

Two Postprocessing CT Techniques for Determining the Composition of Trabecular Bone

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Two dual-energy CT techniques have been developed to analyze the mineral and fat content of trabecular bone. Both are postprocessing techniques that employ calibration standards. Experiments were performed to test these techniques against conventional single-energy techniques and two other dual-energy techniques. As expected, all of the dual-energy methods estimate the mineral content more accurately when fat is present. In contrast to the other dual-energy methods, the new methods described in this article are unique because they make a separate estimate of the fat content of the bone. The results of preliminary tests of these techniques in estimating fat content have been encouraging. Although not exact, the estimates show the correct trend in increasing proportionately as the fat content increases. Possible applications of the techniques in the study of osteoporosis and other bone diseases are described.

Key words: bone mineral analysis, computerized tomography, fat content analysis, osteoporosis.

OSTEOPOROSIS is the most common disorder of the skeletal system. Primarily affecting postmenopausal women, it is manifested by a decrease in the quantity of skeletal bone, which is otherwise histologically and chemically normal. The primary danger to a patient with this disease is increased risk of fracture.

Bone exists in cortical and trabecular forms. Cortical bone is found in the shafts of the long cylindrical bones, and the outer envelope of the vertebrae and flat bone. Trabecular bone is centrally located, primarily within the flat bones and the metaphyses and epiphyses of long bones. It exists in the form of small spicules and trabeculae interspersed with marrow that may contain a variable amount of fat. The chemical composition of the individual spicules of bone does not differ from that of cortical bone.

Because the turnover rate of trabecular bone is approximately eight times greater than that of cortical bone, the trabecular regions of the skeleton should demonstrate osteoporotic changes long before the cortical regions. Computerized tomography (CT) permits separate analysis of trabecular and cortical bone. A quantitative adaptation of CT scanning has gained wide popularity as a method for analysis of bone-mineral content.¹

Both single-energy (kVp) and dual-energy (kVp) CT bone-mineral analysis methods have been developed, although single-energy methods have found far greater clinical application. In general, single-energy methods are more precise and dual-energy methods are more accurate.² The accuracy of single-energy techniques is degraded by the presence of fat within bone marrow. The large negative CT number associated with fat may result in an underestimation of bone-mineral content, an affect that can be minimized using dual energy. Although it has been recognized that dual-energy methods can be used to determine fat plus soft-tissue (nonmineral) content in addition to improving the accuracy of bone-mineral measurement,^{2,3} no one has pursued calculation of the nonmineral content of the marrow. We have developed dual-energy methods that simultaneously estimate both the bone and the fat (separate from soft tissue) concentrations and have tested these methods in

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phantoms. We also have compared these new dual-energy methods to single-energy bone-mineral determination, and two dual-energy techniques drawn from the literature that yield only mineral or both mineral and nonmineral measurements.

Methods

In general, the dual-energy methods presently used can be divided into two categories: (1) preprocessing schemes using raw CT projection data⁴ and (2) postprocessing schemes using image data.^{3,5-7}

The two methods we developed are postprocessing techniques. They will be discussed in this section.

Three-Equation Three-Unknown Method

A volume V of trabecular bone is analyzed. We assume this volume contains a mixture of three materials—bone (calcium hydroxyapatite), soft tissue (or water), and fat. The first equation is derived from the fact that the volume of the mixture is equal to the sum of the volumes of its components.

$$V_{\text{mix}} = v_b + v_s + v_f \text{ or} \\ 1 = v_b/V_{\text{mix}} + v_s/V_{\text{mix}} + v_f/V_{\text{mix}},$$

where v_b = partial volume of bone in the mixture,

v_s = partial volume of soft tissue in the mixture,

v_f = partial volume of fat in the mixture,

and V_{mix} = the total volume of the mixture.

We define the volume fractions of bone, soft tissue, and fat as

$$B = v_b/V_{\text{mix}}, S = v_s/V_{\text{mix}}, \text{ and } F = v_f/V_{\text{mix}}, \text{ respectively}$$

Therefore,

$$1 = B + S + F \quad (1)$$

The second and third equations are drawn from the fact that the CT number of the mixture represents the summation of the CT numbers of the components weighted by their volume fractions.

$$\overline{CT\#}_{\text{mix}}(E_1) = B \times \overline{CT\#}_b(E_1) + S \times \overline{CT\#}_s(E_1) + F \times \overline{CT\#}_f(E_1) \quad (2)$$

$$\overline{CT\#}_{\text{mix}}(E_2) = B \times \overline{CT\#}_b(E_2) + S \times \overline{CT\#}_s(E_2) + F \times \overline{CT\#}_f(E_2) \quad (3)$$

Appendix 1 shows the derivation of these equations.

To use these equations, one must obtain a CT image of a patient's vertebra and reference samples of pure bone, soft tissue (water), and fat at two energies (E_1 and E_2 , eg. 80 and 140 kVp). The mean CT numbers ($\overline{CT\#}$) of these substances are measured within regions of interest in these images. These CT numbers are then substituted into the equations, and the equations are solved for B , S , and F . In our study, an excised sample of femoral cortex was used to represent "pure bone." The bone reference phantom in this method must be scanned separately from the patient to avoid artifacts due to dense cortical bone.

Four-Equation Four-Unknown Method

The x-ray beams used in CT scanning are polyenergetic. Therefore, beam hardening artifacts (eg, cupping) make it difficult to determine accurately the CT number of pure (100% by volume) bone. One possible solution to this problem is to use measurements of the CT numbers of samples containing lower concentrations of bone (eg, mixtures of bone and soft-tissue-mimicking material) to extrapolate to the CT number of pure bone. Another solution is to combine the information from the measurements of the samples containing lower concentrations of bone with slightly modified versions of equations 2 and 3. This essentially is our second technique, which we term the four-equation four-unknown method.

The set of four equations, four unknowns is (Appendix 2 shows the derivation of these equations)

$$(1) \overline{CT\#}_{\text{no fat}}(E_1) = g(E_1) \times [\text{mg/cc}] + i(E_1)$$

$$(2) \overline{CT\#}_{\text{no fat}}(E_2) = g(E_2) \times [\text{mg/cc}] + i(E_2)$$

$$(3) \overline{CT\#}_{\text{with fat}}(E_1) = \overline{CT\#}_{\text{no fat}}(E_1) + F \times [\overline{CT\#}_f(E_1) - \overline{CT\#}_s(E_1)]$$

$$(4) \overline{CT\#}_{\text{with fat}}(E_2) = \overline{CT\#}_{\text{no fat}}(E_2) + F \times [\overline{CT\#}_f(E_2) - \overline{CT\#}_s(E_2)]$$

where the $g(E)$ are the slopes and the $i(E)$ are the intercepts of calibration lines generated with a reference phantom containing known concentrations of bone- and tissue-mimicking material,

mg/cc is the desired bone mineral concentration,

the $\overline{CT\#}_{\text{with fat}}(E)$ are the measured mean CT numbers of the patient's trabecular bone,

the $\overline{CT\#}_{\text{no fat}}(E)$ are the calculated estimates of what the mean CT numbers of the patient's trabecular bone would be if the spongiosa contained no fat,

F = volume fraction of fat,

$\overline{CT\#}_f$ = mean CT number of pure fat (from reference phantom),

$\overline{CT\#}_s$ = mean CT number of pure soft tissue (from reference phantom),

E_1 corresponds with one kV,

and E_2 corresponds with the other kV of the dual energy (kV) technique.

The four unknowns in these equations are mg/cc, $\overline{CT\#}_{\text{no fat}}(E_1)$, $\overline{CT\#}_{\text{no fat}}(E_2)$, and F .

We solve these equations by translating them into their matrix form

$$\begin{bmatrix} 1 & -g(E_1) & 0 & 0 \\ 0 & -g(E_2) & 1 & 0 \\ 1 & 0 & 0 & [\overline{CT\#}_f(E_1) - \overline{CT\#}_s(E_1)] \\ 0 & 0 & 1 & [\overline{CT\#}_f(E_2) - \overline{CT\#}_s(E_2)] \end{bmatrix} \times \begin{bmatrix} \overline{CT\#}_{\text{no fat}}(E_1) \\ \text{mg/cc} \\ \overline{CT\#}_{\text{no fat}}(E_2) \\ F \end{bmatrix} = \begin{bmatrix} i(E_1) \\ i(E_2) \\ \overline{CT\#}_{\text{with fat}}(E_1) \\ \overline{CT\#}_{\text{with fat}}(E_2) \end{bmatrix}$$

and then applying a set of algorithms such as DECOMP and SOLVE.⁸

To use the equations, one obtains images of the patient and a calibration phantom at two energies (E_1 and E_2 , eg, 80 and 140 kVp). The mean CT numbers of the bone calibration mixtures or solutions, 100% fat sample, water or 100% soft tissue sample, and patient's bone marrow are determined at each energy using the region of interest facilities of the CT-image display device. The CT numbers and corresponding concentrations (mg/cc) of the bone calibration solutions are entered into a linear fit computer program and the slopes (g) and intercepts (i) of the CT number vs. milligram per cubic centimeter lines at the two energies are determined. These slopes and intercepts as well as the mean CT numbers of the patient's trabecular bone at the two energies [$CT\#_{\text{with fat}}(E_1)$ and $CT\#_{\text{with fat}}(E_2)$], and the CT# numbers of pure fat and water or tissue at the two energies are entered into the algorithms that solve the set of four equations for the four unknowns. Two of these unknowns are of particular interest: the bone mineral content (mg/cc) and the volume fraction of fat (F).

To evaluate the methods, we performed an experiment in which test solutions containing known amounts of bone, fat, and soft-tissue-mimicking materials were inserted within holes in a 10-inch diameter lucite phantom. The lucite phantom simulated a section of a patient and was placed over a calibration phantom in the tests. Although the components bone, fat, and soft tissue reside as relatively discrete components within the body, it is difficult to devise a reference phantom or test samples using mixtures because of uncertainties associated with the uniformity of the mixtures. Therefore, aqueous solutions were used in both the reference phantom¹ and test samples of our study. Both contained K_2HPO_4 to mimic bone⁹ and water to mimic tissue. Ethyl alcohol (ethanol) was used to mimic fat.² Because our reference phantom does not incorporate an ethanol solution, separate vials containing ethanol were placed on the surface of the lucite phantom to act as "fat" references. The lucite phantom

containing the test solutions and the reference phantom were scanned simultaneously using a General Electric Model 9800 CT scanner (Milwaukee, WI).

The techniques employed were (80kVp, 70 mA) and (140 kVp) 40 mA with a 4-second scan time, 10-mm-slice thickness, and large reconstruction field. To improve the signal-to-noise ratio of our data, we scanned the phantom three times at each energy level and averaged the data.

Results

The results for the four-equation four-unknown method are listed in Table 1 along with the concentrations of K_2HPO_4 predicted using each single kVp technique, and dual-energy methods developed by Cann⁷ (Method A) and Laval-Jeantet et al³ (Method B). (Cann advises they presently employ Method A shown in Appendix 2. This equation differs from that in reference 7 because the intercept values from the calibration curves are used instead of the measured CT numbers of water). The article describing Method B³ states that an equation that is similar in form to the one they developed for determining bone-mineral concentration can be derived for determining the concentration of fat. We derived this equation and used it to calculate the fat concentrations shown in Table 1.

Corresponding results for the same experiment for the three-equation three-unknown method are shown in Table 2. It should be noted that this technique yields volume percentages of bone rather than milligrams per cubic centimeter. This method requires the measurement of the CT

TABLE 1. Comparison of Single- and Dual-Energy CT in Estimating the Mineral (mg/cc of K_2HPO_4) and "Fat" (Volume % of Ethanol) Content of Several Test Solutions

| True Values | Estimate 80 kVp Single Energy | Estimates 140 kVp Single Energy | A* Dual Energy | B† Dual Energy | Estimate Four-Equation Four-Unknown Dual Energy |
|-------------------------|----------------------------------|------------------------------------|-------------------|---------------------|--|
| 50 mg/cc 0% ethanol | 59.0 mg/cc — | 59.2 mg/cc — | 58.2 mg/cc — | 68.1 mg/cc -3.3% | 58.0 mg/cc -0.7% |
| 50 mg/cc 10% ethanol | 48.7 mg/cc — | 45.8 mg/cc — | 57.7 mg/cc — | 69.3 mg/cc 5.7% | 59.7 mg/cc 8.3% |
| 50 mg/cc 20% ethanol | 41.5 mg/cc — | 36.5 mg/cc — | 57.2 mg/cc — | 70.8 mg/cc 11.8% | 60.7 mg/cc 14.4% |
| 50 mg/cc 30% ethanol | 25.8 mg/cc — | 18.9 mg/cc — | 47.4 mg/cc — | 62.3 mg/cc 17.2% | 52.2 mg/cc 19.7% |
| 50 mg/cc 40% ethanol | 15.9 mg/cc — | 6.7 mg/cc — | 44.5 mg/cc — | 61.0 mg/cc 23.6% | 50.9 mg/cc 26.2% |
| 30 mg/cc 0% ethanol | 36.8 mg/cc — | 37.6 mg/cc — | 34.6 mg/cc — | 44.3 mg/cc -4.6% | 34.2 mg/cc -2.0% |
| 30 mg/cc 20% ethanol | 22.8 mg/cc — | 18.9 mg/cc — | 34.9 mg/cc — | 47.7 mg/cc 8.6% | 37.6 mg/cc 11.1% |
| 30 mg/cc 40% ethanol | -0.12 mg/cc — | -6.5 mg/cc — | 19.8 mg/cc — | 34.4 mg/cc 15.7% | 24.2 mg/cc 18.2% |

*Method A is the 2-line dual energy method of Cann (Appendix 2).

†Method B is the 4-line dual energy method of Laval-Jeantet, Cann et al.³

TABLE 2. Three-Equation Three-Unknown Results for Experiment Involving Solutions of K_2HPO_4 and Ethanol

| True Values | Three-Equations Three-Unknown Estimates (Volume % Bone, Volume % Ethanol) |
|-------------------------|---|
| 50 mg/cc 0% ethanol | 3.6% 0.5% |
| 50 mg/cc 10% ethanol | 3.4% 6.0% |
| 50 mg/cc 20% ethanol | 3.5% 11.9% |
| 50 mg/cc 30% ethanol | 3.0% 17.7% |
| 50 mg/cc 40% ethanol | 2.9% 24.0% |
| 30 mg/cc 0% ethanol | 1.9% 0.5% |
| 30 mg/cc 20% ethanol | 1.9% 10.4% |
| 30 mg/cc 40% ethanol | 1.0% 18.3% |

numbers of pure bone, pure tissue, and pure fat. Because of precipitation problems associated with highly concentrated solutions of K_2HPO_4 , and because K_2HPO_4 mimics bone, we used a cadaver bone instead of a 100% K_2HPO_4 solution as the pure-bone sample. The maximum CT numbers in the cortical region in the midshaft of a cadaver femur were used as the "pure-bone" CT numbers. As stated, because of the imaging artifacts that result from scanning a pure-bone sample, the bone calibration reference was scanned separately from the test samples for this method. The CT numbers of a 100% ethyl alcohol solution were used as the CT numbers of "pure fat." Dunscombe et al¹¹ have suggested that greater accuracy in dual-energy CT may be achieved by "assuming a value of 0 for the CT number of water." We found this to be true for the three-equation three-unknown method, and the results in Table 2 were obtained with this assumption. Finally, in solving the three equations for the three unknowns, we imposed the additional constraint that each volume fraction component must be positive because negative volume fractions have no physical meaning. This was achieved by an algorithm that was implemented when any of the solutions to the three equations were negative. This algorithm compared the measured CT numbers of the test sample at each energy to the predicted CT numbers for all possible positive combinations of the volume fractions B, S, and F. The B, S, and F combination that yielded a minimum chi-squared sum for the CT numbers at the two energies was chosen as the solution.

A separate test of the three-equation three-unknown method was also performed. In this test, we placed slabs of

TABLE 3. Test of Three-Equation Three-Unknown Method Using Tissue-Mimicking Plastic Slabs

| | True Value | Predicted Value |
|--------|------------|-----------------|
| % bone | 10 | 11.6 |
| % fat | 0 | 0.2 |
| % bone | 10 | 10.8 |
| % fat | 10 | 0.8 |
| % bone | 10 | 15.8 |
| % fat | 20 | 83.8 |
| % bone | 10 | 10.1 |
| % fat | 30 | 0.0 |
| % bone | 10 | 11.0 |
| % fat | 40 | 34.2 |

bone, soft tissue, and fat-mimicking plastics (bone and water equivalent plastics obtained from Radiation Measurements, Inc., Middleton, WI; polyethylene used to mimic fat) within a 1.2-inch by 1.2-inch square slot in the 10-inch diameter lucite phantom. This slot was lined with 0.1-inch-thick slabs of bone equivalent plastic, representing the cortical bone. To determine the CT numbers of the pure substances, large samples of the tissue-mimicking plastics were placed within the slot and scanned separately at the two energies (80 kVp and 140 kVp). To provide the mixtures, slabs of each material were placed side by side within the slot. The different volume fractions of the components corresponded with different thicknesses of the slabs. For example, a volume fraction of 0.2 corresponded with a slab thickness of 0.2 inch. Each pure substance and mixture was scanned three times at each energy and the data were averaged as before to improve the signal-to-noise ratio. The results are shown in Table 3.

Discussion

Both the three-equation and the four-equation methods yielded encouraging results when tested with the liquid state phantom. Although not exact, they show the correct trend in estimation of the fat (alcohol) content. Specifically, the estimates increase proportionately as the alcohol content increases. A linear regression analysis of the ethanol results in Table 1 for the four-equation four-unknown method shows that the estimated volume percent ethanol is related to the true volume percent ethanol by the expression

$$\text{true \% ethanol} = 1.56 \times (\text{estimated \% ethanol}) + 1.43,$$

with a correlation coefficient of 0.957.

A similar analysis of the data in Table 2 shows that for the three-equation three-unknown method, the linear regression is

$$\text{true \% ethanol} = 1.84 \times (\text{estimated \% ethanol}) - 0.49,$$

with an even better correlation coefficient of 0.981.

The estimates of the K_2HPO_4 concentration are much better than those for the single kVp techniques, and they are approximately equal to those of the dual-energy technique proposed by Cann⁷ (Method A). The good agreement between the four-equation four-unknown method and Method A in estimating the K_2HPO_4 concentrations of the test solutions is to be expected for this particular study. It occurs because of the choice of ethanol to mimic fat. The CT number of ethanol does not vary appreciably with energy (eg, 230 Hounsfield units at 80 kVp and -220 Hounsfield units at 140 kVp), which is an assumption in Method A (Appendix 2). However, a better fat mimicker would have displayed greater variation in its CT number with energy and its use would have resulted in greater differences in the estimated K_2HPO_4 concentrations yielded by the two methods. Ethanol was chosen to mimic fat because it exhibits a negative CT number, is easily placed into solution, and is readily available.

Possible reasons for differences between estimated and true volume percentages of alcohol using the four-equation four-unknown technique include

- (1) inaccuracies introduced by the polyenergetic nature of the x-ray beam (the theory assumes a monoenergetic x-ray beam);
- (2) the fact that the theory assumes a mixture, whereas this was a test of a liquid solution;
- (3) slight errors in mixing the solutions;
- (4) possible existence of undetectable minute air bubbles in the solutions; and
- (5) the dependence of the measured mean CT number of a material on its location within the reconstruction circle of the CT scanner.

In a subsequent study, we found that with our scanner, there is a substantial dependence of measured CT numbers on position within the scanning circle. Water placed within the center of an anthropomorphic phantom may differ from water at the periphery by as much as 20 Hounsfield units. We believe, therefore, that reason five is probably responsible for the systematic overestimation of mineral at 0% ethanol by single- and dual-energy techniques.

Relative to the four-equation four-unknown method, the method proposed by Laval-Jeantet et al³ (Method B) overestimated the bone-mineral content and underestimated the fat content. This may be due to the use of a two-point linear fit that Laval-Jeantet et al suggested for determining the slopes and intercepts of the CT number vs. alcohol concentration lines used in their equations.

There is no simple conversion relation between the volume percent bone in Table 2 and the true milligrams per cubic centimeters of K_2HPO_4 of the samples. However, it is reassuring to note that the ratios of the estimated volume percentages are approximately the same as the ratios of the known concentrations. For example, for the 30 mg/cc 20% ethanol, and the 50 mg/cc 20% ethanol samples, the ratio of

the K_2HPO_4 concentrations (30/50) is 0.6 and the ratio of the estimated volume percentages of bone is 0.54.

The results of the test of the three-equation three-unknown method using solid-state phantoms (Table 3) were disappointing. Reasonably correct answers were obtained in only two of the six cases. We believe that this can be attributed to inaccuracies in the measured CT numbers due to beam hardening, edge artifacts caused by the squared shape of the plastic slab mixture, possible minute air gaps between adjacent slabs and possible nonuniformity of the slab materials. In the future, we will test smooth-shaped objects in which fat, tissue-, and bone-mimicking plastics are uniformly mixed.

Our results suggest an interesting direction for research in dual-energy quantitative CT. It is believed that severe degrees of osteoporosis are accompanied by greater quantities of bone-marrow fat and that these changes are age related.^{12,13} However, there is tremendous individual variation in the quantity of bone-marrow fat, and the potential rate of change in a given individual is unknown. Before the relative roles of single- and dual-energy scanning techniques are decided, it will be necessary to obtain this information.

Perhaps more importantly, there are a number of diseases in which the bone-marrow fat content may be of greater interest than the skeletal-bone measurement. In steroid-induced bone disease, changes in the quantity of bone-marrow fat may precede the complications of osteoporosis and osteonecrosis.¹⁴ In disorders of skeletal-bone marrow, disappearance of the marrow fat may be an important marker of replacement by tumor or other types of pathology. We have had the opportunity to study a limited number of patients with Gaucher's disease in whom we were unable to detect the presence of any bone-marrow fat; in a small series of normal patients, substantial bone-marrow fat content could be identified.

It should be noted that the 50 mg/cc mineral solution tested is equivalent to approximately 30% of the normal mineral concentration of the spinal trabecular bone. This upper limit was selected because of precipitation difficulties associated with greater concentrations of K_2HPO_4 when mixed with alcohol. Since the best diagnostic use of CT is in mildly or moderately affected individuals having mineral measurements of 100 mg/cc or more, the relative fat error will be proportionately less. Furthermore, to the degree that fatty marrow replacement accompanies osteoporosis, the fat error actually enhances the detectability of osteoporosis. Further work will be needed to determine what, if any, clinical role should be assigned to dual-energy CT for osteoporosis detection. As indicated above, however, the evaluation of marrow fat is a worthwhile goal in itself and cannot be accomplished by single-energy CT.

In summary, two methods have been developed for determining the fat and bone content of trabecular bone. Preliminary results of phantom tests have been mixed, but

promising. Future tests using uniform mixtures of bone, soft tissue, and fat-mimicking plastic materials will be conducted to determine the utility of the techniques. Once their value is established, they will be used to study patients with bone diseases.

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Appendix 1

The transmitted intensity of an x-ray beam after it passes through a thickness *t* of trabecular bone is given by the equation

$$I = I_0 \exp(-\mu_{mix}t) \\ = I_0 \exp[-((\mu/\rho)_b \rho_{bmix} + (\mu/\rho)_s \rho_{smix} + (\mu/\rho)_f \rho_{fmix})t],$$

where

- I_0 is the incident intensity,
- μ_{mix} is the linear attenuation coefficient (cm^{-1}) of the mixture of bone, soft tissue, and fat,
- $(\mu/\rho)_{b,s,f}$ are the mass attenuation coefficients ($cm^2/gram$) of bone, soft tissue, and fat, respectively.

and

$\rho_{bmix}, \rho_{smix}, \rho_{fmix}$ are the mass densities or concentrations (grams/ cm^3) of the bone, soft tissue and fat in the mixture.

Equating the exponents and dividing by *t*, we have

$$\mu_{mix} = (\mu/\rho)_b \rho_{bmix} + (\mu/\rho)_s \rho_{smix} + (\mu/\rho)_f \rho_{fmix} \quad (1)$$

The mass densities within the mixture may be described by

$$\rho_{bmix} = m_b/V_{mix} = \rho_{bpure} \times v_b, V_{mix} = \rho_{bpure} \times B,$$

$$\rho_{smix} = m_s/V_{mix} = \rho_{spure} \times v_s, V_{mix} = \rho_{spure} \times S,$$

and

$$\rho_{fmix} = m_f/V_{mix} = \rho_{fpure} \times v_f, V_{mix} = \rho_{fpure} \times F,$$

where

$m_{b,s,f}$ = mass (grams) of bone, soft tissue, and fat,

$\rho_{bpure}, \rho_{spure}, \rho_{fpure}$ = mass densities of pure (100%) bone, soft tissue and fat, V_{mix} = the total volume of the mixture, and

B, S, F = volume fractions of bone, soft tissue and fat.

Also, the mass attenuation coefficients may be described as

$$(\mu/\rho)_b = \mu_b/\rho_{bpure}, \text{ etc.}$$

Substituting the above information into equation (1), we obtain

$$\mu_{mix} = \mu_b B + \mu_s S + \mu_f F \quad (2)$$

The CT number in Hounsfield units is defined by the equation

$$CT_x = 1000 \frac{(\mu_x - \mu_{H_2O})}{\mu_{H_2O}} \quad (3)$$

where μ_x is the linear attenuation coefficient (cm^{-1}) of substance *x*, and

μ_{H_2O} is the linear attenuation coefficient of water.

Solving equation 3 for the linear attenuation coefficient μ_x , we have

$$\mu_x = (0.001 CT_x + 1) \times \mu_{H_2O} \quad (4)$$

Introducing equation 4 into equation 2 and using the fact that the $B + S + F = 1$, it follows that

$$\overline{CT\#}_{mix} = B \times \overline{CT\#}_b + S \times \overline{CT\#}_s + F \times \overline{CT\#}_f \quad (5)$$

Because this is a linear equation, it applies for both individual and mean values of the CT numbers.

Appendix 2

In a sense the four-equation four-unknown method may be considered to be an extension of the dual energy technique proposed by Cann et al.⁷ In their technique, a calibration phantom containing several different dipotassium hydrogen phosphate ($K_2HPO_4 - H_2O$) solutions is placed beneath the patient. The K_2HPO_4 solutions mimic bone in their attenuation of x-rays.⁹ CT

images are acquired at two energies and linear fits of mean CT number vs. mg/cc of K_2HPO_4 are determined at each energy. The linear fit equations are:

$$\overline{CT\#}(E_1) = g(E_1) \times [mg/cc] + i(E_1)$$

$$\overline{CT\#}(E_2) = g(E_2) \times [mg/cc] + i(E_2)$$

where

$g(E_1, E_2)$ are fitted slopes of the lines,

and

$i(E_1, E_2)$ are the fitted intercepts.

Solving these equations for the concentration (mg/cc) of the K_2HPO_4 , we obtain the Cann⁷ (Cann, C.E., personal communication, see text) equation

$$mg/cc = \frac{(\overline{CT\#}(E_1) - \overline{CT\#}(E_2)) - (i(E_1) - i(E_2))}{g(E_1) - g(E_2)}$$

The equivalent K_2HPO_4 concentration of the trabecular bone is determined by measuring its mean CT numbers at the two energies and substituting these two values ($\overline{CT\#}(E_1)$ and $\overline{CT\#}(E_2)$) into the equation.

Cann and Genant¹⁰ state that the K_2HPO_4 concentration that is determined with this method is essentially independent of the fat content in the bone marrow. This implies the concentration (mg/cc) is uniquely determined by the shift in measured CT number with energy and the presence of fat has a minimal effect on the magnitude of this shift (e.g. shift without fat [$\overline{CT\#}(E_1) - \overline{CT\#}(E_2)$] is approximately equal to shift with fat [$\overline{CT\#}(E_1)^* - \overline{CT\#}(E_2)^*$]).

In other words, Cann and Genant assume fat has about the same CT number at each energy and its presence will result in the equivalent decrease in the measured $\overline{CT\#}$ of a substance at the two energies

$$(\overline{CT\#}(E_1))^* = \overline{CT\#}(E_1) - y \text{ and } (\overline{CT\#}(E_2))^* = \overline{CT\#}(E_2) - y,$$

where y is the displacement in $\overline{CT\#}$ due to fat)

This is an approximation since the CT number of fat varies with energy. (In fact, because of the high concentration of hydrogen in fat, the CT number of fat actually increases as the kVp of the CT x-ray beam is increased, which is the opposite of the behavior of most other materials).

Consider two equal volume containers. One holds a mixture of bone or bone mimicking material (eg K_2HPO_4) and H_2O (or a soft tissue mimicking material). The second contains a mixture of bone, soft tissue, and fat materials. The volume of bone material is assumed to be the same in each container. From equation 5 of Appendix 1, the CT numbers of the mixtures in the containers are given by the equations

$$\overline{CT\#}_{no\ fat} = \overline{CT\#}_b \times B + \overline{CT\#}_t \times (1 - B)$$

and

$$\overline{CT\#}_{with\ fat} = \overline{CT\#}_b \times B + \overline{CT\#}_s \times (1 - B - F) + \overline{CT\#}_f \times F$$

where, as before, $\overline{CT\#}_b$, $\overline{CT\#}_s$, and $\overline{CT\#}_f$ are the CT numbers of bone, soft tissue, and fat, B is the volume fraction of bone and F is the volume fraction of fat.

From the above equations, we obtain the equation

$$\overline{CT\#}_{with\ fat} = \overline{CT\#}_{no\ fat} + F \times (\overline{CT\#}_f - \overline{CT\#}_s)$$

This equation holds at both energies, yielding the set of 4 equations as follows:

$$\overline{CT\#}_{no\ fat}(E_1) = g(E_1) \times [mg/cc] + i(E_1)$$

$$\overline{CT\#}_{no\ fat}(E_2) = g(E_2) \times [mg/cc] + i(E_2)$$

$$\overline{CT\#}_{with\ fat}(E_1) = \overline{CT\#}_{no\ fat}(E_1) + F \times [\overline{CT\#}_f(E_1) - \overline{CT\#}_s(E_1)]$$

$$\overline{CT\#}_{with\ fat}(E_2) = \overline{CT\#}_{no\ fat}(E_2) + F \times [\overline{CT\#}_f(E_2) - \overline{CT\#}_s(E_2)].$$