Segment-Specific Resistivity Improves Body Fluid Volume Estimates from Bioimpedance Spectroscopy in Hemodialysis Patients

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Abstract: Discrepancies in body fluid estimates between segmental bioimpedance spectroscopy (SBIS) and gold standard methods may be due to the use of a uniform value of tissue resistivity to compute extracellular fluid volume (ECV) and intracellular fluid volume (ICV). Discrepancies may also arise from the exclusion of fluid volumes of hands, feet, neck and head from measurements due to electrode positions. The aim of this study was to define the specific resistivity of various body segments and to use those values for computation of ECV and ICV along with a correction for unmeasured fluid volumes.

Methods: Twenty-nine maintenance hemodialysis (HD) patients (16 males) underwent body composition analysis including whole body magnetic resonance imaging (MRI), whole body potassium ($^{40}$K) content, deuterium (D$_2$O), and sodium bromide (NaBr) dilution, and segmental and wrist-to-ankle BIS, all performed on the same day before a HD. Segment-specific resistivity was determined from segmental fat free mass (FFM by MRI), hydration status of FFM (by D$_2$O and NaBr), tissue resistance (by SBIS) and segment length.

Results: Segmental FFM was higher and extracellular hydration of FFM was lower in males compared with females. Segment-specific resistivity values for arm, trunk, and leg all differed from the uniform resistivity used in traditional SBIS algorithms. Estimates for whole body ECV, ICV and total body water (TBW) from SBIS using segmental instead of uniform resistivity values and after adjustment for unmeasured fluid volumes of the body, did not differ significantly from gold standard measures.

Conclusion: The uniform tissue resistivity values used in traditional SBIS algorithms result in underestimation of ECV, ICV and TBW. Use of segmental resistivity values combined with adjustment for body volume that are neglected by traditional SBIS technique significantly improves estimations of body fluid volume in hemodialysis patients.
Keywords: Body composition, bioimpedance, whole body, segments, body fluid, magnetic resonance imaging.
Abbreviations:

**BIA**  Bioimpedance analysis

**BIS**  Bioimpedance spectroscopy

**SBIS**  Segmental Bioimpedance spectroscopy

**SBIS\textsubscript{UR}**  Segmental Bioimpedance spectroscopy using uniform resistivity values

**SBIS\textsubscript{SR}**  Segmental Bioimpedance spectroscopy using segmental resistivity values

**WBIS**  Wrist to ankle Bioimpedance spectroscopy

**HD**  Hemodialysis

**ECV**  Extracellular fluid volume

**ECV\textsubscript{W}**  Extracellular fluid volume measured by WBIS

**ECV\textsubscript{S}**  Extracellular fluid volume measured by SBIS

**ICV**  Intracellular fluid volume

**ICV\textsubscript{W}**  Intracellular fluid volume measured by WBIS

**ICV\textsubscript{S}**  Intracellular fluid volume measured by SBIS

**TBW**  Total body water

**D\textsubscript{2}O**  Deuterium oxide

**NaBr**  Sodium bromide

**ECV\textsubscript{NaBr}**  ECV measured by NaBr dilution

**TBK**  Total body potassium

**ICV\textsubscript{TBK}**  ICV measured by TBK

**ECV\textsubscript{G}**  Gold standard ECV

**ICV\textsubscript{G}**  Gold standard ICV

**TBW\textsubscript{G}**  Gold standard TBW
FFM  Fat free mass
SAT  Skin adipose tissue
VAT  Visceral adipose tissue
SM  Skeletal muscle
\(\alpha\)  Ratio of total body ECV to FFM
\(\beta\)  Ratio of total body ICV to FFM
RE  Extracellular resistance calculated by Cole-Cole model
RI  Intracellular resistance calculated by Cole-Cole model
\(\rho_E\)  Extracellular resistivity
\(\rho_I\)  Intracellular resistivity
KB  Coefficient of body height related to limbs’ geometric size
CE  Coefficient of ECV of unmeasured body fluid compartments
CI  Coefficient of ICV of unmeasured body fluid compartments
L  Segment length
INTRODUCTION

Accurate estimation of body fluid volumes in hemodialysis (HD) patients could be of value in managing their hydration state. Since there is no simple and reliable method for measuring extracellular fluid volume (ECV), the hydration status is usually estimated by clinical examination, which, however, lacks accuracy due to the fact that some liters of fluid have to accumulate in the body before edema, the most prominent sign of overhydration, becomes clinically evident. One of the goals of HD treatments is the complete removal of excess ECV and establishment of a normal hydration status (dry weight) at the end of treatment. Dry weight is clinically determined as the lowest post-HD weight a patient can tolerate without developing intra- or interdialytic symptoms. Dry weight needs to be reassessed regularly. This clinical method of dry weight determination, however, may be unpleasant and risky for the patient, especially when associated with cramps and intradialytic hypotensive episodes. Accurate assessment of ECV and ICV by means other than the clinical ‘trial-and-error’ method is desirable and should greatly improve the quality of HD.

Multifrequency bioimpedance spectroscopy (BIS) has been advocated as a noninvasive, simple and inexpensive tool to assess fluid status in hemodialysis (HD) patients as well as other areas of medicine [21, 4, 18, 11, 7]. The BIS method for estimation of intracellular (ICV) and extracellular (ECV) fluid volumes as well as total body water is based on the conductive properties of different body tissues in response to electrical currents of various frequencies [9, 12]. The volume of conductive tissues can be derived from the corresponding electrical resistances. Tissues containing a combination of water and electrolytes are more conductive than bone, air-filled spaces, and fat. Nevertheless, several reports show that current bioimpedance methods may not be accurate enough for clinical use [14, 34, 8].
One of the reasons for inaccuracy of whole body wrist-to-ankle BIS (WBIS) method may be its view of the body as one cylinder, ignoring differences in geometric shape and size of the various body segments [33, 27]. A segmental BIS (SBIS) approach has been developed which measures bioimpedance in arm, trunk and leg segments separately and then estimates total body fluid volumes as a sum of segmental values [22, 2]. However, even with this approach total body ECV is underestimated [3]. This may be due to the use of a uniform resistivity value for all segments in the equations used for calculation of segmental ECV. It is hypothesized that estimates of ECV, ICV and TBW from SBIS could be considerably improved by using segment specific resistivity in the equations. However, assessment of segmental-resistivity remains difficult, because a gold-standard measure of ECV and ICV in each specific segment would be required.

Tracer dilution methods are considered gold standards for assessment of body fluid volumes. Deuterium (D₂O) dilution is generally used for assessment of TBW and sodium bromide (NaBr) dilution for ECV, while ICV can be assessed either from total body potassium content (TBK) or as the difference between TBW and ECV [30, 28]. Dilution methods are not able to directly predict segmental fluid volumes. An approach to define them is the measurement of total body fat-free mass (FFM) and its hydration status, the definition of segmental tissue composition by imaging technology, and then the calculation of fluid volumes based on the hydration index of the segmental fat free masses. The major body segments, arms, trunk and legs are composed of fat, muscle and bone, and their respective masses can be measured by magnetic resonance imaging (MRI). The hydration state of FFM is calculated from MRI and dilution methods and is assumed to be similar in each body segment. The hydration status of FFM is relatively stable (TBW/FFM=0.73) in normal healthy subjects [24]. However, because of fluid retention due to lack of kidney excretory function, the hydration status of FFM in hemodialysis patients may be higher
than in healthy subjects. The aim of this study was to improve the accuracy of SBIS in maintenance hemodialysis patients by measuring the specific resistivity of various body segments and applying those values to algorithms used for calculation of ECV, ICV and TBW.
MATERIALS AND METHODS

2.1 Subjects. 29 maintenance HD patients (26M/13F) (age 54.9±11 y, body weight (BW) 77.9 ±18 kg, height 167 ±10 cm) gave informed, written consent. The study protocol was approved by the IRB of Beth Israel Medical Center, New York, NY.

2.2 Measurement

Dilution methods.

TBW and ECV were measured before HD by D₂O and NaBr dilution methods. Each patient was given an oral dose of 10 g D₂O (ICON: Summit, N.J.) and 5 g of 4 mol/L NaBr solution [26]. Blood samples were collected immediately before and 3 hours after intake of these substances, when equilibration had been reached.

Total body potassium content

⁴⁰K, a natural radioisotope of potassium was used for estimation of total body potassium, using a whole body counter [30]. Total body potassium (TBK, mmol) was estimated as: TBK = ⁴⁰K/0.0118 and body cell mass were measured as BCM = 0.00883*TBK. [24, 26].

Magnetic resonance imaging (MRI)

MRI of the whole body was carried out as reported by Gallagher et al. [15]. Scans were prepared using a 1.5 Tesla scanner (General Electric, 6X Horizon, Milwaukee, WI). Subjects were placed in a prone position with their arms extended overhead and the protocol involved the acquisition of ~40 axial
images of 10-mm thickness and 40-mm spacing from neck to foot. MRI provided estimates of fat, muscle and bone volumes, and a correction was made for hydration of adipose tissue. All MRI scans were segmented into the components mentioned above by highly trained analysts using image analysis software (Tomovision, Montreal, QC, Canada). In a multiple-step procedure, a threshold was selected for adipose tissue and lean tissue and lines were drawn around the selected regions by use of a Watershed algorithm. Thereafter, tissues of interest were color-labeled and the respective tissue areas (cm²) for each MRI image were calculated by summing the specific tissue pixels and then multiplying by the individual pixel surface area. The volume per slice (cm³) was derived by multiplying tissue area by slice thickness and the volume of each tissue for the space between two slices was calculated and converted to mass units (kg) on the basis of specific tissue densities [15].

**Anthropometry**

Body weight was measured by an electrical scale and height was measured to an accuracy of 0.1 cm. The length of each segment (arm trunk and leg) was measured to an accuracy of 0.1 cm, with radiolucent markers indicating the proximal and distal ends of each segment. Maximal and minimal circumferences of each segment were also measured.

**Multifrequency Bioimpedance Spectroscopy**

A multi-frequency device (Xitron 4200) was used for automatic sequential measurements of BIS of arm, trunk, leg and wrist-to-ankle, with frequencies ranging from 5 kHz to 1 MHz. Current was injected through two electrodes placed on one wrist and the ipsilateral ankle. Voltage was recorded from four electrodes placed on the wrist and ipsilateral shoulder, greater trochanter and ankle and the signal was
transferred to the BIS device by a digital switch [33]. The arm not used for dialysis access was used for BIS measurements. With this method segmental BIS (SBIS) and whole body wrist-to-ankle BIS (WBIS) could be recorded together. To allow for equilibration of body fluids patients were positioned supine for at least 15 minutes before the start of measurements. Each measurement was repeated at least 10 times and the average value was used in subsequent computation.

2.3 Calculations

The average of total bromide space (ECV$_{NaBr}$) and the difference between deuterium space (TBW$_{D2O}$) and total body potassium space (ICV$_{TBK}$) ($ECV_{TBK} = TBW_{D2O} - ICV_{TBK}$), was used as the ECV gold standard ($ECVG$), and the average of ICV$_{TBK}$ and the difference between TBW$_{D2O}$ and ECV$_G$ was used as the ICV gold standard ($ICVG$).

Hydration state of FFM

Total body fat free mass ($FFM_{total}$) was calculated as body mass (BW) less total body fat mass. Segmental FFM was calculated as skeletal muscle mass plus bone mass. Extra- and intracellular hydration status of FFM were calculated as the ratios of total body ECV to FFM ($\alpha = ECV_G / FFM_{total}$) and total body ICV to FFM ($\beta = ICV_G / FFM_{total}$), respectively. Factors $\alpha$ and the $\beta$ thus resemble indices of body hydration. It was assumed that the value of the $\alpha$ and $\beta$ in the whole body and each segment were identical.

Segment-specific resistivity
Based on resistance and reactance data derived from BIS, extracellular (R_E, Ohm) and intracellular resistance (R_I, Ohm) were calculated using the Cole-Cole model [15]. Extracellular (ρ_E, Ohm cm) and intracellular segmental resistivity (ρ_I, Ohm cm) were then calculated as

\[ \rho_{E,i} = \alpha \cdot FFM_i \cdot R_{E,i} / L_i^2 \]  
Eq.1

\[ \rho_{I,i} = \beta \cdot FFM_i \cdot R_{I,i} / L_i^2 \]  
Eq.2

where FFM_i is segmental fat free mass, ‘L’ is length of each segment (cm) and ‘i’ represents the individual segment.

**Segmental and total body ECV and ICV**

Segmental ECV_i and ICV_i were calculated as:

\[ ECV_i = \frac{1}{1000} \left( \rho_{E,i} \times \frac{L_i^2}{R_{E,i}} \right) \]  
Eq.3

\[ ICV_i = \frac{1}{1000} \left( \rho_{I,i} \times \frac{L_i^2}{R_{I,i}} \right) \]  
Eq.4

Total body ECV and ICV were calculated respectively as the sum of segmental ECV and ICV, either using segmental resistivity values (ECV_SR, ICV_SR, eq. 5 and 6) or using the uniform resistivity value for each segment (ECV_USR, ICV_USR, eq. 7 and 8, according to [34]):

\[ ECV_{SR} = 2(ECV_A + ECV_T') + ECV_T \]  
Eq.5

\[ ICV_{SR} = 2(ICV_A + ICV_L) + ICV_T \]  
Eq.6

Page 12 of 36
\[ ECV_{UR} = \rho_{ECV} \left( 2 \frac{L_A^2}{R_{E,A}} + 2 \frac{L_L^2}{R_{E,L}} + 4 \frac{L_T^2}{R_{E,T}} \right) \]  
Eq. 7

\[ ICV_{UR} = \rho_{ICV} \left( 2 \frac{L_A^2}{R_{I,A}} + 2 \frac{L_L^2}{R_{I,L}} + \frac{L_T^2}{R_{I,T}} \right) \]  
Eq. 8

where \( \rho_{ECV} \) and \( \rho_{ICV} \) represent the uniform extra- and intracellular resistivity values for SBIS (\( \rho_{ECV} = 47 \) \( \Omega \) cm for males and females, \( \rho_{ICV} = 273.9 \) \( \Omega \)-cm for males and 264.9 \( \Omega \)-cm for females), and \( L_A, L_L, L_T \) and \( R_{E,A}, R_{E,L}, R_{E,T}, R_{I,A}, R_{I,L}, R_{I,T} \) represent lengths and segmental extra- and intracellular resistances for arms, legs and trunk, respectively.

For each method, total body water (TBW) was computed as the sum of ECV and ICV.

\[ TBW_{SR} = ECV_{SR} + ICV_{SR} \]

\[ TBW_{UR} = ECV_{UR} + ICV_{UR} \]

Due to the location of the electrodes the ECV and ICV estimates from SBIS do not include fluid compartments contained in hands, feet, head and neck. Therefore, ECV and ICV results were corrected for the hydrated FFM of each of these compartments. Estimates for the FFM of head, neck, hands and feet were based on the fraction of total FFM contained in these areas, as reported recently [10], and the measured extracellular and intracellular hydration status of total FFM, as described above:

\[ C_E = \alpha \times (FFM_{head+neck} + FFM_{hand} + FFM_{foot}) \]  
Eq. 9

\[ C_I = \beta \times (FFM_{head+neck} + FFM_{hand} + FFM_{foot}) \]  
Eq. 10

Where \( FFM_{head+neck} \) is 5.87%, \( FFM_{hand} \) is 0.97% and \( FFM_{foot} \) is 0.43% of total body weight [10].
Total adjusted $ECV_{SR}$ and $ICV_{SR}$ were then calculated as:

$$ECV_{SR} = 2(ECV_A + ECV_L) + ECV_T + C_E \quad \text{Eq.11}$$

$$ICV_{SR} = 2(ICV_A + ICV_L) + ICV_T + C_I \quad \text{Eq.12}$$

*Whole body bioimpedance measures*

For the WBIS method, whole body $ECV_W$, $ICV_W$ and $TBW_W$ were calculated according to [9] as:

$$ECV_W = K_{ECV} \left(\frac{H^2 \sqrt{W}}{R_E}\right)^{2/3} \quad \text{Eq.13}$$

where $H$ is body height in cm, $W$ is body mass in kg, and $R_E$ is extracellular resistance in Ohms.

$K_{ECV}$ is a factor related to body shape, density and resistivity by the following equation:

$$K_{ECV} = \frac{1}{1000} \left(\frac{K_B \rho_{ECV}^2}{D}\right)^{1/3} \quad \text{Eq.14}$$

where $D$ is body density considered as constant value (kg/L), and $K_B$ is a coefficient relating body height to limb geometry:

$$K_B = \frac{1}{H} \left(\frac{L_A}{C_A^2} + \frac{L_T}{C_T^2} + \frac{L_L}{C_L^2}\right) (2L_A C_A^2 + 2L_T C_T^2 + 2L_L C_L^2) \quad \text{Eq.15}$$

where, $C_A$, $C_T$ and $C_L$ represent segmental circumferences

$ICV_W$ was calculated as:

$$\left(1 + \frac{ICV_W}{ECV_W}\right)^{5/2} = \left(\frac{R_E + R_I}{R_J}\right) \left(1 + \frac{k_\rho ICV_W}{ECV_W}\right) \quad \text{Eq.16}$$

where $k_\rho$ is the ratio of intracellular fluid resistivity to the extracellular fluid resistivity ($k_\rho = \rho_{ICV}/\rho_{ECV}$).
Intracellular resistivity ($\rho_{ICV}$) values used for WBIS were 273.9 $\Omega \cdot \text{cm}$ for males and 264.9 $\Omega \cdot \text{cm}$ for females; extracellular resistivity ($\rho_{ECV}$) values for WBIS were 40.5 $\Omega \cdot \text{cm}$ for males and 30 $\Omega \cdot \text{cm}$ for females.

Total body water (TBW$_W$) was obtained as sum of ECV$_W$ and ICV$_W$.

**Statistical analysis.**

Data are presented as means ± SD. Linear regression analysis was performed to study the relationship between gold-standard measures of body water compartments with estimates generated by SBIS and WBIS. Bland-Altman plot was used to report bias and limits of agreement between gold standard and bioimpedance measurements. Differences between groups were compared using Student’s paired $t$-test and were assumed significant at $p < 0.05$. Statistical analysis was performed using Prism 4 (GraphPad Software, Inc. San Diego CA).
3. RESULTS

Table 1 summarizes results of anthropometric measurements and ECV, ICV TBW value as estimated by classical dilution methods. Total body water by D$_2$O (TBW$_{D2O}$), ECV by NaBr (ECV$_{NaBr}$), ICV by TBK (ICV$_{TBK}$) and fat free mass (FFM) were all significantly higher in males compared to females. The ratio of extracellular volume to FFM (ECV/FFM = $\alpha$) was significantly higher in female patients, indicating a higher hydration state ($\alpha$: 0.39±0.05 vs. 0.34±0.03, L/kg, p<0.001). In contrast, the ratio of intracellular volume to FFM (ICV/FFM = $\beta$) was not different between genders ($\beta$: 0.41±0.04 vs. 0.41±0.02, L/kg, p=ns). Fat free mass of arms, legs and trunk, as estimated from MRI were significantly higher in males vs. females (Table 1).

Whole body extracellular resistance (R$_E$) and intracellular resistance (R$_I$) were measured either directly by wrist-to-ankle BIS (WBIS) or calculated as the sum of segmental resistances from SBIS (Table 2). The mean sum of segmental R$_E$ was not different from mean whole body R$_E$ in men or women (p = n.s.). In contrast, the sum of segmental R$_I$ and whole body R$_I$ were both lower in men than in women.

Specific resistivity values for various body segments were computed from FFM hydration coefficients ($\alpha$ and $\beta$), segmental FFM, and segmental resistance using Eq. 1 and Eq. 2. Extracellular segment-specific resistivity differed significantly between arms, legs and trunk (Table 3). Intracellular segment specific resistivity values for legs and trunk were not different from each other but were significantly higher than for arms. ECV and ICV were calculated for each segment using the classical BIS equations applying a uniform resistivity factor for each segment (SBIS$_{UR}$) and compared to estimates derived from the modified equations using segment specific resistivity values (SBIS$_{SR}$) (Table 4). ECV estimates for arms and legs derived from SBIS with segment-specific resistivity were significantly higher compared
to the traditional method, while estimates for trunk ECV were lower. In contrast, ICV and TBW (ECV+ICV) estimates for arms and trunk were lower when derived from SBIS\textsubscript{SR} than from SBIS\textsubscript{UR}. No difference between the two methods was found for leg ICV estimates. Estimates of total body ECV, calculated as sum of segments, were higher when computed with segment-specific than with uniform resistivity values.

In contrast to gold standard methods, SBIS does not take into account the volumes of hands, feet, head and neck and thus underestimates total body volumes. For direct comparison with gold standards BIS data were adjusted for unmeasured regions of the body according to Eq. 9 – 12. Adjusted total ECV and TBW calculated from SBIS\textsubscript{SR} were not different from gold standards, while calculations from WBIS and SBIS\textsubscript{UR} resulted in significantly lower estimates (Table 5).

The correlations of ECV, ICV and TBW with the respective gold standard methods were stronger for SBIS\textsubscript{SR} than for WBIS (Fig. 1 – 3, (A) and (B)) (ECV\textsubscript{SR}: R\textsuperscript{2}=0.93; ICV\textsubscript{SR}: R\textsuperscript{2}=0.86; TBW\textsubscript{SR}: R\textsuperscript{2}=0.96 vs. ECV\textsubscript{W}: R\textsuperscript{2}=0.83; ICV\textsubscript{W}: R\textsuperscript{2}=0.83; TBW\textsubscript{W}: R\textsuperscript{2}=0.87). Fig.1 – 3 (C) and (D) show Bland-Altman plots for comparison of gold standard and the two BIS methods, demonstrating the superiority of SBIS\textsubscript{SR} over WBIS for the assessment of body fluid volumes.

The geometry of segments differed significantly between males and females with regard to length and circumference (Tab. 6). The specific K\textsubscript{B} values calculated with Eq. 15 were higher than the value currently used in those equations (K\textsubscript{B}=4.3), but was not different between men and women. There is no improvement of accuracy of WBIS by comparing gold standard ECV and ECV\textsubscript{W} using individual K\textsubscript{B} calculated with Eq. 15 (Fig.4).
DISCUSSION

Various approaches to the use of whole body and segmental bioimpedance have been made for assessment of body composition and body fluid volumes in hemodialysis patients [4, 31, 5, 17]. For WBIS the body is assumed to be a uniform cylinder with homogeneous conductivity, while for segmental BIS, the body is viewed as several cylinders of differing sizes connected in parallel and in series. Results derived from both BIS methods are based on measures of tissue resistance and reactance. Equations used for calculation of extracellular fluid volumes from SBIS currently include a factor for tissue resistivity $[\rho]$, which does not differ for the various segments [33]. Resistivity of a specific body segment, however, depends on its tissue composition and hydration status, and, because it is assumed to be a cylinder, on the segment’s length and circumference. In this paper we have defined segment specific resistivity values for arms, legs and trunk separately and have applied those value to the equations for calculation of ICV, ECV and TBW. The results were compared to those obtained with a uniform resistivity factor and to data derived from WBIS. This study shows that both, extracellular and intracellular resistivity differ between segments and indicates that accuracy of body fluid volume measurements from SBIS can be significantly improved by using segment-specific resistivity.

For the definition of segmental resistivity it was essential to measure FFM and the hydration status of FFM with gold-standard methods independent of BIS. Whole body and segmental FFM were determined by MRI, a validated method for assessment of muscle and fat mass [20]. The hydration status of whole body FFM was defined by the ratios of ECV to FFM ($\alpha$) and ICV to FFM ($\beta$), where the gold standard for ECV (ECV$_G$) was determined as the average of total bromide space (ECV$_{NaBr}$) and the difference between deuterium space (TBW$_{D2O}$) and total body potassium space (ICV$_{TBK}$) (ECV$_{TBK} =$ TBW$_{D2O}$ -ICV$_{TBK}$). The gold-standard for the whole body ICV (ICV$_G$) was calculated as the difference
of TBW$_{D_2O}$ and ECV$_G$. The ratio of ECV/FFM was higher in females than in males, and a similar observation was made for the TBW/FFM ratios which were both higher than those reported for normal subjects (0.73 L/kg) [29]. There was no sex difference for the ICV/FFM ratio. Since our data were obtained on a regular dialysis day prior to the start of dialysis treatment, these differences are in accordance with accumulation of water in the extracellular space between dialysis treatments. The sex differences in ECV/FFM are readily explained by generally lower FFM in females compared to males but similar interdialytic weight gain. For further analyses the hydration status of FFM indicated by the factors $\alpha$ and $\beta$ was assumed to be identical throughout the body for each sex.

Extracellular and intracellular segmental resistivities were determined for arms, legs and trunk. Extracellular segmental resistivity of the trunk was significantly higher than that of arm and leg, which also differed significantly from each other. Intracellular segmental resistivity was similar for trunk and leg, but significantly lower in the arm. These differences in segmental resistivities may be due to i) differences in the composition of body tissues within each segment that affect the distribution of body fluid and ii) differences in segmental geometric shape and volume that lead to inhomogeneous distribution of the electrical current. The traditional algorithms for calculation of segmental ECV and ICV (Eq. 7 and 8) from SBIS take into account tissue resistance data specific for each segment but employ only a uniform value for segmental resistivity [34, 33]. In a previous study we have reported that these traditional SBIS equations underestimate trunk ECV, due to inhomogeneous distribution of low voltage current throughout the trunk and we have been able to improve the accuracy of the equation by introduction of a compensatory factor [33]. The present study shows that there are major differences between the uniform resistivity value and those derived from our measurements for each segment. Use
of uniform rather than segmental resistivity values leads to underestimation of segmental and total body fluid volumes.

Due to location of the electrodes, tissue volumes for hands, feet, head and neck are not included in SBIS measurements. We have compensated for these body fluid compartments in our calculations (Eq. 9 - 12) and thus were able to further improve SBIS accuracy. Use of segment-specific resistivity values in combination with correction for unmeasured body fluid compartments resulted in significantly improved estimates of ECV, ICV and TBW from SBIS and the results did not differ statistically from those derived from gold standard methods. One other factor that might interfere with impedance measurements is plasma electrolyte concentration, which changes during and between dialysis treatments. However, the effects of electrolyte concentration on impedance are difficult to separate from changes in body water volumes due to the inherent linkage of changes in electrolyte concentration with those in extracellular fluid volumes in HD patients.

Whole body BIS is the bioimpedance technique used most frequently for assessment of body fluid volumes. This technique assumes the body to be one cylinder and equations include a factor $K_B$ ($K_B = 4.3$) which relates body height to limb geometry. The constant $K_B$ is used under the assumption that limb length and body height are proportionate [12, 31, 9], which may not always be the case. The accuracy of WBIS should be improved by applying individual body segmental coefficients instead of a constant $K_B$ value [12]. We have measured segmental limb lengths and circumferences and introduced individual $K_B$ values for calculation of ECV, ICV and TBW. This, however, did not significantly improve the accuracy of WBIS estimates, which still were significantly lower than both gold standard estimates and estimates from SBIS using segment-specific resistivity.
While data on ECV are clinically useful for estimation of body hydration and prescription of dry weight, data on ICV, which are closely related to muscle mass, may be used for assessment of body composition. Clinically, accurate assessment of segmental or whole body ECV and ICV by BIS will allow differentiation of causes of weight gain (overhydration vs. increase in muscle mass) or weight loss (dehydration vs. loss of muscle mass) in hemodialysis patients.

In conclusion, the accuracy of ECV, ICV and TBW estimates from segmental BIS in maintenance hemodialysis patients is improved by applying segment-specific resistivity values for arms, legs and trunk and by correcting for unmeasured body compartments. Accuracy of whole body BIS was not improved by adjusting for individual limb geometry. Accurate estimation of body fluid volumes is useful in predicting body composition in dialysis and non-dialysis patients and segmental BIS appears to be a most promising tool for these purposes. However, it should be emphasized that the segment-specific resistivity values reported here were obtained from patients with end-stage-renal disease and thus may not be applicable to a non-dialysis population.

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References


Tables

Table 1 Patients’ physical characteristics

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<td>BMI, kg/m2</td>
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<td>TBK, mmol</td>
<td>2607±472</td>
<td>3768±371</td>
<td>0.001</td>
</tr>
<tr>
<td>TBW\textsubscript{D2O}, L</td>
<td>34.4±5.9</td>
<td>45.3±4.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>ECV\textsubscript{NaBr}, L</td>
<td>16.3±4.6</td>
<td>21.0±3.2</td>
<td>0.003</td>
</tr>
<tr>
<td>ICV\textsubscript{TBK}, kg</td>
<td>17.2±3.1</td>
<td>24.8±2.4</td>
<td>0.001</td>
</tr>
<tr>
<td>ICV\textsubscript{D2O-ECVave}, L</td>
<td>18.7±5.4</td>
<td>26.1±3</td>
<td>0.001</td>
</tr>
<tr>
<td>ECV\textsubscript{D2O-ICVT}, L</td>
<td>17.2±3.2</td>
<td>20.5±3.82</td>
<td>0.005</td>
</tr>
<tr>
<td>ECV\textsubscript{ave}, L</td>
<td>16.7±3.8</td>
<td>20.7±3.3</td>
<td>0.005</td>
</tr>
<tr>
<td>FFM, kg</td>
<td>43.0±7.5</td>
<td>60.6±5.7</td>
<td>0.001</td>
</tr>
<tr>
<td>TBW/FFM, L/kg</td>
<td>0.8±0.05</td>
<td>0.75±0.03</td>
<td>0.00056</td>
</tr>
<tr>
<td>ECV/FFM, L/kg</td>
<td>0.39±0.05</td>
<td>0.34±0.03</td>
<td>0.0028</td>
</tr>
<tr>
<td>ICV/FFM, L/kg</td>
<td>0.41±0.04</td>
<td>0.41±0.02</td>
<td></td>
</tr>
<tr>
<td>ECV/ICV</td>
<td>0.92±0.2</td>
<td>0.86±0.14</td>
<td></td>
</tr>
<tr>
<td>FFM-arm, kg</td>
<td>3.4±0.7</td>
<td>5.6±0.6</td>
<td>1.13E-09</td>
</tr>
<tr>
<td>FFM-trunk, kg</td>
<td>22.6±4.5</td>
<td>29.4±3.8</td>
<td>0.00014</td>
</tr>
<tr>
<td>FFM-leg, kg</td>
<td>11.4±2</td>
<td>16.5±2.5</td>
<td>3.13E-06</td>
</tr>
</tbody>
</table>
Table 2 Extracellular and intracellular resistance in male and female

<table>
<thead>
<tr>
<th>Resistance</th>
<th>Female</th>
<th>Male</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-Arm, Ohm</td>
<td>283.7±52</td>
<td>249.9±33</td>
<td>0.04</td>
</tr>
<tr>
<td>RE-Trunk, Ohm</td>
<td>57.1±9</td>
<td>52.8±8</td>
<td>ns</td>
</tr>
<tr>
<td>RE-Leg, Ohm</td>
<td>252.9±43</td>
<td>236±52</td>
<td>ns</td>
</tr>
<tr>
<td>RE-WA, Ohm</td>
<td>593.0±87</td>
<td>538.6±80</td>
<td>ns</td>
</tr>
<tr>
<td>RE-Sum, Ohm</td>
<td>593.6±86</td>
<td>538.2±79</td>
<td>ns</td>
</tr>
<tr>
<td>RI-Arm, Ohm</td>
<td>773.6±189</td>
<td>607.0±113</td>
<td>0.007</td>
</tr>
<tr>
<td>RI-Trunk, Ohm</td>
<td>82.9±17</td>
<td>69.8±13</td>
<td>0.02</td>
</tr>
<tr>
<td>RI-Leg, Ohm</td>
<td>694.7±247</td>
<td>564.7±133</td>
<td>ns</td>
</tr>
<tr>
<td>RI-WA, Ohm</td>
<td>1526.6±396*</td>
<td>1208.8±209*</td>
<td>0.009</td>
</tr>
<tr>
<td>RI-Sum, Ohm</td>
<td>1551.2±411</td>
<td>1241.4±208</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Table 3. Specific segment resistivity in male and female subjects

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\rho_{E}$-Arm, $\Omega$ cm</td>
<td>67 ± 14</td>
<td>67 ± 8</td>
<td>0.918506</td>
</tr>
<tr>
<td>$\rho_{E}$-Trunk, $\Omega$ cm</td>
<td>172 ± 21</td>
<td>159 ± 24</td>
<td>0.138186</td>
</tr>
<tr>
<td>$\rho_{E}$-Leg, $\Omega$ cm</td>
<td>99 ± 15</td>
<td>98 ± 13</td>
<td>0.82964</td>
</tr>
<tr>
<td>$\rho_{I}$-Arm, $\Omega$ cm</td>
<td>191 ± 36</td>
<td>194 ± 29</td>
<td>0.775189</td>
</tr>
<tr>
<td>$\rho_{I}$-Trunk, $\Omega$ cm</td>
<td>266 ± 42</td>
<td>250 ± 38</td>
<td>0.277882</td>
</tr>
<tr>
<td>$\rho_{I}$-Leg, $\Omega$ cm</td>
<td>281 ± 45</td>
<td>281 ± 43</td>
<td>0.992737</td>
</tr>
</tbody>
</table>

Table 4 comparison of ECV and ICV calculated by two segmental BIS

<table>
<thead>
<tr>
<th></th>
<th>ECV ,L</th>
<th>ICV ,L</th>
<th>ECV+ICV, L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBIS$_{SR}$</td>
<td>SBIS$_{UR}$</td>
<td>SBIS$_{SR}$</td>
</tr>
<tr>
<td>Arm</td>
<td>1.69±0.5</td>
<td>1.2±0.3</td>
<td>2.1±0.7</td>
</tr>
<tr>
<td>Trunk</td>
<td>9.6±1.8</td>
<td>11.0±2.1</td>
<td>11.1±2.6</td>
</tr>
<tr>
<td>Leg</td>
<td>5.2±1.3</td>
<td>2.5±0.6</td>
<td>6.0±1.8</td>
</tr>
<tr>
<td>Sum of segment</td>
<td>16.5±3.2</td>
<td>14.6±2.7</td>
<td>19.2±4.5</td>
</tr>
</tbody>
</table>

All differences between specific segments resistivity and uniform resistivity with SBIS are significant (p<0.05).
Table 5 comparison of fluid volume by BIS and gold standard

<table>
<thead>
<tr>
<th></th>
<th>#Gold St</th>
<th>*SBIS&lt;sub&gt;S&lt;/sub&gt;</th>
<th>SBIS&lt;sub&gt;S&lt;/sub&gt;</th>
<th>SBIS&lt;sub&gt;U&lt;/sub&gt;</th>
<th>WBIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECV, L</td>
<td>18.9±4.0</td>
<td>19.0±3.6</td>
<td>16.6±3.2*</td>
<td>14.8±3.1*</td>
<td>17.9±3.7</td>
</tr>
<tr>
<td>ICV, L</td>
<td>21.5±4.3</td>
<td>21.7±4.8</td>
<td>20.12±4.6</td>
<td>20.5±4.6</td>
<td>21.1±5.1</td>
</tr>
<tr>
<td>TBW, L</td>
<td>40.4±7.6</td>
<td>40.7±8.1</td>
<td>36.7±7.4</td>
<td>35.3±7.1*</td>
<td>38.8±8.6</td>
</tr>
</tbody>
</table>

*SBIS<sub>S</sub> data were calculated by sum of segments adjusted for unmeasured regions of the body

# Gold standards refer to ECV<sub>G</sub>, ICV<sub>G</sub> and TBW<sub>G</sub>

*p < 0.05 vs. gold standard measure by ANOVA and Dunnett’s multiple comparison test

Table 6 Anthropometric measurement

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm length, cm</td>
<td>52.8±5.6</td>
<td>59.7±3.3</td>
<td>0.000289</td>
</tr>
<tr>
<td>Trunk length, cm</td>
<td>53.5±5.4</td>
<td>57.9±3.9</td>
<td>0.016267</td>
</tr>
<tr>
<td>Leg length, cm</td>
<td>74.5±4.6</td>
<td>81.7±5.7</td>
<td>0.001047</td>
</tr>
<tr>
<td>Arm circumference, cm</td>
<td>24.8±4.2</td>
<td>25.9±2.3</td>
<td>0.374207</td>
</tr>
<tr>
<td>Trunk circumference, cm</td>
<td>99.7±16.4</td>
<td>102.2±11.4</td>
<td>0.632169</td>
</tr>
<tr>
<td>Leg circumference, cm</td>
<td>38.9±4.8</td>
<td>40.1±2.9</td>
<td>0.443259</td>
</tr>
<tr>
<td>K&lt;sub&gt;B&lt;/sub&gt;</td>
<td>4.63±0.6</td>
<td>4.56±0.5</td>
<td>0.720578</td>
</tr>
</tbody>
</table>
Legends

Fig. 1 A, B: Prediction of extracellular fluid volume (ECV) from segmental bioimpedance spectroscopy in hemodialysis patients. Segmental BIS including segment-specific resistivity (SBIS, 1A) and wrist-to-ankle bioimpedance (WBIS, 1B) were correlated with gold standard ECV (ECVG) derived from averaging total bromide space and the difference between total body water (deuterium space) and ICV (total body potassium) (r²=0.9287 for SBIS and r²=0.8345 for WBIS). C, D: Bland-Altman plot comparing total body gold standard ECV (ECVG) and bioimpedance estimated ECV, using segmental BIS including segment-specific resistivity (SBIS, 1C) and wrist-to-ankle bioimpedance (WBIS, 1D).

Fig. 2 A, B: Prediction of intracellular fluid volume (ICV) from segmental bioimpedance spectroscopy in hemodialysis patients. Segmental BIS including segment-specific resistivity (SBIS, 2A) and wrist-to-ankle bioimpedance (WBIS, 2B) were correlated with gold-standard ICV (ICVG) derived from averaging TBK-derived ICV and the difference between total body water (deuterium space) and ECVG (total body potassium) (r²=0.8629 for SBIS and r²=0.8345 for WBIS). C and D: Bland-Altman plot comparing total body gold standard ICV (ICVG) and bioimpedance estimated ICV, using segmental BIS including segment-specific resistivity (SBIS, 2C) and wrist-to-ankle bioimpedance (WBIS, 2D).

Fig. 3 A, B: Prediction of total body water (TBW) from segmental bioimpedance spectroscopy in hemodialysis patients. Segmental BIS including segment-specific resistivity (SBIS, 3A) and wrist-to-ankle bioimpedance (WBIS, 3B) were correlated with gold standard TBW (TBWG) calculated as sum of ECVG and ICVG (r²=0.9599 for SBIS and r²=0.8345 for WBIS). C, D:
Bland-Altman plot comparing gold standard TBW (TBW_G) and bioimpedance estimated TBW, using segmental BIS including segment-specific resistivity (SBIS, 3C) and wrist-to-ankle bioimpedance (WBIS, 3D).

Fig.4: Bland-Altman plot comparing total body, gold-standard ECV (ECV_G) and bioimpedance estimated ECV, using wrist-to-ankle bioimpedance computed with individual KB-values according to Eq.9 (ECV_{WBIS,KB})
Fig. 1
Fig. 2
Fig. 3
Figure 4