Comparison of Single- and Dual-Photon Absorptiometry in Postmenopausal Bone Mineral Loss

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We describe a single photon absorptiometric (SPA) technique, which enables differential estimation of the rates of loss from trabecular and cortical bone. Ten scans are obtained in the forearm: six in an area with about 7% trabecular bone and four scans in the adjacent distal area with a trabecular bone content of 25%. By comparing bone masses of these two sites in 19 postmenopausal and 53 premenopausal women, the postmenopausal trabecular bone loss was estimated to be approximately seven times greater than cortical loss within the first years of cessation of regular vaginal bleeding. On a group basis the bone loss at the distal forearm scan site (by SPA) corresponded closely to the spinal bone loss (by dual-photon absorptiometry). The reproducibility of the two scan sites in the forearm was 1–1.5% (CV%), which makes the method suitable for longitudinal studies. Corrections for variations in fatty tissue covering can be made without deterioration of the reproducibility. The high precision can only be achieved with a good calibration procedure; if calibration is not done the reproducibility error increases two- or threefold.

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Increasing interest in the causes, prevention, and treatment of metabolic bone disease has led to demands for reliable, easy, and inexpensive methods for measuring bone mass. Interest has especially centered on measurements of trabecular bone mass, and one of the most widely used techniques for evaluating predominantly trabecular bone is the dual-photon technique applied to the spine. However, a third of the spinal bone mass is cortical and measurement solely of trabecular bone can only be done with expensive methods such as computerized tomography (*1*).

In the last 10 yr measurements of bone mass in the forearms by single photon absorptiometry have become one of the most widely used methods for evaluating the cortical bone mass primarily. There are several different scanners with minor differences in the measurement set up. The scan site varies from the midshaft site to the distal and some scanners measure only one of the forearm bones. Our technique, using six scans over 2 cm of the bone length, minimizes the reposition error and thereby increases the precision. The aim of this study was to examine the possibility of measuring trabecular bone mass by extending the scan procedure in the distal direction without losing the high reproducibility of the method, and to evaluate the fit of the trabecular bone mass in the forearm to the bone mass in the spine.

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Fifty-three premenopausal women and 19 women who had passed a natural menopause 5.5 ± 0.8 yr previously (Table 1) entered the study. All were free from present or past diseases known to affect calcium metabolism and none of the postmenopausal women had received hormonal substitution therapy. All the women were measured twice with a 3-mo interval in between.

MATERIALS AND METHODS

Bone mineral content (BMC) in the ulna and radius

TABLE 1
Age, Weight, Height, LBM, and Biochemical Values in 53 Premenopausal and 19 Postmenopausal Women

Item	Premenopausal $\bar{x} \pm 1$ s.d.	Postmenopausal $\bar{x} \pm 1$ s.d.
Age (yr)	44.7 ± 7.3	53.0 ± 0.6*
Weight (kg)	61.7 ± 8.4	59.5 ± 12.4
Height (cm)	163.3 ± 6.0	160.2 ± 6.1
LBM (kg)	43.0 ± 2.2	41.2 ± 2.8
Serum calcium (mmol/l)	2.45 ± 0.08	2.46 ± 0.09
Log serum alk.phos (U/l)	2.09 ± 0.10	2.17 ± 0.08†
F.U. Calcium/Cr (mmol/mol)	196 ± 117	371 ± 216*

* $p < 0.001$ compared with premenopausal women, Student's t-test.
† $p < 0.01$.

was measured by single photon absorptiometry (Nuclear Data Bone density scanner 1100) (*2*). Six scans, 4 mm apart are obtained on each forearm. The first scan is taken at the site where the distance between the two forearm bones is 8 mm. This site is automatically found by the controller software by stepwise registration of distances between the bones at intervals of 2 mm. We have now extended the scan procedure by obtaining four additional scans 2 mm apart distal to the starting point. The scan procedure thus starts at the 8 mm site (Fig. 1) and moves proximally (mean of scans 1 to 6 = proximal BMC), returns to the starting point and then moves distally in the opposite direction (mean of scans −1 to −4 = distal BMC). The system is calibrated once a week by measuring an aluminum standard nine times (= a total of 54 scans) in order to eliminate drift of the system. The calculated calibration factor is used for correction of BMC measurements in the following week. In addition a control scan of the standard is done daily. BMC_1 is the "raw value" of the bone mineral and BMC_2 is the value obtained after correction for varying amounts of fat in the subcutaneous tissue by means of a special computer algorithm. BMC_2 is BMC_1 with a percentage added depending on the amount of fat measured (the more the fat the larger the percentage). The correction assumes that the arm is circular, and the fat is measured as an intensity increase of the sides of the arm. The correction percentage ranges from 0% in lean patients to about 30% in very obese patients. The 8-mm site corresponds on the average in adult bones to 10% of

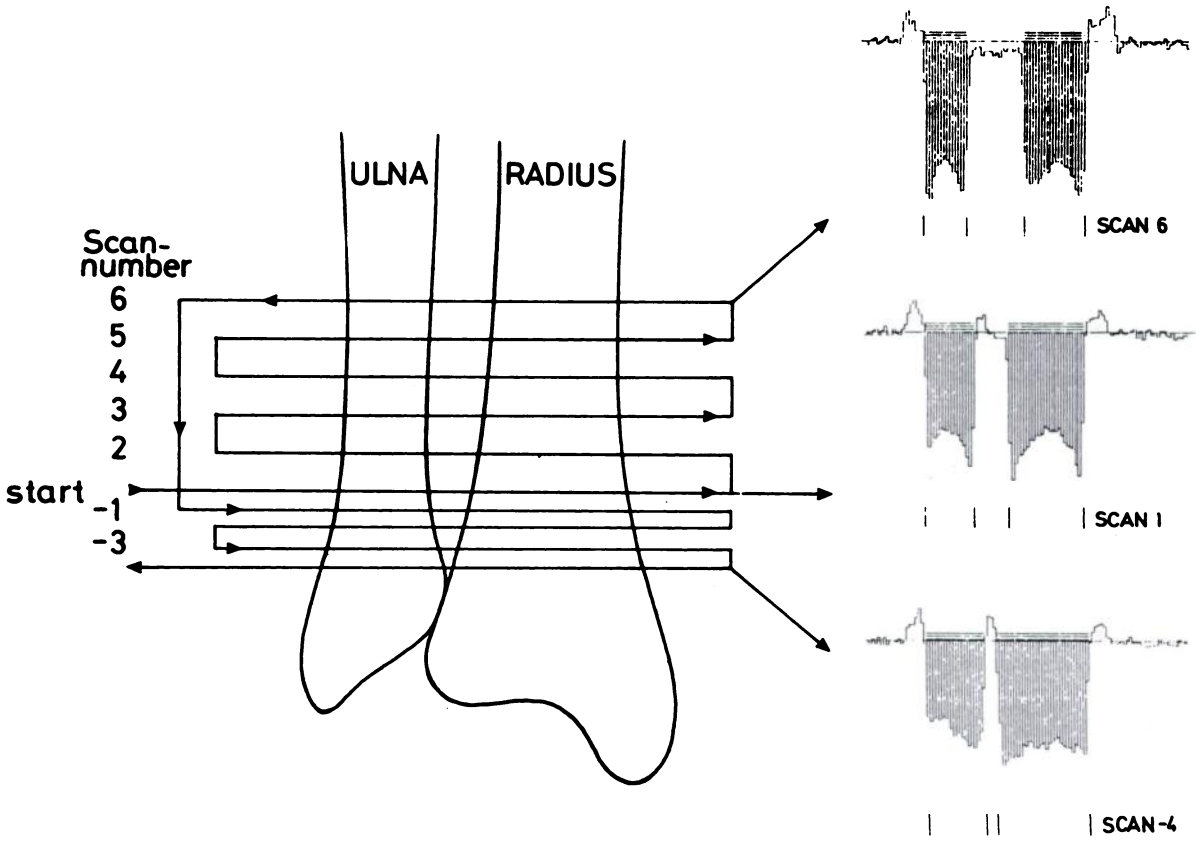

FIGURE 1
Measurement set-up in forearm with examples of scan print-outs. Fat correction is illustrated by horizontal lines moving baseline upwards

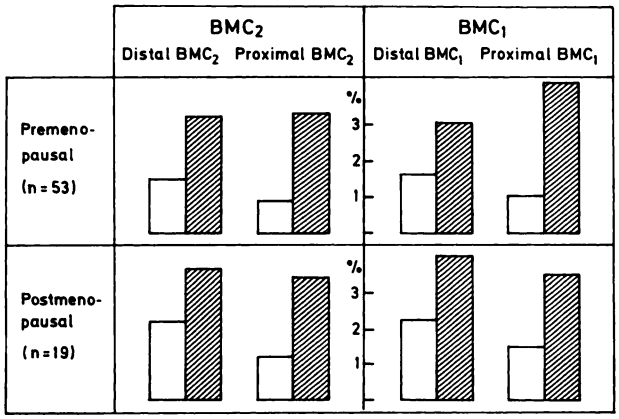

FIGURE 2
Coefficient of variation between two scan procedures 3 mo apart with calibration (□) and without calibration (▨)

the length from the styloid tip for the ulna and 14% for the radius. The most distal scan will therefore contain 30–40% trabecular bone (*3*). This value rapidly declines in the proximal direction to about 5% in the most proximal scans.

Bone mass in the spine was measured by dual-photon absorptiometry using a 1 Ci gadolinium-153 source (Lunar Radiation Corporation dual-photon spine scanner) (*4*). The person is placed on the scan table with flexed hips and knees and the scanning is started along a line joining the tops of the iliac crests. 40 scan lines 4.5 mm apart are obtained with a transverse speed of 2.5 mm/sec. Counts are accumulated in 0.5 sec. intervals. At all sample sites not containing bone the lean/fat composition of soft tissue is calculated and the average value is used to calculate bone mass at each bone-containing site. Baseline and bone edges are adjusted on displayed profile of each scanline. Bone mass (spinal BMC) is calculated in the vertebrae L_2 to L_4, including the intervertebral discs, and is given in grams mineral after calibration to standards. Bone mineral density (spinal BMD) is bone mass per unit projected scan area. In 29 premenopausal women measured twice with a 6-mo interval the precision (CV%) is 4.6% for spinal BMC and 3.9% for spinal BMD.

Lean body mass (LBM) was calculated by the formula of Boddy et al. (*5*). The serum calcium concentration was determined by atomic absorption and corrected for variations in serum concentrations of proteins. Alkaline phosphatase and the fasting urinary concentrations of calcium and creatinine were measured by routine techniques. The alkaline phosphatases were transformed logarithmically before the calculations were done.

Comparison between two groups was done by a Student's t-test and relationships between two bone mass measurements were evaluated by second order regression analysis.

RESULTS

The reproducibility of the conventional scan procedure in the forearm, using the mean of the six *proximal* scans, was about 1% in premenopausal women, both when the raw values (BMC_1) and the fat-corrected values (BMC_2) are used (Fig. 2). Nor had fat correction much influence on the reproducibility of the *distal* scan. The reproducibility of the distal scans is about 50% higher than for the proximal site. Without the weekly calibration the coefficients of variation increased by 2 to 3% at all scan sites. The same trends were found in the postmenopausal group, but all values were higher than in the premenopausal group. The reproducibility of the single scans was of the same magnitude in the proximal six scans, but increased gradually in the distal direction. During a 2-mo period the precision of the standard measurement was 0.4% (CV%).

The BMC_2 values at each scan site for both the premenopausal and the postmenopausal women are illustrated in Fig. 3. Compared to the younger women, bone mass is reduced at all scan sites in the postmenopausal women, but the difference is greatest at the most distal sites, which suggests a greater loss of trabecular bone. From the data in Schlenker's paper (*3*) we have estimated that the proximal BMC_2 contains about 7% trabecular bone, whereas the trabecular bone content in the four distal scans averages 25% in premenopausal women. On the assumption that chronological age has only minor importance for bone loss, it is possible to calculate the rates of bone loss from the two types of

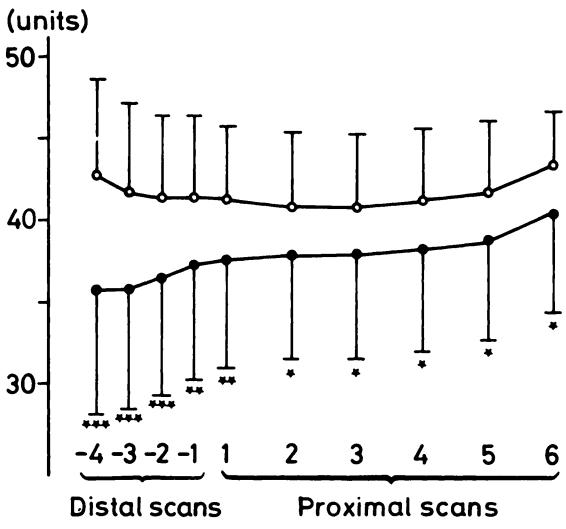

FIGURE 3
BMC_2 (i.e., fat corrected values) in 53 premenopausal women (O) and 19 postmenopausal women (●) at each scan site in forearm. Values are given as mean +/− 1 s.d. (* = p <0.05; ** = p <0.01; *** = p <0.001 postmenopausal vs. premenopausal women. Student's t-test)

TABLE 2
Bone Mass at Different Measuring Sites in Pre- and Postmenopausal Women (values are given as mean ± 1 s.d.)

Item	Proximal BMC_2 (units)	Distal BMC_2 (units)	Spinal BMD (g/cm^2)	Spinal BMC (g)
Premenopausal (n = 53)	41.4 ± 4.2	42.0 ± 5.1	1.01 ± 0.12	46.2 ± 6.5
Postmenopausal (n = 19)	38.3 ± 6.3*	36.4 ± 7.3†	0.86 ± 0.13†	38.5 ± 7.5†
Percent of premenopausal values	93.7 ± 15.2%	86.8 ± 17.4%	85.0 ± 12.9%	83.3 ± 16.2%

* = $p < 0.05$.
† = $p < 0.001$ compared with premenopausal women, Student's t-test.

bone by applying the following equations where T = the rate of trabecular bone loss (% per 5.5 yr) and C = the rate of cortical bone loss (% per 5.5 yr):

$$\text{Prox. } BMC_2 \text{ prem.} \times 7\% \times T + \text{Prox. } BMC_2 \text{ prem.} \times 93\% \times C = (\text{Prox. } BMC_2 \text{ prem.} - \text{Prox. } BMC_2 \text{ postm.}) \times 100 \quad (1)$$

$$\text{Dist. } BMC_2 \text{ prem.} \times 25\% \times T + \text{Dist. } BMC_2 \text{ prem.} \times 75\% \times C = (\text{Dist. } BMC_2 \text{ prem.} - \text{Dist. } BMC_2 \text{ postm.}) \times 100. \quad (2)$$

The calculated values are divided by 5.5 which is the time elapsed since the menopause. This gives an average annual rate of trabecular bone loss of 7% and a cortical loss of 1%.

The relationships between forearm and spinal bone masses or densities were modest with coefficients of regression of 0.56 to 0.59 and standard errors of estimates of 11.8 to 14.1% (Table 3, Fig. 4). Nearly identical results were obtained with distal and proximal forearm scans. The regression lines of spinal bone mass or density on forearm BMC had, however, smaller intercepts and slopes closer to one when distal BMC was the independent variable than when proximal BMC was used. We have here expressed the single observations as a percentage of the mean value in the premenopausal group in order to obtain similar units on the two axis. When the postmenopausal women were compared to the premenopausal the reduction of bone mass of the distal forearm site (on a group basis 13.2%) was in agreement with the reduction in the spine (15% for BMD and 16.7% for BMC),while the reduction at the proximal forearm site was only 7.3%.

DISCUSSION

The rate of bone loss in calcium metabolic disorders ranges from a 300 mg calcium loss daily during development of severe osteomalacia (*6*) to 50 mg daily in normal postmenopausal women (*7*). Since the female skeleton contains about 900 g calcium, the changes in bone mass are small. This implies the necessity of having methods with a high reproducibility in order to access differential rates of bone loss. Measuring set-ups suitable for repeated measurements would have to be quick and convenient. The described single photon absorptiometry scan procedure in the most distal part of the forearm fulfills these criteria. The important factor is a good calibration procedure. Without it, our scanning procedure would have had a reproducibility error two to three times higher than that found with calibration. The normal calibration procedure, which is also recommended by the manufacturers, is a single measurement of the standard before each patient is examined. If this is followed the error in measuring the standard is added to the imprecision of the patient's BMC measurements. The technique described here,

TABLE 3
Relationships Between Bone Mass Measurements in Forearm and Spine (Values are Expressed as Percent of Mean Values in Premenopausal Group)*

x/y	Spinal BMC		Spinal BMD	
BMC_2 proximal	r = 0.60	s.e.e. = 13.8%	r = 0.56	s.e.e. = 11.8%
	α = 1.65	yo = −66.2	α = 1.23	yo = −25
BMC_2, distal	r = 0.58	s.e.e. = 14.1%	r = 0.59	s.e.e. = 11.5%
	α = 1.21	yo = −20.6	α = 0.87	yo = 11.9

* α = slope and yo = intercept of second order regression line.

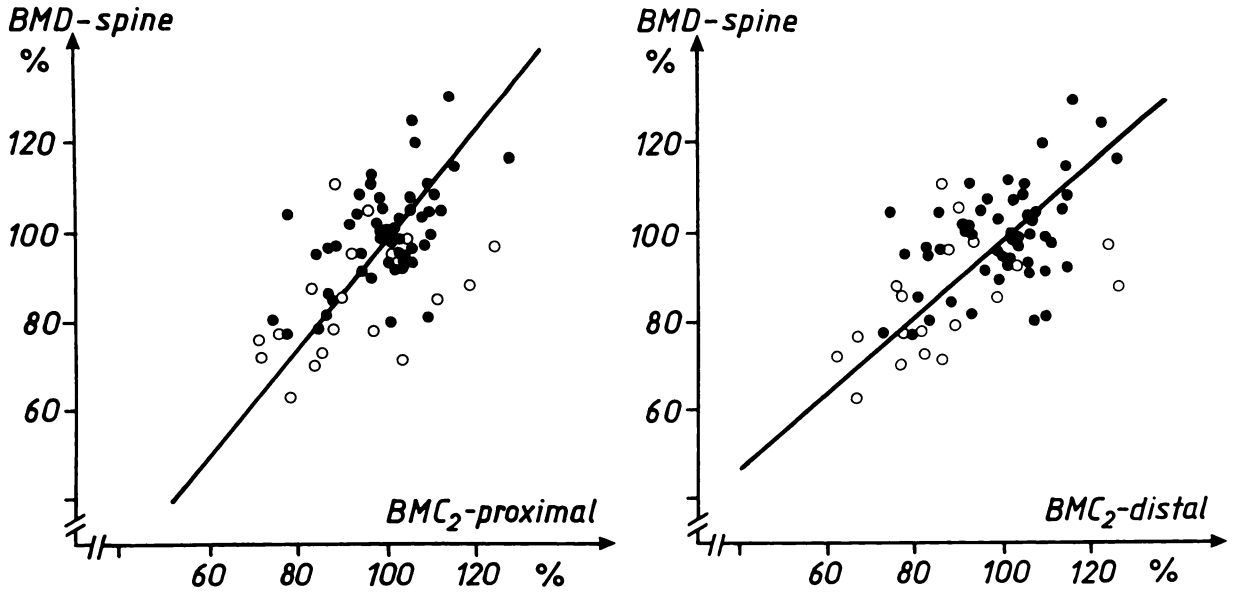

FIGURE 4
Relationships between BMC in forearms and bone density in spine. Values are given in percent of mean value in premenopausal group

with several measurements of the standard once a week, eliminated the error of the standard measurement and thereby gives a long-term reproducibility of 1%.

Considering the large number of papers published on bone measurements, there are surprisingly few reports on composition in different anatomical regions. In the region where our BMC distal scans are measured, the percentage of trabecular bone increases rapidly in the distal direction, while it is more constant at the proximal site. We have used bone composition values derived from Schlenker's results in four women, of whom only two were premenopausal. Since his results are given for percentage of total bone length of the two individual forearm bones and we use the 8-mm site as starting point, many assumptions must be made before the relative trabecular bone content can be estimated at our sites. We used 7 and 25%, respectively, as values of relative trabecular bone content at the two scan sites, but, irrespective of the exact figures used to solve the equation, the estimated rate of trabecular bone loss will exceed the rate of cortical loss. The smaller the differences between bone composition at the two sites the greater the differences in estimated rates of bone loss. The equation also presupposes that the rate of premenopausal bone loss is negligible. This may be an approximation since trabecular bone loss has been found in younger women (*8,9*). However, in our premenopausal women, the regression of spinal BMC on age had a positive slope and that of spinal BMC was only slight (−0.07%./yr). Many authors (*10,11*) have pointed out that bone loss in some endocrine diseases in site specific and it cannot at present be concluded that the rate of postmenopausal bone loss is identical in central and peripheral parts of the skeleton in the individual patient. A preferential trabecular bone loss in the years following the menopause has been found by others (*9,12*), and accordingly we estimated trabecular bone loss to be approximately seven times greater than the cortical loss within the first 5 to 6 postmenopausal yr. This figure is an average value and does not exclude the possibility of even greater differences within the first 1 or 2 yr of the menopause.

There are uncertainties both with the arm and spinal scanning procedure. In the spine, difficulties in correcting for variations in soft-tissue covering will lead to variations in the baseline from scan to scan; problems of defining edges will lead to unsystematic, false high values; and in some subjects there are problems of separating individual vertebrae. With the distal arm scanning procedure slight movements of the forearm will reduce the precision. In almost all our subjects the most distal scan was taken at the site where the two forearm bones join. In some, this point was not reached within the scanning procedure, while in others it was reached at scan number −2 or −3. These differences are probably caused by differences in body size, and scanning over a certain percentage of the bone length of the forearms may improve both precision and accuracy.

The relationships between forearm and spinal bone masses are modest and spinal BMC or BMD cannot therefore be predicted from the arm BMC in individuals. The standard error of estimate between the two types of measurement was, however, only 12 to 14%. Similar values have been found in other studies con-

cerning healthy women (*13*) where forearm scans are obtained at a radius site with a bone composition corresponding to that at our proximal site. Distal forearm scanning is not a more precise indicator of spinal bone mass, i.e., the s.e.e.s are similar when distal or proximal forearm scans are used as the dependent variable. Distal BMC may, however, be a more accurate estimator of spinal BMC. This is concluded by the fact that this regression had smaller intercepts and slopes closer to one. Furthermore, the percentage reduction in spinal bone mass in the postmenopausal women showed greater resemblance to reduction at the most distal forearm scans than to the more proximal. The study of Mazess (*13*) showed that the relationship between the peripheral and central bone measurements deteriorated when diseased persons were included. Whether the differences described here between the two forearm measurements also exists in such persons needs further evaluation.

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