Assessing total body and extracellular water from bioelectrical response spectroscopy

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Exercise Physiology Laboratory, Space Biomedical Research Institute, National Aeronautics and Space Administration, Johnson Space Center, Houston 77058; University Space Research Association, Houston 77058; Stable Isotope Program, United States Department of Agriculture Agricultural Research Service Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine, Houston 77030; Biochemistry Research Laboratory, KRUG Life Sciences, National Aeronautics and Space Administration, Houston, Texas 77058.

Siconolfi, Steven F., Randal J. Gretebeck, William W. Wong, Robert A. Pietrzyk, and Sheril S. Suire. Assessing total body and extracellular water from bioelectrical response spectroscopy. J. Appl. Physiol. 82(2): 704–710, 1997.—We developed and validated assessments for total body water (TBW) and extracellular water (ECW) by using two resistance values of a new electric circuit model (CM) (two resistors: a capacitor and an inductor) with or without body mass. Fluid shifts occurring after 40 min of supine rest did not decrease the validity of either estimate. CM estimates were valid; r = 0.941 to 0.969, low SE of estimates of 1.15–2.28 kg, nonsignificant mean differences (CM dilution; %Δ = −0.4 to 1.3%) that were close to the expected measurement errors for TBW (±1%) and ECW (±5%), and Bland-Altman pairwise comparisons that showed equivalence between methods. The CM estimates of TBW and ECW had marginally better validity than the previously published bioimpedance models. The advantage of the CM model is its assessments of multiple fluid spaces and that it does not require gender-specific equations. We conclude that CM estimate of TBW is acceptable, whereas further validation is needed before the ECW estimate should be used in a clinical or research setting.

Bioimpedance; frequency; body fluids

Bioresistance is a technique that estimates body fluids by using a variety of models. All of these models use the relationship that states the volume of a conductor is the product of the specific resistivity and the ratio of the squared length of the conductor to the measured resistance (12). The specific resistivity of the conductor is a characteristic of the conductor (12). The following equation shows this relationship

\[ \text{volume} = \rho \times \frac{\text{length}^2}{R} \]

where \( \rho \) is the specific resistivity (Ω*cm) of the conductor and \( R \) (Ω) is the measured resistance. The specific resistivity is a different constant for each conductive medium. In human applications, the length of the conductor is generally the subject's height (Ht).

Previous researchers used a variety of input frequencies to determine different fluid spaces (4, 7–10, 15–17). The capacitive nature of cell membranes led researchers to use currents at higher frequency (50–100 kHz) to assess total body water (TBW) (8–10, 15, 17, 22) and lower frequencies (1–5 kHz) to estimate extracellular water (ECW) (4, 9, 17, 22). These researchers empirically chose the frequencies and evaluated their effectiveness as predictors of specific fluid volumes. Other investigators used an electric circuit model (CM), with multifrequency inputs, to determine the size (magnitude in ohms, faradays, and henrys) of the resistors, capacitors (22), and inductors (19, 20) of different CM. These investigators used regression models, with the size of the electric components as the dependent variable when estimating fluid volumes.

This investigation sought to evaluate a new CM. The new electric CM consists of two series circuits (resistor and capacitor, resistor and inductor) placed in parallel to each other (Fig. 1). Similar to other circuits (19, 20), the intracellular water was the resistor (R1 in Fig. 1) in series with the capacitor. ECW was the value of the other resistor (R2 in Fig. 1). The sum (for parallel circuits) of R1 (ECW) and R2 (intracellular water) is the resistance of the total circuit and represents the TBW. The capacitor is on the intracellular water side of the circuit and represents the capacitance of cell membranes (1, 7). The inductor is on the extracellular side of the circuit and represents blood and plasma volumes. The induction of an inductor in this model is different from the circuits used by other investigators (22). An inductor produces an electric field (resistance that is orthogonal to electron flow) when electrons flow through a wire coil (12). Siconolfi et al. (20) theorized that the inductor in the new circuit represented the electric field produced when the subjects' blood and plasma carry the electric charge through the net of the vascular system. The Siconolfi et al. (20) bioelectrical response spectroscopy (BRS) model for blood and plasma volumes used the inductor and estimated vascular volumes to within
5% of clinical (125I-labeled human serum albumin) values. The capacitance and inductance values from this model were not used to estimate TBW or ECW. As in other models (8–10, 15, 17, 22), regression analyses determined the conversion of RT to TBW and R2 to ECW.

We hypothesized that estimates of TBW and ECW could be made by using components of the new CM and would not be affected by fluid shifts (occurring within the ECW) associated with supine rest. We evaluated the new estimates by comparing values from chemical dilution and estimates from previously published single-frequency (SF) models. The comparison of these assessments with the chemical dilution value helped determine the degree of accuracy of the proposed and previously published models.

METHODS

Subjects All subjects passed an Air Force Class III physical or equivalent and were briefed on the study. After all questions about the study were answered, subjects signed an approved informed-consent statement. NASA’s institutional review board approved all procedures in this study. We randomly assigned subjects to a development or validity group for TBW and ECW. The subjects in the TBW development group (n = 23) had their TBW evaluated with 18O-labeled water. The subjects in the TBW validity group (n = 31) were evaluated with deuterium oxide (D2O). The unavailability of 18O-labeled water and the desire to demonstrate the robust nature of the CM estimate led us to use 2H2O for the validity group. Wong et al. (25) reported a 0.3-kg difference in TBW measurements from saliva samples. In addition, Wong et al. (25) for 18O/16O or 2H/H isotope-ratio measurements by gas-isotope-ratio mass spectrometry.

Dilution space was calculated from baseline, 4-h, and 5-h sample collections by using the equation (10)

\[ N = \frac{W (A - s \cdot d)}{18.02 (A - s \cdot p)} \]

where N is the pool space; W is the amount of water used to dilute the dose; A is the amount of dose administered; d is the dose diluted for analysis; s is enrichment of dose A, tap water (t), peak postdose sample (s), and predose baseline sample (p). To account for incorporation of tracer into nonaqueous tissue, a correction factor of 1.04 (deuterium) or 1.01 (18O-labeled water) was used for the relationship between the isotope dilution space and TBW (15). The error rate in our laboratory for this measurement is <1% (based on difference between 4- and 5-h samples).

ECW. We assumed that ECW was the bromide dilution space. Baseline bromide levels were determined from an initial blood sample. Subjects then ingested an oral dose of bromide (12.2 g of NaBr). Additional blood samples were collected 3 and 4 h after administration of the dose. All samples were centrifuged, and the plasma was stored at −20°C. Plasma proteins were removed from the sample before ion chromatography by using 0.3 mol of the sample to Ultra-free-PF Filter units (10,000 nominal mol mass limit; Millipore, Bedford, MA). Pressurizing the filter assembly with 10 ml of air from a plastic syringe activated the units (23). The protein-free filtrate (10 µl) was diluted 1:100 with ion chromatography eluant (1.8 mM Na2CO3/1.7 mM NaHCO3). Recovery of bromide-spiked plasma samples was >90%.

Bromide concentration in the samples was determined by using ion chromatography (Dionex model 2000i suppression-based system; Dionex, Sunnyvale, CA). Samples (500 µl) were automatically injected onto the AS4A column (Dionex) by using the Dionex autosampler module with a flow rate set at 1 ml/min. Bromide was determined by suppression-based conductivity detection and quantitated by using a calibration curve (least squares linear regression).

ECW volumes were determined from the difference in plasma bromide concentrations between the baseline and 3- and 5-h samples. ECW were calculated as

\[ ECW = \text{Br}_{dose}/[\text{Br}] = 0.90 \times 0.95 = 0.94 \]

where \( \text{Br}_{dose} \) was the amount of bromide orally administered to the subject, [Br] was the plasma bromide concentration obtained from the difference between the 0- and 3-h blood samples, 0.90 was the fraction of the bromide assumed to be extracellular, 0.95 was the Donnan equilibrium factor, and 0.94 was the assumed water content of plasma (11, 21).

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Development Groups</th>
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<th>Validity Groups</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TBW</td>
<td>ECW</td>
<td>TBW</td>
<td>ECW</td>
</tr>
<tr>
<td>Age, yr</td>
<td>32.0 ± 6.6</td>
<td>33.8 ± 5.8</td>
<td>35.9 ± 6.4</td>
<td>34.0 ± 7.0</td>
</tr>
<tr>
<td>Height, cm</td>
<td>168 ± 6</td>
<td>170 ± 11</td>
<td>170 ± 10</td>
<td>170 ± 9</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>67.8 ± 13.0</td>
<td>64.7 ± 11.4</td>
<td>69.2 ± 14.0</td>
<td>72.9 ± 17.1</td>
</tr>
<tr>
<td>TBW, kg</td>
<td>38.8 ± 7.7</td>
<td>34.6 ± 6.3</td>
<td>36.8 ± 7.8</td>
<td>38.6 ± 9.6</td>
</tr>
<tr>
<td>ECW, kg</td>
<td>NA</td>
<td>15.4 ± 2.9</td>
<td>16.0 ± 3.4</td>
<td>16.2 ± 3.8</td>
</tr>
<tr>
<td>Gender</td>
<td>10 M/13 F</td>
<td>6 M/11 F</td>
<td>16 M/15 F</td>
<td>6 M/3 F</td>
</tr>
</tbody>
</table>

Values are means ± SD. TBW, total body water; ECW, extracellular water; M, male; F, female.
BRS. BRS was the impedance, phase angle, capacitance, and inductance responses of the human body to a multifrequency input current. We recorded BRS from a Hewlett-Packard model 4284A Precision LCR Meter through electrodes placed on the hand, wrist, ankle, and foot at standard locations (1, 4, 6, 8–10, 17, 19, 20, 22), before subjects assumed the supine position. BRS uses an input current of ∼250 μA (at frequencies of 5, 50, 67, 85, 100, 150, 166, 200, 250, and 300 kHz). Subjects reclined to a supine position, and a computer recorded the BRS immediately and after 40 min of quiet rest. A blanket or extra clothing kept the subjects warm during the rest period and reduced possible variation in BRS caused by skin temperature changes. Unpublished pilot studies in our laboratory (n = 10) showed increases in impedance of 25–30 Ω after 40 min of supine rest in gym shorts and T-shirts. This increase was minimized (∼10–15 Ω) when subjects were kept warm with a blanket. The difference between the BRS TBW at 0 and 40 min evaluated the effects of shifting fluids between interstitial and vascular fluid spaces (5, 14, 18). This comparison is important, because Roos et al. (14) and Sherriff and Maughan (18) showed an association between the increases in total body resistance (measured at a set frequency) and decreases in hematocrit that accompany a change in posture.

Determination of circuit components. The determination of circuit components did not use the Cole-Cole method but used a new approach (6) that has been shown to produce resistances similar to graphic techniques based on the Cole-Curtis theory (Cole and Curtis (3)). We regressed (3rd-order least square regression) each subject’s impedance and resistance values on frequency. The R2 (ECW) resistor (Fig. 2) was the intercept (when frequency was zero) of the resistance on frequency regression. At a zero frequency, the current flow went preferentially through the extracellular side of the circuit, because the capacitor acts as a gap on the intracellular side of the circuit. This figure represents data for a typical subject who had a correlation of 0.99 for impedance on frequency. The mean ± SD of the correlations for the individualized regressions was 0.99 ± 0.02. The resistance of the total circuit (RT) was the resistance at the frequency where impedance changed by only 1% with a frequency increase of 25 kHz (Fig. 2). We used the 1% limit because it is an industry standard for high-precision resistors (12). This analytical approach uses the theory that, at very low frequencies, the electrical current does not enter cells, whereas at high frequencies, the current enters both the intracellular and extracellular fluid spaces (1, 3, 4, 9, 17). The R1 (intracellular water) resistor was the difference between one divided by the RT and one divided by R2 (ECW).

This new method of circuit analysis represents a teleological approach. This is different from the traditional Cole-Cole analysis that solves for resistances when reactance is zero (3, 7). The Xitron BIS 4000B analyzer (Xitron Technologies, San Diego, CA) uses a modified Cole-Cole approach with iterative curve fitting (26). Unlike the Cole-Cole approach, this statistical approach allows for the removal of 25% of the data to increase the fit of the resistance and reactance values. Our approach uses all the data. Our laboratory (6) reported a high correlation (r = 0.987–0.994) between the analysis techniques for the R2 and RT resistors. However, the main predictor of TBW from BRS (Ht2/RT) had a significantly weaker correlation and larger SE of the estimate (SEE; r = 0.693 ± 5.6 kg) for the Cole-Cole analysis than that observed from our model (r = 0.945 ± 2.6 kg). Therefore, we concluded that the new circuit analysis was preferable.

SF estimates of TBW and ECW. The gender-specific equations by Kushner and Schoeller (8) estimated TBW from Ht2/RT (resistance at 50 kHz) and body mass (M) by using the following sex-speciﬁc equations

\[
\text{TBW(kg)} = 0.396 \times (\text{Ht}^2/\text{RT}) + 0.143 \times M + 8.399
\]

males: model R = 0.988; SEE = 1.658 kg, and

\[
\text{TBW(kg)} = 0.382 \times (\text{Ht}^2/\text{R}) + 0.105 \times M + 8.315
\]

females: model R = 0.975; SEE = 0.884 kg.

Two regression equations estimated ECW. The Segal et al. equation (17) estimated ECW by using Ht2/R (resistance at 5 kHz) and body mass, whereas Lukaski and Bolonchuk (10) estimated ECW by using Ht2/R (resistance at 50 kHz), Ht2/Xc (Xc is the capacitive reactance at 50 kHz), and body mass. The models used the following equations

\[
\text{ECW(kg)} = 0.264 \times (\text{Ht}^2/\text{R}) + 0.112 \times M - 6.115
\]

[Segal et al. (17)]; model R = 0.930; SEE = 1.94 kg;

\[
\text{ECW(kg)} = 0.189 \times (\text{Ht}^2/\text{R}) + 0.052 \times M - 0.0002 \times (\text{Ht}^2/\text{Xc}) + 1.03
\]

[Lukaski and Bolonchuk (10)]; model R = 0.943; SEE = 1.00 kg.

Statistical analyses. Stepwise multiple regression produced equations to estimate TBW and ECW from the RT and R2 values (determined with a new method) of new electrical CM of the body. TBW used Ht2/RT and body mass, whereas ECW only used Ht2/R2. We evaluated the validity of these estimations with four statistical tests: mean differences (analysis of variance, Newman-Keuls post hoc testing), strength of linear relationship (Pearson product-moment correlations), SEE, and Bland-Altman pairwise comparisons (2).

The Bland-Altman pairwise comparison (2) evaluates the validity of a new method to an accepted technique. This comparison was a graphical representation of the difference (absolute or %) of accepted) between methods and the average of these methods. Bland and Altman (2) suggest that if all the values are within the ±2 SD of the averaged values (±2 coefficient of variations for %Δ) and there is no correlation between the differences vs. the averaged values, then the methods are clinically equivalent. Validity of a new method decreases if 1) the mean difference is greater than the
measurement error, 2) the Bland-Altman plot shows data points outside confidence intervals, and 3) there is a significant relationship indicating that one method overestimates or underestimates the other as a function of size.

RESULTS

Development groups. The stepwise multiple regression for TBW yielded the following prediction equation for TBW with a multiple $R$ of 0.987 and SEE of 1.26 kg

$$\text{TBW(kg)} = 2.584 + 0.379 \cdot \text{Ht}^2/\text{RT} + 0.168 \cdot \text{M}$$

where $\text{RT}$ is the resistance ($\Omega$) of the circuit and $\text{M}$ is the mass (in kg) of the body. The mean ± SD of RT for the development group was 465 ± 83 Ω. The stepwise multiple regression for ECW yielded the following prediction equation for ECW with a multiple $R$ of 0.858 and SEE of 1.72 kg

$$\text{ECW(kg)} = 2.854 + 0.2877 \cdot \text{Ht}^2/\text{R}_2$$

where $\text{R}_2$ is the resistance ($\Omega$) of the circuit at a frequency of 0 Hz. The mean ± SD of $\text{R}_2$ for the development group was 683 ± 68 V.

Validity of TBW assessment. We examined the validity of the TBW and ECW estimations at time 0 (BRS taken immediately after subjects became supine) and after 40 min of supine rest. The CM estimate of TBW had high correlations ($r = 0.956$ to 0.964) and low SEE ($2.08$–$2.28$ kg) compared with measures using isotopic dilution in the validation group. The CM estimate of TBW was not significantly different from the isotopic values for both time points ($1.3 \pm 6.1$ and $-0.4 \pm 5.5\%$ for 0 and 40 min, respectively). These results were similar to those observed for the SF-BRS estimates ($r = 0.951$–0.956, SEE $= 2.39$–$2.42$ kg). The Kushner and Schoeller (8) estimate of TBW was significantly ($P < 0.05$) greater than isotopic dilution at 0 min ($4.2 \pm 6.2\%$) but not at 40 min ($2.7 \pm 6.2\%$). The Bland-Altman correlations for %D (BRS–$^2\text{H}_2\text{O}$) vs. averaged TBW (Fig. 3 and Table 2) were not significantly different from zero. This indicated there was no trend for either CM or Kushner and Schoeller (8) BRS assessment of TBW. Values for both BRS assessments were within two coefficients of variation of the averaged values. Similar values were observed for the BRS-estimated TBW after 40 min of supine rest (Table 2).

Validity of ECW assessment. The CM estimate of ECW had high correlations ($r = 0.941$–0.949) and low SEE ($1.27$–$1.12$ kg) compared with measures using bromide dilution in the validation group. These results were similar to those observed for the Lukaski and Bolonchuk (10) and Segal et al. (17) BRS estimates of ECW (Table 2). The Segal et al. (17) BRS estimate of ECW was significantly ($P < 0.05$) greater than dilution

Table 2. Dilution and BRS TBW and ECW, correlations, and Bland-Altman pairwise comparisons for TBW and ECW

<table>
<thead>
<tr>
<th>Study Condition</th>
<th>Min</th>
<th>Dilution, kg</th>
<th>BRS, kg</th>
<th>Dilution vs. BRS</th>
<th>Bland-Altman</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$r$</td>
<td>SEE, kg</td>
</tr>
<tr>
<td>TBW (n = 31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K&amp;S</td>
<td>0</td>
<td>38.23 ± 7.68</td>
<td>90.951</td>
<td>2.42</td>
<td>-0.083</td>
</tr>
<tr>
<td>CM</td>
<td>0</td>
<td>37.22 ± 7.80</td>
<td>0.956</td>
<td>2.28</td>
<td>0.013</td>
</tr>
<tr>
<td>K&amp;S</td>
<td>40</td>
<td>37.50 ± 7.84</td>
<td>0.952</td>
<td>2.39</td>
<td>-0.079</td>
</tr>
<tr>
<td>CM</td>
<td>40</td>
<td>36.42 ± 7.86</td>
<td>0.964</td>
<td>2.08</td>
<td>-0.007</td>
</tr>
<tr>
<td>ECW (n = 9)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Segal</td>
<td>0</td>
<td>18.07 ± 5.11</td>
<td>0.912</td>
<td>1.56</td>
<td>0.736*</td>
</tr>
<tr>
<td>L&amp;B</td>
<td>0</td>
<td>18.20 ± 5.32</td>
<td>0.951</td>
<td>1.18</td>
<td>0.331</td>
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<tr>
<td>CM</td>
<td>0</td>
<td>16.93 ± 4.62</td>
<td>0.941</td>
<td>1.27</td>
<td>-0.008</td>
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<tr>
<td>Segal</td>
<td>40</td>
<td>18.20 ± 5.32</td>
<td>0.936</td>
<td>1.34</td>
<td>0.734*</td>
</tr>
<tr>
<td>L&amp;B</td>
<td>40</td>
<td>18.62 ± 5.68</td>
<td>0.954</td>
<td>1.15</td>
<td>0.107</td>
</tr>
<tr>
<td>CM</td>
<td>40</td>
<td>17.09 ± 5.08</td>
<td>0.949</td>
<td>1.12</td>
<td>-0.073</td>
</tr>
</tbody>
</table>

Values are means ± SD. BRS, bioelectric response spectroscopy; SEE, standard error of estimate; %Δ, percent change; K&S, estimate of TBW by Kushner and Schoeller (5); CM, new circuit model estimates of TBW and ECW; Segal, estimate of ECW by Segal et al. (14); L&B, estimate of ECW by Lukaski and Bolonchuk (7). *Significant correlation or mean difference, $P < 0.05$. 

Fig. 3. Bland-Altman plots for Kushner and Schoeller (8) (solid line) and multifrequency (MF) CM (dashed line) bioelectrical response spectroscopy (BRS)-estimated total body water (TBW) vs. $^2\text{H}_2\text{O}$-determined TBW at time 0 min. Solid arrow, mean difference for single frequency (SF; $4.2 \pm 6.2\%$); open arrow, mean difference for CM ($1.3 \pm 6.1\%$).
The Bland-Altman correlations for %Δ (BRS-ECW) vs. averaged ECW (Fig. 4) were not significantly different from zero for CM or Lukaski and Bolonchuk (10) at 0 and 40 min. This indicated there was no trend for these BRS assessments of ECW. However, the Segal et al. (17) estimate of ECW had significant correlations for both time points (Table 2). Segal et al. (17) BRS assessment of ECW was within two coefficients of variation of the averaged values at 0 and 40 min, whereas CM estimates and the results of Lukaski and Bolonchuk (10) were within one coefficient of variation (Table 2).

**DISCUSSION**

We developed and validated assessments for TBW and ECW from the resistor values of a new electric CM and body mass (TBW only). These BRS estimates of TBW and ECW were not affected by fluid shifts that occur after 40 min of supine rest. These estimates have good validity, based on the strength of the correlations (r = 0.941–0.969), low SEE (1.15–2.28 kg), nonsignificant mean differences (CM – dilution; %Δ = –0.4 to 1.3%) that were close to the expected measurement errors for TBW (±1%) and ECW (±5%), and the Bland-Altman pairwise comparisons that showed no significant trend. These findings are not surprising because other researchers have shown that BRS estimates of fluid volumes have been successful (2, 5–7, 13, 14, 18).

Kushner and Schoeller (8) reported similar correlations (r = 0.93–0.96) and SEE (2.03–2.25) when assessing TBW in their validity group. In a review by the same authors (15), estimates of TBW from SF-BRS had correlations with dilution methods ranging from 0.87 to 0.98 and SEE of 1.37–3.03 kg. All the prediction equations minimally used Ht²/R and body mass. The resistance was measured at 50 kHz for these studies. The present study only used Ht²/RT and body mass, not needing gender-specific equations or gender and age as factors.

We evaluated the validity of the Kushner and Schoeller (8) model with data from the present study. This model yielded similar correlations, SEE, and Bland-Altman pairwise comparisons (Table 2) as those derived from CM. The only difference between the methods was the significantly higher (4.2% greater than ²H₂O) mean values at 0 min. This difference may have been due to the amount of time between placing electrode on the subject and recording of BRS. In the present study, a technician placed the electrodes on the subjects before they became supine; in the Kushner and Schoeller study (8), the amount of time in the supine position before the resistance was recorded may have varied. This is supported by the lack of a difference after 40 min of rest for this model (Table 2). The CM estimate of TBW may be an improvement over the Kushner and Schoeller (8) model because of the following findings: 1) no significant mean difference between dilution and CM, 2) mean differences closer to measurement error for CM, and 3) CM does not require sex-specific equations for the estimation of TBW.

The stability of RT during the 40 min of supine rest provides a stable estimate of TBW when internal fluid shifts are occurring. This may be due to our definition of RT as the resistance where impedance is changing at 1% over increments of 25 kHz. The use of 1% of impedance (not resistance) kept RT-sensitive changes in all of the electrical components representing fluid volumes. Therefore, shifts of fluids may have altered one or more of the components [as shown with inductance by Siconolfi and Gretebeck (19)], but these did not affect the 1% impedance value and kept RT stable.

BRS models that estimate ECW by using a resistance response from a single frequency have reported results similar to those found in the present study with the use of the CM model. Lukaski and Bolonchuk (10) reported a correlation of 0.907 with a SEE of 1.40 kg when they applied their model to a validation group. Segal et al. (17) did not report a validation (n = 18) group's correlation or SEE, but they did report nonsignificant mean differences between their model's estimate and their validity group's dilution value. They also reported that the residuals were not related to either the predicted or measured values. Van Loan et al. (22) developed an estimate of ECW with the use of a similar electrical circuit. Their circuit does not contain an inductor. They determined the value of their resistors through iterative statistical regression (repeating curvilinear regression while removing up to 25% of the data points). They report a correlation of 0.893 (SEE of
0.947) and no significant difference between their BRS estimate and their reference method (22).

The Van Loan et al. (22) regression estimates of ECW and TBW are based on the resistances when reactance is zero. The Cole-Cole model (3) assumes that these resistances represent the points where fluids (TBW and ECW, for our purposes) become pure conductors. Van Loan et al. (22) computed (by statistical semicircle regression of reactance on resistance) the Cole-Cole values from resistance and reactances over a wide frequency range obtained from the Xitron 4000B bioimpedance analyzer (Xitron Technologies, San Diego, CA). However, the Xitron computation of the TBW and ECW resistances allows for removal of data (up to 25%). This is not part of the Cole-Cole method for determining these resistances. We compared resistance, capacitance, and inductance values for the Xitron 4000B to the Hewlett-Packard LCR, by using standard electrical components. We found differences between the instruments (6). Therefore, we could not compare the Van Loan et al. (22) regression estimates of body fluids to those in the present study.

The present study compared the three BRS estimates for ECW with the dilution-determined value. All models had good correlations (r > 0.9) with low SEE (< 1.6 kg). The Segal et al. (14) model yielded significantly lower ECW after 40 min of supine rest. The CM model had low mean differences (< 2%) that were less than the expected measurement error (5%). The means for the Lukaski and Bolonchuk (10) model were not significantly different from the dilution values, but they did exceed the expected measurement error. Significant Bland-Altman correlations at 0 and 40 min were observed only for the Segal et al. (17) model. These correlations suggest this model overestimated the high ECW values and underestimated the low values (Fig. 4). This was not found for the other two models. Lohman (9) recommends that the regression weight for body mass should be as small as possible in an assessment of body fluids. The model of Lukaski and Bolonchuk (10) met this recommendation, but it was not evident for the Segal et al. (17) model. The Segal et al. (17) model uses a regression weight for body mass that is twice that used by Lukaski and Bolonchuk (10). In the SF models, body mass accounts for 50 and 23% of the predicted ECW, using the Segal et al. (17) and Lukaski and Bolonchuk (10) equations, respectively. The high contribution of body mass in the Segal et al. (17) estimate of ECW may have produced the significant Bland-Altman trends since ECW and body mass were correlated (r = 0.783) for these subjects. The CM estimate of ECW did not require body mass as a factor in its model and therefore has very small Bland-Altman correlations. A limitation of the present study’s analysis of these three models is the small number of subjects in the validation group. Therefore, these validation results for ECW are preliminary and should be verified with an appropriate number (n = 30) of subjects.

The CM estimates of TBW and ECW had marginally better validity than the previously published models that used SF-BRS inputs plus body mass and gender. The advantage of the CM model is that it provides assessments of TBW, ECW, and blood volume (20) using only body mass as an additional independent factor. The second advantage was the stability of the estimates during fluid shifts. We conclude that CM estimate of TBW is acceptable, although further validation is needed for the ECW estimate before it could be used in a clinical or research setting.

We thank Alice Rogers for helping with data collection. Address for reprint requests: S. F. Siconolfi, Space Biomedical Research Institute SD3/Space Biomedical Research Institute, NASA Johnson Space Center, Houston, TX 77058.

Received 21 November 1994; accepted in final form 11 July 1996.

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