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Measurement of bone mineral using multiple-energy x-ray absorptiometry

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Abstract. Our laboratory has previously reported a method of determining the amount of bone mineral using triple-energy absorptiometry with a continuous x-ray spectrum. In the present study, the experimental properties of the technique were examined. The accuracy, the influence of fat content and body thickness and the *in vitro* and *in vivo* precision were analysed. The results found in this investigation showed that despite the complexity of the technique, the amount of bone mineral can be accurately determined. The *in vivo* precision was determined to be 3.4%, expressed as the coefficient of variation (CV), for different skeletal parts. The *in vitro* precision was found to be 2.1% (CV). Neither the fat content nor the body thickness had any effect on the measured bone mineral values. Excellent linearity and a close correlation were found between the true and the measured bone mineral values.

1. Introduction

Photon absorptiometry techniques are standard measurement procedures for the determination of bone mineral *in vivo*. Single-energy x-ray absorptiometry (SXA) and dual-energy x-ray absorptiometry (DXA) are, for example, well established methods. There are also other photon scattering and absorptiometry techniques, e.g. Rayleigh-to-Compton scattering and triple-energy x-ray absorptiometry (TXA), for bone mineral determination (Puumalainen *et al* 1976, Ling *et al* 1982, Jonson *et al* 1986). However, these techniques are in less frequent use since they are complex, and they require photon spectroscopy analysis.

When single- and dual-energy absorptiometry methods are used, an uneven distribution of adipose tissue in the human body will considerably influence the accuracy of the measured bone mineral values (Tothill and Pye 1992). In this context, triple-energy absorptiometry may provide an improvement, since this technique corrects for fat inhomogeneity. The validity of triple-energy absorptiometry for quantification of bone mineral in a three-tissue-compartment system composed of bone mineral, lean soft tissue and adipose tissue is the subject of discussion (Lehmann *et al* 1981, Kotzki *et al* 1991, Farrell and Webber 1990, 1992, Tothill and Pye 1992, Sutcliffe 1996). A comprehensive analysis concerning the theoretical feasibility of triple-energy absorptiometry has been presented in an earlier study by our laboratory (Swanpalmer *et al* 1998).

The aim of the present work was to examine the experimental properties of triple-energy absorptiometry when a continuous x-ray spectrum is used as the photon source.

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2. Materials and methods

In body composition analyses involving photon absorptiometry, the human body is assumed to consist of three different tissue constituents, i.e. bone mineral, lean soft tissue and adipose tissue. If a narrow-beam geometry is used the assumption that the photons in every arbitrary energy interval of the continuous x-ray spectrum are attenuated exponentially is valid. When n energy intervals are selected in the energy distribution of the x-ray spectrum, the attenuation of the radiation beam for the three-tissue compartments is described by n exponential equations as follows

$$N_i = N_{0,i} \exp(-\mu_{b,i} m_b - \mu_{s,i} m_s - \mu_{f,i} m_f) \tag{1}$$

where $i = 1, 2, \ldots, n$, N_i is the observed number of counts in the energy interval i, $N_{0,i}$ is the number of counts in the energy interval i without attenuation, μ is the mass attenuation coefficient in $cm^2\ g^{-1}$, m is the mass of attenuator per unit area in $g\ cm^{-2}$, and b, s and f are indices for bone mineral, lean soft tissue and fat respectively. Note that the same measurement set-up may be used for the determination of the experimental mass attenuation coefficients and for the measurement of bone mineral.

Three energy intervals can be randomly selected among the n energy intervals of the x-ray spectrum and an equation system containing three independent attenuation equations can then be written for these three energy intervals. Thus

$$N_1 = N_{0,1} \exp(-\mu_{b,1} m_b - \mu_{s,1} m_s - \mu_{f,1} m_f) \tag{2}$$

$$N_2 = N_{0,2} \exp(-\mu_{b,2} m_b - \mu_{s,2} m_s - \mu_{f,2} m_f) \tag{3}$$

$$N_3 = N_{0,3} \exp(-\mu_{b,3} m_b - \mu_{s,3} m_s - \mu_{f,3} m_f). \tag{4}$$

The notation is the same as in equation (1).

The above system of equations (2)–(4) contains three equations and three unknowns (i.e. m_b, m_s and m_f) and can be uniquely solved by using, for instance, Cramer's rule. Depending on the number of possible energy intervals, a number of combinations containing three energy intervals can be obtained. In this study, the x-ray tube high voltage was set at 60 kV_p and the energy intervals in the x-ray spectrum were between 35 and 57 keV, each interval being 1 keV. Thus, the number of permutations in this case is given by the following expression

$$\left(\frac{n}{3}\right) = \left(\frac{23}{3}\right) = \frac{23!}{3! \times 20!} = 1771. \tag{5}$$

Thus, 1771 values (for m_b, m_s and m_f) were calculated according to Cramer's rule for the three-tissue-component system. Since the adjacent energy intervals differed by only 1 keV, the mass attenuation coefficients for all the three tissue classes differed only slightly. This means that the three-equation system was ill-conditioned and some of the calculated values of m_b, m_s or m_f were negative in some combinations. In such cases the three-energy combinations with the corresponding calculated values (m_b, m_s, m_f) lead to cancellations, so generally fewer than 1771 positive values were obtained. These values were then statistically analysed to give the median and the mean values.

The set-up contained the following equipment: a stabilized x-ray generator (maximum load 100 kV_p, the tube current continuously variable between 0 and 6 mA), an x-ray tube, a planar high-purity germanium detector (the detector had a beryllium window of 0.254 mm, an active area of 500 mm^2 and a 7 mm crystal thickness), a 1.5 μs fixed conversion time analogue to digital converter (ADC), a fast spectroscopy amplifier and a computer-supported multichannel analyser (MCA). The x-ray tube was a water-cooled analysis tube. The anode

material was tungsten and the anode angle was 26°. The size of the focus was 6 × 8 mm. The radiation beam was filtered by 1 mm of beryllium. The source to detector distance was 1198 mm. The opening of the detector collimator had a diameter of 12 mm and a length of 136 mm. The source collimator was placed at a distance of 540 mm from the source with an opening diameter of 6 mm. The couch was positioned at 585 mm from the surface of the detector.

Table 1. Experimental and theoretical mass attenuation coefficients for bone, soft tissue and fat ($cm^2\ g^{-1}$).

Energy (keV)	$\mu_{b,\mathrm{exp}}$	$\mu_{b,\mathrm{theor}}$[a]	Ratio	$\mu_{s,\mathrm{exp}}$	$\mu_{s,\mathrm{theor}}$[a]	Ratio	$\mu_{f,\mathrm{exp}}$	$\mu_{f,\mathrm{theor}}$[a]	Ratio
35	1.312	1.390	0.944	0.297	0.307	0.967	0.250	0.249	1.004
36	1.221	1.290	0.947	0.288	0.298	0.966	0.247	0.244	1.012
37	1.139	1.200	0.949	0.280	0.289	0.969	0.243	0.240	1.012
38	1.066	1.120	0.952	0.273	0.282	0.968	0.240	0.236	1.017
39	1.001	1.050	0.953	0.266	0.275	0.967	0.235	0.233	1.009
40	0.942	0.988	0.953	0.260	0.268	0.970	0.231	0.230	1.004
41	0.888	0.929	0.956	0.255	0.262	0.973	0.227	0.227	1.000
42	0.839	0.876	0.958	0.250	0.257	0.973	0.224	0.224	1.000
43	0.793	0.828	0.958	0.245	0.252	0.972	0.222	0.221	1.005
44	0.752	0.784	0.959	0.241	0.248	0.972	0.219	0.219	1.000
45	0.715	0.744	0.961	0.237	0.244	0.971	0.217	0.217	1.000
46	0.679	0.707	0.960	0.233	0.240	0.971	0.215	0.215	1.000
47	0.647	0.673	0.961	0.230	0.236	0.975	0.214	0.213	1.005
48	0.618	0.642	0.963	0.227	0.233	0.974	0.212	0.211	1.005
49	0.592	0.613	0.966	0.224	0.230	0.974	0.210	0.209	1.005
50	0.567	0.587	0.966	0.221	0.227	0.974	0.207	0.207	1.000
51	0.545	0.562	0.970	0.219	0.224	0.978	0.206	0.206	1.000
52	0.525	0.540	0.972	0.216	0.222	0.973	0.203	0.204	0.995
53	0.505	0.519	0.973	0.214	0.219	0.977	0.202	0.203	0.995
54	0.488	0.499	0.978	0.212	0.217	0.977	0.200	0.202	0.991
55	0.472	0.481	0.981	0.210	0.215	0.977	0.199	0.200	0.995
56	0.457	0.464	0.985	0.209	0.213	0.981	0.198	0.199	0.995
57	0.448	0.448	1.000	0.208	0.211	0.986	0.196	0.198	0.990

[a] The theoretically determined mass attenuation coefficients were derived from Berger and Hubbell (1987).

The mass attenuation coefficients were experimentally determined using the same geometry as in the measurement of bone material. To determine the mass attenuation coefficients, for bone material, fat and lean soft tissue, phantoms with varying thicknesses of pure hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), triolein ($C_{57}H_{104}O_6$) and water were used. A comparison was made between these experimental mass attenuation coefficients and the theoretically determined values.

We have examined the influence of fat and body thickness on the measured bone mineral values as well as the accuracy in the bone mineral areal mass (BMA) values. The accuracy measurements were performed on phantom layers of pure hydroxyapatite submerged in a water bath. For the analyses of fat and body thickness dependence, phantoms with varying thickness of homogeneous layers of triolein and water were used.

Both the *in vitro* and the *in vivo* precisions were analysed. The *in vitro* precision was determined from 25 phantom measurements on the hydroxyapatite phantom over an interval of one week. One of these 25 phantom measurements was chosen for examination of the distribution of the calculated bone mineral values. The reproducibility or the precision *in vivo* of the present method was determined by repeating measurements on 10 volunteers, at

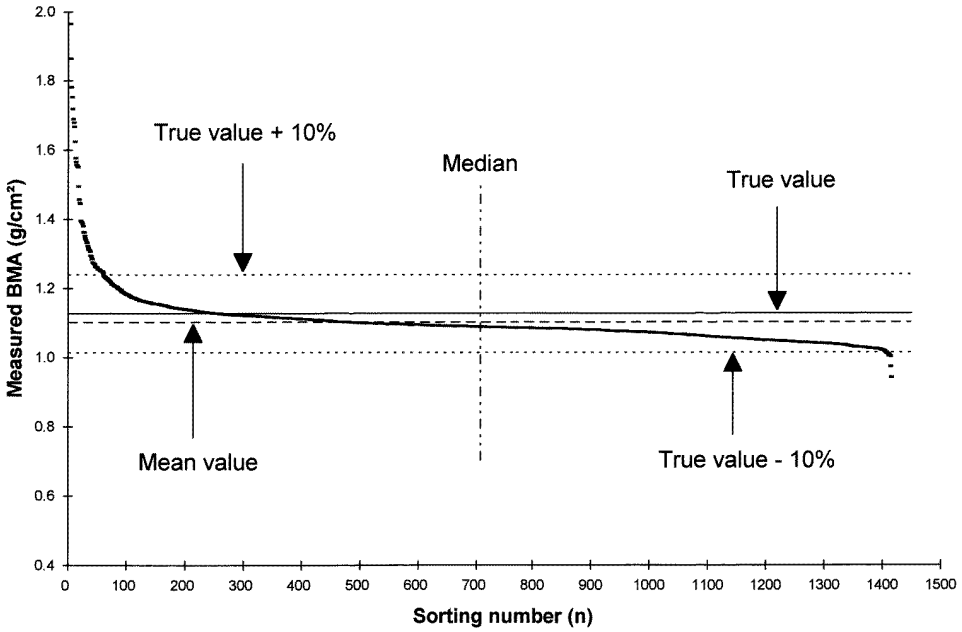

Figure 1. Distribution of BMA values ($n = 1413$). The sorting number is associated with the order number when the BMA values were arranged from the highest to the lowest value.

the same position in the body, over a period of one week. The tibial condyle (anteroposterior (AP) measurement) and the third lumbar vertebral body (lateral measurement) were chosen as measurement sites. Five subjects were investigated in both cases.

The measurements were performed as stationary measurements. The measured bone volume was cylindrical and had a diameter of 8 mm. For both *in vitro* and *in vivo* measurements the number of photons detected in the different energy intervals (i.e. energy channels with 1 keV width) of the continuous x-ray spectrum were between 55 000 and 300 000 with the former value being a precondition, either in the 35 keV or 57 keV energy channel. For these values the patient measurement time was about 5 min. The number of primary photons (i.e. the $N_{0,i}$ values) and primary photon rate in every single energy interval (i.e. the 23 selected energies) for the detected photons above were approximately 10^8 and 3.3×10^5 photons/s respectively.

3. Results

The experimentally obtained mass attenuation coefficients for hydroxyapatite, fat (triolein) and water are compared with the theoretically determined values in table 1. Since the mass attenuation coefficients were expressed in $cm^2\ g^{-1}$, the amount of bone mineral is expressed in g cm^{-2}, i.e. the BMA (Jonson 1993).

The distribution of the calculated BMA values ($n = 1413$) for one of the phantom measurements with 19 cm water, 1.127 g cm^{-2} bone mineral (hydroxyapatite) and 3.5 cm fat (triolein) is shown in figures 1 and 2. It can be seen from these figures that both the mean (1.102 g cm^{-2}) and the median (1.088 g cm^{-2}) of the calculated BMA values are close to the true value (1.127 g cm^{-2}). The mean and the median values were 2.2% and

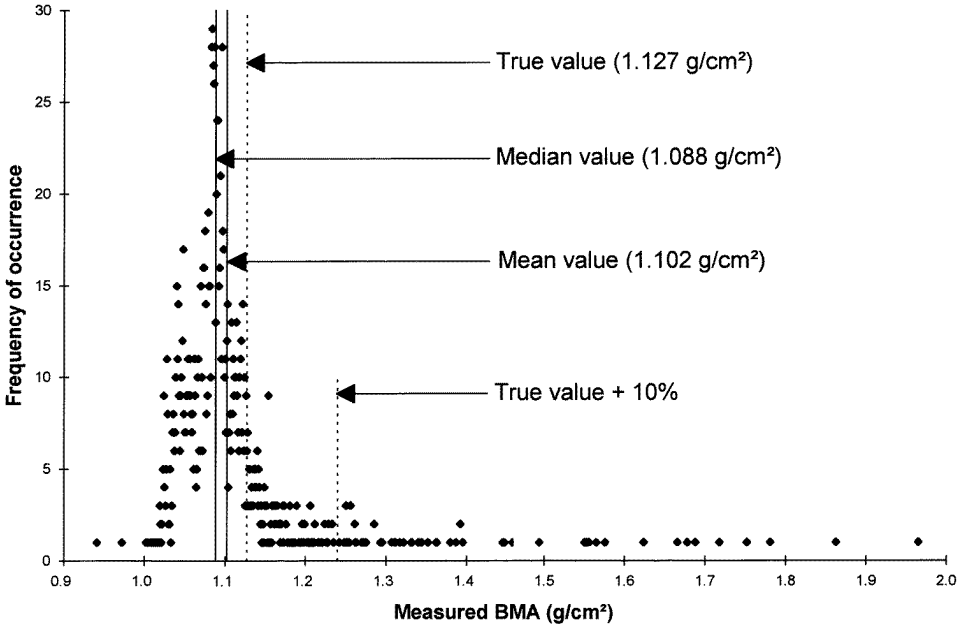

Figure 2. Frequency distribution of BMA values ($n = 1413$). The BMA values were rounded off to three decimals.

3.5% lower than the true value respectively. It can also be seen from figure 1 that 95% ($n = 1344$) of the calculated BMA values were within the range (true value $\pm$ 10%). As can be seen in figure 2, when the values greater than (true value + 10%) are omitted ($n = 58$) the distribution of the remaining BMA values ($n = 1355$) has the shape of a normal or Gaussian distribution with the centre at the median value. (Note, the BMA values presented in this study were rounded off to three decimals).

Figure 3 summarizes the hydroxyapatite phantom measurements performed in order to examine the linearity and the agreement with the true value for bone mineral. For the mean as well as for the median bone mineral value a close correlation and excellent linearity were found between the true and the measured bone mineral values. As can be seen in figure 3, the lines for the mean and the median values are parallel and the discrepancy between them is small.

No correlation was found between measured BMA values and fat content when the influence of fat on the BMA values was examined. The results of this analysis are presented in figure 4 ($r = 0.096$, $P = \text{NS}$ (0.84)).

The effect of body thickness on the measured BMA values is shown in figure 5. It can be seen from the figure that body thickness had no significant effect on the measured BMA values ($r = 0.16$, $P = \text{NS}$ (0.66)).

The reproducibility in the *in vitro* analysis based on 25 phantom measurements during one week gave a coefficient of variation of 2.1% when the median BMA values were chosen for the calculation of the precision. The corresponding coefficient of variation for the mean BMA values was 2.3%. Since the median BMA values showed less variability than the mean values, the former were used in the analyses of fat content and body thickness effects on the measured BMA values (figures 4 and 5).

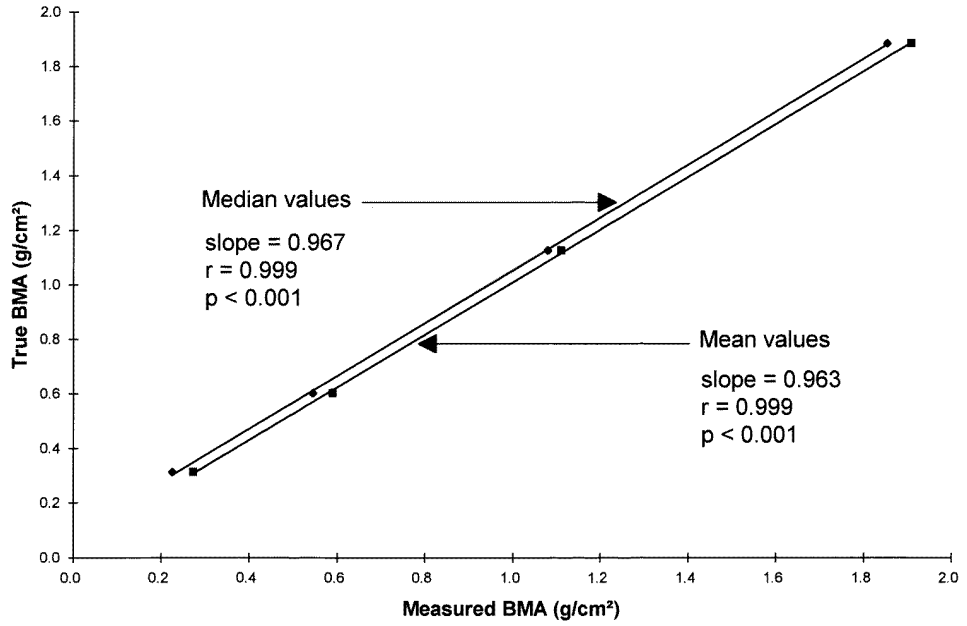

Figure 3. Linearity between true and measured BMA. (The standard errors of estimate (SEE) for the median and mean values were 1.1% and 1.2% respectively.)

The *in vivo* precision was determined by repeating measurements on 10 subjects at the same measurement site. The values obtained from these measurements are shown in table 2. As can be seen, the precision, expressed as the coefficient of variation, ranged between 0.57% and 6.36% with a mean of 3.35% and a standard deviation (SD) of 2.24% for the tibial condyle (AP) measurements. For the third lumbar vertebral body (lateral) measurements the values (CV) ranged between 2.3% and 4.14% with a mean of 3.4% and an SD of 0.68%.

4. Discussion

In body composition investigations, particularly in quantitative analyses of the amount of bone mineral, a three-component tissue system consisting of bone, lean soft tissue and adipose tissue is analysed when photon absorptiometry techniques are used. When photon absorptiometry methods with less than three photon energies are used, certain approximations and assumptions must be made to solve the three-tissue-component system since in these cases only one or two attenuation equations can be set up. A common approximation is the fat approximation, which assumes a uniform adipose tissue distribution at the measurement site. When photon absorptiometry techniques with two photon energies are used the total thickness of the attenuator can be introduced as an additional parameter and in this case the fat approximation is superfluous (Jonson *et al* 1990). An alternative method of analysing the three-component system without the fat approximation or knowledge of the total thickness of the attenuator is to use triple-energy absorptiometry. Triple-energy absorptiometry is less widely used as it is complex and requires a high number of photons to be detected. However, Jonson *et al* (1986) have overcome this problem by introducing

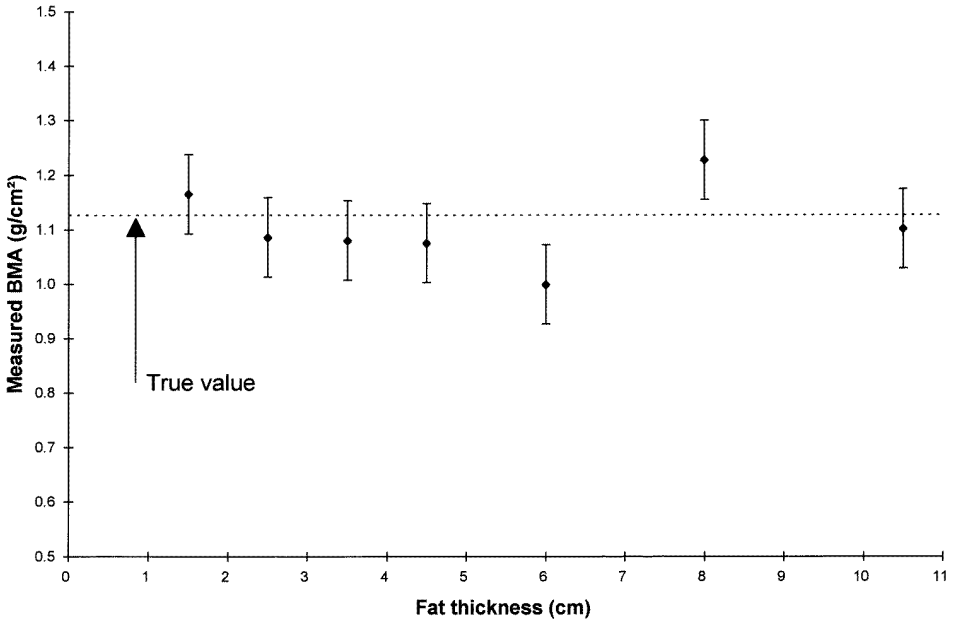

Figure 4. Dependence of the measured BMA values on fat thickness ($r = 0.096$, $P =$ NS (0.84)). The error bars denote one standard deviation of the mean.

Table 2. Reproducibility in *in vivo* measurements.

	Repeated measurements BMA (g cm^{-2})			
Subject	1	2	3	CV (%)
1[a]	0.891	0.878	0.821	4.31
2[a]	0.684	0.719	0.67	3.65
3[a]	0.81	0.801	0.807	0.57
4[a]	0.628	0.617	0.557	6.36
5[a]	1.117	1.143	1.159	1.86
				Mean[a]: 3.35
6[b]	0.351	0.339	0.363	3.42
7[b]	0.37	0.359	0.386	3.65
8[b]	0.504	0.483	0.464	4.14
9[b]	0.548	0.533	0.558	2.3
10[b]	0.694	0.73	0.743	3.51
				Mean[b]: 3.4

[a] Tibial condyle (anteroposterior measurement).
[b] Third lumbar vertebral body (lateral measurement).

a method of triple-photon absorptiometry employing a continuous x-ray spectrum as the photon source.

For accurate determination of the bone mineral content using photon absorptiometry, accurate experimental determination of the mass attenuation coefficients is a prerequisite. The agreement between the coefficients determined in this work and theoretical data are

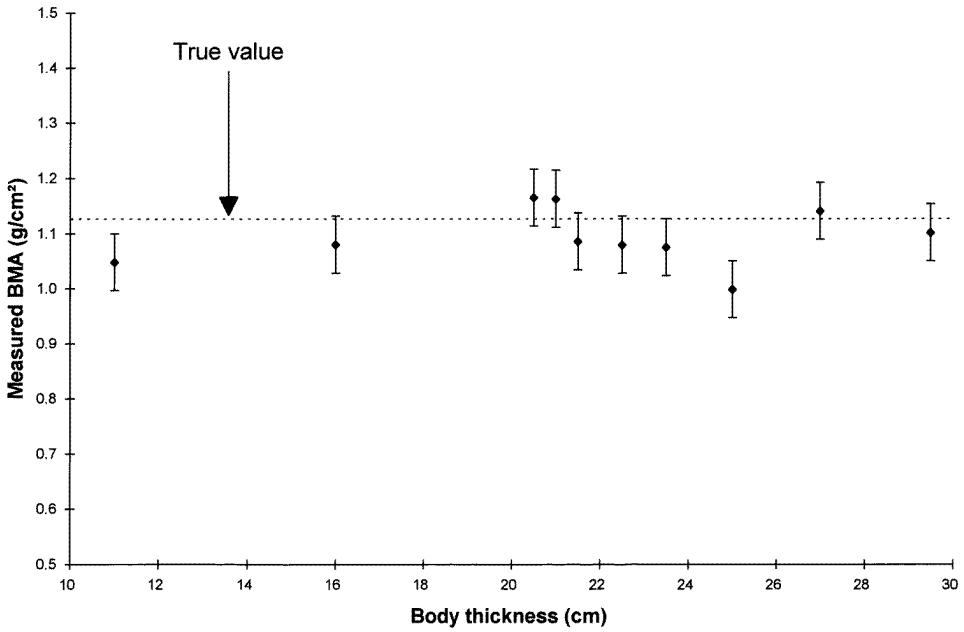

Figure 5. Influence of body thickness on the measured BMA values ($r = 0.16$, $P =$ NS (0.66)). The error bars denote one standard deviation of the mean.

well within the limits of acceptance. This is shown by the agreement between the measured and true BMA values. However, as can be seen in table 1, the mass attenuation coefficients, particularly for lean soft tissue and fat, differ slightly. In consequence, the equation system (2)–(4) is ill-conditioned. An insufficient number of detected photons or a slight change in the mass attenuation coefficients will substantially influence the accuracy. Despite the fact that the experimental mass attenuation coefficients were accurately determined, some of the three-energy combinations in this permutation technique gave negative values due to the above described conditions. This indicates that a large number of permutations is required to avoid uncertainties of scatter of data which occur with a low number of permutations. In other words, the number of energy intervals is of major importance in this particular method of triple-energy absorptiometry. The number of BMA values which can be obtained (from a single measurement) with this technique is directly dependent on the number of energy intervals selected and indirectly on the number of photons detected and the accuracy of the mass attenuation coefficients.

It has been shown in this study that during calculations of BMA a large number of positive values can be obtained (figures 1 and 2). It can be seen from these figures that ~95% of the BMA values obtained were close to the true value. This close relationship between the true and calculated BMA values can also be observed in figure 3, where true BMA values are shown together with the mean and median values of the calculated BMA values.

Figures 4 and 5 show that the fat content and body thickness had no significant influence on the measured BMA value. The present technique measures the bone mineral in a single point. No adipose or soft tissue values along a beam path outside the bone are necessary as in dual-energy absorptiometry. The present technique enables determination of the bone

mineral without any influence of homogeneous and non-homogeneous soft or adipose tissue within or around the measured bone.

The short-term *in vitro* precision (2.1% CV) is poorer that the precision in DXA measurements of $<1\%$ (Lai *et al* 1992). One source of error is probably associated with small variations in the output from the x-ray tube and in insufficient pulse transfer.

The *in vivo* precision was determined for different skeletal parts, i.e. the tibial condyle and the third lumbar vertebral body. As shown in table 2, the present system had an *in vivo* reproducibility or precision of 3.35% and 3.4%, expressed as the coefficient of variation for the tibial condyle and the third lumbar vertebral body measurements respectively. Further optimization is required to lower the variability, for example by modifying the positioning of patients for the measurements.

The results obtained in this work show that the amount of bone material can be accurately determined using triple-energy absorptiometry with a continuous x-ray spectrum as the photon source.

Acknowledgments

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