

## The value and limitation of dual-energy X-ray absorptiometry

J. E. Harrison<sup>a</sup>, C. Muller<sup>a</sup>, S. S. Krishnan<sup>b</sup>, S. W. Kooh<sup>c</sup>, E. Noriega<sup>c</sup>, C. Leslie<sup>c</sup> and K. G. McNeill<sup>d</sup>

<sup>a</sup>The Toronto Hospital and the Department of Medicine, <sup>b</sup>Department of Chemical Engineering, <sup>c</sup>Department of Paediatrics, <sup>d</sup>Department of Physics, University of Toronto, Toronto, Canada.

In population studies, in which patients and controls are of comparable size, bone mineral area density (BMD) gives reliable results for mean bone mass data although, with sequential data, BMD may underestimate the degree of change in bone mass. In children BMD data should be reliable, provided that patients and controls, matched for age and sex, are also of the same size. With disease children may be small for their age so that low bone mass by BMD may be due to small body size and not necessarily to osteopenia. In these situations the bone mineral content (BMC) index may be more reliable than BMD. To assess bone mass status in individuals, BMC index, as well as BMD, should be used, particularly with adults at the extremes of body size (the very small or very tall).

### Introduction

The procedure, dual-energy X-ray absorptometry (DXA), is used widely for measurements of bone mass. DXA gives minimal radiation exposure (< 5 mrem), has excellent precision (1-2%) and costs are acceptable (\$100-\$200)<sup>1</sup>, but the validity of DXA data is uncertain.

The DXA procedure measures bone mineral content (BMC g) and bone area cm<sup>2</sup> (height × lateral width). BMC is then normalized to this bone area to give a bone mineral area density (BMD g/cm<sup>2</sup>). This BMD calculation would not be expected to normalize adequately for body size since the normalization does not take into consideration variation in anterior posterior (AP) bone thickness that also would vary with body size. Children do show a BMD dependency on body height<sup>2</sup>, (although controls for paediatric studies are usually matched for sex and age but not for body size), but in adults this height dependency is not observed. Some problem with DXA BMD data that obscures the adult height dependency is suggested.

DXA measurements on aluminium samples have demonstrated a lower limit of sensitivity for BMD of 0.3 g/cm<sup>2</sup> with spine scans and 0.4 g/cm<sup>2</sup> with whole body scans<sup>1</sup>. In all subjects mean BMD values are inevitably above the lower limit of sensitivity, ie BMD >0.3 g/cm<sup>2</sup> for lumbar scans, but, throughout the area of the bone, local BMD values will vary widely. In normal adults, with Lumbar BMD 1.0-0.8 g/cm<sup>2</sup>, the areas of bone with local BMD values < 0.3 g/cm<sup>2</sup> would be small. With increasing loss in bone mass, however, a greater proportion of bone area will have local BMD values below detection, causing a slight under-estimation of BMC (observed < true) and an over-estimation of BMD which will be greater than the under-estimation of BMC (observed > true). Similar errors in BMC and BMD may occur in small compared to tall subjects, eg in children. Possibly, the lack of BMD height dependency in adult populations is related to this problem with DXA lower limit sensitivity, ie a small reduction in BMD associated with smaller adults, due to

smaller AP thickness, may be offset by a comparable over-estimate in BMD due to the effect of DXA lower-limit sensitivity.

In clinical studies, significant discrepancies have been observed between DXA BMD data and normalized bone data by neutron activation analysis (NAA), (with NAA the normalization is to overall body height (Calcium Bone Index, CaBI))<sup>2</sup>. In individual cases results by either DXA or NAA may be unreliable but results of a study on patients with anorexia nervosa (AN) indicate that, at least in some cases, BMD values are unreliable and that BMC normalized to body height may be preferable.

### Clinical study and procedures

Bone mass measurements with DXA and with NAA, were carried out on 22 adolescent women with AN. Each patient was studied on the initial hospital visit and, in 11, measurements were repeated after a 1-2 year follow-up (mean 15 months). DXA but not NAA measurements were also carried out on 24 age-, height- and sex-matched volunteers. Consistent with the diagnosis of anorexia, the AN patients had body mass index (BMI, Wt/H<sup>2</sup> kg/m<sup>2</sup>) 73(3)% (m(lsd)) of controls. Over the follow-up period BMI increased by 11.5 (19)% but remained significantly below the control group. (BMI, m(sd) was 16(2), 17(4) and 22(2) kg/cm<sup>2</sup> in AN initially, in AN follow-up and in controls, respectively).

The NAA procedure measures calcium in an area 30 × 60 cm<sup>2</sup>, incorporating trunk and upper thighs. The calcium activity, proportional to the total bone mineral in the area of measurement, is normalized to body size based on height<sup>3</sup> (the CaBI)<sup>3</sup>.

DXA measurements were made with the Holmic QDR-1000W facility. Lumbar vertebrae L<sub>1-4</sub> were measured. L-BMC and L-BMD were recorded. In addition, L-index values were calculated that normalized L-BMC to body size (based on a Height<sup>3</sup> function similar to that for the CaBI calculation).

## Results

A significant correlation was obtained with L-BMC to Ca count by NAA ( $r=0.84$ ,  $p<0.0001$ ). The correlation with the normalized data, L-BMD to CaBI, was not significant ( $R=0.29$ ,  $P<0.2$ ) while the correlation with L-index to CaBI ( $R=0.71$ ,  $P<0.002$ ) was stronger than the BMD correlation. The degree of bone loss would be expected to be associated with duration of anorexia. A significant correlation was observed with duration of disease to CaBI ( $R = -0.60$ ,  $P = -0.003$ ) but the correlation to L-BMD was not significant ( $R = -0.3$ ,  $P = 0.18$ ). The correlation to L-index ( $R = -0.43$ ) just reached significance at 5% Figure 1.

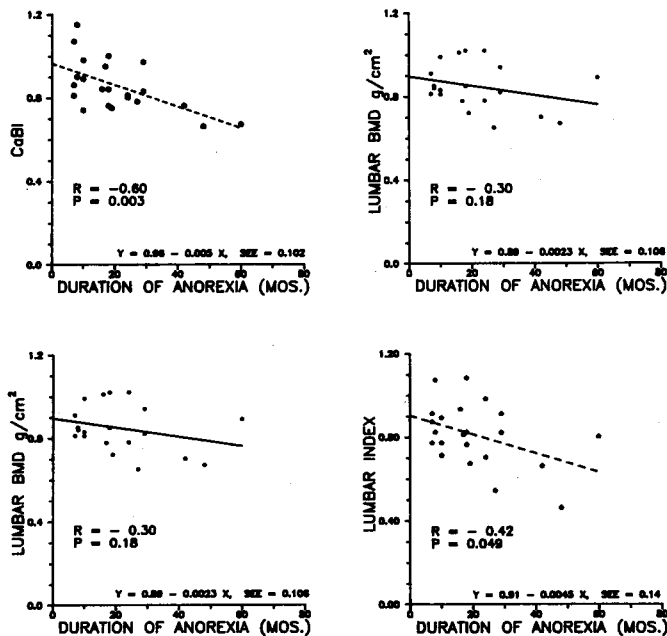


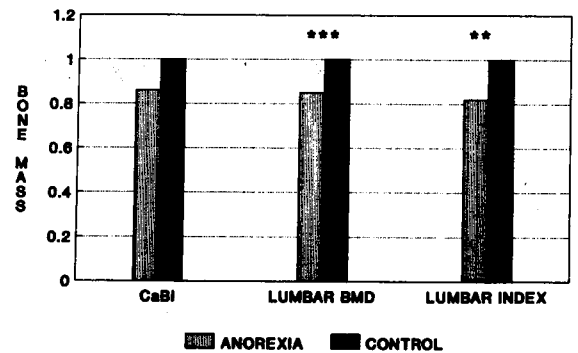
Figure 1. Correlations for CaBI to L-BMD (top), and to L-Index (above). Data obtained on patients with anorexia nervosa.

In spite of the poor correlation between BMD and CaBI, on average, comparable bone mass values with the two procedures were obtained at the initial investigation (Fig. 2) and, at follow-up, further losses in bone mass were comparable (Fig. 3). The losses in bone mass during follow-up by the three estimates were equally significant,  $P < 0.001$ . The mean loss by L-BMD was less than mean losses by L-index and by CaBI but the differences were not significant.

## Discussion

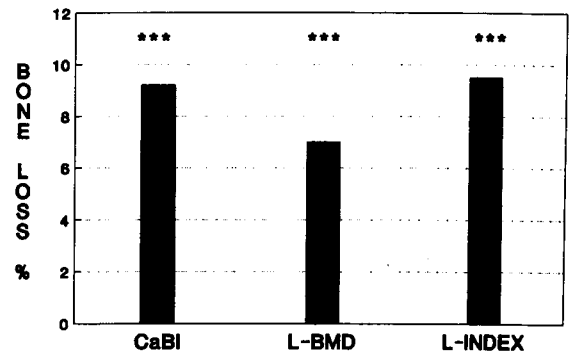
BMC normalized to body height (L-index) gave a stronger correlation to CaBI than BMC normalized to bone area (BMD). L-index also gave a stronger correlation than L-BMD to duration of disease. These findings suggest that some of the discrepancies between BMD and CaBI data are due to errors associated with the normalization of BMC to bone area, and that normalization to body height may be more reliable.

In spite of significant discrepancies between BMD and CaBI data, mean values of bone mass in the AN population were similar with the three estimates, both when initial values were compared to controls and when follow-up data were compared to initial values. In the sequential study, the mean bone loss was less by BMD than by estimates based on height normalizations, (L-index or CaBI). Although the differences were not significant a smaller reduction in bone mass by BMD, compared to L-index or to CaBI, is consistent with the



Significance, \*\*\*  $p < 0.0001$ , \*\*  $p < 0.003$

Figure 2. Mean bone mass data on patients with anorexia studied prior to treatment compared to control data. L-BMD and L-index values are compared to data on matched controls. CaBI data are compared to historical controls and, therefore, significance is not reported.



Significance \*\*\*  $P < 0.001$

Figure 3. Mean percent changes in bone mass in the patients in Figure 1 followed over 1-2 years. \* Significant differences from no change.

prediction that BMD is over-estimated proportionately to the degree of bone loss.

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