# **Dual-energy X-ray absorptiometry and body composition**

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### Purpose of review

Dual-energy X-ray absorptiometry is now widely adopted for the measurement of the fat, fat-free soft tissue and bone mineral compartments of the body. Whereas it is regarded by many as a reference technique for such measurements, it is not without limitations. Inter and intra-manufacturer differences have been areas of concern. This review focuses on recent literature addressing these areas and the issue of validity.

#### **Recent findings**

Body composition measurements using newer generation dual-energy X-ray absorptiometry machines compared between different manufacturers and compared with earlier instruments continue to show differences that may be unacceptable, particularly for investigators upgrading their machines or involved in multicentre studies using different machines. In terms of validity, significant deviations at a group level are reported when compared with reference four-component models, and perhaps more importantly, wide limits of agreement are seen that are a concern for the interpretation of results at an individual level.

#### Summary

It is important that investigators recognize the limitations of dual-energy X-ray absorptiometry technology in the interpretation of their results. There is a continuing need both for inter-machine comparisons and validation studies against accepted criterion methods, particularly as new software or technological changes are introduced. Such studies permit the development of translation equations for the crosscalibration of devices, and may be vital for cross-sectional studies. For longitudinal studies in many populations, dualenergy X-ray absorptiometry is without question a valuable technique for the measurement of compositional changes, both at the total body and regional levels.

#### Keywords

body fat, fan-beam, four-compartment model, pencil-beam, regional-body composition

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#### Abbreviations

CT computed tomography DEXA dual-energy X-ray absorptiometry

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### Introduction

Dual-energy X-ray absorptiometry (DEXA) is now one of the most frequently used techniques for body composition measurement as a result of the increasing worldwide availability of these scanners. The technique is attractive because it is non-invasive, is easily applied for both healthy individuals and patients, and the radiation dose is extremely small. Scanning times, which may have been an impediment to its use in paediatric studies, have decreased substantially with newer technology. A further attractive feature is its ability to provide regional-body composition analysis.

This technique is increasingly being viewed as a laboratory reference method for the estimation of total body fat. Since its introduction its status as a gold standard for body fat measurement has been examined by several commentators [1-3]. Such a method should be capable of high accuracy and precision and be free of major assumptions that may limit its usefulness to individuals with 'normal' body composition. DEXA is capable of good precision for the measurement of body fat, fat-free mass and bone mineral, and this has been well documented [4,5]. This attribute makes it potentially a valuable tool for longitudinal studies in the clinical setting. DEXA accuracy is more difficult to judge, because apart from the chemical analysis of cadavers, a technique for the direct measurement of body fat is not available. Such human cadaver analysis has not been performed to validate DEXA measures of whole-body composition. Postmortem chemical analysis of animals has been compared with DEXA measurements in a number of studies, with variable results depending on the equipment and software used [6–9]. Perhaps more appropriately, in the area of human body composition, multicompartment body composition models have been used as criterion methods for DEXA validation [10].

Recurring issues that are relevant to acceptance as a reference method are the reported differences between machines from different manufacturers [11] and from the same manufacturer [12]. Concern has also been reported about the consistency of results between machines of the same model [13,14]. Software upgrades that appear from time to time often include changes in the algorithms used for body composition calculation, which can affect the measurements for an individual [11,15,16]. Both inter and intra-manufacturer comparisons are clearly important for investigators upgrading their machines, particularly

during the course of longitudinal studies, and in the context of multicentre trials.

This review focuses on recently published studies addressing the validation of DEXA measurements of body composition and the comparability of such data between instruments from the same and different manufacturers.

#### Principles and assumptions

The underlying concept of DEXA technology is that photon attenuation in vivo is a function of tissue composition. Rectilinear scanning of the supine body is performed that divides the body into a series of pixels, within each of which the photon attenuation is measured at two different energies. The ratio of the attenuations at these two energies is referred to as the R value. The DEXA body composition approach assumes that the body consists of three components that are distinguishable by their X-ray attenuation properties: fat, bone mineral and fat-free or 'lean' soft tissue. Within any pixel the proportions of only two components can be resolved by the differential absorption of two photon energies. Soft tissues, consisting largely of water and organic compounds, reduce photon flux to a much lesser extent than bone mineral, and pixels containing bone are relatively easily distinguished from those with no bone present. In areas where bone is not present suitable calibration allows fat and lean fractions to be resolved from soft tissue. The composition of these areas of soft tissue is extrapolated to the soft tissue overlying bone to produce total body fat and lean soft tissue. The algorithms to accomplish these extrapolations vary between manufacturers and have not been publicly released. Technical details of the methodology may be found in the review by Pietrobelli et al. [17].

A fundamental assumption is that the soft tissue is normally hydrated for accurate partitioning into fat and lean fractions. The addition of fluid, for example normal saline, which has a higher R value than normally hydrated lean tissue, results in an underestimation of fat mass change [18,19]. The addition of fluid having a similar R value to lean tissue would not be expected to alter the estimate of fat mass. In practice, any differences in measured composition that can be ascribed to fluid changes are likely to be relatively minor [18]. Bone density and fat mass measured in haemodialysis patients were found to be unaffected by fluid changes [20]. Paracentesis of ascites did not change total fat mass measurements by DEXA [21].

### **Equipment developments**

DEXA scanners capable of whole-body composition measurement are currently available from three

manufacturers, Hologic, GE-Lunar and Norland. First-generation DEXA scanners utilized pencil-beam X-ray fields, in which a single detector was used to measure the transmission of X-rays from a highly collimated source. Such scanners are typified by the Hologic ODR-1000, GE-Lunar DPX and DPX-L, and the Norland XR-26. More recently, fan-beam technology was introduced, which allowed faster scanning speeds and offered higher resolution compared with pencilbeam DEXA. However, magnification and projection effects at the boundaries of the beam may compromise accuracy in these systems. These machines are generally designed with a slit collimator X-ray source and multiple detectors. Hologic introduced fan-beam technology with the QDR-2000 (also operable in pencilbeam mode) and GE-Lunar with the Expert. Current generation fan-beam machines include the QDR-4500 and Delphi (Hologic) and Prodigy (GE-Lunar). Typical adult whole-body scanning times of 15-25 min using the GE-Lunar DPX have been reduced to approximately 5 min with the Delphi and Prodigy. The introduction of newer generation pencil-beam machines such as the GE-Lunar DPX-IQ and Norland XR-46 has also seen a substantial reduction in scan times. The narrow-angle fan beam in the Prodigy reduces the magnification effects compared with the wide-angle fan beams found in the QDR-2000 and Expert. Within the two broad categories of beam geometry, technical differences in both hardware and software mean that results from one instrument are not necessarily the same as those from another [11]. Interest has also focused, understandably, on the comparability of results from pencil-beam and fan-beam devices [22].

# Machine comparisons

A study comparing the Prodigy and Delphi A fan-beam instruments with the DPX and DPX-L pencil-beam machines in adult healthy volunteers [23] identified significant differences in estimates of total body fat between machines from the same manufacturer and from different manufacturers. These differences were sex dependent. Data were not provided for the limits of agreement between pairs of instruments nor on whether the differences were dependent on the absolute amount of total body fat measured. A comparison of the Hologic QDR-1000W pencil-beam with the 4500W fan-beam instruments in 13-18-year-old youths showed that at the lower values of body fat the fan-beam scanner gave higher measurements, whereas the reverse was true at higher fat readings [24]. In addition, the variation in individual differences in fat-free soft tissue tended to be markedly greater at higher levels of fat-free soft tissue. These results supported earlier reports comparing Hologic pencil-beam (QDR-2000W or QDR-1000W) and fan-beam (QDR-4500A) instruments in children and adults [25,26].

Agreement between Hologic QDR-2000 and GE-Lunar DPX-L scanners was examined by Bairos *et al.* [27] in male and female adult volunteers. On average, the Hologic scanner yielded higher total body fat results than the DPX-L in both men and women. However, whereas the bias was consistent across the range of fat mass for women it was greater in men at higher fat levels than at lower levels. A comparison of pencil-beam and fan-beam machines from the same manufacturer (GE-Lunar) indicated that for total fat mass measurement the bias was small between the Prodigy and the DPX-IQ and between the Expert and the DPX-IQ, with no dependence on mean fat mass [28]. Noticeably higher scatter in the differences was observed for the Expert-DPX comparison.

In a group of infants (body weight range 1.8–13.1 kg) Hologic pencil-beam (QDR-2000) and fan-beam (QDR-4500) machines using paediatric software yielded differing results for fat and lean tissue mass [29]. Fat mass was 19% greater for the pencil-beam machine.

A comparison of two fan-beam machines (Expert and QDR-4500A) in adult volunteers showed that the differences in the percentage of body fat by the two machines were correlated with the mean percentage of body fat, with the Expert giving higher readings at high body fat and lower readings at low body fat values [26].

Limited data are available on the comparison of regionalbody composition between DEXA scanners. Bairos et al. [27] found that fat in the arms and legs was significantly greater when measured by the Hologic QDR-2000 (fan beam) than by the GE-Lunar DPX-L. Truncal fat, however, was less with the Hologic. Some sex dependence was seen in the behaviour of the differences as a function of the average amount of tissue. In a study of 24 HIVinfected patients [30] carried out with a GE-Lunar Prodigy and a Hologic QDR-2000, the Hologic machine generated markedly higher values for the fat content of the arms, the legs and total body, but significantly lower values for the trunk. The fat percentage in the arms was almost twice the result given by the Prodigy. Fat distribution, as measured by the trunk-to-limb fat percentage ratio, was  $0.89 \pm 0.28$  (SD) for the QDR-2000 and  $1.62 \pm 0.47$  for the Prodigy. Similar findings to the two studies were reported earlier between the Hologic and GE-Lunar machines in young men [31] and diabetic females [32].

#### Validation studies: whole-body composition

Considerable work has been published on the validation of earlier generation DEXA instruments against suitable reference standards [22]. Such work is ongoing, mainly in terms of the application to populations not previously examined. A generally accepted reference standard is the four-compartment model in which body fat is estimated from measurements of body density (by hydrodensitometry), total-body water (usually by deuterium dilution), and DEXA bone mineral values. The recent study by van der Ploeg *et al.* [33°] compared body composition measurements by a GE-Lunar DPX-L with a four-compartment model in 152 healthy adults. The study sample was predominantly men (n = 118), with a high proportion (21%) of lean athletic individuals (< 10% body fat). It was notable that whereas the difference between the two methods was small at the higher body fat levels (> 25% body fat), DEXA progressively underestimated the body fat of leaner individuals, and there was wide intra-individual variation.

Another large study was conducted in a paediatric population [34<sup>•</sup>], and compared percentage body fat measurements using a four-compartment model with those using GE-Lunar DPX or DPX-L machines and paediatric software. At low percentage fat levels DEXA underestimated body fat, whereas the reverse was true at higher levels of body fat. Again there was considerable intra-individual variation.

Few validation studies have been reported using the more recently developed DEXA machines. In overweight and obese children, the Prodigy significantly overestimated body fat in both males and females compared with a four-compartment model [35]. These results were consistent with those in 9–17 year-old females, in whom a QDR-2000W in pencil-beam mode overestimated the percentage of body fat by 3.9% on average, compared with the four-compartment model, with 95% limits of agreement  $\pm 6.7\%$  [36]. A more limited validation study, using a three-compartment model as reference [37], showed that the Prodigy overestimated the percentage of body fat in male and female adults.

# Validation studies: regional-body composition

Although computed tomography (CT) and magnetic resonance imaging are the reference standards for measuring skeletal muscle mass and abdominal adipose tissue, access to such technology is limited. DEXA regional analysis offers a much more accessible approach and at a substantially lower radiation dose than CT. The measurement of muscle mass has been of particular relevance to investigations of sarcopenia in the elderly [38], and DEXA has been used in a number of recent reports [39–43]. The quantification of totalbody skeletal muscle mass by magnetic resonance imaging in a large number of healthy adults has enabled this parameter to be predicted from DEXA appendicular lean soft tissue mass [44].

#### 308 Pharmaceutical aspects, devices and techniques

The measurement of abdominal obesity has assumed increased importance because of the association of this parameter with the risk of obesity-associated diseases, independent of total adiposity [45]. Abdominal fat is usually measured between the L1 and L4 vertebral bodies as an operator-defined region of interest on the DEXA scan image. The validation of this measure against single-slice CT scanning has been carried out, and more recently against multi-slice CT [46<sup>•</sup>], the latter providing a more accurate reference measure. Abdominal fat mass measured by the two methods was highly correlated, although DEXA systematically underestimated the CT-derived fat mass. Inter-rater reproducibility was high for the DEXA assessments. That study was carried out using a GE-Lunar DPX-IQ (software version 4.5c), and the results do not necessarily translate to other machines.

#### Measurement of body composition changes

For an assessment of longitudinal changes in body composition, DEXA may be a sensitive tool as a result of its good precision [47]. Although the technology is widely used for such studies, there are limited data on the accuracy with which these changes are measured by the DEXA systems available. In 19 diabetic patients, the DPX-IQ overestimated total body fat at baseline and after 6 months of insulin treatment compared with a fourcompartment model [48]. The DEXA measurement of the change in body fat was within 0.2 kg of the change registered by the four-compartment model. However, the limits of agreement were wide  $(\pm 4 \text{ kg})$ . In a study of a group of adults measured before and after weight change [49], the changes in fat mass measured by the QDR 4500 (fan beam) and QDR-2000 (pencil beam) differed significantly, with the pencil-beam system providing results that more closely matched the changes derived from estimates of fat mass based on total body water determinations.

For optimal results from longitudinal studies, especially for the detection of small changes, close attention needs to be paid to technical issues that can affect measurements. A consistency of technique for data acquisition and analysis is perhaps more critical for infant studies than adults. For example, the quantity of clothing necessary for neonate/infant scans may be a significant fraction of body weight, and will interfere with the body composition measurement. Although this is also an issue for cross-sectional studies, in the longitudinal setting the standardization of clothing is essential. Concerns such as these have recently been addressed using a piglet model to simulate experimental and clinical conditions as well as in a group of infants [50,51].

# Conclusion

Differences between machines continue to be a concern for whole-body and regional-body composition assessment. Machines from different manufacturers tend to show greater differences than those from the same manufacturer. However, in both situations this concern is an issue for investigators upgrading their machines or embarking on multicentre studies. There remains a need for more in vivo cross-calibration studies between scanners, including comparisons between the same models in different centres, thus allowing translational equations to be developed for data adjustment when necessary. The reasons for the inter-manufacturer differences are not clear, but no doubt involve differences in the approaches taken by manufacturers in both the technological and software areas [52]. The assumptions used, particularly for the determination of soft-tissue composition in areas overlying bone, are proprietary information and are thus not able to be scrutinized.

DEXA accuracy for whole-body composition remains an issue, and whereas the four-compartment and similar multicompartment models are considered to provide reference data, it must be borne in mind that these models demand considerable care in execution if the data are to be of the highest quality. The wide 95% limits of agreement generally seen for the comparison of DEXA and four-compartment model fat estimates appear greatly to exceed the expected variability, based on the contributing precisions for fat measurement by DEXA (approximately 3%) and by the four-compartment model (better than 3%). Whereas DEXA is a valuable tool for body composition analysis and may have its greatest value in longitudinal studies, its limitations must be appreciated.

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