BONE MINERAL CONTENT DETERMINED BY FUNCTIONAL IMAGING

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Quantitation of bone mineral by photon absorptiometry is a simple and accurate method for determining changes in bone volume and mineral content in serial studies. An extension of the scintillation camera method for studying such changes in the calcaneous is described. This technique is applicable to large areas of bone, thereby minimizing the effect of repositioning errors. Using a 40-mCi ^{241}Am sheet source, a 2.1% reproducibility in bone phantoms and a 2.4% reproducibility in normal patients was achieved. Several case studies are presented to illustrate sensitivity and clinical application of the method. Although bone mineral determinations are now performed in a limited number of health care facilities, the scintillation camera method described in this report could increase the availability of these determinations significantly.

In 1962 Cameron, et al, described a scanning technique for determinating bone mineral content in which a collimated monoenergetic photon beam coupled to a scintillation detector moved across the selected bone in a linear fashion (*1,2*). The bone mineral content was related to the intensity of radiation transmitted through bone and overlying soft tissue compared with that transmitted through soft tissue alone. This technique eliminated problems associated with the poorly defined beam energy and nonuniform film response inherent in roentgenographic film methods for determining bone mineral content, and it avoided intersystem calibration since photon energy was constant (*3*). Because of the irregular bone shape and thickness and the uneven distribution of mineral content, however, values obtained from a single linear scan may not be representative of the entire bone and may in fact vary significantly depending on the site of the scan path. To overcome these potential problems, we have extended our previously reported method of photon transmission scanning with the scintillation camera (*4*); we now use a dedicated minicomputer to produce functional images representing mineral content. A large area of interest in the selected bone is defined for computations, thereby obtaining a more representative sampling of total bone mineral content and minimizing errors due to imprecise repositioning of the bone in sequential patient studies. Because of the intrinsic flexibility of the technique, mineral content may be determined for irregularly shaped bones and for various regions of interest.

METHODS

A simplified two-component model can be used to explain the theoretical basis of the technique. One compartment consists of bone compressed to a thickness of x_b after all soft components have been extracted whereas the other compartment, of thickness x_s, is composed of water-equivalent soft tissue surrounding the bone, and extracted from its intramedullary spaces (Fig. 1). The intensity of incident photons (I_o) transmitted through the bone, water, and water-equivalent tissue (I) and through an equivalent thickness of water alone (I_o^*) can be expressed as follows:

$$I = I_o e^{-\mu_s x_s - \mu_b x_b}$$

$$I_o^* = I_o e^{-\mu_s (x_s + x_b)}.$$

The μ_s is the linear attenuation coefficient of water for the ^{241}Am photons and is a constant. The linear attenuation coefficient of bone mineral, μ_b, depends on its chemical composition. The remaining parameter, x_b, is a variable that depends on both the anatomic thickness of the bone and the

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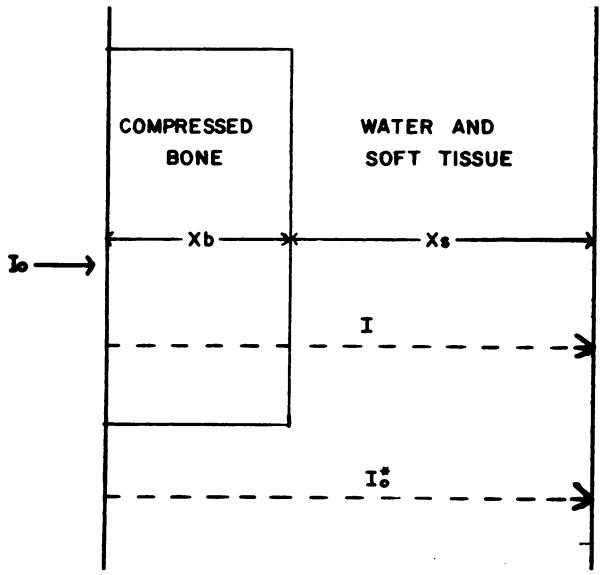

FIG. 1. Simplified model for BMI determination. x_s represents combined thickness of water and soft tissue surrounding bone, and x_b is thickness of remaining material after all intramedullary components have been removed. I_o is intensity of incident photon beam; I is intensity transmitted through bone, soft tissue and water combined; and I_o^* is intensity through soft tissue and water alone.

actual bone density. The bone mineral per square centimeter of projected surface is proportional to the natural logarithm of the ratio I_o^*/I, which we define as the bone mineral index (BMI).

$$BMI = \ln \frac{I_o^*}{I} = (\mu_b - \mu_s)\, x_b.$$

The calcaneus is used routinely for the bone mineral measurement (*5,6*). The photon source is a 10-by 14-cm sheet containing 40 mCi of ^{241}Am, which emits 60-keV gammas. The patient's heel is fitted snugly into a Plexiglas trough filled with water and placed between the source and the low-energy, high-resolution collimator of the scintillation camera (Fig. 2). To prevent rotation and movement, several troughs were constructed to fit heels of various widths.

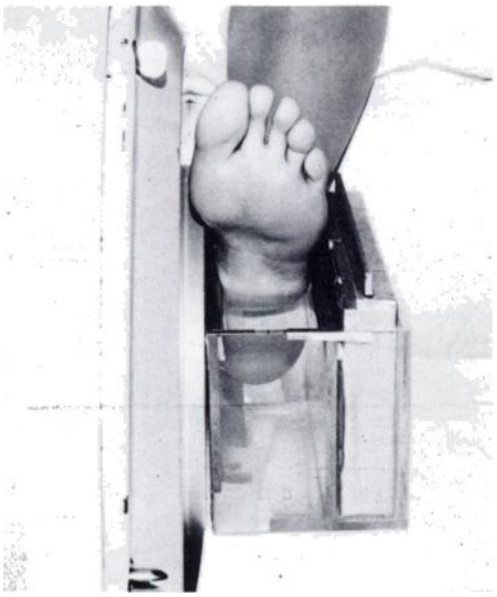

FIG. 2. To measure bone density, heel is fitted snugly into narrow water-filled trough and placed between high-resolution collimator (left) and 40-mCi ^{241}Am source (right).

Photon transmission through the immersed heel (I) and then through the trough filled with water alone (I_o^*) is monitored in a 64 × 64 matrix with each cell measuring 4.3 × 4.3 mm at the camera face. An information density of 26,000 counts/cm^2 over the region of the calcaneus is required on both the bone and no-bone data matrices in order to maintain the statistical deviation in a single BMI calculation at a value less than 2% (1 s.d.). Our system currently requires a 10-min data-collection period for each image, resulting in an absorbed radiation dose of 20 mrems to the patient's heel. Using a dedicated minicomputer, the natural logarithm of the ratio I_o^*/I is then computed for each cell and the results are displayed in a maximum of seven levels on a cathode-ray tube (CRT) as a functional image of BMI (Fig. 3A).

Scattered radiation and poor resolution (⅜ in.) at 60 keV create an apparent zone of decreased BMI outside the actual bounds of the calcaneus. To eliminate this zone and to correct for variation in image size due to long-term instrument drift, a steel plate with holes drilled at fixed points is imaged with each study to determine a detector-to-CRT minification factor. The size of the functional image is adjusted by an edge-cutting technique so that the width of the image is equal to the minification factor times the width of the calcaneus at its narrowest point as determined by a lateral roentgenogram of the heel (Fig. 3B). For each patient the distal 5 cm along the axis of the calcaneus on the roentgenogram is multiplied by the minification factor and marked with the light pen on the functional image. Because this area is represented by at least 80 computer cells, small measurement errors have relatively little effect on the BMI averaged over the entire area.

RESULTS

To evaluate this method, a BMI was determined for each of 12 cylindrical bone phantoms composed of a uniform mixture of calcium carbonate and tissue-equivalent plastic. The BMI values obtained were representative of the range of values encountered in patients and normal control subjects. The correlation coefficient of BMI to actual phantom calcium content was 0.99 with a significance, $p < 0.001$ (Fig. 4).

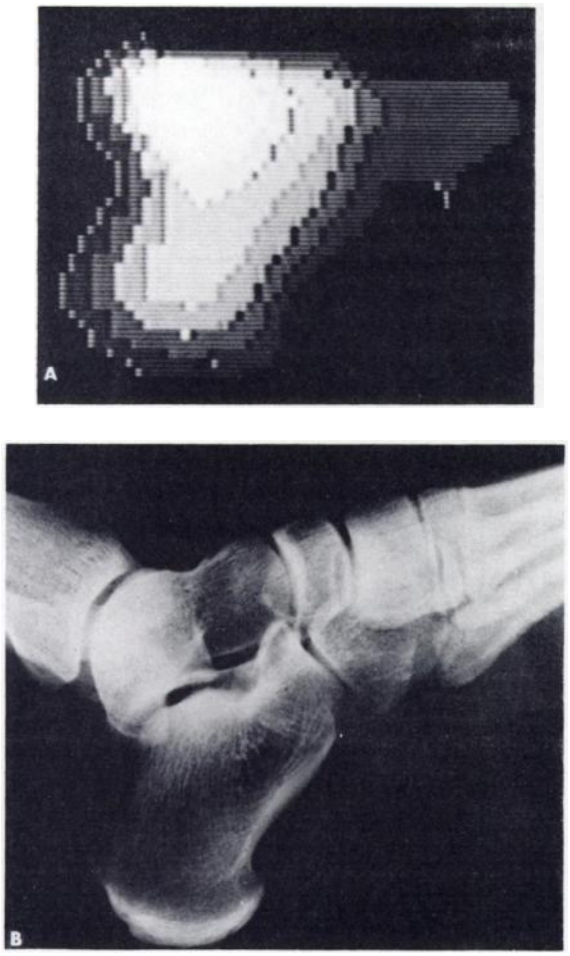

FIG. 3. (A) Lateral roentgenogram of heel. (B) Corresponding functional image of calcaneus obtained from computer display.

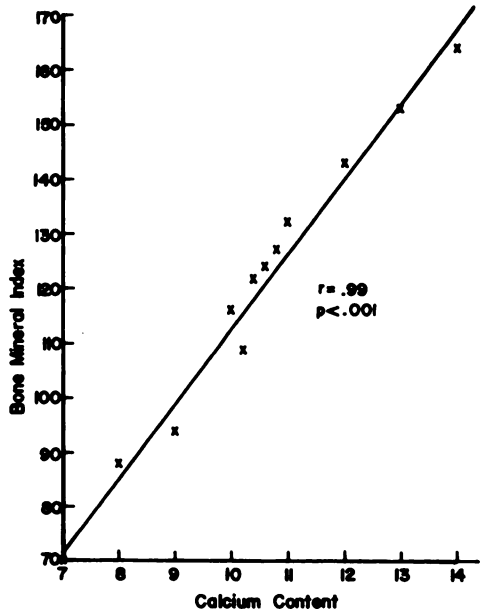

FIG. 4. Correlation of measured BMI with percent calcium content (by weight) in phantoms.

Sixteen repeated determinations over a 1-week period using a representative phantom yielded an average coefficient of variation of 2.1% with a maximum variation of 2.8%. Six BMI determinations at monthly intervals on each of four healthy subjects yielded an average coefficient of variation of 2.4% with a maximum variation of 2.9%.

CASE REPORTS

The following cases illustrate the clinical application of this technique.

Case 1. A 39-year-old woman had an 8-month history of weight loss, heat intolerance, and palpitations. A diagnosis of diffuse toxic goiter (Grave's disease) was made based on physical examination and laboratory testing. Following ^{131}I therapy, she improved clinically with return to an ideal body weight. Serial BMI determinations for a 3-month period revealed progressive bone remineralization (Fig. 5).

Case 2. A 25-year-old woman underwent a total thyroidectomy and ^{131}I ablation for thyroid carcinoma 3 months prior to the initiation of our study. At that time she was placed on a balanced combination of thyroxine and triiodothyronine, equivalent to 3 grains of thyroid daily. At the time of her first bone mineral determination, she was clinically euthyroid. Over the subsequent 4 months, however, she developed progressive weight loss, tremor, and palpitations. Clinical re-evaluation at that time indicated that she had become thyrotoxic, necessitating a reduction in the dose of thyroid replacement. Serial bone mineral determinations revealed progressive demineralization parallel with the development of her hyperthyroid state (Fig. 5).

Case 3. A 59-year-old woman with documented metastatic breast carcinoma had constipation, abdominal pain, and progressive disorientation. Admission laboratory data revealed a serum calcium of 14.8% and phosphorous of 4.5 mg%. After receiving 2 mg mithramycin intravenously, the serum calcium fell to 8.2 mg% with a subsequent rapid return to hypercalcemic levels. Singer, et al postulate that mithramycin may act in part to inhibit bone resorption (*7*). A rise in BMI was demonstrated corresponding to the transient decrease in serum calcium level (Fig. 6).

DISCUSSION

Because of the large trabecular surface exposed to remodeling activity, cancellous bone is three to four times more susceptible to changes in mineralization than cortical bone (*8,9*). Mineralization of the calcaneus is affected not only by normal metabolic processes and disease but also by stress-bearing,

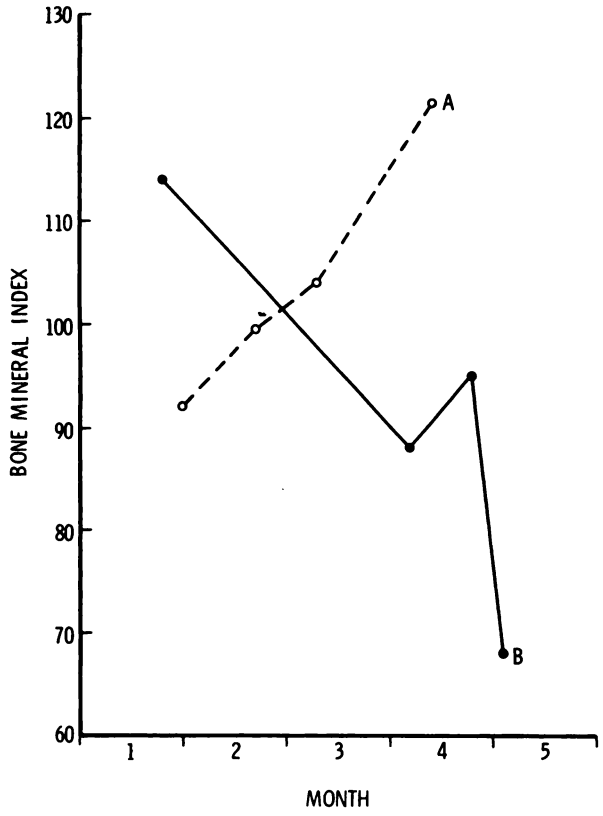

FIG. 5. A, serial BMI determinations showing remineralization of calcaneus in 39-year-old woman after ^{131}I treatment of Grave's disease. B, Serial BMI determinations indicating demineralization of calcaneus accompanying drug-induced thyrotoxicosis after total thyroidectomy for thyroid carcinoma.

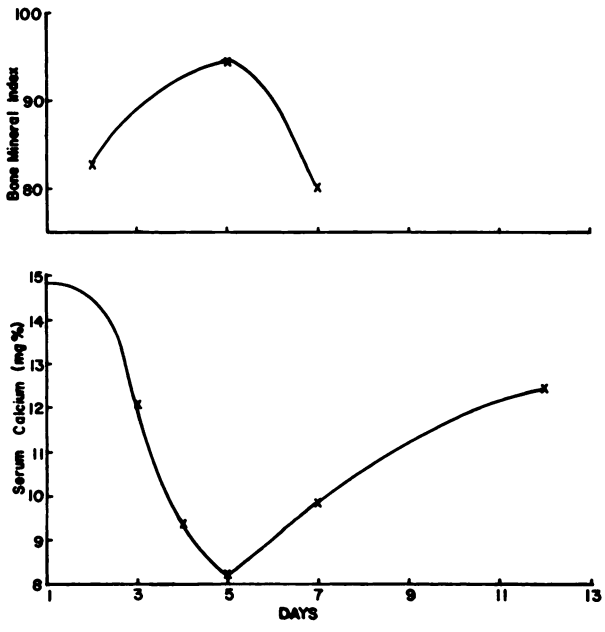

FIG. 6. Serial BMI determination showing relationship of BMI to serum calcium levels in patient treated for hypercalcemia secondary to metastatic breast carcinoma.

including ambulation. For these reasons, as well as for its relatively large size, sparsity of overlying soft tissue, and easy accessibility, the calcaneus was selected for the study.

The calculated BMI in an average normal patient is reduced artifactually by approximately 8% due to adipose tissue in the radiation path, which is not considered in our simple two-compartment model. The intramedullary and subcutaneous fat has a density less than that of water and therefore transmits a greater fraction of the penetrating radiation than does other soft tissue. This effect is probably not significant in serial measurements in the same patient for most diseases such as chronic arthritis, postmenopausal osteoporosis, or hypertension since the fat content generally does not change greatly within a short period of time. With marked shifts in body mass which may occur, for example, in patients with acute spinal cord injuries, such changes may prove to be of significance.

The potential importance of the determination of bone mineral content relates not only to research pertaining to calcium metabolism in various gastrointestinal, vitamin deficiency, endocrine, and renal disorders but also to a significant clinical need for a means of monitoring such changes. For example, osteoporosis is statistically the most widespread bone disease in humans, affecting approximately 25% of all white females in the United States by the age of 60 (*10*). Roentgenographic techniques require approximately 30–60% demineralization before the characteristic findings of cortical thinning and porosity of long-bones, "codfish" vertebrae, Schmorl's nodes, or compression fractures evolve (*11*). The most important consideration is that once such a reduction in the volume of bone occurs, there are no known measures that are permanently effective in restoring bone mass. Consequently, it is critical to determine osteoporotic changes early in their course since the process often can be arrested by a combination of measures including physical therapy, mineral supplements, fluoride, and gonadal hormones (*10*). Such changes can be measured either by determining actual bone mass or by serial measurements of BMI obtained during progression of the disease. Since we have not attempted to normalize BMI values to the thickness of the calcaneus, the method is applicable primarily to serial studies in a single patient. In order to compare bone mineral content between patients, the volume of the calcaneus should be determined so that an actual bone density in grams per cubic centimeter may be calculated. In vivo estimations of bone volume have been based mainly on orthogonal radiographic views or on mathematical methods that assume a cylindrical

shape for the bone, neither of which is valid for irregularly shaped bones. Recently, Grob and Binswanger have used ultrasonic scanning to measure the thickness of the calcaneus (*12*). This technique in conjunction with photon absorptiometry appears to be a promising method of estimating actual bone density.

REFERENCES

1. CAMERON JR, GRANT R, MACGREGOR R: An improved technic for measurement of bone mineral content in vivo. *Radiology* 78: 117, 1962

2. CAMERON JR, SORENSON J: Measurement of bone mineral in vivo: An improved method. *Science* 142: 230–232, 1963

3. MAZESS RB: *Proceedings of International Conference on Bone Mineral Measurement*, NIH-NIAMD, Chicago, Ill, 1973

4. DEPUEY EG, BURDINE JA: Determination of bone mineral content using the scintillation camera. *Radiology* 105: 607–610, 1972

5. VOGEL JM, FRIEDMAN RJ: Mineral content changes in the os calcis, ulna, and radius induced by prolonged bedrest. In *Proceedings of Bone Measurement Conference*, AEC CONF-700515, Oak Ridge, Tenn, Atomic Energy Commission, 1970, pp 408–423

6. VOGEL JM, ANDERSON JT: Rectilinear transmission scanning of irregular bones for quantification of mineral content. *J Nucl Med* 13: 13–18, 1972

7. SINGER FR, NEER RM, MURRAY TM, et al: Mithramycin treatment of intractable hypercalcemia due to parathyroid carcinoma. *N Engl J Med* 283: 634–636, 1970

8. MARSHALL JH, LLOYD BL, RUNDO J, et al: Alkaline earth metabolism in adult man. *Health Phys* 24: 125–221, 1973

9. FROST HM: *Bone Remodeling and its Relationship to Metabolic Bone Diseases.* Springfield, Ill, CC Thomas, 1973, pp 13, 19, 121

10. HEANY R: *Cecil-Loeb Textbook of Medicine.* Philadelphia, Pa, WB Saunders, 1971, p 1863

11. LACHMAN E: Osteoporosis: the potentialities and limitations of its roentgenologic diagnosis. *Am J Roentgenol Radium Ther Nucl Med* 74: 712–715, 1955

12. GROB N, BINSWANGER U: Ultrasound measurement of os calcic width for photon absorption studies. *Invest Radiol* 8: 156–159, 1973