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**QUANTITATION OF THE DEGREE OF OSTEOPOROSIS BY
MEASURE OF TOTAL-BODY CALCIUM EMPLOYING NEUTRON ACTIVATION***

by

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A basic assumption underlying the measurement of bone mass for the evaluation of osteoporosis is that there exists a relationship between the level of bone mineral and the occurrence of spontaneous fractures characteristic of the condition. If the hypothesis that the structural integrity of the skeleton, (particularly of the vertebrae), is associated with a critical level of mineral is accepted, it is then essential to determine the threshold value and to establish degrees of osteoporosis in terms of the deficiency of calcium from a "normal" value. Since osteoporosis occurs chiefly in postmenopausal women, age 50 or greater, who "normally" exhibit an increase in the rate of Ca loss associated with the regression of the gonadal hormones, the problem of distinguishing osteoporotic individuals from normal women in the same age range is a particularly difficult one.

In the present study, two techniques for measuring the amount of Ca in the total skeleton were employed: total-body neutron activation analysis (TBNA) and the determination of the mineral content of a bone of the appendicular skeleton (absorptiometric measurement of the radius, BMC).

Methods

Thirty-six women were selected on the basis of having either one or more compression fractures of the vertebrae or radiological evidence of severe osteoporosis. Twenty-three "normal" women, manifesting no clinical evidence of osteoporosis, and ranging in age from 50 to 78 years, served as controls. The patients were uniformly exposed to a beam of partially moderated fast neutrons which induces the reaction $^{48}\text{Ca} (n, \gamma) ^{49}\text{Ca}$. The induced ^{49}Ca was then measured with the Brookhaven whole-body counter which gives an absolute measurement of the ^{49}Ca . From these data, absolute levels of total-body calcium were calculated with an accuracy of $\pm 5\%$ and a precision of $\pm 1\%$ (1SD) (1). The radiation dose to the patient in this technique is 0.028 rad

(or 0.28 rem). The bone mineral content (BMC) of the radius and width (W) were measured with a Norland-Cameron absorptiometer (2,3). Measurements were made at the 8 cm site on the left radius.

Results and Discussion

The range in absolute levels of TBCa in the osteoporotic patients was very large (344 - 865 g), reflecting the effects of the parameters of body habitus, age and sex (see Table 1). In order to assess the relative deficit of TBCa in an individual, it is necessary that the calcium level be compared with a "normal" value for that individual. This variability in TBCa diminishes the usefulness of the average value as the basis for comparison. For this reason, a previously developed algorithm was used to predict the normal TBCa in each subject based on lean body mass (potassium), height, sex and age (4,5). The formula used was:

$$Ca_p = \alpha HK^{\frac{1}{2}} \quad (1)$$

where Ca_p = predicted total body Ca (g)

H = height (m)

K = total body potassium (g)

α = 56.62-0.38 (age - 55)

for subjects > 55 yrs

α = 56.62 for subjects $\leq$ 55 yrs

The measured total-body Ca expressed in terms of the predicted normal value (Ca_p) is referred to as the calcium ratio (TBCa/ Ca_p). The difference between the value of this ratio and 1 is referred to as the Ca deficit.

In the group of female osteoporotics, the mean calcium ratio was 0.858 ± 0.110 (SD); the mean was 0.996 ± 0.072 (SD) for the normal contrast group (Table 1).

In patients with kyphosis, correction was made for loss of stature due to the kyphotic changes by estimation of the height from a radiograph of the tibia length (5). Correction was also made for the abnormally low K values observed in a few patients. The predicted normal K was calculated from a previously derived relationship involving height and weight (6).

The BMC values varied from 0.362 to 1.028 g/cm in the osteoporotic population. To facilitate intercomparison of bone mineral content (BMC), measured by absorptiometry, the data must be normalized for size and age as was necessary for the TBCa data. While division of the BMC value by the width of the radius (W) tends to reduce the variability in the group, the procedure is not satisfactory as a normalization. Inasmuch as TBCa and BMC measurements correlate well, BMC data can also be normalized by a modification of the same algorithm employed for the normalization of the TBCa data (7). The new algorithm with an age correction factor was derived as follows:

$$\text{BMC} = 0.00112 \text{ TBCa} - 0.0664 \quad (2)$$

$$\text{TBCa} = \alpha \text{ HK}^{\frac{1}{2}} \quad (3)$$

$$\text{BMC}_p = 0.0635 \text{ HK}^{\frac{1}{2}} - 0.0664 \text{ for age} \leq 55 \quad (4)$$

$$\text{BMC}_p = [0.0635 - 0.00043 (\text{age} - 55)] \text{ HK}^{\frac{1}{2}} - 0.0664 \text{ for age} > 55 \quad (5)$$

The normalized TBCa and BMC values are shown in Figure 1. The values of 75% of all the calcium ratios for the osteoporotic subjects were more than 1 SD below the normal mean, while 70% of the BMC ratios of the osteoporotic subjects fell within 1 SD of the mean of the normal subjects.

A highly significant correlation was found between the directly measured BMC and TBCa values. The correlation coefficient was 0.826 ($p < 0.001$); it was almost the same as that found for the age matched normal population (0.813). This finding is surprising in light of the probable differential rates of loss in different bones in osteoporotic patients. Ca loss is known to occur primarily

from the trabecular bone of the vertebrae in the osteoporotic patients, and only secondarily from the radius. The correlation coefficient relating TBCa and BMC reported here is in good agreement with the results reported by Chesnut (8).

Thirty-four of these osteoporotic patients underwent various therapeutic regimes: calcitonin, calcium, estrogen and growth hormone administration, and were studied both before and following therapy by both TBNA and photon absorptiometry.

The correlation coefficient between the change in TBCa ($\Delta\%$) and the change in BMC ($\Delta\%$) was very poor ($r = 0.17$). These findings suggest that changes in radial BMC values, at the 8 cm site, do not always reflect changes in skeletal mass in response to treatment of osteoporosis.

As previously reported, there is a large statistical variability in the BMC of the peripheral skeleton in normal populations up to 18% (10). This variability, even in data normalized for sex, age and size of the individual, make it unsatisfactory to diagnose osteoporosis solely on the basis of the measurement of radial BMC. The TBCa value, normalized for sex, age and skeletal size, appears to be statistically more reliable than the BMC values of the radius as an index for quantitating the degree of osteoporosis in an individual. The normal loss of calcium with age in post-menopausal women often makes it difficult to distinguish between osteoporotic and non-osteoporotic individuals. The degree of osteoporosis in an individual can be assessed in terms of their calcium deficit, as measured by TBNA, but only on a statistical basis.

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**SKELETAL CALCIUM AND BONE MINERAL
CONTENT IN ADULT FEMALES**

No.	Age	Wt kg	Ht cm	TBCa g	$\frac{TBCa}{Ca_p}$	BMC g/cm	W cm	BMC/W g/cm ²	$\frac{BMC}{BMC_p}$
<u>Osteoporotic Females (44-81 y)</u>									
36	65.7	56.9	153.3	589.8	0.858	0.646	1.234	0.528	0.917
		±24.3*	±5.4	±18.4	±12.8	±23.8	±12.5	±22.4	±16.9
<u>Normal Females (50-79 y)</u>									
23	61.7	64.4	156.3	728.3	0.996	0.752	1.173	0.638	0.993
		±14.7	±4.6	±13.6	±7.2	±16.3	±10.9	±13.2	±10.7

* Coefficient of variation (%SD)

TBCa - total body calcium, measured

Ca_p - total body calcium, predicted

BMC - bone mineral content of radius (g/cm), measured

BMC_p - bone mineral content of radius (g/cm), predicted

W - radius width (cm)

Fig. 1 - Neg. #5-70-75