Multicomponent methods: evaluation of new and traditional soft tissue mineral models by in vivo neutron activation analysis[1–3]

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ABSTRACT

Background: Practical and accurate methods for quantifying the soft tissue mineral component of multicomponent fat-estimation models are needed.

Objectives: The aims were to develop a new complete model for estimating soft tissue minerals based on measured total body water (TBW) and extracellular water (ECW) and a simplified new model based on TBW measurements only and to compare these estimates with those determined with 2 traditional models (ie, the Brožek and Selinger models) and with criterion estimates based on in vivo neutron activation (IVNA) analysis.

Design: The subjects were 156 healthy adults and 50 patients with AIDS. Total body potassium, sodium, chlorine, and calcium were measured by IVNA; TBW by ^3H_2O or D_2O dilution; ECW by bromide dilution; and bone mineral by dual-energy X-ray absorptiometry.

Results: The mean (± SD) mass of total-body soft tissue minerals in healthy adults was 467 ± 62 g with the IVNA model, 492 ± 62 g with the new model, and 487 ± 59 g with the simplified new model. Compared with the IVNA model, the complete and simplified new models overestimated soft tissue minerals by 5.4% and 4.6% (both $P < 0.001$), respectively. In contrast, the Brožek and Selinger models overestimated overall mean soft tissue minerals by 35% and 99% (both $P < 0.001$), respectively. Overall results for soft tissue mineral prediction with the 2 new models were less satisfactory for the patients with AIDS, although the results were better than those with the traditional models.

Conclusions: The physiologically formulated complete new model for estimating soft tissue minerals provides the opportunity to upgrade the accuracy of current multicomponent models for estimating total body fat. *Am J Clin Nutr* 2002;76:968–74.

KEY WORDS Extracellular water, intracellular water, body composition, multicomponent methods, neutron activation analysis, soft tissue mineral, AIDS

INTRODUCTION

Early body-composition investigators introduced the 2-component model in which body mass is divided into fat and fat-free mass (ie, body mass = fat + fat-free mass) (1, 2). An important recent advance is the introduction of multicomponent models that partition body mass into ≥3 components (3). Because the addition of measured components usually reduces the number of applied assumptions, multicomponent models are often considered the criterion against which other methods of estimating total body fat are validated.

One important group of multicomponent models is based on body-volume measurements that are usually estimated by hydrodensitometry or air plethysmography (4, 5). Body-volume estimates are used in one term of the classical 2-component model (4, 5) that serves as the basis for this group of multicomponent models. The addition of an estimate of total body water (TBW) by isotope dilution allows the development of a 3-component model (1, 2). The 3-component model can then be extended to a 4-component model by adding an estimate of bone mineral by dual-energy X-ray absorptiometry (DXA) (3, 6). Three- and 4-component models are now widely applied in body-composition laboratories throughout the world. However, both the 3- and 4-component models do not include a discrete estimate of soft tissue mineral, a small but important molecular level component (7).

Soft tissue minerals consist largely of soluble minerals and electrolytes found in the extracellular and intracellular compartments of soft tissue. Although the mass of soft tissue minerals (≈400 g) is relatively small in adults, its contribution to body density should be considered because soft tissue minerals collectively have a higher density (3.317 g/cm^3) at normal body temperature than do each of the other components, including fat (0.900 g/cm^3), water (0.994 g/cm^3), protein (1.34 g/cm^3), and bone mineral (2.982 g/cm^3) (8).

There are currently only 3 in vitro cadaver studies that report estimates of total-body soft tissue minerals (9–11). On the basis of these in vitro studies, Brožek and Selinger developed 2 traditional models to predict total-body soft tissue mineral mass (1, 12). No previous studies have critically evaluated or challenged the 2 prevailing models of soft tissue minerals as applied in conventional

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Received March 15, 2001.

Accepted for publication October 22, 2001.

multicomponent-model methods (7, 13). Although total-body soft tissue mineral mass can be measured in vivo by delayed-γ in vivo neutron activation (IVNA) analysis, this method cannot be applied in most laboratories because of the complex instrumentation required and the radiation exposure that precludes use in some subject groups (14).

The aim of the present study was to advance a new physiologically formulated method of quantifying total-body soft tissue mineral mass. Our intent in developing this approach was to provide a practical means of estimating soft tissue mineral mass in vivo. We examined results provided by the new model and a simplified version of the new model along with the previously reported traditional models of Brožek and Selinger with the use of IVNA estimates as the criterion.

METHODS

Soft tissue mineral models

Three models are currently used to estimate soft tissue minerals: the IVNA, Brožek, and Selinger models. Each of these models is described below, as is a new model for estimating soft tissue minerals.

IVNA model

The established criterion method is to estimate soft tissue minerals separately by IVNA and whole-body counting. Total-body sodium (TBNa) and total-body calcium (TBCa) are measured with delayed-γ IVNA. Sodium is found as a cation in soft tissues and is also bound to the crystalline matrix of bone mineral (15, 16). Because the ratio of sodium to calcium in bone mineral is known (15), bone mineral sodium can be estimated from TBCa as 0.038 × TBCa. Sodium in soft tissues can then be calculated as the difference between TBNa and sodium in bone mineral. With the use of similar approaches, 6 main soft tissue minerals electrolytes (K^+, Na^+, Mg^{2+}, Cl^-, $H_2PO_4^-$, and HCO_3^-) can be calculated from 4 measurable elements (potassium, sodium, chlorine, and calcium) and then summed for total-body soft tissue minerals (Ms) mass (17, 18):

$$Ms = 2.76 \times TBK + TBNa + 1.43 \times TBCl - 0.038 \times TBCa \quad (1)$$

where Ms, TBK (total-body potassium), TBNa, TBCl (total-body chlorine), and TBCa are all in grams.

Brožek model

Total-body soft tissue minerals in this model are assumed to be present in a constant amount relative to bone mineral. According to 3 cadaver studies, it follows that 1000 g whole-body mineral will give rise to 819.3 g bone mineral plus 180.7 g mineral from nonosseous mineral (9–11). A corresponding model was thus developed by Brožek, which suggests a constant ratio of 0.221 between soft tissue minerals and bone mineral (both in g) (1):

$$Ms = 0.221 \times Mo \quad (2)$$

where Mo is bone mineral.

Selinger model

Selinger (12) assumed in this model that 1.02% of body mass (BM) is Ms with the corresponding equation:

$$Ms = 0.0102 \times BM \quad (3)$$

New model

All soft tissue minerals distribute within intracellular water (ICW) and extracellular water (ECW) compartments; thus, total-body soft tissue minerals can be expressed as follows:

$$Ms = \text{intracellular Ms} + \text{extracellular Ms} \quad (4)$$

In Equation *4*, intracellular Ms = $[Ms]_{ICW} \times ICW$ and extracellular Ms = $[Ms]_{ECW} \times ECW$, where $[Ms]_{ICW}$ and $[Ms]_{ECW}$ are the intracellular soft tissue minerals concentration and extracellular soft tissue mineral concentrations, respectively. Equation *4* can thus be converted to a cellular-level model for soft tissue minerals:

$$\begin{aligned} Ms &= [Ms]_{ICW} \times ICW + [Ms]_{ECW} \times ECW \\ &= [Ms]_{ICW} \times (TBW - ECW) + [Ms]_{ECW} \times ECW \\ &= [Ms]_{ICW} \times TBW - \{[Ms]_{ICW} - [Ms]_{ECW}\} \times ECW \end{aligned} \quad (5)$$

Equation *5* indicates that total-body Ms is determined by 4 factors: $[Ms]_{ICW}$, $[Ms]_{ECW}$, TBW, and ECW.

The intracellular fluid compartment is separated from extracellular fluid by a selectively permeable membrane. On the basis of limiting membrane effects and the Na^+:K^+ adenosinetriphosphatase (EC 3.6.1.3) pump, cation and anion concentrations across cell membranes are maintained stable. For example, the K^+ concentration of intracellular fluid is maintained at ≈5.943 g/kg H_2O (≈152 mmol/kg H_2O) and the Na^+ concentration of extracellular fluid is ≈3.312 g/kg H_2O (≈144 mmol/kg H_2O) (**Table 1**) (19, 20). Therefore, both $[Ms]_{ICW}$ and $[Ms]_{ECW}$ are maintained relatively stable at 16.168 g/kg H_2O and 9.543 g/kg H_2O, respectively (Table 1). The stability of cation and anion concentrations across cell membranes is also reflected by a relatively constant body fluid osmolality of ≈300 mOsmol/kg H_2O (20–22). According to Equation *5*, total-body soft tissue minerals can thus be estimated as follows:

$$Ms = 16.168 \times TBW - 6.625 \times ECW \quad (6)$$

where Ms is in g and both TBW and ECW are in kg.

Equation *6* requires an estimate of ECW, a measured compartment that is not always available to investigators. We therefore extended our model development by simplifying Equation *6* to a TBW-only version. Because ECW can be expressed as (ECW/ICW) × TBW/[1 + (ECW/ICW)], Equation *6* can be converted to the following equation:

$$Ms = \left(16.168 - 6.625 \times \frac{ECW/ICW}{1 + ECW/ICW}\right) \times TBW \quad (7)$$

We evaluated water distribution in a previous study and observed a mean (±SD) ratio of ECW to ICW of 0.97 ± 0.20 for adults: 0.82 ± 0.16 for healthy men and 1.07 ± 0.22 for healthy women (23).

A feature of Equation *7* is that relative changes in water distribution (ie, ECW/ICW) have only a small effect on estimates of soft tissue minerals. When the ratio of ECW to ICW increases by 50% (eg, from 0.8 to 1.20), soft tissue minerals decrease by only 5% (from 13.22 × TBW to 12.55 × TBW). Hence, although the ratio of ECW to ICW is variable between and within subjects, the effect of this variability on the total-body soft tissue minerals component is relatively small. Because the average magnitude of the ratio of ECW to ICW, as observed in our previous study, is 0.97 for healthy adults (23), Equation *7* can be simplified as follows:

$$Ms\ (g) = 12.9 \times TBW, \text{ or } Ms\ (kg) = 0.0129 \times TBW \quad (8)$$

TABLE 1
Electrolyte composition of the intracellular and extracellular fluids observed in healthy adult humans[1]

	Intracellular fluid		Extracellular fluid	
	Osmolality	Concentration	Osmolality	Concentration
	mOsmol/kg H_2O	*g/kg H_2O*	*mOsmol/kg H_2O*	*g/kg H_2O*
Cations				
K^+	152	5.943	4	0.156
Na^+	3	0.069	144	3.312
Ca^{2+}	4	0.080	3	0.060
Mg^{2+}	32	0.389	1.5	0.018
Anions				
Cl^-	5	0.178	114	4.047
$H_2PO_4^-$	93	9.021	2	0.194
HCO_3^-	8	0.488	28	1.708
SO_4^{2-}			1	0.048
Total	297	16.168	297.5	9.543

[1] Data adapted from references 19 and 20.

Both the complete and simplified versions of the new model were evaluated in the present study.

Experimental approach

IVNA model

All subjects completed IVNA and whole-body ^{40}K counting. Soft tissue mineral mass was calculated by using Equation *1* from measured TBK, TBNa, TBCl, and TBCa masses and served as the reference.

Brožek model

Bone mineral was measured by DXA, and Equation 2 was then used to estimate soft tissue minerals.

Selinger model

Soft tissue minerals were calculated from measured body mass by using Equation 3.

New model

The subjects completed tritium or deuterium dilution studies for TBW and a bromide-dilution study for ECW. Equations *6* and *8* were then applied to predict total-body soft tissue minerals.

Subjects

Healthy adult subjects and patients with AIDS were evaluated in the present study. Healthy adults were recruited from hospital staff and local residents. Each subject completed a medical examination that included routine blood studies. AIDS patients had varying degrees of body mass loss since the onset of their illness, although all were clinically stable at the time of the study. All study participants signed an informed consent form that was approved by the hospital's institutional review board.

Body-composition measurements

Consenting subjects were studied after an overnight fast. Body mass was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. Total-body contents of potassium, sodium, chlorine, and calcium were quantified by using the whole-body counting–IVNA facilities at Brookhaven National Laboratory (24). The precisions for elemental measurements are 1.5% for TBK, 2.5% for TBNa, 2.5% for TBCl, and 0.8% for TBCa (25).

Tritium space (^3H_2O; in L) or deuterium space (^2H_2O; in L) were measured at the Body Composition Unit of St Luke's–Roosevelt Hospital with precisions (CV) of 1.5% and 1.2%, respectively. The dilution space was then converted into kilograms TBW by correcting for nonaqueous hydrogen exchange and water density at 36 °C (TBW = dilution space × 0.96 × 0.994) (26).

Bromide-dilution space (sodium bromide, in L) was measured at the Body Composition Unit of St Luke's–Roosevelt Hospital with a precision of 1.4%. The dilution space was then converted into kilograms ECW by correcting for the weight fraction of water in plasma (0.94), the Gibbs-Donnan effect (0.95), and the penetration of bromide into the intracellular space of erythrocytes (0.90) (26).

The subjects were scanned with a whole-body DXA system (Lunar DPX with software version 3.6; Madison, WI) at peak energies of 40 and 70 keV. The DXA system software first divides pixels into bone mineral content and soft tissue compartments. Soft tissue is then further separated by system software into fat-free soft tissue and fat. The bone mineral content measured by DXA represents ashed bone. One gram of bone mineral yields 0.9582 g ash because labile components such as bound water and carbon dioxide are lost during heating (8). Bone mineral content was therefore converted to bone mineral (bone mineral = bone mineral content/0.9582). The precision of the DXA system used is 1.3% for bone mineral (8).

Statistical analysis

The results are expressed as group means ± SDs. Simple linear regression analysis was applied to describe the relation between soft tissue minerals measured by the IVNA model and those predicted by the other 4 models. The differences in estimates of soft tissue minerals between the IVNA model and the other 4 methods were related to the mean of the IVNA model and the method under examination, as described by Bland and Altman (27).

RESULTS

Physical characteristics and body composition

A total of 206 subjects were evaluated in 2 groups: healthy adults and patients with AIDS (**Table 2**). The 156 healthy adults

TABLE 2
Physical characteristics and body-composition results for the 2 subject groups[1]

	Healthy subjects (n = 3 M, 153 F)	AIDS patients (n = 17 M, 33 F)
Age (y)	44.3 ± 10.7	39.6 ± 10.5[2]
Body mass (kg)	91.0 ± 11.2	59.4 ± 8.3[3]
Height (m)	1.63 ± 0.07	1.64 ± 0.10
BMI (kg/m^2)	34.2 ± 4.0	22.0 ± 2.3[3]
Body fat (%)[4]	43.9 ± 5.4	23.5 ± 10.7[3]
Mo (kg)	2.712 ± 0.358	2.387 ± 0.442[3]
TBK (g)	120.4 ± 17.9	102.9 ± 27.0[3]
TBNa (g)	71.1 ± 7.5	66.7 ± 12.0[5]
TBCl (g)	63.4 ± 10.4	55.2 ± 10.6[3]
TBCa (g)	718 ± 96	724 ± 138
TBW (kg)	37.7 ± 4.6	33.3 ± 8.0[3]
ECW (kg)	17.8 ± 2.6	14.8 ± 3.1[3]
Ms (g)	467 ± 62	402 ± 93[3]
Ms/Mo (kg/kg)	0.174 ± 0.018	0.170 ± 0.031
Ms/BM (kg/kg)	0.0052 ± 0.0005	0.0067 ± 0.0010[3]

[1] $\bar{x}$ ± SD. ECW, extracellular water measured by bromide dilution; Mo, bone mineral by dual-energy X-ray absorptiometry; Ms, total-body soft tissue minerals by in vivo neutron activation model (Equation *1* in Methods); TBCa, total-body calcium by delayed-γ in vivo neutron activation; TBCl, total-body chlorine measured by delayed-γ in vivo neutron activation; TBK, total-body potassium measured by whole-body counting; TBNa, total-body sodium measured by delayed-γ in vivo neutron activation; and TBW, total-body water measured by ^2H_2O or ^3H_2O dilution methods.

[2,3,5] Significantly different from healthy subjects (Student's t test): [2] $P \leq 0.01$, [3] $P \leq 0.001$, [5] $P \leq 0.05$.

[4] Measured by dual-energy X-ray absorptiometry.

ranged in age from 25 to 74 y, in body mass from 55.0 to 116.1 kg, and in body mass index (BMI; in kg/m^2) from 21.7 to 50.1. The 50 patients with AIDS ranged in age from 22 to 66 y, in body mass from 44.7 to 76.3 kg, and in BMI from 17.6 to 28.8. The healthy adults were older, were heavier, and had a greater BMI and percentage body fat than did the AIDS patients (all $P < 0.01$–0.001). The body-composition results for the 2 groups are presented in Table 2. TBK, TBNa, TBCl, bone mineral, TBW, and ECW were greater in the healthy adults than in the AIDS patients (all $P \leq 0.05$), although there was no significant difference in TBCa between the 2 groups.

Total-body soft tissue mineral measurements

IVNA model

Total-body soft tissue minerals determined with the IVNA model were 467 ± 62 g in the healthy subjects and 402 ± 93 g in the AIDS patients (**Table 3**).

New model

The total-body soft tissue mineral component predicted by the new model (ie, Equation *6*) was 492 ± 62 g in the healthy subjects (Table 3), an average overestimate of 25 g, or 5.4% ($P < 0.001$). The estimates of soft tissue minerals by the new model were highly correlated with estimates of soft tissue minerals by the IVNA model in the healthy subjects:

$$\text{Ms by IVNA} = 0.818 \times \text{Ms by new model} + 64.7 \quad (9)$$

where $r = 0.82$, $P < 0.001$, and SEE = 35.3 g. Bland-Altman analysis (27) indicated that the differences between estimates of soft tissue minerals by the IVNA and the new models were not significantly associated with the mean soft tissue mineral estimates by the 2 models ($r = 0.008$, $P > 0.05$) (**Figure 1**).

TABLE 3
Total-body soft tissue minerals assessed by the five models[1]

	Healthy subjects	AIDS patients
IVNA model (g)	467 ± 62	402 ± 93
New model (g)	492 ± 62	441 ± 112
New/IVNA model	1.054 ± 0.081	1.097 ± 0.079
Simplified new model (g)	487 ± 59	430 ± 103
Simplified/IVNA model	1.046 ± 0.076	1.070 ± 0.066
Ms by Brožek model (g)	625 ± 83	550 ± 102
Brožek/IVNA model	1.346 ± 0.148	1.401 ± 0.258
Selinger model (g)	928 ± 114	606 ± 84
Selinger/IVNA model	1.987 ± 0.195	1.507 ± 0.223

[1] $\bar{x}$ ± SD. Soft tissue mineral prediction models (equations in Methods): Brožek model (Equation *2*), IVNA model by in vivo neutron activation (Equation *1*), new model (Equation *6*), Selinger model (Equation *3*), and simplified new model (Equation *8*).

The total-body soft tissue mineral component predicted by the new model was 441 ± 112 g in the AIDS patients (Table 3), an average overestimate of 39 g or 9.7% ($P < 0.001$). Bland-Altman analysis indicated that the differences between estimates of soft tissue minerals by the IVNA and new models were significantly associated with the mean estimates of soft tissue minerals by the 2 models ($r = 0.60$, $P < 0.05$)

Simplified new model

The total-body soft tissue mineral component predicted by the simplified new model (ie, equation 8) was 487 ± 59 g for the healthy subjects (Table 3). Compared with IVNA-measured soft tissue minerals, the simplified model overestimated soft tissue minerals by an average of 20 g, or 4.6% ($P < 0.001$). The estimates of soft tissue minerals by the simplified model and of those by the IVNA model were highly correlated in the healthy subjects:

$$\text{Ms by IVNA} = 0.882 \times \text{Ms by simplified model} + 37.9 \quad (10)$$

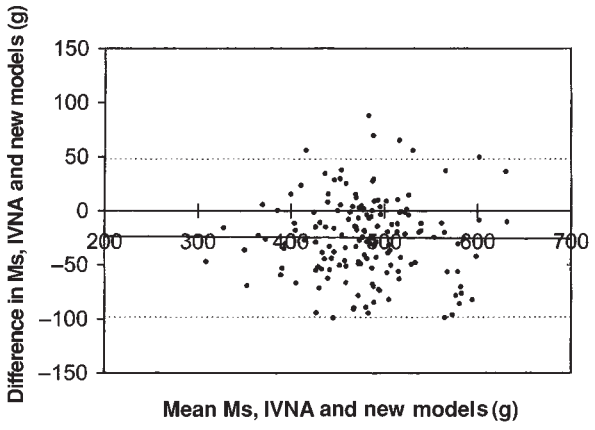

FIGURE 1. Difference between estimates of soft tissue minerals (Ms) by in vivo neutron activation (IVNA) and the complete new model plotted against the corresponding mean Ms values provided by IVNA and the new model in 156 healthy adult subjects. $y = -0.005x - 22.3$ ($r = 0.008$, $P > 0.05$). The dashed lines indicate 95% confidence limits ($\bar{x} \pm 2$SD).

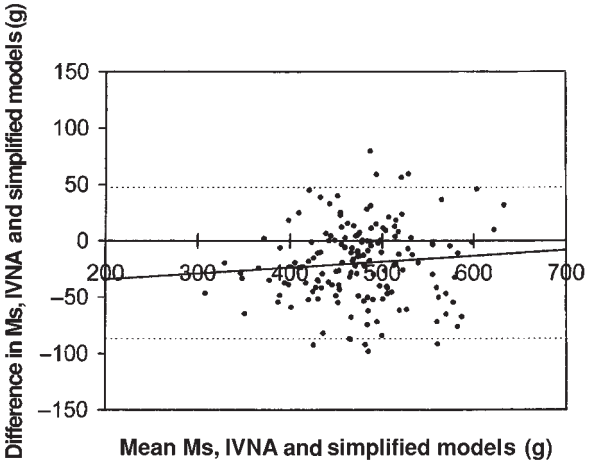

FIGURE 2. Difference between estimates of soft tissue minerals (Ms) by in vivo neutron activation (IVNA) and the simplified new model plotted against the corresponding mean Ms values provided by IVNA and the simplified new model in 156 healthy adult subjects. $y = 0.045x - 41.6$ ($r = 0.075$, $P > 0.05$). The dashed lines indicate 95% confidence limits ($\bar{x} \pm 2$SD).

where $r = 0.84$, $P < 0.001$, and SEE = 32.0 g. Bland-Altman analysis indicated that the differences between estimates of soft tissue minerals by IVNA and the simplified models were not significantly associated with the mean estimates of soft tissue minerals by these 2 models ($r = 0.075$, $P > 0.05$) (**Figure 2**).

The total-body soft tissue mineral component predicted by the simplified new model (ie, Equation *8*) was 430 ± 103 g in the AIDS patients (Table 3). Compared with IVNA-estimated soft tissue minerals, the simplified model overestimated soft tissue minerals by an average of 28 g, or 7.0% ($P < 0.001$). Bland-Altman analysis indicated that the differences between estimates of soft tissue minerals by IVNA and the simplified models were significantly associated with the mean estimates of soft tissue minerals by the 2 models ($r = 0.40$, $P < 0.05$).

Brožek and Selinger models

Total-body soft tissue minerals predicted by the Brožek and Selinger models are presented in Table 3. Compared with the IVNA model, the Brožek model overestimated soft tissue minerals by an average of 35% for the healthy subjects and by 40% for the AIDS patients, whereas the Selinger model overestimated soft tissue minerals by an average of 99% for the adult subjects and by 51% for the AIDS patients (all $P < 0.001$).

Although estimates of soft tissue minerals by the Brožek and Selinger models were correlated with estimates of soft tissue minerals by the IVNA model in the healthy subjects, the *r* values were much lower and the SEEs were much larger than those with Equations *9* and *10*:

$$\text{Ms by IVNA} = 0.501 \times \text{Ms by Brožek model} + 154.2 \quad (11)$$

where $r = 0.67$, $P < 0.001$, and SEE = 61.9 g.

$$\text{Ms by IVNA} = 0.382 \times \text{Ms by Selinger model} + 112.8 \quad (12)$$

where $r = 0.70$, $P < 0.001$, and SEE = 81.2 g.

Bland-Altman analysis indicated that the differences between estimates of soft tissue minerals by the IVNA and Brožek and IVNA and Selinger models were significantly associated with the corresponding mean estimates of soft tissue minerals.

DISCUSSION

The relatively small and chemically diverse soft tissue mineral component is not easily quantified in vivo, even at specialized laboratories that measure body composition. In the present study we derived a physiologically based soft tissue mineral model along with a simplified form and we showed good agreement with the IVNA criterion approach in healthy subjects. These supportive findings thus provide the opportunity to upgrade current body volume (BV)–based 4-component models. Accordingly, simultaneous body mass (in kg) and body volume (in L) models can be written as follows:

$$\text{BM} = \text{fat} + \text{TBW} + \text{protein} + \text{Mo} + \text{Ms} \quad (13)$$

$$\text{BV} = \text{fat}/0.9007 + \text{TBW}/0.9937 + \text{protein}/1.34 + \text{Mo}/2.982 + \text{Ms}/3.317 \quad (14)$$

In resolving Equations *13* and *14*, a 5-component total-body fat model can be derived as follows:

$$\text{Fat} = 2.748 \times \text{BV} - 0.715 \times \text{TBW} + 1.129 \times \text{Mo} + 1.222 \times \text{Ms} - 2.051 \times \text{BM} \quad (15)$$

Rather than a single total mineral component, this 5-component model accounts for both the bone mineral and soft tissue minerals components. Whereas Equation *15* may reduce model error by accounting for the 2 separate mineral components, an increase in measurement error can be anticipated by estimating ECW, which is needed to calculate soft tissue minerals.

IVNA criterion model

In the present study we selected IVNA-estimated soft tissue minerals as the criterion because measurement precision is high for total-body potassium, sodium, chloride, and calcium. Furthermore, the models used incorporate a limited number of assumptions that are formulated on physicochemical principles. The error associated with measurement of the IVNA model components (σ_{Ms}) can be estimated for the healthy subjects by assuming an average body composition as shown in Table 2 and measurement precisions as stated in Methods. Accordingly,

$$(\sigma_{Ms})^2 = (2.76 \times 120.4 \times 0.015)^2 + (1 \times 71.1 \times 0.025)^2 + (1.43 \times 63.4 \times 0.025)^2 + (0.034 \times 718 \times 0.008)^2 \quad (16)$$

The propagated soft tissue mineral measurement error for the healthy subjects was 5.8 g. Because IVNA systems are not widely available and expose subjects to ionizing radiation, the IVNA model can only be used as in the present study to evaluate other methods for predicting soft tissue minerals.

New model

The new soft tissue mineral model has a firm physiologic basis: all soft tissue minerals are distributed within the ICW and ECW compartments, and the mineral and electrolyte concentrations and osmolarity of intracellular and extracellular fluids are highly regulated. Model error, therefore, should be small unless subjects have clinically significant electrolyte and mineral disturbances.

According to Equation *6*, the new model has 2 sources of model error, the assumed values of 16.168 and 6.625 g/kg for the concentrations of intracellular and extracellular soft tissue minerals, respectively. In addition, there are 2 sources of measurement error, TBW and ECW estimations by dilution methods. The error caused by measurement of TBW and ECW can be evaluated in the healthy subjects by assuming an average body composition as shown in

Table 2 and by assuming measurement precisions as described in Methods.

$$(\sigma_{Ms})^2 = (16.168 \times 37.7 \times 0.012)^2 + (6.625 \times 17.8 \times 0.014)^2 \quad (17)$$

The propagated measurement error of the new model was 7.5 g, which is minimally larger than that of 5.8 g for the IVNA-criterion method.

Compared with IVNA-measured soft tissue minerals, the new model overestimated soft tissue minerals by an average of 25 g in the healthy subjects. When the new soft tissue mineral model was applied in a 5-component model, according to Equation *15*, it introduced a mean error of 0.03 kg in total-body fat. This small error can be neglected in most circumstances. The new soft tissue mineral model for the aforementioned reasons provides an improved means of estimating total-body fat as part of a 5-component model.

The new complete model (ie, Equation *6*) requires bromide dilution, and this technique may not be available at some laboratories. Assuming that water distribution is constant (ie, ECW/ICW = 0.97), a simplified model (ie, Equation *8*) was developed. Compared with the complete model, the simplified version has a smaller measurement error in the healthy subjects: $\sigma_{Ms} = 12.9 \times 37.7 \times 0.012 = 5.8$ g. The simplified version of the new model can provide an improved estimate of soft tissue minerals for the 4-component model. Inserting Equation *8* into Equation *15*, a 4-component model can be derived as follows:

$$\text{Fat} = 2.748 \times \text{BV} - 0.699 \times \text{TBW} + 1.129 \times \text{Mo} - 2.051 \times \text{BM} \quad (18)$$

Equation *18* is similar to other 4-component models, including the Lohman-Selinger model (28) and the Baumgartner model (13).

Limitations of new model

Although the new model can provide reasonable estimates of soft tissue mineral mass for healthy adults, note should be made of some model limitations. One concern about the complete model is that the ECW space depends on the selected tracer. In addition to bromide dilution, as used in the present study, there are several other radioactive and nonradioactive materials that can be used to determine ECW. However, not all of these materials yield the same ECW dilution spaces. For example, the dilution spaces of SO_4^{2-} and inulin are smaller than those measured by bromide, although both have been used as measures of extracellular fluid (29, 30). When sulfate dilution is applied, for instance, the estimate is smaller than that from bromide dilution; therefore, Equation *6* will provide a higher estimate of total-body soft tissue minerals. Our validation study applies only to bromide ECW estimates; thus, other ECW methods need to be evaluated.

When the new model was applied in AIDS patients, as shown in Table 3, the complete and simplified versions of the new model overestimated soft tissue minerals by an average of 9.7% and 7.0%, respectively. Bland-Altman analysis also indicated a significant bias in the prediction of soft tissue minerals relative to IVNA for both the complete and simplified versions of the new model. Most of our AIDS patients had experienced clinically significant weight loss and acute medical conditions. The new models, based on assumed stable mineral-electrolyte distributions and concentrations, may thus be less accurate when applied outside of the healthy adult population. Nevertheless, the results of the new model were still much better than those provided by the 2 traditional models for estimating soft tissue minerals.

Traditional models

Two traditional models are currently applied to estimate whole-body soft tissue mineral mass. The Brožek model has a measurement error similar to that for the complete new soft tissue mineral model and IVNA model: $\sigma_{Ms} = 0.231 \times 2712 \times 0.0128 = 8.0$ g. The measurement error of the Selinger model is very small, $\sigma_{Ms} = 0.0102 \times 100 = 1.0$ g. However, neither the Brožek nor the Selinger model derive theoretical support because there is no plausible reason why the relation between soft tissue minerals and bone mineral and between soft tissue minerals and body mass should form simple stable ratios. In the adult subjects, the ratio of soft tissue minerals to bone mineral is 0.174 ± 0.018 (CV: 10.3%), the ratio of soft tissue minerals to body mass is 0.0052 ± 0.0005 (CV: 9.6%) (Table 2), and the ratio of soft tissue minerals to fat-free mass is 0.0095 ± 0.0010 (CV: 10.5%). These results indicate that all 3 ratios are highly variable.

For these collective reasons, it is not surprising that the Brožek model overestimated soft tissue minerals in the healthy subjects by an average of ≈160 g. When estimates of soft tissue minerals by the Brožek model were applied as part of a 5-component model, according to Equation *15*, it overestimated total body fat by 0.2 kg. The Selinger model overestimated soft tissue minerals by ≈460 g and overestimated total body fat by ≈0.5 kg when applied as part of a 5-component model.

Conclusions

In the present study we applied physiologic principals and observed mineral and electrolyte distributions in deriving a new model for estimating soft tissue minerals. When incorporated into the traditional body volume–based 4-component model, ≥5 components of biological interest can be derived, and improved estimates of soft tissue minerals can be obtained. In contrast, model error is introduced into the traditional 4-component model when the Brožek or Selinger model is applied for estimating total body fat, although the magnitude of this error is <0.5 kg. The present study provides new insights into derived multicomponent models and suggests new and potentially improved 4- and 5-component model equations.

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