QUANTITATIVE COMPUTED TOMOGRAPHY ASSESSMENT OF SPINAL TRABECULAR BONE. I. AGE-RELATED REGRESSION IN NORMAL MEN AND WOMEN

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Computed tomography, utilized in conjunction with a calibrated phantom containing a set of reference densities (K_2HPO_4 and water), is capable of determining the mineral content of the trabecular bone of the spine with an accuracy of about 6% of the ash weight of the vertebrae scanned [specimen studies). Other modalities measure a composite of cortical and trabecular bone. Computed tomography is capable of exclusively measuring the mineral content of the trabecular bone of the spine, where the earliest and most pronounced changes of spinal osteoporosis occur. Quantitative computed tomography measurements are useful for a precise and objective assessment of the spinal mineral content and its changes with age, disease, and drugs.

KEY WORDS:
Computed tomography, Normal values; Spine; Bone mineral content

A reliable, noninvasive, and readily available modality for in vivo measurement of bone mineral content is necessary as an objective yardstick for diagnosis of various skeletal disorders associated with bone loss. In recent years, a number of techniques for measurement of bone mineral content (BMC) have been developed. These include bone biopsy, radiogrammetry, radiographic densitometry, single and dual photon absorptiometry, Compton scattering, neutron activation analysis, and computed tomography quantitative (CT) (1-8). The only modality capable of measuring the trabecular or cortical bone selectively in the axial or peripheral skeleton is CT.

TECHNIQUE OF QUANTITATIVE COMPUTED TOMOGRAPHY ASSESSMENT OF BONE MINERAL CONTENT

A General Electric 8800 CT/T unit was used to quantitatively assess BMC. Our technique is similar to that described by Cann and Genant (8), with some modifications. The patient is positioned as for a lumbar spine CT examination. A lo-mm-thick axial slice is reconstructed through the midportion (spongiosum) of the bodies of T-12, L-l, L-2, and L-3 vertebrae. To correct for the scanner and patient-related factors affecting the x-ray beam, a set of reference densities are also scanned simultaneously with the patient (Figure 1). These consist of water, fat, and bone mineral equivalent solutions (K_2HPO_4) in the density range of the trabecular bone.* Then, the Hounsfield number of the vertebral trabecular bone is determined, making certain that the measured volume is composed exclusively of trabecular bone and does not include the vertebral cortex or the basivertebral vein. The BMC of each vertebra is then determined by calibration

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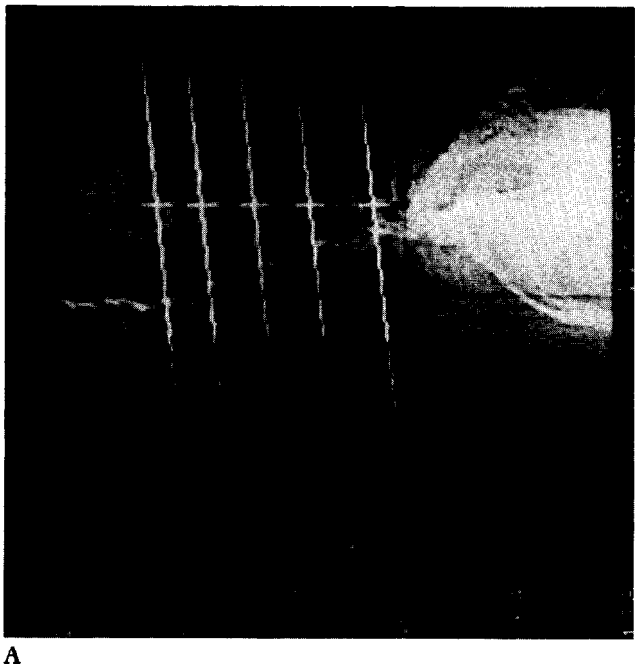

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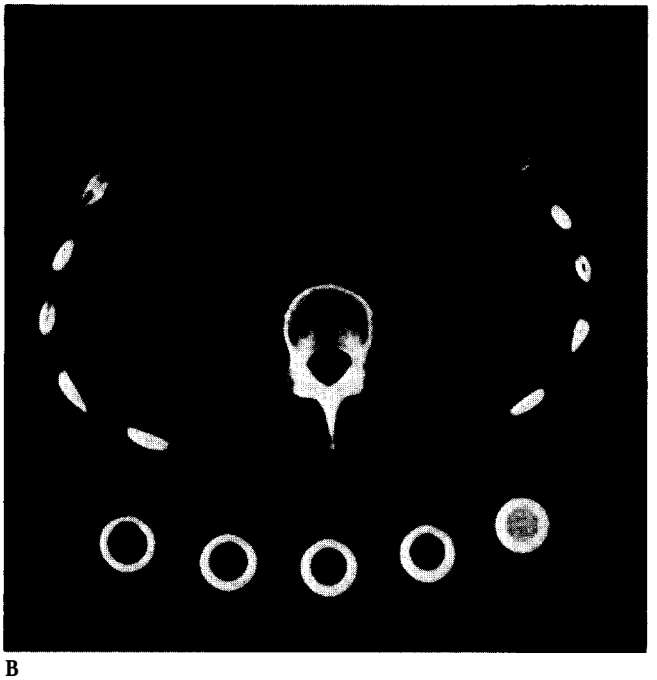

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FIGURE 1. (A) A lateral computed radiograph of the thoracolumbar spine reveals positioning of the CT slices for bone mineral determination. **(B)** An axial image obtained through the central portion of the body of L-2 with the calibrating densities in place.

against the values obtained for the reference densities scanned with the patient, and is expressed in milligrams per cubic centimeter of K_2HPO_4 (bone mineral equivalent). The BMC of four vertebrae, usually **T-12, L-l, L-2,** and L-3, is averaged and reported as the spinal BMC. In serial studies, when a fracture has developed, only nonfractured vertebrae are measured, and the results are compared to the recalculated values of the same vertebrae in the prefracture study.

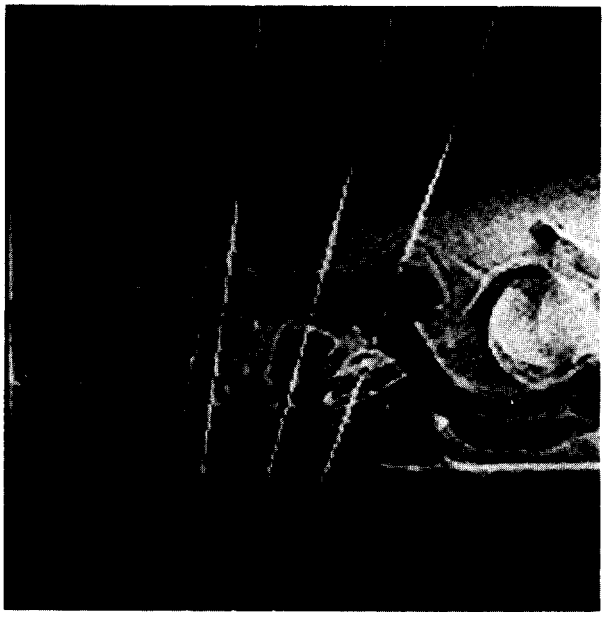
The accuracy of CT spinal mineral measurement values were checked against the ash weight of the trabecular bone of sample vertebrae. Fresh lumbar vertebrae removed at autopsy were inserted into the lumbar spine of a specially designed human torso phantom, constructed from natural bone and soft tissue equivalent material, with an abdominal cavity equipped with a colon-like conduit containing saline and air. The phantom was then scanned while positioned on the reference densities with the same technique as for a person (Figure 2). The error in the CT values thus obtained was 6% or less. The precision (reproducibility) of the study in serial specimen measurements was 2 to 3%.

STATISTICAL METHODS

A total of 448 observations was made: 316 on males, 132 on females. These observations covered an age range of **19** to 83 years in males, and from 19 to 85 years in females.

Males and females were considered separately. For each age represented, the measurements were examined for distribution properties by normal

FIGURE 2. A lateral computed radiograph reveals a torso phantom consisting of lumbosacral spine (natural bone), abdominal cavity, and a conduit for colon containing air and saline. Note the removable L-3 vertebra in its specially designed compartment.



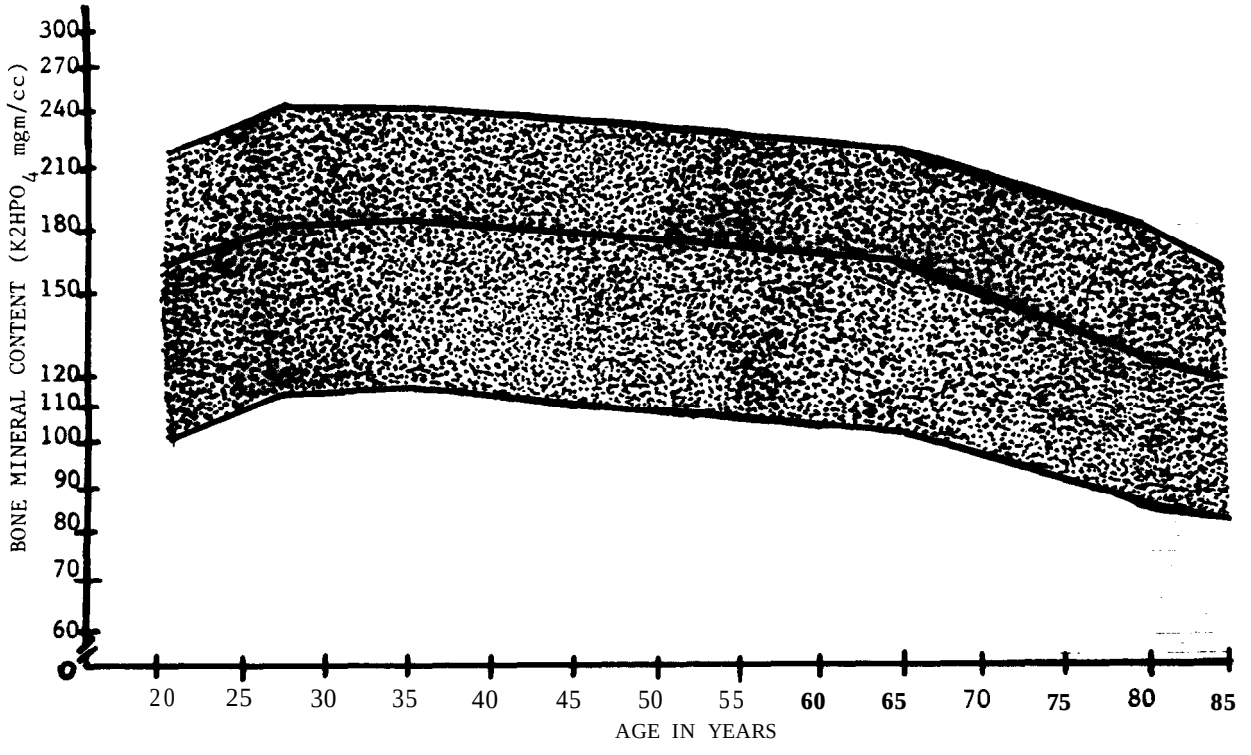
equivalent deviate (NED) analysis. For females, this could be carried out at all ages represented except for 24, 25, and 35 years, where only one or two observations were available. For males, this could be carried out at all ages represented except for 48, 49, 53, and 75 years, where only one or two observations were available. The NED analysis demonstrated clearly that both the male and female values were distributed in log-normal fashion. Consequently, geometric means were calculated as the characteristic value for each age plotted in Figures 3 and 4. Standard deviations and coefficients of variation were also calculated, taking into account the log-normal property of these measurements.

Estimation of the standard deviations and coefficients of variation, as described above, showed no statistically significant variation from age to age for either males or females. The results of the individual computations for standard deviation and coefficients of variation were therefore pooled for each sex; approximately 6% of the coefficient of variation may be attributed to technical rather than biologic sources of variability, as determined in our computations for specimens. These pooled factors representing variability for each sex were then multiplied by **1.645** to give the 90% confidence band for the log-normal distribution. This band may be seen surrounding the graph of average results shown in Figures 3 and 4.

SUBJECTS

There were **316** men, ranging in age from 19 to 83 years, with a mean age of 47 years. There were **132** women. Fifty-eight of the women were premenopausal, ranging in age from 19 to 48 years, with a mean age of 45 years; 74 were postmenopausal, ranging in age from 44 to 85 years, with a mean age of **61** years. These men and women were considered normal as regards calcium metabolism and skeletal mass. All were ambulatory outpatients, with no history of debilitating or chronic illness. None had a history of fracture of spine, ribs, hip, shoulder, or wrist with minor trauma, or metabolic bone disease, thyroid, parathyroid, or renal disease. All subjects with milk intolerance (lactase deficiency), oophorectomized women, and men and women receiving sex hormones for any reason were excluded from the study. The subjects were referred for CT examination of the abdomen or spine for various complaints of recent onset (1 to 4 months' duration], including pain, suspicion of pelvic and abdominal mass, metastasis, and other conditions. All

FIGURE 3. The center line depicts spinal trabecular bone in 316 normal men. The stippled area depicts the 90% limits of age-related normal.



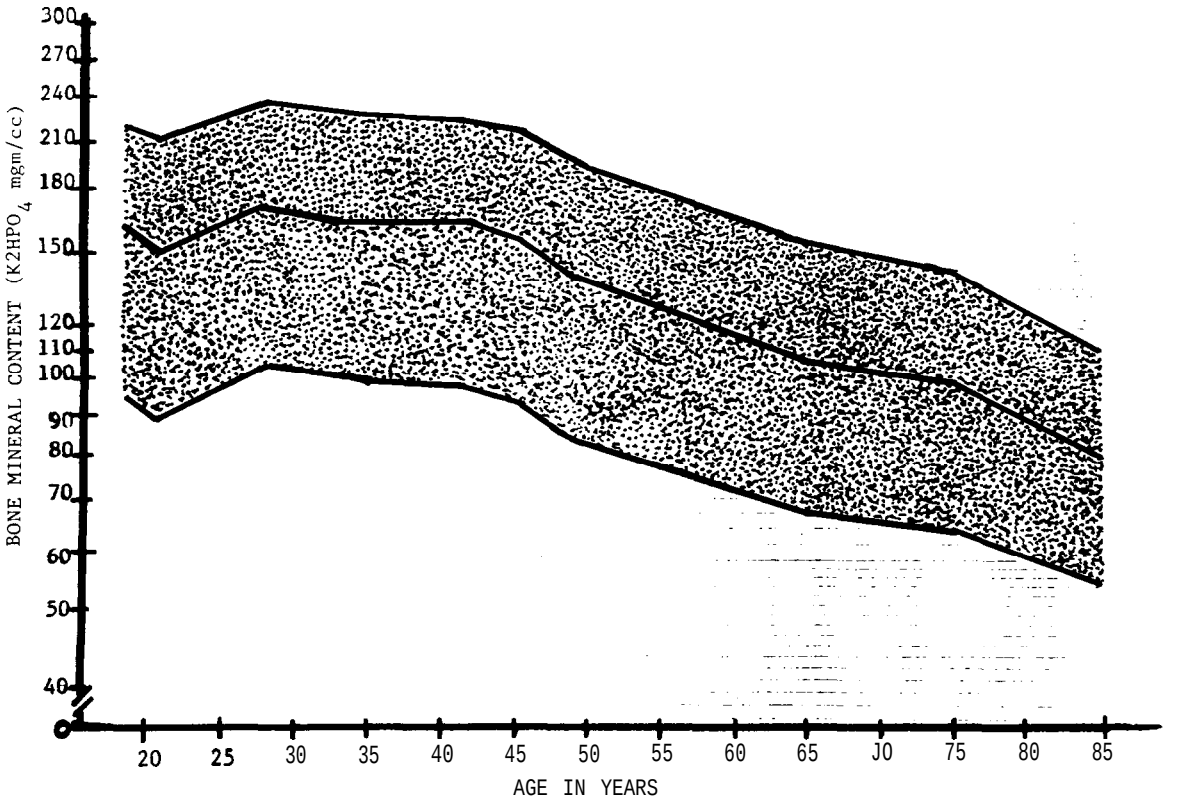


FIGURE 4. The center line depicts spinal trabecular bone in 132 normal women. The stippled area depicts the 90% limits of age-related normal.

subjects found to have a fracture of the spine or other significant pathology were excluded from the study.

RESULTS

The values of spinal trabecular bone for men (Figure 3) and women (Figure 4) were plotted as a function of age. In men, the BMC of the spinal trabecular bone was at its maximum between the ages of 20 to 30 years. There was a gradual decrease after this age, with a more rapid rate of bone loss after the age of 60 years. The total lifetime diminution was about 30%; more than half of it occurring after 60 years of age. In women, the trabecular BMC of the spine, after reaching its maximum level around 25 to 30 years of age, decreased gradually with an overall lifetime (to age 85) diminution of about 45 to 50%. Between the ages of 20 and 40 years the spinal trabecular BMC decreased minimally. After age 40 years, the rate of bone loss was slightly faster, with a more rapid acceleration in a period lasting 5 to 10 years immediately following menopause.

DISCUSSION

Normal Bone Mass

A large number of factors, including race (blacks generally have more total body bone mass), heredity, sex (women generally have less bone mass than men), diet, and exercise, affect the regional (eg, the playing arm in tennis players) and total body bone mass (9, 10). The total body bone mass increases rapidly from birth to about age 20 to 30 years, when it reaches its maximum level. It may stay fairly constant to age 35 to 40 years, or it may decrease gradually at a very slow rate. After age 40 years, men lose bone (spinal trabecular bone) at the rate of 0.5 to 0.9% per year, while women, in general, lose bone at the rate of 0.7 to 1.3% per year (3, 11-13). However, in our experience, as well as that of others (12), a subgroup (10 to 15%) of postmenopausal women without any apparent illness may lose bone at an accelerated rate of 2 to 8%, or even more, per year. These women may develop symptomatic osteoporosis within 10 to 15 years of menopause.

Measurement of Bone Mineral Content

Bone biopsy is an invasive technique, but is a reliable modality for the pathologic diagnosis of various metabolic bone diseases. However, assessment of BMC requires use of the specialized technique of histomorphometry (1, 12). This technique, however, is not widely available, and in our experience is not capable of a precise and reproducible quantification of small changes in the bone mass. Qualitative evaluation of the peripheral cortical bone, eg, assessment of endosteal and subperiosteal resorption, and intracortical tunneling usually provide helpful information regarding the status of various metabolic diseases of bone. However, precise and reproducible quantification is also virtually impossible with this technique. The quantitative measurement of the metacarpal cortical thickness (on radiographs), and assessment of mineral content of the diaphysis and metaphysis of the peripheral limb bones (eg, radius] by photon absorptiometry provides helpful information regarding the BMC of the peripheral bones. This is particularly important in patients with systemic arthritides and hyperparathyroidism. In the latter patients, there may be marked bone resorption affecting the peripheral skeleton, whereas quantitative CT assessment may reveal normal or higher than normal values for the spine (rugger-jersey spine). Thus, it is desirable to include assessment of the peripheral bones as an integral part of evaluation of the total body bone mineral status. Comptom scattering (14) and neutron activation analysis (7) have not so far been widely used in clinical settings. Dual photon absorptiometry (3, 4, 15) is highly accurate and may be used to assess the mineral content of the spine or the peripheral skeleton. However, this modality is not capable of measuring the cortical and trabecular BMC separately, and an unavoidable mixture of trabecular and cortical bone is included in the sampling site. Recent studies (15) suggest the trabecular and cortical bone to be separate compartments, with differences in respect to the onset and rate of bone loss. Thus, interpretation of the composite values obtained, particularly in longitudinal studies, becomes complex. Furthermore, a slight change in the point of measurement in serial studies may yield widely varying values, not so much because of a change in the BMC, but because of inclusion of varying amounts of trabecular and cortical bone in the sampling site. Detection of bone loss is not possible by conventional radiography unless at least 30% of bone mineral content is lost (13).

Quantitative Computed Tomography Measurement of Bone Mineral Content. Computed tomography is currently the modality of choice as a noninvasive tool for in vivo measurement of BMC of spinal trabecular bone because it can selectively measure either the trabecular or cortical bone, with a high degree of accuracy and precision (8). The potential usefulness of CT for bone mineral measurement was realized almost immediately after the introduction of the first commercial CT units. These early scanners, however, were hampered by a number of shortcomings, including difficulties in precise positioning and errors related to the spectral hardening of the x-ray beam and geometric distortion. Most recently introduced scanners, however, are capable of precise and reproducible positioning so that the same exact point can be measured on serial measurements, and incorporate some corrections for beam hardening and geometric distortion.

Measurement of the bone mineral content by CT is based on the ability to measure the density (CT number) of any tissue in the cross-sectional CT slice. The CT number (Hounsfield number) is related to the mean of the linear absorption coefficient of all the tissues within the volume examined. For CT measurements to be reliable, a number of precautions have to be observed to ensure the accuracy and the precision of the procedure. The accuracy is affected by a number of factors, including the spectral hardening of the x-ray beam and the biologic variations of the vertebral body composition, particularly the relative amount of fat present in the vertebrae. The precision of serial measurements is affected by the scanner drift with time (correctable against the reference densities), and the reliability of duplicating the positioning of the patient.

When the fat content of the vertebral body is increased significantly, it can lower the measured CT values by about 1 Hounsfield unit per 1% fat by weight. This error can be reduced by dual-energy CT. In our experience, dual-energy CT provides generally more accurate values for the BMC (specimen studies) when the fat content is significant. However, the precision of the study is significantly less. Thus, in most clinical studies, dual-energy CT may not be necessary (16).

Cross-Sectional Studies of Spinal Trabecufar Bone in Normal Subjects

Our results are based on cross-sectional studies, and the longitudinal inferences suggested by them cannot be absolutely verified because the same vari-

ables may not be operative during the 65-year span of the age regression curve (3, 15). However, Smith et al (17) reported virtually identical results on comparison of cross-sectional and longitudinal data for the appendicular skeleton on the same subjects. Our results show a curvilinear pattern of bone loss in normal subjects. In women there was an accelerated rate of bone loss following the menopause. This is in agreement with a number of reported studies (3, 4, **18)** and the pattern noted in iliac crest biopsies (1). However, Riggs et al (15) reported a linear vertebral mineral diminution starting at young adulthood and continuing throughout life, with no evidence of an accelerated rate following the menopause. This apparent discrepancy may be due to the statisical methods used, differences in populations studied, and differences between the two measuring modalities employed. We measured exclusively the trabecular bone of the vertebral spongiosum by CT. Dual-photon absorptiometry measures a composite of the trabecular bone of the vertebral body and the cortical bone of the vertebral cortex, endplates, osteophytes, vertebral elements, and the calcification present in the atherosclerotic aorta (3).

Assessment of spinal bone mineral content has been recommended as a base-line in all women passing through menopause (11). Serial yearly measurements thereafter would reveal the rate of bone loss. Thus, it would be possible to identify the following two groups: those women who for one reason or another have substantially less bone than normal; and the subgroup of women who lose bone more rapidly than is normal (3, 10). These two groups of women are in danger of developing severe osteoporosis and are candidates for rigorous preventive treatment.

The total radiation to the patient's abdomen with this technique is approximately 200 to 300 mrem (19). Furthermore, virtually no gonadal radiation is received by either men or women.

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CONTINUING MEDICAL EDUCATION QUESTIONS

1. Spinal bone loss in association with aging occurs most profoundly:
   a. In trabecular bone.
   b. In cortical bone.
   c. Equally in trabecular and cortical bone.
   d. In lumbar spine only.
2. The maximum total body bone mineral content:
   a. May be attained by age 20 to 30 years.
   b. May be higher in blacks.
   c. May be influenced by diet.
   d. All of the above.
   e. None of the above.
3. The rate of bone loss in normal adult women:
   a. May be temporarily accelerated following the menopause.

b. Is generally slightly faster than that in men.
c. Both.
d. Neither.

4. Computed tomography is useful for measurement of spinal mineral content because:
a. It can separately and independently measure the trabecular bone.
b. It is more accurate than methods utilizing conventional radiography.
c. Both.
d. Neither.