Total body protein: a new cellular level mass and distribution prediction model\textsuperscript{1–3}

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ABSTRACT

Background: Protein is an important body component, and the presently accepted criterion method for estimating total body protein (TBPro) mass—in vivo neutron activation (IVNA) analysis—is unavailable to most investigators and is associated with moderate radiation exposure.

Objective: The objective was to derive a theoretical cellular level TBPro mass and distribution model formulated on measured total body potassium, total body water, and bone mineral and to evaluate the new model with the IVNA method as the criterion.

Design: The new model was developed on the basis of a combination of theoretical equations and empirically derived coefficients. TBPro mass estimates with the new model were evaluated in healthy women \((n = 183)\) and men \((n = 24)\) and in men with AIDS \((n = 84)\). Total body nitrogen was measured by IVNA, total body potassium by whole-body \(^{40}\)K counting, total body water by tritium dilution, and bone mineral by dual-energy X-ray absorptiometry.

Results: The group mean \((\pm SD)\) TBPro mass estimates in healthy women and men with AIDS \((8.2 \pm 0.9, 11.0 \pm 1.8,\) and \(10.5 \pm 1.1 \text{ kg},\) respectively) with the new model were similar to IVNA criterion estimates \((8.9 \pm 0.9, 11.1 \pm 1.6,\) and \(10.9 \pm 1.2 \text{ kg},\) respectively). TBPro mass estimates with the new model correlated highly with the IVNA estimates in all subjects combined \((r = 0.92, P < 0.001)\). The new model suggests that the composite TBPro mass within each group consists mainly of cellular protein \((75–79\%)\) and, to a lesser extent, protein in extracellular solids \((19–23\%)\) and extracellular fluid \((\approx 2\%)\).


KEY WORDS Body composition, nutritional assessment, total body nitrogen, total body potassium, total body water, whole-body counting

INTRODUCTION

Protein is a functionally important component at the molecular level of body composition. Protein mass in healthy adults is relatively large, representing 10.6 kg, or 15.1%, of body mass in the reference man \((1)\). The actual amount of protein found in living humans is based on 2 study sources, in vivo neutron activation (IVNA) and non-IVNA methods \((2, 3)\).

The chemical formula for protein is assumed to be \(\text{C}_{105}\text{H}_{159}\text{N}_{32}\text{O}_{32}\text{S}_{0.7}\) with a ratio of nitrogen to protein of 0.16. Assuming that all body nitrogen is incorporated into protein, a total body protein (TBPro) model that can be measured by IVNA was derived from total body nitrogen (TBN) \((5, 6)\):

\[
\text{TBPro}_{(\text{IVNA})} = \text{TBN}/0.16 = 6.25 \times \text{TBN} \tag{1}
\]

This method is now considered the criterion for TBPro measurement, and cadaver validations were reported by Knight et al \((7)\). However, IVNA systems are costly to construct and expose subjects to ionizing radiation \((\approx 0.26 \text{ mSv})\). Accordingly, the number of evaluated healthy subjects is relatively small \((\approx 500)\).

The importance of protein in nutritional and physiologic research has led to alternative non-IVNA measurement methods, including model and empirical approaches. The model approach, based on measurements of TBN and total body potassium (TBK), provides estimates of TBPro and protein distribution \((8, 9)\). Although an innovative advance at the time, the models reported by Burkinshaw et al \((8)\) and Cohn et al \((9)\) were later shown to have many theoretical limitations and, in some cases, were inaccurate \((10, 11)\). James et al \((12)\) subsequently reported another TBN-TBK model for estimating cellular and collagen proteins. Fuller et al \((13)\) recently suggested TBPro models based on a 4-compartment approach or dual-energy X-ray absorptiometry (DXA) estimations. However, none of these earlier models were evaluated with IVNA as the criterion.

Empirical TBPro prediction formulas were developed by using anthropometry or total body water (TBW) as the main predictors \((2, 14)\). Ellis et al \((2)\) reported a high correlation between TBPro and TBK. Using IVNA to measure TBN as the criterion, these authors derived empirical TBPro prediction equations based on TBK measured with the whole-body \(^{40}\)K\textsuperscript{2}

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counting method. We modified the form and units (TBPro in kg and TBK in mmol) of the equations to be consistent with those in the present study.

For healthy men: 
\[
\text{TBPro}_{\text{Ellis et al}} = 0.00248 \times \text{TBK} + 2.54
\]
where \( r = 0.87, P < 0.05, \) and SEE = 0.74 kg.

For healthy women: 
\[
\text{TBPro}_{\text{Ellis et al}} = 0.00317 \times \text{TBK} + 0.95
\]
where \( r = 0.79, P < 0.05, \) and SEE = 0.79 kg.

Equations 2 and 3 show that TBK is a good predictor of TBPro, although there are no available theoretical models that provide a basis for this empirical association.

In the present study we derived a theoretical model linking protein mass and distribution with the cellular body-composition level. Available human data are then used to fit the model with empirical coefficients that require 3 estimates: TBK, TBW, and level. Available human data are then used to fit the model with empirical association.

TBPro, although there are no available theoretical models that provide a basis for this empirical association.

Almost all body potassium exists in ICF and ECF and the intracellular and extracellular potassium concentrations are relatively constant at 152 and 4 mmol/kg H2O, respectively (20). The ICW can thus be calculated from TBK and TBW (17, 21) via the following simultaneous equations:

\[
\text{TBK} = 152 \times \text{ICW} + 4 \times \text{ECW}
\]
\[
\text{TBW} = \text{ICW} + \text{ECW}
\]
where TBK and TBW are in mmol and kg, respectively. Resolving these simultaneous equations, ICW and ECW can be calculated if TBK and TBW are known:

\[
\text{ICW} = (\text{TBK} - 4 \times \text{TBW})/148
\]
\[
\text{ECW} = (152 \times \text{TBW} - \text{TBK})/148
\]
By combining Equations 7 and 10, BCM protein can be expressed as a function of TBK and TBW:

\[
\text{BCM protein} = 0.3838 \times (\text{TBK} - 4 \times \text{TBW})/148
\]
\[
= 0.00259 \times \text{TBK} - 0.0104 \times \text{TBW}
\]

Protein in extracellular fluid

The ECF is a nonmetabolizing fluid that surrounds cells and provides a medium for gas exchange, transfer of nutrients, and excretion of metabolic end products. ECF consists of ECW, a small amount of protein, and ECF minerals. ECF protein can be calculated as follows:

\[
\text{ECF protein} = \text{ECW/0.98} - (\text{ECW + ECF minerals})
\]

As previously reported, ECF can be expressed as ECW/0.98, where 0.98 is the mean hydration of ECF (17). Our recent study indicated that ECF minerals are a function of ECW and ECF minerals = 0.009543 \times ECW, where 0.009543 is ECF mineral concentration (in kg/kg H2O) (18). Equation 13 can thus be converted to

\[
\text{ECF protein} = \text{ECW/0.98 - (ECW + 0.009543 \times ECW)}
\]
\[
= 0.01087 \times \text{ECW}
\]

By combining Equations 11 and 14, ECF protein can be calculated as follows:

\[
\text{ECF protein} = 0.01087 \times (152 \times \text{TBW} - \text{TBK})/148
\]
\[
= 0.0112 \times \text{TBW} - 0.000073 \times \text{TBK}
\]

Protein in extracellular solids

The ECS compartment consists of 2 parts: organic and inorganic. Organic ECS include 3 types of protein (collagen, reticular, and elastic), whereas the inorganic ECS of bone mineral includes calcium hydroxyapatite as the major constituent. ECS are distributed in several tissues and organs, including cortical and trabecular bone, cartilage, periarticular tissue, tendons, and fascia. In the reference man, the ECS protein is 2.08 kg (ie, 1.0 kg in cortical bone, 0.24 kg in trabecular bone, 0.18 kg in cartilage, 0.14 kg in periarticular tissue, and 0.52 kg in tendons and fascia), and the ECS bone mineral content is 2.84 kg (ie, 2.2 kg in cortical bone, 0.50 kg in trabecular bone, 0.045 kg in cartilage, 0.037 kg in periarticular tissue, and 0.057 kg in tendons and fascia) (1). Assuming that the ratio of ECS
protein to bone mineral (i.e., 2.08/2.84 = 0.732) is relatively stable across subjects, the ECS protein compartment can be predicted as follows:

\[ \text{ECS protein} = 0.732 \times \text{bone mineral} \]  \hfill (16)

**Total body protein mass**

By inserting Equations 12, 15, and 16 into Equation 5, TBPro mass can be calculated as follows:

\[
\text{TBPro}_{\text{new model}} = (0.00259 \times \text{TBK} - 0.0104 \times \text{TBW}) \\
+ (0.0112 \times \text{TBW} - 0.000073 \times \text{TBK}) + 0.732 \\
\times \text{bone mineral} = 0.00252 \times \text{TBK} + 0.0008 \times \text{TBW} \\
+ 0.732 \times \text{bone mineral} \]  \hfill (17)

where TBPro, TBW, and bone mineral are in kg, and TBK is in mmol. Because the contribution of the TBW term to Equation 17 is very small, only 0.03 kg protein for the 42 kg TBW in the reference man, the TBPro prediction model can be simplified to the following:

\[
\text{TBPro}_{\text{new model}} = 0.00252 \times \text{TBK} + 0.732 \times \text{bone mineral} \]  \hfill (18)

**Experimental approach**

The subjects completed prompt-\(\gamma\) IVNA, whole-body \(^{40}\text{K}\) counting, tritium-labeled water dilution, and DXA studies. The completed evaluations were then used to estimate TBPro mass and distribution according to the IVNA model and new models.

**Subjects**

The subject pool consisted of healthy adults and men with AIDS. The rationale for inclusion of patients with AIDS and body weight loss was 2-fold: it provided the opportunity to examine the new TBPro model in clinical patients, and body weight loss might show limitations of the new TBPro model that are not evident in healthy subjects with a normal body weight.

The ethnically mixed healthy subjects were recruited in the New York (St Luke’s–Roosevelt Hospital and Winthrop University Hospital) and Boston (Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging) areas. Each subject in the healthy group completed a medical history, a physical examination, and routine screening blood studies to exclude the presence of underlying diseases. The men with AIDS were recruited from among patients with nutritional disorders and weight loss cared for by physicians at the St Luke’s–Roosevelt Hospital in New York City. The patients were ambulatory and afebrile and met the Centers for Disease Control criteria for AIDS. The study participants signed an informed consent form that was approved by the Institutional Review Boards of St Luke’s–Roosevelt Hospital, Winthrop University Hospital, and the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging. Some subject data came from our earlier unrelated body-composition studies (22, 23).

**Body-composition measurements**

Consenting subjects were studied after an overnight fast. Body weight was measured to the nearest 0.1 kg (Weight Tronix, New York) and height to the nearest 0.5 cm with the use of a stadiometer (Holtain, Crosswell, United Kingdom).

Total body nitrogen was determined by prompt-\(\gamma\) IVNA at Brookhaven National Laboratory with a precision (CV) of 2.7% (24). TBK was calculated as 40 K/0.000118. The tritium-labeled water dilution volume, in liters, was measured at Brookhaven National Laboratory with a precision of 1.5%. The tritium dilution volume was then converted into TBW mass by correcting nonaqueous hydrogen exchange and water density at 36°C (TBW = \(\text{H}_2\text{O} \) dilution volume \( \times 0.96 \times 0.994 \)) (26). Total-body bone mineral was quantified at the 3 evaluation centers by whole-body DXA (Lunar DPX, Madison, WI). The estimated precision is 1.28% for bone mineral (27).

**Statistical methods**

Results are expressed as group means ± SDs unless otherwise noted. Simple linear regression analysis was applied to describe the relation between TBPro by IVNA and TBPro predicted by the new model. Mean differences between TBPro by IVNA and TBPro predicted by the new model among the 3 subject groups were evaluated for statistical significance by analysis of variance. \(P \leq 0.05\) was considered statistically significant. In Tables 1 and 3, a Bonferroni adjustment to the significance level was made. The differences in TBPro between IVNA and the new model were related to the mean of the 2 methods as described by Bland and Altman (28) to evaluate bias. Statistical calculations were carried out by using Microsoft EXCEEL (Redmond, WA) and SPSS version 10 for WINDOWS (SPSS Inc, Chicago).

### Table 1

Baseline characteristics and body composition of the 3 subject groups

<table>
<thead>
<tr>
<th>Subject Group</th>
<th>Healthy women (n = 183)</th>
<th>Healthy men (n = 24)</th>
<th>Men with AIDS (n = 84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>50.3 ± 12.8</td>
<td>49.3 ± 17.6</td>
<td>39.7 ± 9.1</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>64.3 ± 7.9(^a)</td>
<td>71.3 ± 9.5</td>
<td>65.5 ± 6.6(^a)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.64 ± 0.06(^a)</td>
<td>1.73 ± 0.09</td>
<td>1.75 ± 0.05</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>23.9 ± 2.8</td>
<td>23.7 ± 2.0</td>
<td>21.5 ± 2.1(^a)</td>
</tr>
<tr>
<td>TBK (kg)</td>
<td>1.42 ± 0.15(^a)</td>
<td>1.77 ± 0.26</td>
<td>1.75 ± 0.19</td>
</tr>
<tr>
<td>TBW (mmol)</td>
<td>2485 ± 281(^a)</td>
<td>3531 ± 391</td>
<td>3340 ± 396</td>
</tr>
<tr>
<td>TBW (kg)</td>
<td>31.7 ± 3.11(^a)</td>
<td>41.1 ± 6.2</td>
<td>41.2 ± 4.5</td>
</tr>
<tr>
<td>Bone mineral (kg)(^a)</td>
<td>2.62 ± 0.42(^a)</td>
<td>2.85 ± 0.54</td>
<td>2.90 ± 0.30</td>
</tr>
<tr>
<td>TBPro (kg)</td>
<td>8.9 ± 0.9(^a)</td>
<td>11.1 ± 1.6</td>
<td>10.9 ± 1.2</td>
</tr>
<tr>
<td>By IVNA(^a)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By new model(^a)</td>
<td>8.2 ± 0.9(^a)</td>
<td>11.0 ± 1.8</td>
<td>10.5 ± 1.1</td>
</tr>
</tbody>
</table>

\(^{a}\) \= SD. IVNA, in vivo neutron activation; TBK, total body potassium measured by whole-body \(^{40}\text{K}\) counting; TBN, total body nitrogen measured by prompt-\(\gamma\) in vivo neutron activation analysis; TBPro, total body protein; TBW, total body water measured by \(\text{H}_2\text{O}\) dilution.

Significantly different from healthy men (Student’s \(t\) test with Bonferroni adjustment): \(^{P} P < 0.02, {P} P < 0.002, {P} P < 0.000118\).

\(^{a}\) Measured by dual-energy X-ray absorptiometry (22).

\(^{a}\) TBPro (kg) = 6.25 × TBN (kg).

\(^{a}\) TBPro (kg) = 0.00252 × TBK (mmol) + 0.732 × bone mineral (kg).
RESULTS

Subject characteristics

A total of 291 adult subjects (183 healthy women, 24 healthy men, and 84 men with AIDS) were evaluated in the study (Table 1). The healthy women ranged in age from 23 to 81 y, in body mass from 48.0 to 82.0 kg, and in body mass index (in kg/m²) from 18.4 to 29.8. The healthy men ranged in age from 25 to 78 y, body mass from 57.6 to 89.1 kg, and body mass index from 20.2 to 28.4. The men with AIDS ranged in age from 22 to 62 y, in body mass from 46.6 to 77.2 kg, and in body mass index from 16.7 to 25.9.

There were significant differences between healthy women and healthy men in all measures (P < 0.01–0.001), except age and body mass index (Table 1). The men with AIDS weighed on average 5.8 ± 7.4 kg (P = 0.009) less than the healthy men. There were no significant differences between the 2 groups of men in TBN, TBK, TBW, or bone mineral (Table 1; all P > 0.05).

Correlations between TBPro and TBK

There were good correlations between TBPro (kg) by IVNA and TBK (mmol) in all 3 groups.

Healthy women: \(\text{TBPro}_{(IVNA)} = 0.00250 \times \text{TBK} + 2.79 \) (19)

where \(r = 0.76, P < 0.001,\) and SEE = 0.60 kg.

Healthy men: \(\text{TBPro}_{(IVNA)} = 0.00240 \times \text{TBK} + 2.63 \) (20)

where \(r = 0.89, P < 0.001,\) and SEE = 0.75 kg.

Men with AIDS: \(\text{TBPro}_{(IVNA)} = 0.00250 \times \text{TBK} + 2.56 \) (21)

where \(r = 0.85, P < 0.001,\) and SEE = 0.63 kg.

The slopes and intercepts of these equations did not differ significantly by analysis of variance, and a single prediction equation was calculated for all of the subjects (\(n = 291\)).

\(\text{TBPro}_{(IVNA)} = 0.00240 \times \text{TBK} + 2.96 \) (22)

where \(r = 0.91, P < 0.001,\) and SEE = 0.62 kg (Figure 1).

Total body protein

IVNA model

TBPro mass measured by IVNA was 8.9 ± 0.9 kg in the healthy women, 11.1 ± 1.6 kg in the healthy men, and 10.9 ± 1.2 kg in the men with AIDS (Table 1).

New model

There were moderate-to-high correlations between TBPro by IVNA and the new model in all 3 groups (\(r = 0.80\) for healthy women, 0.90 for healthy men, and 0.85 for men with AIDS; all \(P < 0.001\)). TBPro by IVNA was also highly correlated with estimates of TBPro by the new model when all of the subjects were combined in one group (\(r = 0.92\)) (Table 2). Compared with IVNA, the new model on average underestimated TBPro by 7.6% for the healthy women, 10% for the healthy men, and 3.5% for the men with AIDS (all \(P < 0.001\)). Bland-Altman analysis indicated that the differences between TBPro by IVNA and the new model were not significantly correlated with the mean TBPro estimates by the 2 models for the healthy women (\(r = -0.06\)), healthy men (\(r = -0.30\)), and men with AIDS (\(r = 0.15, all P > 0.05\)). However, a small significant bias between the methods was observed for all subjects pooled (Table 2).

Although the new model of TBPro, which is based on cellular-level principles, provides estimates in good agreement with IVNA measures, the estimates are systematically biased low, as noted above. Thus, a regression equation can be constructed by using TBPro estimates from the new model:

\(\text{TBPro}_{(IVNA)} = 0.834 \times \text{TBPro}_{(\text{new model})} + 2.07 \) (23)

where \(r = 0.92, P < 0.001,\) and SEE = 0.59 kg; \(n = 291\) (Figure 2). The use of this regression equation significantly reduced the SEE to 0.59 kg from 0.86 kg when values directly from the new model are used. Nevertheless, this regression equation is empirically derived without a theoretical foundation and should not be confused with Equation 18.

Protein distribution

Protein distribution was calculated according to Equations 12, 15, and 16. Cellular protein, ECF protein, and ECS protein accounted for 75–79%, ≈2%, and 19–23% of TBPro (new model), in the 3 groups, respectively (Table 3). Compared with the healthy women, the healthy men had a higher fraction of TBPro as cellular protein and a lower fraction as ECS protein (both \(P < 0.001\)). Compared with the men with AIDS, the healthy men also had a higher fraction of TBPro as cellular protein (\(P < 0.001\)) and a lower fraction as ECS protein (\(P < 0.003\)).

DISCUSSION

IVNA criterion method

Because the “true” value of body protein is not measurable in vivo, a reference method with high accuracy is necessary to evaluate less accurate methods. The applied TBPro reference method should ideally meet 2 criteria: the method should avoid major assumptions and have maximal precision. Because of its unique role as an essential component of protein, the assessment of TBN by IVNA has been used as the well-validated
criterion for TBPro (5, 6).

The mean measurement error associated with the IVNA model can be estimated for the healthy subjects by assuming an average TBN of the healthy men and women as shown in Table 1 and measurement precision as stated in Subjects and Methods. Accordingly,

$$\sigma_{TBPro} = 6.25 \times 1.60 \times 0.027 = 0.27 kg$$ (24)

The propagated TBPro measurement error for the healthy subjects was 0.27 kg. Because IVNA is not practical for longitudinal studies and for use in children and young women, the IVNA model can be used as the reference in the present study to evaluate the new model for predicting TBPro.

**TBK-TBPro association**

Both potassium and protein are mainly distributed within the intracellular compartment, and TBK was thus applied by Ellis et al (2) as a predictor of TBPro. Our experimental results confirmed that there were good correlations between TBPro and TBK for all 3 groups. The slopes and intercepts of the derived empirical equations for TBPro compared with TBK for healthy women (0.00250 and 2.79), healthy men (0.00240 and 2.63), and men with AIDS (0.00248 and 2.54) were similar to the slope and intercept of Ellis’s equation for healthy men (0.00248 and 2.54). Moreover, assuming that the average bone mineral value for healthy women and men is 2.74 kg (Table 1), our derived model (ie, Equation 18) takes the form $TBPro = 0.00252 \times TBK + 2.00$. The slope and intercept of this formula calculated from the new model are also similar to the results of Ellis et al in men (0.00248 and 2.54). These observations thus cross-validate Ellis et al’s empirical prediction formula for men (Equation 2). However, Ellis et al’s prediction equation for TBPro from TBK in women has a larger slope (0.00317) and a smaller intercept (0.95) than those observed in the current study. We have no explanation for this discrepancy.

**New TBPro model**

Because there is a lack of a strong theoretical basis for the empirical TBK prediction formulas, we focused in the present study on the development of a new TBPro model derived as the combination of 3 separate protein compartments. Our results support the new TBPro model’s validity relative to the criterion IVNA model in both the healthy adults and the men with AIDS, although, overall, the model provided slightly lower TBPro estimates.

The new model has 2 sources of measurement error, one from estimates of TBK and the other from bone mineral. The total measurement error can be evaluated in our healthy subjects by assuming an average body composition of men and women, as shown in Table 1, and by assuming measurement precisions as described in Methods. The total measurement error is equal to the combination of error in TBK and bone mineral measurement:

$$\sigma_{TBPro}^2 = (0.00272 \times 3008 \times 0.024)^2 + (0.732 \times 2.74 \times 0.0128)^2 = 0.0386 + 0.0007$$

$$= 0.0393$$ and $\sigma_{TBPro} = 0.20 kg$ (25)

The propagated measurement error of the new model is 0.20 kg, which is smaller than that of the IVNA-criterion model (0.27 kg). This calculation also shows that the measurement of TBK is the major source of measurement error.

The new TBPro model has a firm physiologic basis, and our results indicate that the new model can also be applied in men

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**TABLE 3**

<table>
<thead>
<tr>
<th>Fractional distribution of total body protein at the cellular level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Protein compartment</td>
</tr>
<tr>
<td>Cellular</td>
</tr>
<tr>
<td>Extracellular fluid</td>
</tr>
<tr>
<td>Extracellular solids</td>
</tr>
</tbody>
</table>

$^1 \bar{x} \pm SD$.

$^2$Significantly different from healthy men (Student’s t test with Bonferroni adjustment): $^2P < 0.002, ^2P < 0.006$. 

---

**FIGURE 2.** Total body protein (TBPro) mass measured by in vivo neutron activation (IVNA) and TBPro predicted by the new model (Equation 18). The equation of the regression line is $TBPro_{IVNA} = 0.834 \times TBPro_{new model} + 2.07$ ($r = 0.92, P < 0.001, \text{SEE} = 0.59$ kg), $n = 291$. The SEs of the coefficient and intercept are 0.020 and 0.20, respectively. The line of identity is shown in the figure.
with AIDS. However, it is questionable whether the new model would be accurate when applied in some patient populations with significant intracellular and extracellular electrolyte disturbances (ie, in patients without constant potassium concentrations of 152 mmol/kg H₂O in ICF and of 4 mmol/kg H₂O in ECF). Further studies are thus needed to validate the new model in patients with various acute and chronic disease states. In addition, the reason for the systematic underestimate of mean TBPro in comparison with IVNA requires further investigation.

An important characteristic of the new model is that it provides estimates of protein distribution among BCM, ECF, and ECS compartments. On the cellular level, both BCM and ECF contain potassium and protein. Potassium can thus be used as a predictor of BCM and ECF proteins. The new model also considers the third protein compartment, ECS protein. Both bone mineral and protein are the major constituents of ECS; thus, bone mineral measured by DXA can be used as a predictor of ECS protein. At present, however, the accuracy of the protein distribution estimates cannot be evaluated, and there are no published independent estimates of protein in cellular, ECF, and ECS components. Further studies are thus needed to validate our estimates of protein distribution.

**Conclusion**

In the present study we developed and then validated a new approach for estimating TBPro mass in vivo. The model, formulated on a series of theoretical equations combined with physiologically and empirically based coefficients, provides TBPro estimates similar to those of the criterion IVNA method. Our new model, which also gives an estimate of protein distribution, may also be applicable in patients with AIDS. Further validation studies are needed in longitudinally monitored populations and in patients with various acute and chronic diseases.

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ZMW and SBH designed the study; ZMW and SH analyzed the data; ZMW, SH, WS, and SBH wrote the manuscript; and DPK, LW, JFA, MEN, SBH, and RNP collected the data. None of the authors had any financial or personal interest in any company or organization sponsoring the research, including advisory board affiliations.

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