, cellular; IV, tissue-organ; V, whole body [4] (Fig. 2 on page 6). The second area is represented by the development of techniques and methods to investigate the body composition at each of the five steps, as previously mentioned. The third linked area deals with the influence of different genetic, biological and environmental factors on BC [5].

The lack of available, acceptable or accurate clinical tools restricted the diffusion of BC analysis in past research and overall clinical practice. Today, whole-body, organ-tissutal, and molecular levels are the most investigated ones in the human BC, due to the simplicity of anthropometric methods and the widespread availability of imaging techniques [6] (Fig. 3 on page 6 Fig. 4 on page 7 Fig. 5 on page 8).

Magnetic resonance and spectroscopic imaging (MRI, MRSI), and computed tomography (CT) represent an attractive opportunity in the study of BC. Advantages of these "heavy" techniques are commonly referred to the high spatial resolution, to the high accuracy and reproducibility in mass quantification and BC investigation, to the accurate differential quantification of elements (CT) or to fine quantitative and qualitative biochemical analysis (MRI, MRSI). However, these techniques are definitely unthinkable in clinical practice or limited in research field, because of the high costs, the presence of contraindications, and the exposure to ionizing radiations (CT) associated with their use [5,6]. Moreover these techniques are often not suitable for heavier patients.

On the other hand, DXA and US are low cost technologies, accurate, easy to perform and close-at-hand imaging tools, and they are widely available. Both techniques allow methods to assess bone and soft tissue properties. US can distinguish between visceral and subcutaneous fat depots, regionally and lipid storage in organs such as liver; moreover, quantitative ultrasound equipments (QUS) are designed to evaluate bone physical properties [7,8]. There are no risks related to US, but this method is strictly dependent on operator experience. DXA measurements are based on the molecular
level that can be simplified in a 3-compartment model with fat mass (FM), non-bone lean mass (LM) and bone mineral content (BMC). This technique is able to assess FM, LM, BMC regionally and whole-body as well as it can measure whole-body bone mineral density (BMD) in the same scan mode. DXA is accurate, reproducible, fast, relatively inexpensive, and involves very low radiation dose to the patient. All these advantages make this densitometric method ideal for clinical use and longitudinal studies, in both adults and children. New DXA equipments and software allow an accurate and differential estimate of visceral fat (in spite of projective limitations of DXA imaging acquisition) and to scan obese and heavier patients with precise half-body evaluations [9]. Furthermore, notwithstanding the advancement in bone imaging and knowledge related to metabolic bone diseases, DXA is still central in diagnosing and managing osteoporosis. The classical use of DXA in the assessment of bone metabolic status (BMD, T-Score and Z-Score for lumbar, femur, forearm and whole-body scans) is today integrated by new structural parameters of hip geometry (axis length, cross-sectional area, cross-sectional moment of inertia, femoral strength index) [10] (Fig. 6 on page 9) and by other fundamental applications (vertebral fracture assessment # VFA).

Both DXA and US methods can be proposed in the management of metabolic disorders, but they still need to find a position in this field.
**Fig. 2:** The five-level model in the organization of body composition.

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Fig. 3: Methods in the assessment of human body composition: imaging techniques investigate molecular and tissueal levels.

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**Fig. 4**

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Fig. 5

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Fig. 6

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Imaging findings OR Procedure details

BC assessment is integral in the study of diseases wherein human metabolism is directly or indirectly involved or affected.

Our population

From December 2008 to nowadays we enrolled different categories of individuals, from healthy people to patients affected by several diseases to investigate the potential role of DXA in the clinical management and in the research field. Three hundred "healthy" people from 18 to 70 years old were enrolled among the volunteer blood donors of our hospital in order to define the BC profile and to obtain a local reference standard database of BC parameters for comparative evaluations among "healthy" and "unhealthy" populations. We also studied the BC of 213 obese patients submitted to different treatments, from nutritional treatment to bariatric surgery; on the other hand, 70 patients affected by anorexia were evaluated. One hundred twenty patients undergoing organ transplantations (heart, liver, kidney) and submitted to chronic corticosteroid therapy were analyzed for the basal BC profile determined by their chronic diseases and for the follow-up in their BC evolution. Several studies investigating BC distribution were also conducted in order to study oncological diseases, to manage the pharmacokinetic effect of drugs (e.g. testosterone), and to investigate other particular disorders.

The enrolled patients underwent whole-body analysis and lumbar, femur, and VFA scans, before treatment and during the follow-up period at different established steps according to specific protocols.

Healthy people and patients affected by obesity and metabolic disorders were also submitted to US evaluations for the assessment of abdominal adiposity indexes. To prove US accuracy in the assessment of fat indexes we also conducted a comparative study using CT as gold standard [11].

In the bone metabolic context we compared densitometric (VFA) and radiographic images of 68 patients with clinical indication for morphometric evaluation of the spine to evaluate diagnostic performance of VFA.

DXA assessment

**Whole-body:** Subjects were placed in a supine position with arms at sides slightly separated from the trunk and correctly centered on the scanning field. The regions of interest on whole-body scans were defined by the analytical program including six different corporeal districts: total body, trunk, upper limbs, lower limbs, android region
(a portion of the abdomen included between the line joining the two superior iliac crests and extended cranially up to the 20% of the distance between this line and the chin) and gynoid region (a portion of legs leaving from the femoral great trocanter, directed caudally up to a distance double of the android region) (Fig. 7 on page 15). For each region, DXA scanned the weight (in g) of total mass, FM, LM, and BMC. A whole-body BMD was also assessed, and the percentage of FM and LM, and whole-body T-score were calculated.

**Lumbar:** Measurements were obtained with the subject laying in a supine position and legs supported on a padded box to flatten the pelvis and lower spine (from the first to the fourth lumbar vertebra); the bright pointer was centred on the midpoint of the line joining the two superior iliac crests. The analysis was based upon the mean values of each vertebral BMD. Total and lumbar BMD and T-score were used to evaluate bone metabolic status (Fig. 8 on page 15).

**Femur:** For hip DXA scan, the patient was positioned supine on the scanner table, centered on the table, with the long axis of the femoral diaphysis aligned with the long axis of the scanner table. A positioning device was used to place the femur in internal rotation, to elongate the femoral neck. Hip BMD measurement was obtained for various regions of interest including the femoral neck, trochanter, Ward's area, intertrochanteric region, and total hip (Fig. 9 on page 16).

**VFA:** Patients were placed on the scanning bed in left lateral decubitus with knees and femurs flexed, positioning a lumbar brace in order to help the column alignment. The scanner determine the starting position of the lateral spine scan by pointing a laser spot 2 cm below the iliac crest so that all of L5 vertebrae was visible. VFA acquisition was performed with smartscan, a system with self-limitation scanned field to vertebral column area to reduce further radiation exposure. After the scan, the program automatically performed vertebral morphometry. The software automatically placed 6 points in each vertebral body from L4 to T4 to calculate the vertebral heights, their ratios, and average height. The operator analyzed all scans to manually reposition points that were not correctly placed by software.

**US evaluation**

US abdominal fat thicknesses and indexes were measured and calculated according to the method of Vlachos et al. [12]; all parameters investigated are described below and showed in Fig. 10 on page 17.
Minimum subcutaneous fat thickness (a): linear probe, longitudinal scan on the xiphoumbilical line, just below the xiphoid process in the epigastric region, measured as the distance between the anterior surface of linea alba and the fat-skin barrier.

Maximum preperitoneal fat thickness (b): linear probe, longitudinal scan on the xiphoumbilical line, just below the xiphoid process in the epigastric region, measured as the major distance between the anterior surface of the peritoneum covering the liver to the posterior surface of linea alba.

Maximum subcutaneous fat thickness A (c): linear probe, longitudinal scan on the xiphoumbilical line, measured 2 cm above the umbilicus, measuring the distance between the linea alba and the skin-fat barrier.

Maximum subcutaneous fat thickness B (e): linear probe, longitudinal scan in the middle line of the abdomen, measured 2 cm below the umbilicus, measuring the distance between the linea alba and the skin-fat barrier. This parameter has never been described before.

Intra-abdominal fat thickness (d): convex probe, transversal and longitudinal scan on the xiphoumbilical line, 2 cm above the umbilicus, measured as the distance between the anterior wall of the aorta and the posterior surface of the rectus abdominis muscle.

Wall fat index (WFI) and maximum abdominal fat index (MAFI) were calculated as maximum preperitoneal fat thickness/minimum subcutaneous fat thickness ratio and intra-abdominal fat thickness/maximum subcutaneous fat thickness A ratio respectively.

Our results

According to our results DXA proved to be a useful tool in the assessment of body mass composition, and to be more accurate than those anthropometric parameters commonly used in clinical practice.

Total FM/LM ratio can be proposed as a sort of therapeutic index in the follow-up of obese patients undergone both medical and surgical programs, in order to understand and to monitor the evolution of obesity under treatment and to provide risk factors for associated complications such as diabetes and cardiovascular diseases (Fig. 11 on page 18).

WFI and MAFI may be proposed as a valid index of compartmental fat distribution (visceral/subcutaneous adipose tissue ratio). US is a fast, accurate and simple tool for fat assessment. It offers a regional evaluation of subcutaneous and visceral fat compartments, and it is well known how different is their weight on the pathogenesis of cardiovascular and metabolic diseases.

DXA BC parameters and US adiposity indexes of the "healthy" sample are shown in Fig. 12 on page 19.
Moreover, our study confirms that latest improvements in DXA technology allow a very reliable assessment of VFs and make VFA more competitive with traditional radiographic gold standard (Fig. 13 on page 20). Modern DXA systems are able to obtain images of the lumbar and thoracic spine in a single view with relatively high spatial resolution. Finally, DXA offers the opportunity to assess in a single session with very low exposure to ionizing radiation the two most clinically relevant and followed markers of bone metabolism, from an imaging point of view: BMD and VFs.
**Fig. 7:** DXA is based on a three-compartment model and it allows a quantitative direct estimate of fat mass, lean mass, bone mineral content, both whole-body and regionally (android region, gynoid region, superior arms, inferior arms and trunk).
Fig. 8: DXA screen of the lumbar scan (L1-L4). The acquired image of the lumbar spine is represented on the right, while BMD and T-score values of the relative vertebral bodies are on the left.

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Fig. 9: DXA screen of the hip scan.

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**Fig. 10:** Anatomic draft (on the left) and imaging (on the right) of US adiposity indexes: minimum subcutaneous fat thickness (a), maximum preperitoneal fat thickness (b), maximum subcutaneous fat thickness A (c), maximum subcutaneous fat thickness B (e), intra-abdominal fat thickness (d).

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Fig. 11

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Fig. 12: In the top-left whole-body fat mass/lean mass ratio; in the down-left android fat mass/lean mass ratio; in the top-right WFI ratio (maximum preperitoneal fat thickness/minimum subcutaneous fat thickness); in the down-right MAFI ratio (intra-abdominal fat thickness/maximum subcutaneous fat thickness A).

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**Fig. 13:** On the left: densitometric vertebral fracture assessment. On the right: the same patient evaluated with conventional radiography.

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Conclusion

BC analysis has gained a relevant role in studying and understanding the physiopathology induced by several and different diseases [1-3; 13].
The study of BC is a transversal field that does not only make use of medical imaging techniques. However, the lack of available, acceptable and accurate clinical tools restricted its diffusion in past clinical practice. Nowadays imaging evolutions and improvements may give an important contribution. Although CT and MRI have been shown to be useful in distinguishing and quantifying fat tissue depots, DXA is less expensive, invasive, more available and exposes patients to a small amount of ionizing radiations. DXA and US should deserve more consideration and attention for the use in this field by radiologists (Fig. 14 on page 23).
Efforts to define indications of such techniques in the clinical management of patients affected by different diseases should be made by all clinicians.
Fig. 14: Features and advantages of main imaging techniques involved in body composition analysis.

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