

Quantitative Bone Mineral Analysis Using Dual Energy Computed Tomography

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This preliminary evaluation indicates that CT scanning permits measurement of cancellous, cortical or integral bone. With the single energy technique, precision is high and with the dual energy technique, accuracy is high. In the total body mode, CT scanning may prove an important tool for assessing the axial skeleton in osteoporotic conditions.

Key words: bone mineral analysis, computed tomography.

CURRENTLY available in vivo techniques for quantifying skeletal mass are generally restricted to measurements of the peripheral tubular bones and reflect primarily cortex. A technique capable of separately quantifying cancellous bone may be a more sensitive determinant of metabolic bone disease. To this end, we have assessed the potential of computed tomography for bone mineral determination.

Materials and Methods

For preliminary evaluation of the EMI head unit was used, and phantoms were constructed to simulate mineral, soft tissue and fat, either separately or in composite. Dipotassium hydrogen phosphate (K_2HPO_4) solution was chosen since it has absorption properties⁴³ similar to calcium hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$).³ Water was used to simulate lean soft tissue, and ethyl alcohol (C_2H_5OH) to simulate fat.^{24,28,30} Single chamber cylinders (16 mm diameter) were filled with combinations of these solutions. Coaxial dual chamber cylinders were constructed with the outer circumferential chamber (42 or 33 mm diameters) containing

high concentrations of phosphate solution and the inner chamber (31 or 22 mm diameters) containing lower concentrations to simulate cancellous bone. Variable amounts of alcohol were added to the central chamber to simulate marrow fat. Monitor displays of single and coaxial phantoms, and the corresponding digital print-outs were used for quantitation.

The manner of converting EMI number to fractional mineral content is given by the following formulas. First, the relationship between EMI number and linear attenuation coefficient is defined by the formula given by McCullough²⁴:

$$N = \frac{\mu_L - \mu_{LH_2O}}{.0038}$$

where N is EMI number, μ_L is mean linear attention coefficient, and μ_{LH_2O} is attenuation coefficient of water. This relationship between EMI number and the linear attenuation coefficient is linear for any given energy such as 80 kVp and 140 kVp. If we next assume a dual component system consisting of bone and lean soft tissue, ignoring fat for the moment, then the following applies: $\mu_L = X\mu_{LB} + (1-X)\mu_{LT}$ where X is the unknown fractional component of mineral, μ_{LB} and μ_{LT} the known linear attenuation coefficients of mineral and lean soft tissue or water, respectively.^{24,28,30}

We examined the CT number of our tissue-equivalent substances as a function of the tube operating kilovoltage, and evaluated the effect of beam hardening. We then determined the accuracy of CT for measuring mineral content in known standards of potassium phosphate in water. This was accomplished by a summation of CT numbers for the entire slice of solid cylinder and reflects the total bone mass (bone integral) in a volume defined by the cross sectional area and the slice thickness.

We compared these CT results on known standards with those obtained by means of the widely used Norland-Cameron device⁶ which measures, by iodine-125 photon absorption, an integral of bone in a 1 cm wide path of the radius. We further explored the unique capability of CT for determining separately, cortical and cancellous bone, as well as, integral bone. The digital print-out of a coaxial phantom with delineation of the cortex and cancellous core was the manner in which separate calculation of CT numbers was accomplished.

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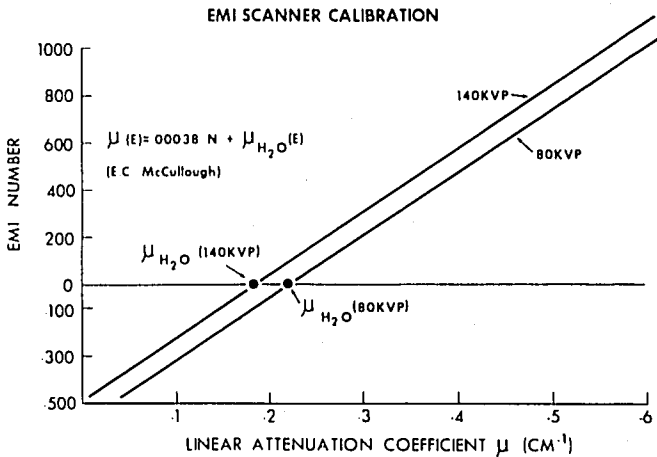


Fig. 1. Linear relationship between the EMI number and the linear attenuation coefficient for 80 kVp and 140 kVp. Water is calibrated 0 at both energies.

In vivo determination of cancellous bone, however, measures mineral in the presence of soft tissue with variable amounts of fat which, if uncorrected, can introduce substantial errors.³⁷ The dual energy beam technique may correct these inaccuracies using the following formulas:

$$\bar{\mu}_L(E_1) = X\mu_{LB}(E_1) + Y\mu_{LT}(E_1)$$

$$\bar{\mu}_L(E_2) = X\mu_{LB}(E_2) + Y\mu_{LT}(E_2)$$

Solution:

$$X = \frac{1}{a} [\bar{\mu}_L(E_1) - b\bar{\mu}_L(E_2)]$$

Where:

$$a = \mu_{LB}(E_1) - b\mu_{LB}(E_2)$$

$$b = \mu_{LT}(E_2) / \mu_{LT}(E_1) \approx \mu_{LH_2O}(E_2) / \mu_{LH_2O}(E_1)$$

Thus, the mean linear attenuation coefficient is determined at two divergent energies such as 80 and 140 kVp. The X factor, representing the fractional mineral component, can then be determined by simultaneous solution of the two equations. The Y parameter which describes the equivalent density of the soft tissue fat component may be solved for in a similar fashion. The use of simple algebraic formulas is made possible by the linear relationship between EMI number and the linear attenuation coefficient (Fig. 1).

Results

The EMI numbers for our tissue equivalent substances as a function of tube operating kilovoltages are shown in Figure 2. Of importance with the EMI head scanner, the CT number of water is 0 at all energies, which is accomplished by internal calibration. The CT number of potassium phosphate is considerably higher than water due to its high Z and high density. The number changes greatly with energy, ie, 1100 EMI units at 80 kVp and 650 EMI units at 140 kVp for a 100 gm% solution. The CT number of 100% ethyl alcohol is

approximately minus 100, and changes slightly with operating kVp. Thus, it is apparent that unknown amounts of fat mixed with soft tissue can affect the determination for bone mineral.

In Figure 3 the measured integral CT number is plotted against the mineral content calculated on the basis of the known concentration and size of phantoms. The correlation coefficient is high and the scatter of points about the regression line low, giving an accuracy of 1.9%.

A similar plot of the Norland-Cameron densitometric determination versus the calculated mineral content for the same known standards is shown in Figure 4. The correlation is again high, but the scatter or standard error is slightly greater with this determination, approximately 4%. Thus, the Norland-Cameron measurement and the integral CT determination show similar close correlations against known standards, and as seen in Figure 5, show a close correlation one measurement to the other. Additionally, the two patients measured with both methods show close agreement with the phantom measurements.

Figure 6 shows a plot of the mean CT numbers versus the fraction or percent potassium phosphate solutions for the coaxial phantom simulating cortical and cancellous bone. The high correlation previously shown for integral bone is likewise shown here for cancellous determination and for cortical determination done separately. This separate determination cannot be done with the Norland-Cameron technique.

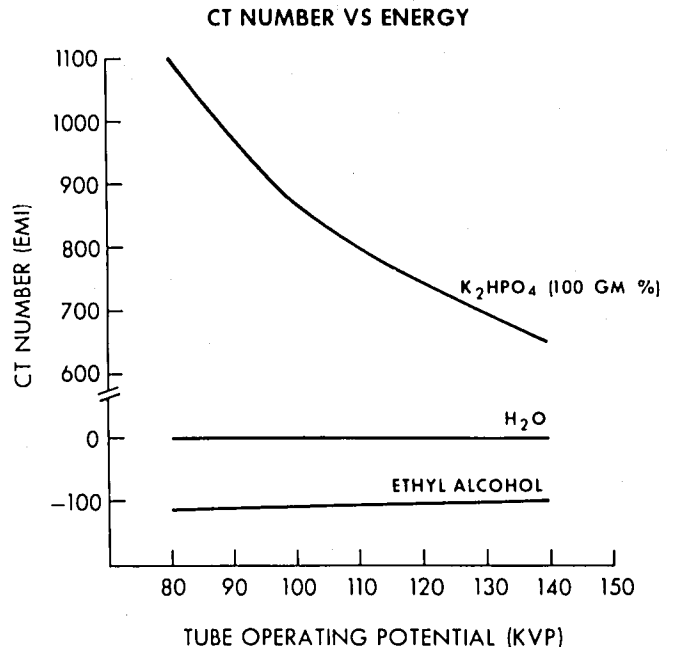


Fig. 2. CT number versus tube operating kilovoltage plotted for our tissue equivalent substances. Ethyl alcohol has a value of approximately minus 100 EMI units. The value for dipotassium hydrogen phosphate changes greatly with energy.

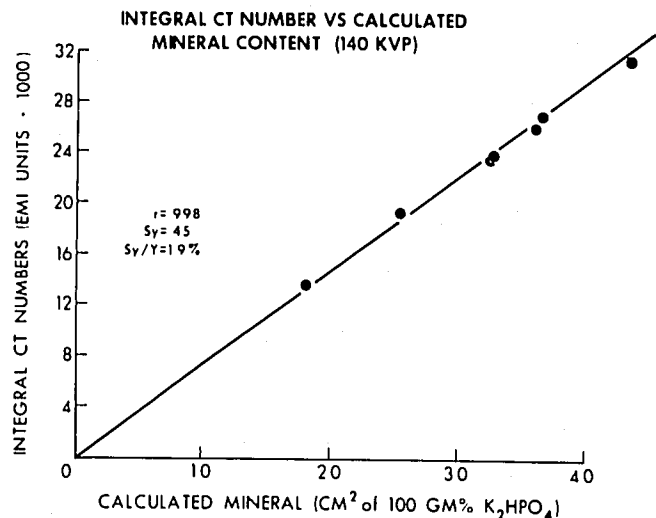


Fig. 3. Summation of integral of CT number (140 kVp) for a slice of solid cylinder plotted against the known standards of dipotassium hydrogen phosphate expressed as centimeters squared of 100 gm% K_2HPO_4 equivalent.

Figure 7 demonstrates the basis for the dual determination. It is made possible by the large change in linear attenuation coefficient for the mineral component as a function of kVp. The fat (C_2H_5OH) and soft tissue (H_2O) components show a smaller, predictable and *paralleling* change in linear attenuation coefficient. Thus, if we know the change in CT number for an unknown mixture, the mineral fraction can be derived independent of fat and water.

This is shown graphically in Figure 8 where the CT number of $K_2HPO_4-C_2H_5OH-H_2O$ mixtures obtained at 140 kVp are plotted against the CT number obtained at 80 kVp. The determined fractional component, X, for mineral concentrations are shown by the diagonal lines in steps of 20 gm% each. For example, The CT number for a mixture containing 100 gm% potassium phosphate, will fall somewhere along the lowest diagonal line depending upon the relative amounts of fat and soft tissue.

The accuracy and precision of the dual and single energy techniques are shown in Figure 9. Here we have used a series of phantoms with a constant 5 gm% potassium phosphate concentration but with the various mixtures of alcohol ranging from 0-40% by volume and plotted on the axis. The measured value for mineral content *should* be 5% for all determinations. With the single energy techniques, however, the measured value becomes progressively lower with increasing alcohol content such that at 40% added alcohol, one obtains a result of approximately 2 gm% for the 80 to 140 kVp techniques. The error is greater than 50%. The precision, however, is very high as indicated by the very small standard deviation bars, approximately 1-2%.

With the dual energy technique the error is greatly reduced; we obtain values close to the correct 5 gm% value. In other words, the accuracy of this determination relative to the single energy mode is considerably improved although its magnitude was not determined by multiple measurements. The precision, however, is poorer as evidenced by the standard deviation of approximately 10%. Thus, the dual energy technique reduces the inaccuracy resulting from unknown amounts of fat at the sacrifice of precision.

It would appear that for serial determinations in a given patient, the single energy technique will be most useful since precision is high. For a diagnostic determination, however, to separate a patient from a normal population, accuracy is required, and thus the dual energy technique must be used.

The precision or coefficient of variation, as a function of the mineral content or fractional K_2HPO_4 , is plotted in Figure 10. The higher precision of single compared to dual energy determination is demonstrated as well as the relatively higher precision for determining high rather than low fractions of mineral.

The potential effect of beam hardening²⁴ on accuracy is demonstrated in Figure 11 which shows a "cross sectional" plot of a coaxial phantom simulating the radius. It can be seen that for this relatively thin-walled cortical equivalent, the inaccuracy from beam hardening for determining the inner cancellous equivalent core is negligible with the EMI head scanner. For thicker and denser cortical equivalents, however, beam hardening error can be considerable as shown in Figure 12. Here the CT number at the center of a cylinder of 16 mm diameter is plotted as a function of mineral fraction at two energies indicating nonlinearity in the system.

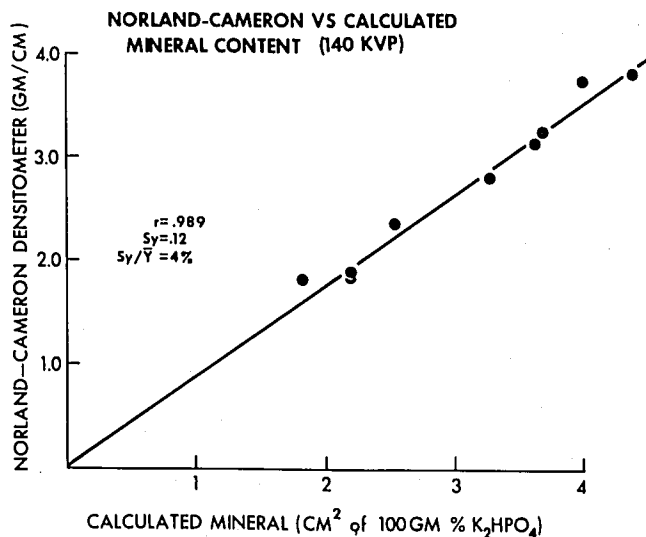


Fig. 4. Norland-Cameron determination versus the same known standards as in Fig. 3.

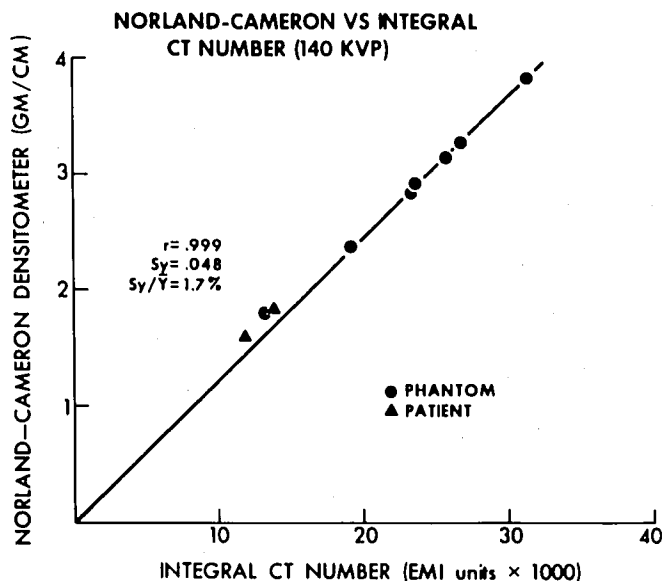


Fig. 5. Norland-Cameron determination versus integral CT number for the known standards. Both phantom and 2-patient measurements fall close to the regression line.

Discussion

Potential advantages of the computed tomographic technique^{4,5,13,29,33} over other modalities for bone mineral determination include: 1) transaxial display of data which permits identification of anatomy and separate determination of cortical, cancellous or integral bone; 2) capability of determining linear absorption coefficient for a readily defined volume of bone; and 3) in the dual energy mode, the ability to determine mineral content in the presence of variable fat and soft

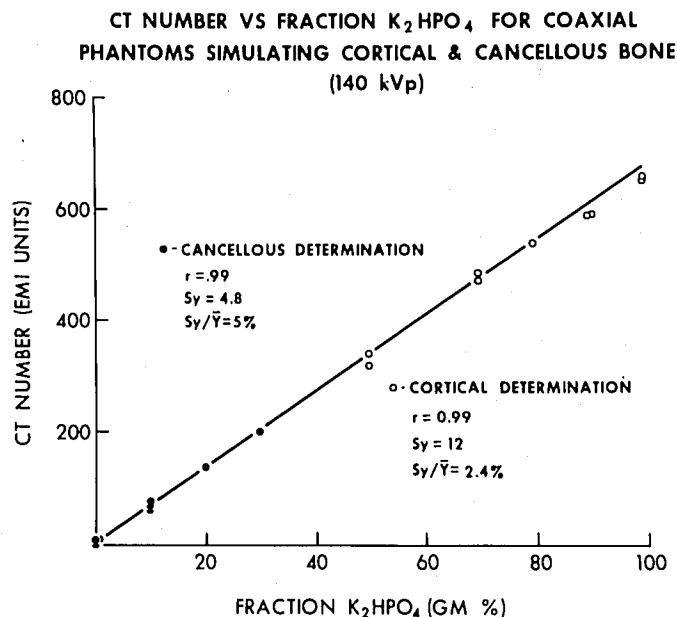


Fig. 6. Mean CT numbers versus the fraction K_2HPO_4 for co-axial phantoms simulating cortical and cancellous bone.

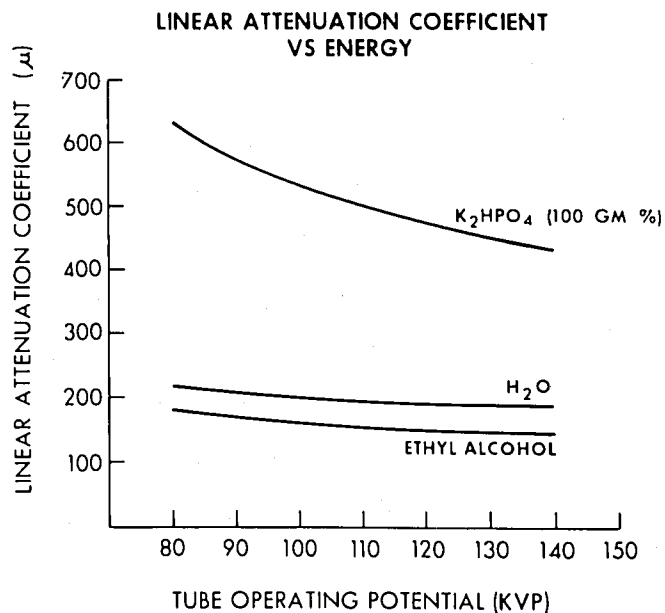


Fig. 7. Linear attenuation coefficient versus kVp for the tissue equivalent substances. The large change in linear attenuation coefficient for the mineral component is demonstrated. Water and ethyl alcohol show a smaller and paralleling change with tube operating potential.

tissue. Other procedures available for determining bone mineral content in the peripheral skeleton include the following:

First, there is the simple measurement of cortical thickness which is easy to perform, reproducible and is backed by a large body of normative data.^{11,12,27,40} This technique may lack sensitivity in assessing many metabolic bone disorders since only endosteal bone resorption is reflected by this measurement. Intracortical resorption (cortical porosity) and trabecular bone resorption which are important determinants of high bone turnover states are not measured.^{9,14-16,26,36,38}

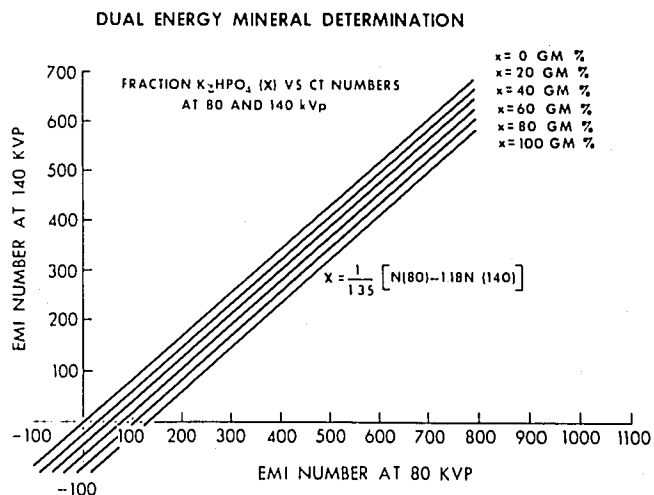


Fig. 8. The fraction K_2HPO_4 (X) is plotted on the diagonal in 20 gm% steps. These values are determined by obtaining the EMI number at 140 and 80 kVp.

ACCURACY FOR MINERAL DETERMINATION

MEASURED K_2HPO_4 FRACTION (5 GM %) VS ALCOHOL ADMIXTURES (0-40%)
FOR DUAL ENERGY AND SINGLE ENERGY TECHNIQUES

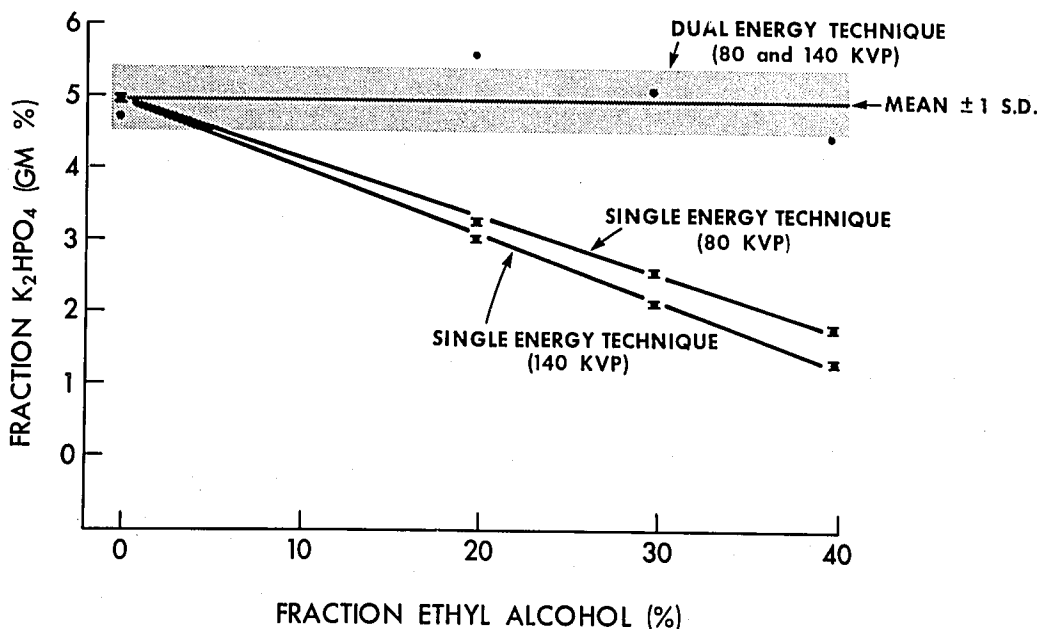


Fig. 9. Measured K_2HPO_4 fraction determined from fixed 5 gm% solutions with various admixtures of alcohol for dual and single energy techniques. The higher precision but poorer accuracy for single energy techniques is shown.

Second, photodensitometry^{7,8,21,26} is a technique using an x-ray source, radiographic film, and a known standard wedge which has proved reproducible in experienced hands and is possibly more sensitive than simple cortical measurement. Complicated technical requirements have limited the clinical scope of this technique, however.

Third, a more widely used, easier and more precise technique is photon absorptiometry using an iodine-125 source interfaced with a sodium iodine scintillation detector.^{1,6,20,36} Many such devices have been used but the most widely accepted is the Norland-Cameron⁶ which measures the radial shaft (although other tubular bones can be examined). Considerable normative data are available and many clinical studies have supported its usefulness.^{17,36} A reproducibility of 2% and an accuracy of approximately 6% have been demonstrated.⁶ The measurement is primarily an integral of cortical bone since the diaphysis, where measurements are generally made, contains little cancellous bone, and the metaphysis, which contains proportionally more trabecular bone (up to 25-40% of total integral bone),³⁵ is more difficult to measure due to repositioning errors and, consequently, precision may be poor. The impetus for measuring cancellous bone is that this bone tissue has a greater surface-to-volume ratio than cortical bone and shows alteration earlier and more dramatically in many metabolic disorders.^{11,16,17,31,38} It is for this reason that the quantized cross sectional display of CT may prove particularly valuable. Addi-

tionally, a technique such as CT, capable of measuring various sites in the skeleton, may be advantageous.^{11,12,42}

A study recently reported by Reich²⁹ utilized a Delta CT scanner and correlated the results with those obtained using the Norland-Cameron densitometer, both techniques measuring an integral of bone in the radial shaft. A fairly high correlation was obtained: $r = 0.72$. Additionally, accuracy was determined by measuring tubular bones devoid of soft tissue and placed in a water bath. The CT results correlated well with sub-

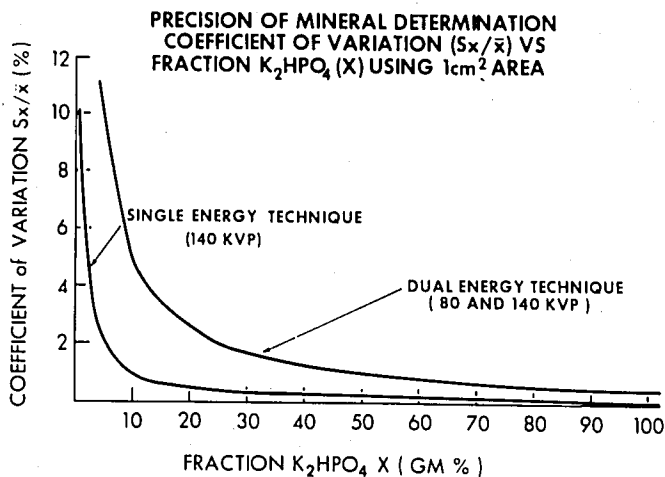


Fig. 10. The precision for single and dual energy mineral determination (coefficient of variation) plotted as a function of fraction K_2HPO_4 .

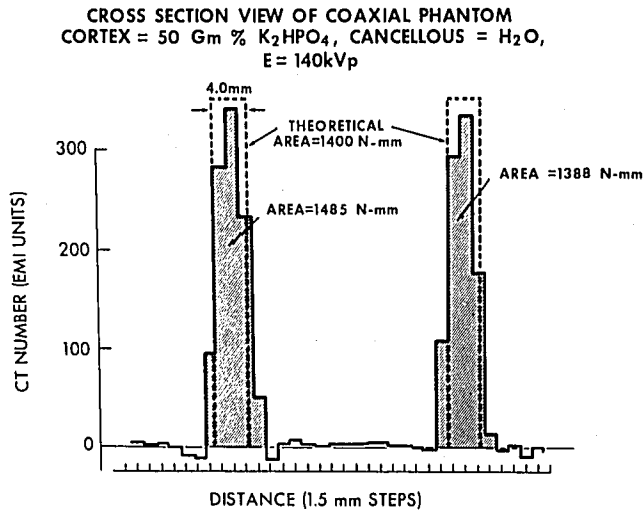


Fig. 11. Cross-sectional view of a co-axial phantom with the outer cortex containing 50 gm% solution K_2HPO_4 , and a central core containing water. We do not see falsely low CT numbers for the central portion to indicate beam hardening error.

sequent calcium determination in specimens ($r = 0.97$) indicating a high accuracy achievable in vitro. Precision was not determined and there was no attempt to separately determine the mineral content of cortical and cancellous bone, or the mineral in the presence of variable soft tissue components.

A specially devised CT technique for bone mineral analysis was recently reported by Rügsegger³³ which used an iodine-125 source and computer assisted reconstruction. It showed excellent capability for separate determination of cortical and cancellous bone in the radius and provided approximately 2% precision. Accuracy was not determined. However, it should be

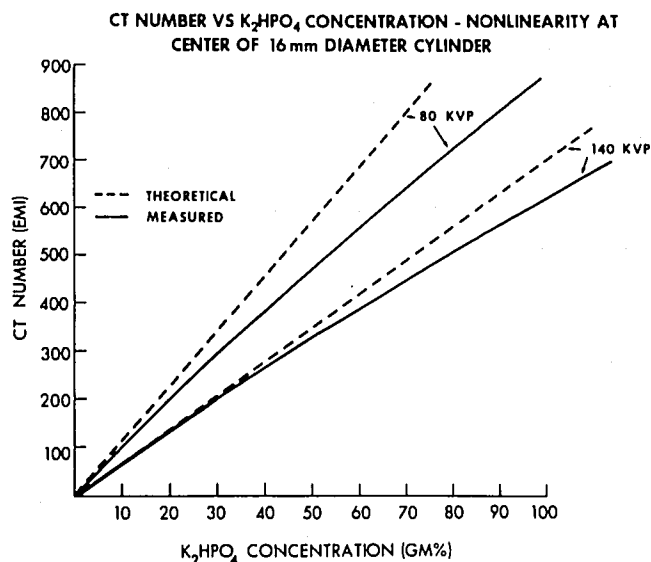


Fig. 12. Theoretical and measured values for CT number versus K_2HPO_4 concentration for determinations made at the center of a 16 mm diameter cylinder. The wide discrepancies seen at values greater than 60 gm% are due to non-linearity and precipitation of potassium phosphate from solution.

noted that the error due to unknown fat will depend greatly upon the beam energy as well as the relative amount of fat.³⁷ Thus with a low energy source such as iodine-125 (mean energy 27 keV) the attenuation by mineral is accentuated relative to fat and soft tissue due to the Z^3 dependence of the photoelectric attenuation process which dominates at low photon energy. At this low energy the error in determining bone mineral content due to variable fat in the marrow space of the radius has been estimated at less than 3%.¹⁸ Moreover, beam hardening error which can be considerable with a low energy polychromatic source is eliminated by the nearly monochromatic ¹²⁵I photon spectrum. It is apparent then that this technique of CT reconstruction using an iodine-125 source may be superior to that achievable with commercially available CT scanners for peripheral small bones.

The current study addressed the problems of separate mineral quantitation of cortical and cancellous bone in the presence of variable fat complicated by beam hardening of the polychromatic photon beam. The EMI head scanner was used at 80 and 140 kVp to measure coaxial phantoms containing solutions of dipotassium hydrogen phosphate, water and ethyl alcohol which simulate variable bone, soft tissue and fat. The results indicated that the CT technique at a single energy can readily and accurately determine mineral content for cortical, cancellous or integral bone in a two component system containing mineral and soft tissue. It can do this in dual component phantoms with accuracy matching or surpassing the Norland-Cameron technique which can only measure integral bone. Additionally, in the dual energy mode,³⁴ mineral content of a three component system containing mineral, soft tissue and fat can be relatively accurately determined at a considerable sacrifice of precision. Furthermore, for the small tubular bones such as the radius, the hardening of the polychromatic beam at the relatively high energy levels used is rather minimal. Thus, the CT technique discussed here shows considerable promise for quantitating mineral in the peripheral skeleton although it may not compare favorably with the low-energy, monochromatic CT technique of Rügsegger.³³

For analysis of the axial skeleton, however, particularly the spine where complications of bone loss frequently become manifest,^{16,38} the dual energy CT technique discussed herein may prove particularly valuable. Since higher energies must be used for statistical and dosimetric reasons, the relative error due to marrow fat may be considerable (up to 30%).^{4,18,37} This indicates the necessity for dual energy technique for the thicker body parts. The beam hardening effects for a polychromatic source, however, will necessarily be greater and repositioning errors may be large. Further analysis of computed tomography for spinal mineral

quantitation will be necessary to determine the potential of this technique in comparison with other modalities currently under investigation, i.e., single projection dual-energy photonabsorptiometry and x-ray spectrophotometry.^{10,18,19,30} total or partial body neutron activation,^{2,23,25} and Compton scattering.⁴¹

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