British Journal of Nutrition (1997), 77, 151–163

Review article

Measurement of soft tissue composition by dual energy X-ray absorptiometry

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(*Received 11 April 1996 – Revised 23 July 1996 – Accepted 20 September 1996*)

INTRODUCTION

The importance of soft-tissue composition in studies of health and disease is increasingly recognized. There is a need for reference standards for body composition, to define normal and abnormal growth, to examine sex and ethnic differences and to evaluate the effects of disease. Body-fat mass in particular is an important predictor of morbidity or mortality and changes in body composition provide an objective method of evaluating the efficacy of therapeutic interventions designed to reduce health risks.

Until recently reference methods to measure body composition were confined to specialist research centres, whilst simpler field techniques were unable to offer the necessary accuracy and precision to substantiate their use (Coward *et al.* 1988). Dual-photon absorptiometry (DPA) and dual-energy X-ray absorptiometry (DXA) are novel techniques which offer the potential for precise measurement of bone and soft-tissue composition (Mazess *et al.* 1990; Chan, 1992). The principle of absorptiometry is based on the exponential attenuation of X-rays at two energies as they pass through body tissues. DPA has been in use for over 15 years, using a radionuclide source, usually ^{153}Gd, to generate gamma rays. In modern DXA machines the radionuclide source has been replaced by a low-current X-ray tube, offering improved resolution, precision, reduced scan times and less maintenance. DXA has now largely superseded DPA.

DXA machines are available in a large and increasing number of hospitals and research centres across the country. In addition to gross body composition DXA is able to measure the regional distribution of bone, fat and lean tissue (Mazess *et al.* 1990), as shown in Fig. 1. Methods have also been described to measure muscle mass (Heymsfield *et al.* 1990; Fuller *et al.* 1992*b*), abdominal and intra-abdominal fat (Svendsen *et al.* 1993*a*).

However a number of technical problems remain, such that DXA cannot yet be considered to be a 'gold standard' for soft-tissue measurements (Roubenhoff *et al.* 1993). These include generic issues such as the effect of hydration, tissue thickness and fat distribution, and there are also important inter-machine differences which need to be resolved if this technology is to fulfil its potential (Tothill *et al.* 1994).

Each manufacturer offers variations of the system for the analysis of soft tissue in 'adults' (generally > 10 kg), paediatric subjects (approximately 2–10 kg) and small animals. The present review will focus on the human systems alone.

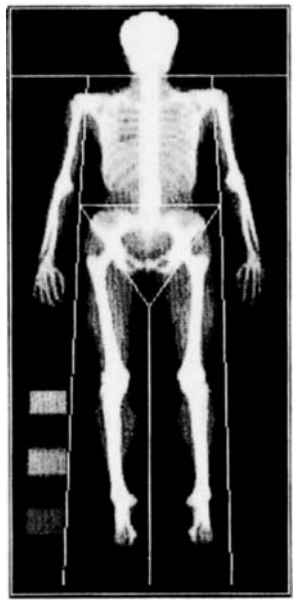

Fig. 1. An example of the information obtained from whole-body soft-tissue analysis by dual-energy X-ray absorptiometry using the Hologic QDR-1000W machine.

MEASURING SOFT TISSUE BY DUAL-ENERGY X-RAY ABSORPTIOMETRY

DXA machines were originally developed to measure bone mineral and this remains their primary purpose (reviewed by Prentice, 1995). In order to measure soft-tissue composition the machines must be capable of whole-body scans and linked to appropriate software. Each of the three manufacturers (Hologic Inc., Waltham, MA, USA; Lunar, Madison, WI, USA; and Norland, Fort Atkinson, WI, USA) include at least one machine within their range that is able to perform such measurements.

In practice patients are placed in a supine position and scanned in a rectilinear manner using X-rays at two energies (e.g. 70 and 140 kvP for Hologic QDR-1000W). Older machines may take up to 25 min for a single scan, but newer models, capable of whole-body scans within 5 min and rapid data processing, make this an attractive method even for large-scale surveys. In theory patients are not required to undress, although the need to eliminate items containing metal means that it is often easier to scan individuals in a hospital gown or nightwear.

The effective dose equivalent per whole-body measurement is less than 5 μSv and is close to background radiation levels. This low radiation exposure makes even repeated scans suitable for all subjects, including babies and children, although prudence continues to advise against scanning pregnant women. Although not truly portable, machines can be

housed in mobile units if necessary since the low radiation exposure makes additional screening unnecessary.

The ratio of soft tissue attenuation (R_{ST}) of the low- and high-energy beams is measured as they pass through the body. The attenuations of pure fat (R_F) and of bone-free lean tissue (R_L) are known from theoretical calculations and *in vitro* measurements. Thus, one can solve an equation for each X-ray energy with two unknown factors to calculate the proportion of fat (∞) and lean tissue (β) in each pixel containing soft tissue only:

$$R_{ST} \text{ (low energy)} = \infty(R_F) + \beta(R_L),$$
$$R_{ST} \text{ (high energy)} = \infty(R_F) + \beta(R_L).$$

Approximately 40 % of pixels in the body contain bone and have to be processed in an indirect manner due to the beam hardening caused by the bone. In simple terms, the bone analysis calculates the grams of bone mineral (BMC) at the bone pixel. In addition, the total mass at that point can be determined from the attenuation of the two X-rays since the attenuation is roughly proportional to the mass that is present. The amount of soft tissue is the difference between the total tissue mass and the BMC at that point. To determine the amount of this tissue mass that is fat, the algorithm looks at neighbouring pixels that do not contain bone, calculates the proportion of fat in these points and applies this percentage to the bone pixel. In the head, where the brain tissue is totally surrounded by bone, an assumption is made regarding the percentage of fat. This figure (e.g. 17 % for Hologic machines) is used for all pixels in the head which contain bone. More detailed descriptions of the analytical procedures can be found elsewhere (e.g. Peppler & Mazess, 1981; Gotfredsen *et al.* 1986).

Machines from different manufacturers use different forms of external calibration. However in each case errors in the absolute accuracy of the measurements can arise because of fundamental errors in the attenuation coefficients assumed for fat and lean tissue. Changes in hydration or in the concentration of elements of high atomic number such as Na, K and Cl, also influence soft-tissue attenuation, causing deviations from the assumed R_L in the given equations. Furthermore the attenuation of pixels that include a small amount of bone may be closer to that of lean tissue than to bone and will thus overestimate lean tissue and underestimate bone.

DXA measurements of bone are sensitive to the anteroposterior thickness of the body and this may also affect soft tissue determinations. *In vitro* measurements of water and oil/lard mixtures (Laskey *et al.* 1992; Jebb *et al.* 1995 *a,b*), meat samples (Jebb *et al.* 1995*a*) and whole-body phantoms (Tothill *et al.* 1994) show significant increases in measured fat mass at extremes of thickness. The study of Tothill *et al.* (1994) is particularly useful since measurements were made in an anthropomorphic phantom and the results compared for the three different brands of machine. Fig. 2 shows significant changes in measured fat with thickness in the phantom with a nominal 22 % fat. However the differences between manufacturers are much greater than the differences attributable to thickness (Tothill *et al.* 1994).

The differential effects of tissue thickness may present particular problems in the obese where the range of thickness is at its greatest. However the principal limitation in studies of obesity or its treatment, is the size of the scanning area. Large subjects must be scanned in a cramped position which hinders regional analysis, indeed for some subjects only part of the body can be measured at a time. In an attempt to resolve this problem a method has recently been described in which half the body is scanned at a time (Tataranni & Ravussin, 1995).

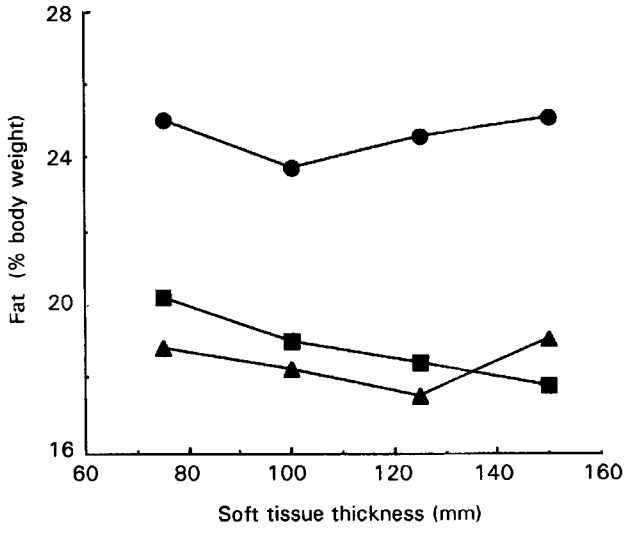

Fig. 2. Effect of tissue thickness on the estimation of fat mass by dual-energy X-ray absorptiometry using machines from different manufacturers: (●), Norland; (■), Hologic; (▲), Lunar. (Data from Tothill *et al.* 1994.)

GROSS BODY COMPOSITION

In vivo assessments of the absolute accuracy of measurements of gross body composition are hindered by the lack of an appropriate reference standard. Much of the available data supporting the accuracy of DXA is based on its ability to determine accurately the total mass of tissue present. However, this does not ensure its accurate division into fat and fat-free mass. For most DXA machines body weight represents the sum of soft tissue plus bone mineral, where soft tissue represents the sum of fat and lean tissues.

Some comparisons with direct chemical analysis have been made in pig cadavers (Brunton *et al.* 1993; Svendsen *et al.* 1993*a*; Ellis *et al.* 1994; Picaud *et al.* 1996; Pintauro *et al.* 1996), small animals (Chan, 1992) or meat samples (Jensen *et al.* 1993; Jebb *et al.* 1995*a*,*b*) for adult and paediatric software. Svendsen *et al.* (1993*a*) measured the composition of seven pigs ranging from 35 to 95 kg by DXA (Lunar DPX) and direct chemical analysis. The correlations between the two sets of measurements were not significantly different from the line of identity and the standard errors of the estimates (SEE) were 2·9 %, 1·9 kg and 2·7 kg for percentage fat, fat mass and lean tissue respectively. The mean difference between DXA and direct analysis was − 1·7 (SD 0·8) kg, although the differences between methods were not statistically significant. A similar study using sixteen smaller pigs weighing 5–35 kg, showed that although the results were highly correlated (r^2 0·98), the mean difference in the fat mass measured by DXA (Hologic QDR-2000 Adult Whole Body) compared with direct analysis was − 1·16 (SD 0·21) kg for the initial version of software and + 0·75 (SD 0·12) kg using an updated software package (Ellis *et al.* 1994).

Early studies using DXA (Hologic QDR-1000W) in small piglets showed that DXA overestimated fat mass by twofold compared with direct analysis (Brunton *et al.* 1993). Using an updated version of the software Picaud *et al.* (1996) have shown improved

agreement, although in a group of piglets ranging from 30 to 570 g fat the average SEE was 32 g. DXA overestimated fat mass in small piglets but progressively underestimated fat as the size of the animal increased. In the study of Pintauro *et al.* (1996) eighteen pigs weighing 25·5 (SD 7·0) kg (9·9–32·8 % fat) were scanned using both the adult fast detail and paediatric medium scan mode (Lunar DPX-L). Although the results for both fat and lean were highly correlated in both scan modes ($r > 0{\cdot}98$) the relationship between fat mass values determined by chemical analysis and DXA was significantly different from the line of identity.

Comparison with a four-compartment model of body composition techniques shows reasonable agreement at the group level but substantial errors in individual subjects (Fuller *et al.* 1992*a*), and the same applies for comparisons with neutron activation analysis (NAA) (Heymsfield *et al.* 1989). DXA underestimated fat mass by 1·16 (SD 4·07) kg compared with a four-compartment model (mean fat mass 22·3 (SD 5·4) kg) and DPA by 0·91 (SD 2·06) kg relative to NAA (mean fat mass 17·6 (SD 5·9) kg). Other studies have compared DPA and/or DXA with densitometry (Mazess *et al.* 1984; Hassager *et al.* 1989; Heymsfield *et al.* 1989; Wang *et al.* 1989; Fuller *et al.* 1992*a*; van Loan & Mayclin, 1992; Johansson *et al.* 1993; Tothill *et al.* 1994; Wellens *et al.* 1994), total body water (Heymsfield *et al.* 1989; Fuller *et al.* 1992*a*; van Loan & Mayclin 1992; Wellens *et al.* 1994) or total body potassium (Hassager *et al.* 1989; Heymsfield *et al.* 1989; Slosman *et al.* 1992; Jensen *et al.* 1993) but such studies are limited by the inherent errors of two-compartment models for body composition analysis. There is some suggestion that DXA may tend to underestimate body fat increasingly with increasing fatness (Aloia *et al.* 1995) or age (Snead *et al.* 1993). Much less information is available in relation to the infant software. For fourteen infant cadavers DXA underestimated fat mass by 32·7 (SD 32·2) g compared with fat measured by NAA (mean fat mass 244 g; Ellis *et al.* 1995). Gutin *et al.* (1996) have compared DXA with skinfold thicknesses and bioimpedance in forty-three 9–11-year-olds. Again, although highly correlated ($r > 0{\cdot}83$), DXA measures of fat mass were higher than fat estimates from skinfold thicknesses or impedance.

Other studies have tried to validate DXA by measuring short-term changes in composition as a result of changes in water balance (Lands *et al.* 1991; Formica *et al.* 1993; Going *et al.* 1993; Stenver *et al.* 1995). The results of some studies are difficult to interpret because the imposed change in water balance is close to the measurement precision of DXA. The largest changes have been observed in a study of twenty patients measured pre- and post-dialysis where the change in water balance ranged from +200 to −3700 ml. Here the correlation with the change in fat-free mass measured by DXA was 0·68 with a SEE of 0·9 litres (Stenver *et al.* 1995).

Further validation studies are necessary to define the absolute accuracy of soft-tissue measurements. The differences between manufacturers and software packages inevitably cast doubts on the absolute accuracy of the method. However it is clear that the precision is excellent, with CV of approximately 2 % for the proportion of fat and approximately 1 % for lean tissue mass (Mazess *et al.* 1990; Pritchard *et al.* 1993; Tothill *et al.* 1994). This is better than most other *in vivo* methods to measure soft-tissue composition and makes DXA an attractive option for studies in which small changes in composition are to be measured.

One such example is a study of changes in soft-tissue composition following renal transplantation (Hart *et al.* 1993). Fig. 3 shows that although there is a steady increase in weight following transplantation this is solely attributable to significant increases in body fat mass and not lean tissue.

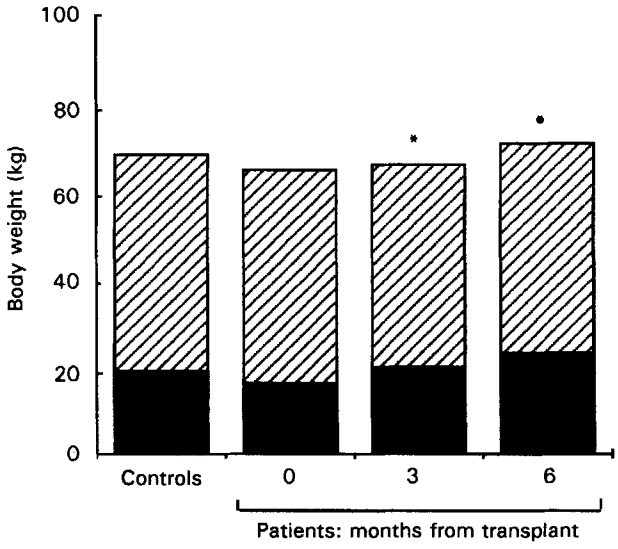

Fig. 3. Changes in body composition following renal transplantation, measured using dual-energy X-ray absorptiometry. (■), Fat mass; (▨), fat-free mass. *Mean values were significantly different from baseline, $P < 0.03$. (Data from Hart *et al.* 1993.)

REGIONAL FAT DISTRIBUTION

A particular advantage to DXA measurements of soft tissue compared with many other *in vivo* composition techniques is the ability to analyse segments of the body in addition to making whole-body estimates (Mazess *et al.* 1990; Fuller *et al.* 1992*b*; Chilibeck *et al.* 1994; Tothill *et al.* 1994). Although different manufacturers offer different degrees of flexibility in the regional analysis it is always possible to subdivide the body into at least arms, legs and trunk.

Table 1 shows that the precision of measurements in each region is poorer than at a whole-body level. There is the potential for observer error in delineating the regions. This becomes increasingly problematic as the size of the subject increases, making regional measures of soft-tissue composition in the obese virtually impossible. In the trunk the arrangement of the ribs and spine means that few pixels are bone free and hence a large proportion of measurements in this region are estimated from neighbouring tissue composition, making the estimate less reliable. Regional measures of the abdomen may be sensitive to the effects of ectopic calcification.

Validation of the accuracy of regional measures of soft-tissue composition requires comparison with techniques such as computed tomography (CT) or magnetic resonance imaging (MRI). Limited data for the abdominal region show good agreement for the measurement of adipose tissue volume (Schlemmer *et al.* 1990; Svendsen *et al.* 1993*b*; Jensen *et al.* 1995) but information is not yet available for the composition of limbs.

Regional measurements of soft tissue have been used to assess the changes in body composition in Cushing's disease (Wajchenberg *et al.* 1995). Fig. 4 shows data from groups of lean controls, patients with Cushing's disease and weight-matched obese patients. Unsurprisingly both patient groups had significantly more fat than the lean controls. The only significant difference between Cushing's patients and their obese controls was that they had less fat in the arms, reflecting the characteristic peripheral wasting associated with Cushing's disease.

Table 1. *Precision of regional measures of fat mass made using different models of dual-energy X-ray absorptiometer*

(Data for Hologic and Norland from Tothill *et al.* 1994 and data for Lunar from Mazess *et al.* 1990)

Model...	Hologic QDR-1000W (*n* 19)	Lunar DPX (*n* 12)	Norland XR 26 MkII (*n* 7)
Total body fat (kg)			
Mean	11·4	13·3	19·5
SD	0·214	0·735	0·513
CV (%)	1·9	6·9	2·7
Trunk fat (%)			
Mean	12·9	20·8	33·0
SD	0·5	1·18	0·8
CV (%)	4·3	7·0	2·9
Arms fat (%)			
Mean	26·9	20·8	39·3
SD	1·2	1·35	2·4
CV (%)	5·2	8·3	6·8
Legs fat (%)			
Mean	26·3	23·8	32·3
SD	0·6	1·44	0·9
CV (%)	2·9	8·1	2·3

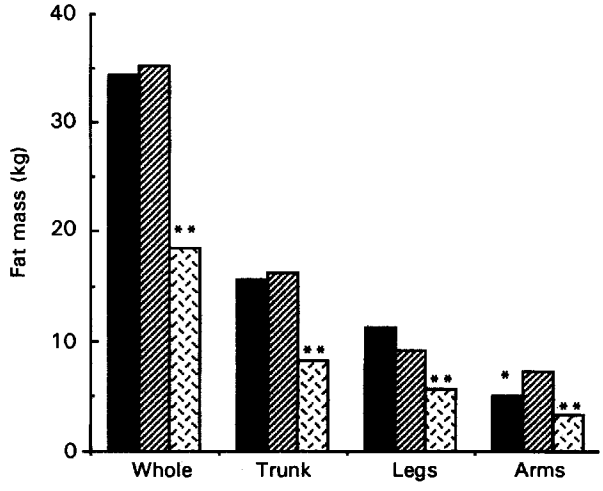

Fig. 4. Effect of Cushing's disease on body composition, measured using dual-energy X-ray absorptiometry. (■), Patients with Cushing's disease (*n* 8); (▨), obese subjects (*n* 10); (⊠), lean subjects (*n* 8). * Mean value was significantly different from that for obese subjects only, $P < 0{\cdot}04$. **Mean values were significantly different from those for obese subjects and patients with Cushing's disease, $P < 0{\cdot}005$. (Data from Wajchenberg *et al.* 1995.)

ABDOMINAL FAT

Tissue composition in the abdomen can be distinguished using DXA by identifying it as a specific region of interest within the analysis program. This is usually defined as the upper edge of the second lumbar vertebra to the lower edge of the fourth lumbar vertebra. The reference standard for abdominal fat is CT or MRI. The precision of DXA measurements of total abdominal fat (CV < 10 %) is significantly worse than that of CT (CV < 2 %), but similar to or better than that of MRI (CV > 10 %) (van der Kooy & Seidell, 1993).

DXA alone cannot distinguish intra-abdominal from subcutaneous fat. However, attempts have been made to do so by estimating the subcutaneous fat mass by anthropometric measures and calculating intra-abdominal fat by difference from the total abdominal mass (Svendsen *et al.* 1993*b*; Jensen *et al.* 1995; Treuth *et al.* 1995). This procedure yields a SEE of approximately 15 % for the prediction of intra-abdominal fat mass.

Despite the superiority of CT, DXA will be the preferred option in most situations because of the relative ease of access to machines, simplicity of measurement and low radiation exposure. Clearly MRI measurements can compete with DXA in terms of radiation exposure, but problems of cost, availability and precision may be even worse than for CT.

MUSCLE MASS

Limb muscle mass can be assessed based on a theoretical model of body composition in which it is assumed that the majority of fat-free tissue in the limbs is accounted for by skeletal muscle (Heymsfield *et al.* 1990; Fuller *et al.* 1992*b*). The total volume of the limbs is measured and the volume of skin, bone and adipose tissue subtracted.

The precision of this measurement is estimated to be approximately 1·5 % (Fuller *et al.* 1992*b*). It is difficult to establish the absolute accuracy because of the lack of definitive methods to quantify whole-body skeletal mass *in vivo*. However results correlate well with whole-body measures of total body potassium, which is commonly used as a marker of lean tissue mass, and estimates based on anthropometric measurements of limb muscle mass (Heymsfield *et al.* 1990).

Changes in muscle mass have been measured in patients with small-cell lung cancer (Jebb *et al.* 1994). Fig. 5 shows changes in body composition in patients who either responded or failed to respond to cytotoxic therapy. Non-responders lost 4.8 kg body weight of which 71 % was fat-free mass; of this 76 % was estimated to be muscle mass, suggesting that visceral tissue was relatively preserved.

APPLICATIONS

DXA has been widely employed and some examples have already been described. The availability of machines in many hospitals and ease of measurement have made a particular impact in the clinical sphere where other reference methods to assess body composition are unavailable or impractical. There are reports of cross-sectional measures of body composition in many patient groups including those with diabetes (Rosenfalak *et al.* 1995), renal disease (Hart *et al.* 1993) and Cushing's syndrome (Wajchenberg *et al.* 1995), but these have done little more than demonstrate group differences in body composition between patients and controls. The most useful data have come from studies in which a change in composition has been measured. These include the effect of growth hormone treatment (Taaffe *et al.* 1994; Beshyah *et al.* 1995), nutritional repletion following renal transplantation (Hart *et al.* 1993), composition of weight loss in lung cancer (Jebb *et al.*

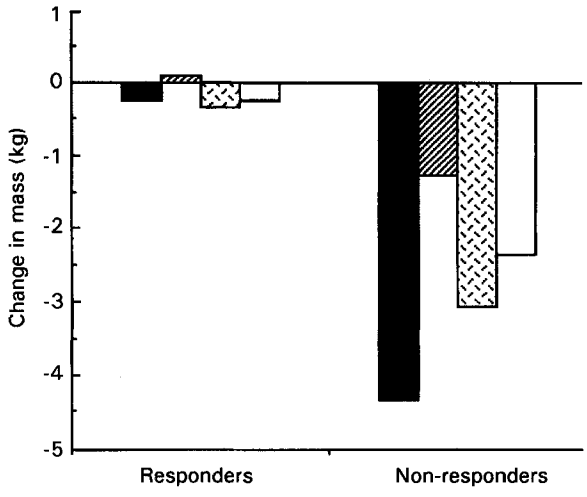

Fig. 5. Changes in body composition of patients with small-cell lung cancer, who responded or did not respond to cytotoxic therapy, measured by dual-energy X-ray absorptiometry. (■), Total body weight, (▨), fat mass; (▧), fat-free mass; (□), muscle mass. (Data from Jebb *et al.* 1994.)

1994) and the composition of weight loss during voluntary weight reduction (Koyama *et al.* 1990; Webber *et al.* 1994).

In such cases the precision of DXA determines the magnitude of the change which can be detected or the number of subjects required to show a significant change. Fig. 6 shows the numbers of subjects that would be required to detect differences in fat mass using DXA, assuming a range of different values for measurement precision. Measurements of whole-body fat mass can be made with a precision of 1 %, so a change of only 2 % can be detected

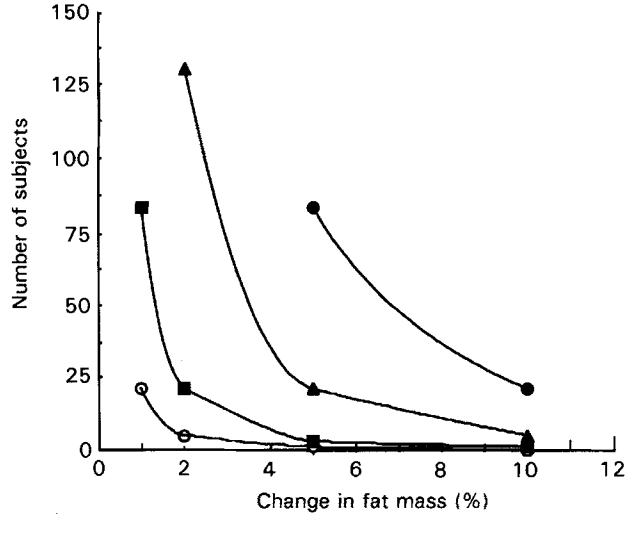

Fig. 6. Numbers of subjects needed to detect a change in fat mass (90 % power, 5 % significance) with varying precision of dual-energy X-ray absorptiometry measurement: (○), 1 %; (■), 2 %; (▲), 5%, (●), 10 %.

with less than ten subjects, whereas a similar change in fat mass in the trunk along, with a precision of 5%, would require more than 125 subjects (90% power, 5% significance).

DXA has also been used to establish reference values for body composition and fat distribution in large surveys of children and adults (Rico *et al.* 1994; Baumgartner *et al.* 1995; Ogle *et al.* 1995), but in this respect DXA alone is not ideal. The use of DXA in combination with other *in-vivo* techniques to produce a four-compartment model (bone mineral, water, fat and fat-free soft tissue) provides a more appropriate reference model of *in-vivo* body composition, but the technical complexity of this approach limits its application (Jebb & Elia, 1995).

INTER-MACHINE DIFFERENCES

Differences in both hardware and software make differences in measured composition between manufacturers unsurprising, but cast doubts on the absolute accuracy of DXA estimates of soft-tissue composition. In a comprehensive study Tothill *et al.* (1994) suggested that the total body fat measured by Hologic produced the best agreement with estimates derived from body density measurements. Lunar machines gave values of +3·7% and Norland +6·3% compared with Hologic. Furthermore the deviation between machines increased with increasing adiposity, predominantly due to differences in the measurement of fat in the trunk. This suggests that the differences cannot be entirely explained by differences in calibration standards, but also relate to the assumptions about fat distribution. This implies that the data cannot be adjusted to achieve comparability by a simple 'correction factor'.

Of greater concern are the substantial differences between machines by the same manufacturer which have been reported, despite apparently high standards of quality control within individual machines (Paton *et al.* 1995). Table 2 shows a comparison of measurements in six subjects on two different Lunar machines, each running similar software. BMC and total tissue mass were not significantly different but there was a mean difference of 3 kg fat. Measurements on a single subject measured on four machines showed differences of 0·9, 3·5 and 6·0 kg fat relative to machine 1. This is of particular concern for multicentre clinical trials. Unless these problems are quickly resolved the promising future of DXA will be unfulfilled.

CONCLUSIONS

Without doubt, DXA has already provided a new stimulus to studies of body composition and fat distribution. Its greatest advantage compared with other *in vivo* techniques to

Table 2. *Intra-manufacturer differences in measured composition of body compartments, using dual-energy X-ray absorptiometry*

(Data from Paton *et al.* 1995)

	Machine A	Machine B	Difference	*P*
BMC (kg)	2·9	2·8	+0·53	0·1
Total tissue (kg)	57·8	56·9	+0·90	0·11
Fat (%)	9·8	15·1	−5·3	0·001
Fat (kg)	5·9	8·9	−3·0	0·0006
Lean (kg)	51·9	48·0	+3·9	0·0001

BMC, bone mineral content.

measure soft-tissue composition is its precision, which should allow accurate measurements of changes in composition. However questions still remain regarding its absolute accuracy particularly at extremes of composition.

DXA is not the 'gold standard' sometimes claimed, but if used intelligently it can provide useful and valid measures. This caveat means it should not be viewed as a 'black box', but as a method which requires informed interpretation with an understanding of both the capabilities and limitations of the technique.

It seems probable that an investment in the technology by manufacturers could produce significant improvements in soft-tissue analysis, as has already occurred in the bone mineral aspects of DXA. Unfortunately it is a classic chicken-and-egg scenario; the market is restricted by the limitations of the technology and manufacturers seem unwilling to invest in the technology without a market. The economic reality is that few machines are sold for their capacity to measure soft tissue.

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