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ORIGINAL ARTICLE

Extracellular volume measurements using bioimpedance spectroscopy-Hanai method and wrist–ankle resistance at 50 kHz

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Abstract A method for extrapolating the extracellular water (ECW) resistance from wrist–ankle resistance at 50 kHz (R_{50}) is proposed in this paper, in order to enable 50 kHz impedancemeters to use the BIS-Hanai equation for determination of ECW. Values of R_{50} and the ECW resistance extrapolated at zero frequency R_e were measured in a first group of 57 healthy volunteers, using a Xitron 4200 multifrequency impedancemeter and mean values (b) of the ratio R_{50}/R_e in men and women were used to determine individual values of R_{e50}, the ECW resistance extrapolated from R_{50}, which were substituted to R_e in the BIS-Hanai equation. For validation, the method was compared against ECW measured with the Xitron (V_{ex}) in a second group of 31 healthy volunteers, using values of b of first group. Values of R_{e50} in this second group were found to be not significantly different from corresponding values of R_e with p-values of Student test of 0.346 for men and 0.300 for women. ECW volumes (V_{e50}) calculated from R_{e50} were also found not significantly different from those of the Xitron with Student paired test p values of 0.277 in men and 0.393 in women. Our method gave a better agreement with V_{ex} than two bioimpedance analysis methods from the literature, especially in women. It was also tested on a 50 kHz single frequency impedancemeter (BodyExplorer, Juwell Medical) on a third group of 21 subjects and gave ECW volumes not significantly from those of the Xitron with $p = 0.531$ for men and 0.096 for women.

Keywords Extracellular water · Bioimpedance analysis

Abbreviations

BCM Body cell mass
BIA Bioimpedance analysis
BIS Bioimpedance spectroscopy
BMI Body mass index
ECW Extracellular water
ICW Intracellular water
TBW Total body water

List of symbols

b mean value of R_{50}/R_e
c volume fraction of non conducting elements
D_B body density (kg m^{-3})
H height (m)
K_B body shape factor
k_e coefficient defined by Eq. (5)
R_{50} resistance at 50 kHz (Ω)
R_e ECW resistance extrapolated at zero frequency by the Xitron (Ω)
R_{e50} ECW resistance calculated from R_{50} (Ω)
V_B body volume (L)
V_{ex} ECW volume calculated by the Xitron from R_e (L)
V_{e50} ECW volume calculated from R_{50} (L)
W weight (kg)
X_{50} reactance at 50 kHz (Ω)
ρ resistivity (Ω m)

Subscripts

b BodyExplorer
s Sergi's method
h Hannan's method

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1 Introduction

While there are several methods for measuring total body water (TBW) using bioimpedance analysis (BIA) from the wrist-ankle impedance at 50 kHz [2, 4, 5, 10, 11, 19], the number of BIA methods from measuring extracellular water (ECW) from the same impedance is more limited [7, 17]. ECW and TBW measurements can be useful in several pathologies, such as hemodialysis [8, 13], as the major part of water removed by ultrafiltration comes from ECW, or in cardiac disease, often leading to extracellular edema [12]. In addition, the difference between TBW and ECW yields the intracellular volume (ICW) which gives access to body cell protein mass BCM_{pro} [20] by

$$BCM_{pro} = 0.3838\ ICW \qquad (1)$$

At frequencies below 1 kHz, the current will not penetrate cell membranes and only circulates in the ECW. The bioimpedance spectroscopy (BIS) method [3, 18] uses this property to calculate the ECW resistance R_e by extrapolating the impedance measured at various frequencies along a circle until the resistance axis, when it becomes a pure resistance at zero frequency (Fig. 1). The human body is then approximated as the sum of 5 cylinders (the limbs and the trunk) by multiplying the resistance-volume relationship for a single cylinder by a dimensionless shape factor K_B calculated from the length and perimeters of the limbs and the trunk to give the body resistance R as shown by De Lorenzo et al. [3]

$$R = \frac{K_B \rho_a H^2}{V_B} \qquad (2)$$

where V_B is the body volume, H the height and ρ_a the apparent tissue resistivity. De Lorenzo et al. [3] obtained a value of 4.3 for the shape coefficient K_B from statistical anatomical measurements in adults. The apparent tissue resistivity is given by Hanai's [6] "mixture" conductivity theory, where c is the volume fraction of non-conducting tissues and ρ the resistivity of fluid inside tissues

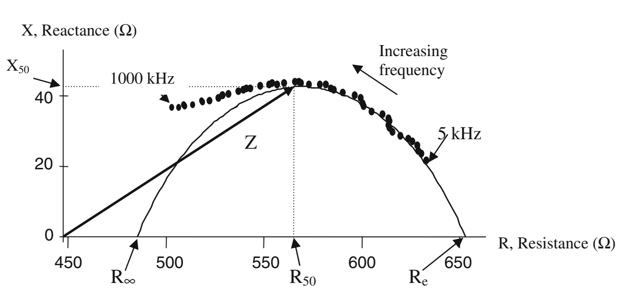

Fig. 1 Schematic of determination of resistances R_e and R_∞ by extrapolation in R–X plane

$$\rho_a = \frac{\rho}{(1-c)^{3/2}} \qquad (3)$$

At low frequency, c is equal to $1 - V_e/V_B$, as only ECW is conducting and Eqs. (2) and (3) lead to the following expression for ECW volume in L, where H is the height in cm, and W the body weight in kg

$$V_{ex} = k_e \left(\frac{H^2 W^{1/2}}{R_e} \right)^{2/3} \qquad (4)$$

with

$$k_e = \left(\frac{K_B^2 \rho_e^2}{D_B} \right)^{1/3} \qquad (5)$$

where D_B is the body density and ρ_e the ECW resistivity. Values of the coefficient k_e were determined from measurements of ECW volumes by bromide dilution technique, and found to be 0.306 for men and 0.299 for women, when V_e is in liter, the body density D_B is 1.05 kg L^{-1} and ECW resistivity ρ_e is in Ω cm. When these values of k_e are introduced in Eq. (4), ECW resistivities ρ_e are found equal to 40.3 Ω cm for men and 39.0 Ω cm for women, close to values of saline (40 Ω cm).

In a recent paper [9], we have used Eq. (4) to calculate ECW volumes from the provided by a single frequency foot-to-foot impedancemeter which featured a square signal at 114 kHz, using the low frequency resistance R_{lf} extracted from the top of the square signal. Individual coefficients k_{ie} in this case were determined by substituting R_{lf} to R_e in Eq. (4) and equating V_e with the ECW volume V_{ex} measured by a Xitron 4200 multifrequency impedancemeter (Xitron Technology, San Diego, Ca, USA) to obtain

$$k_{ie} = V_{ex} \left(H^2 W^{1/2} / R_{lf} \right)^{-2/3} \qquad (6)$$

Mean values of these individual coefficients k_{ie} were used as k_e in Eq. (4) to measure ECW with the foot-to-foot impedancemeter. These ECW volumes were found not significantly different from corresponding ones measured by the Xitron.

Because many commercially available impedancemeters operate at a single frequency of 50 kHz, this paper investigates whether the BIS method could be implemented by replacing R_e in Eq. (4) by an ECW resistance R_{e50} deducted only from R_{50}, the body resistance measured at 50 kHz, rather than by extrapolation of impedances measured at various frequencies, as the Xitron does. The study was first performed using R_{50} and R_e measured by a Xitron 4200 on two groups of subjects, the second being used for validation and the method was later applied to a third group, using a recently commercialized 50 kHz impedancemeter, the BodyExplorer (Juwell Medical, Gauting, Bavaria, Germany).

2 Material and methods

2.1 Principle of method

Our method consists in estimating the ECW resistance (R_{e50}) from R_{50} by assuming that the ratio $b = R_{50}/R_{e50}$ remains constant in men and in women, although it may be slightly different between the two sexes. In order to determine this parameter b, we have measured, using a Xitron 4200, R_{50} and R_e in a first group of 27 men and 28 women (method definition group) from the student body and staff of our university. The parameter b was taken as the mean value of the R_{50}/R_e ratio in men and women, so that the ECW resistance R_{e50} is given by

$$R_{e50} = R_{50}/b \quad (7)$$

Then the ECW volume V_{e50} was calculated from Eq. (8), in which R_{50}/b was substituted to R_e, and V_{e50} to V_{ex}.

$$V_{e50} = k_e\left(\frac{bH^2W^{1/2}}{R_{50}}\right)^{2/3} \quad (8)$$

with the same values of k_e as for the BIS method of Eq. (7), $k_e = 0.306$ for men and 0.299 for women.

For an independent validation of the method, the same impedance measurements were made in a second group (validation group) of 15 men and 16 women and values of V_{e50} were calculated from Eq. (8) using values of b found for the first group. These values of V_{e50} were compared with corresponding values of V_{ex} calculated by the Xitron from Eq. (4).

2.2 Subjects and measurement protocol

Whole body impedance data were recorded in the first and second groups of healthy volunteers aged from 16 to 71 years. Their characteristics are summarized in Table 1. Their weight (W) was measured by a Bodymaster Vision scale (Tefal SA, Rumilly, France) and their height (H) by a wall mounted measuring tape. A Xitron 4200 was used in the supine position with four gel electrodes placed on the dorsal surfaces of the right hand and foot. Current electrodes were placed, respectively, proximal to metacarpal and metatarsal phalangeal joints, in accordance with standard tetrapolar electrode placement [2]. Proximal (voltage) electrodes were separated by 5 cm from current ones. This device operates at 50 frequencies between 5 and 1,000 kHz and calculates resistances at zero (R_e) and infinite (R_∞) frequencies by extrapolating its data to the real axis in the resistance-reactance plane as shown in Fig. 1, plotted using impedance values given by the Xitron software. The reproducibility of resistances measurements has been checked and found to be within 3–5 Ω or about 1%.

Once the method was validated after comparing values of R_{e50} with corresponding ones of R_e from the Xitron in the second group of subjects, it was applied to the BodyExplorer, a BIA impedancemeter. To this effect, impedance measurements were made on a third group of 21 healthy subjects (11 men and 10 women) using successively the Xitron 4200 and the BodyExplorer supplying a resistance (R_{50b}), a reactance (X_{50b}) and phase at 50 kHz according to the protocol described previously. The third group characteristics are also summarized in Table 1. A block diagram showing the purpose and measurements in each group is given in Fig. 2.

2.3 Comparison with other methods for calculating ECW volume at 50 kHz

We have used the equation of Sergi et al. [17]

$$V_{es} = -5.22 + 0.2H^2/R_{50} + 0.005H^2/X_{50} + 0.08W + 1.9 + 1.86\ \text{sex} \quad (9)$$

where X_{50} is the reactance at 50 kHz and sex is equal to 0 for men and to 1 for women and that of Hannan's et al. [7]

$$V_{eh} = 0.0119H^2/X_{50} + 0.123H^2/R_{50} + 6.15 \quad (10)$$

2.4 Statistical analysis

The comparison of ECW resistances and volumes measured by the Xitron at zero frequency and at 50 kHz were presented using linear regressions with squared correlation

Table 1 Mean values and standard deviations of physical characteristics of the three groups of subjects

	Method definition group		Validation group		BodyExplorer group	
	Men, first group (n = 27)	Women, first group (n = 30)	Men, second group (n = 15)	Women, second group (n = 16)	Men, third group (n = 11)	Women, third group (n = 10)
Height (m)	1.78 ± 0.05	1.63 ± 0.04	1.78 ± 0.06	1.65 ± 0.05	1.79 ± 0.06	1.67 ± 0.04
Age (year)	33.3 ± 16.86	35.0 ± 15.4	28.2 ± 10.9	28.2 ± 11.8	33.6 ± 16.0	30.7 ± 12.5
Weight (kg)	75.42 ± 14.53	62.66 ± 9.3	78.8 ± 12.7	66.75 ± 14.6	80.8 ± 21.4	72.3 ± 12.3
BMI (kg/m^2)	23.83 ± 4.46	23.40 ± 3.1	24.69 ± 3.6	24.5 ± 5.3	25.15 ± 6.2	26.1 ± 4.4

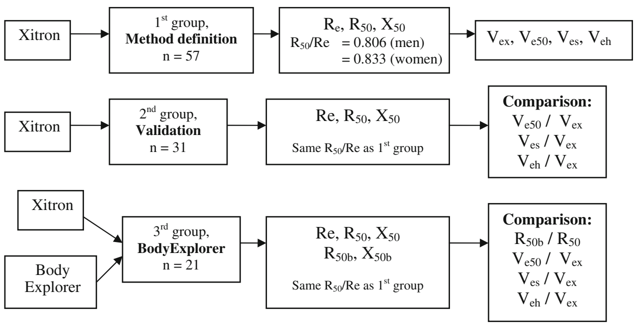

Fig. 2 Block diagram of impedance measurements in various groups

coefficients (R^2). A Bland–Altman graph [1] was used to present differences $V_{e50} - V_{ex}$ in the second group, their standard deviations (SD) and limits of agreement (mean ± 2 SD), which include, in principle 95% of these differences. These resistances and ECW volumes by different methods for both groups were compared using paired Student tests (*t* tests). Results are considered to be significatively different if *p* values are less than 0.05.

3 Results

3.1 Determination and validation of method using the Xitron 4200

3.1.1 Determination of R_{e50} from R_{50}

The mean and SD of R_{50}, measured by the Xitron at 50 kHz, those of R_e, extrapolated by the Xitron at zero frequency and their ratio R_{50}/R_e, are listed in Table 2 for the first and second groups of subjects. This table shows that values of R_e are higher than those of R_{50}, since the resistance decreases with increasing frequency. The values of coefficient b to be used in Eq. (8) are given by the mean values of R_{50}/R_e ratios obtained for the first group which are equal to 0.806 for men and 0.833 for women, as shown in Table 2. The mean values of R_{e50} calculated by Eq. (7) with these values of b were 622.4 Ω versus 623.4 for R_{ex}, in men, and 742.2 Ω versus 741.6 for R_e in women. To avoid any confusion, *p* values of Student test for comparing R_{e50} with R_e for the first group were deleted as this group was used for determination of R_{e50}.

Values of R_{e50} for the second group (Validation group) were calculated using the values of b obtained with the first group, and mean differences with R_e were larger, equal to −4.63 Ω for men and 5.99 Ω for women. However, R_{e50} were not significantly different from corresponding values of R_e with *p* values equal to 0.346 in men and 0.30 in women. Figure 3 shows the comparison of ECW resistances extrapolated from 50 kHz with values of R_e given by the Xitron in the first group. Figure 4 displays the same comparison for the second group and shows that values of R_{e50} were very close to those of R_e.

3.1.2 Determination of ECW volumes V_{e50} using the Xitron

Values of V_{ex}, calculated by the Xitron using Eq. (4), and V_{e50}, calculated from Eq. (8) in first and second group, and differences $V_{e50} - V_{ex}$, are given in Table 3, together with *p* values of Student test, deleting again values for the first group. It can be seen that values of V_{e50} and V_{ex} were close, and not significantly different in the second group, with *p* values of 0.277 in men and 0.393 in women. Values of V_{es}, ECW volumes calculated from Sergi's method (Eq. (9)) also shown in Table 3 together with differences $V_{es} - V_{ex}$, were slightly above those of V_{ex} and V_{e50} in first group, especially in women where they were significantly different. Values V_{eh} calculated from Hannan's method (Eq. (10)) are given in the last column of Table 3. Hannan's method overestimates the ECW as compared to the Xitron by an average of 2 L in men and 3 L in women of first and second groups.

Similar results for the comparison of ECW volumes by different methods were found in the second group. Differences between V_{e50} and V_{ex} were larger than in the first

Table 2 Mean values and SD of ECW resistances R_e, resistances R_{50} and reactances X_{50} measured at 50 kHz by the Xitron in the 3 groups

	Men, first group ($n = 27$)	Women, first group ($n = 30$)	Men, second group ($n = 15$)	Women, second group ($n = 16$)	Men, third group ($n = 11$)	Women, third group ($n = 10$)
R_e Ω	623.4 ± 68.7	741.6 ± 69.7	623.6 ± 67.8	733.8 ± 75.5	615.8 ± 60.8	749.5 ± 79.3
R_{50}, Ω	501.7 ± 56.0	618.3 ± 63.6	498.6 ± 58.0	616.2 ± 65.6	494.8 ± 48.3	626.9 ± 61.3
X_{50}, Ω	62.7 ± 9.4	68.8 ± 6.4	63.5 ± 7.4	69.77 ± 8.8	65.0 ± 8.1	72.9 ± 9.7
R_{50}/R_e	0.806 ± 0.02	0.833 ± 0.02				
R_{e50}, Ω	622.4 ± 69.4	742.2 ± 76.3	618.6 ± 72.0	739.7 ± 78.8	613.85 ± 59.9	752.6 ± 73.6
$R_{e50} - R_e$	−1.0 ± 19.9	0.6 ± 16.4	−4.6 ± 18.4	6.0 ± 22.3	−1.9 ± 20.9	3.1 ± 22.4
p(R_{e50}/R_e)			0.346	0.300	0.766	0.669

Mean values and SD of R_{e50}, the ECW resistance calculated from R_{50}. *p* values of Student paired tests comparing R_{e50} and R_e

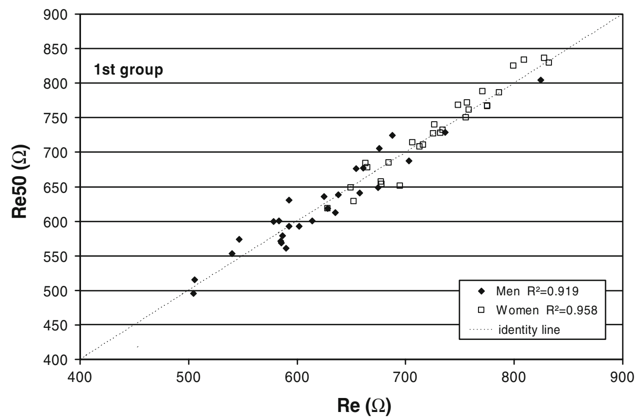

Fig. 3 Comparison of ECW resistances extrapolated from 50 kHz (R_{e50}) with R_e, extrapolated by the Xitron in the first group

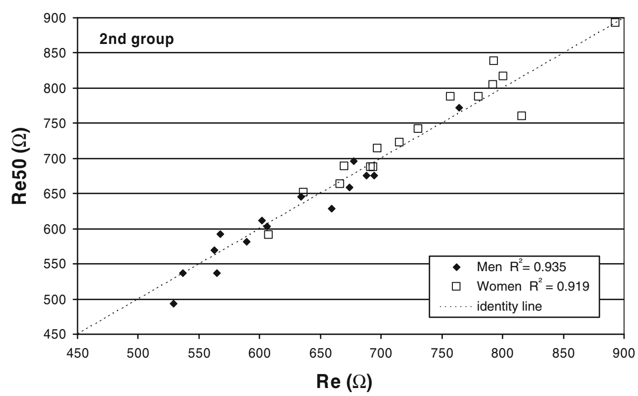

Fig. 4 Comparison of ECW resistances extrapolated from 50 kHz (R_{e50}) with R_e, extrapolated by the Xitron in the second group

group and p values were smaller but V_{e50} were not significantly different from V_{ex} with p values of 0.277 for men and 0.393 for women. Values of V_{es} were not significantly different from those of V_{ex} in men, but they overestimated V_{ex} by 1.0 L in women. As for the first group, values of V_{eh} for the second group overestimated V_{ex} by 1.72 L in men and by 1.85 L in women.

Measurements of V_{e50} in the third group can also be considered as a validation test for our method, since they use the value of b for the first group. For this third group also, values of V_{e50} were not significantly different from V_{ex} with p values of 0.545 for men and 0.096 for women.

The detailed comparison of ECW volumes V_{e50} calculated from R_{50} and Eq. (8) with V_{ex}, given in Fig. 5a for men of first group, shows that their values are very close. This is true also for V_{es} calculated by Sergi's method (Eq. (9)). The same comparison displayed in Fig. 5b for women of first group shows that, if values of V_{e50} were also very close to those of V_{ex}, this was not the case for V_{es} which overestimated V_{ex} by an average of 1.25 L. Perhaps the coefficient 1.86 of the last term of Eq. (9) was too high. The same comparison for the second group is depicted in Fig. 6. Values of V_{e50} are very close to the identity line for both men and women, while values of V_{es} for women generally overestimate ECW as compared to the Xitron. A Bland–Altman [1] graph of differences $V_{e50} - V_{ex}$ is shown in Fig. 7 for the second group. Only one point for men and one for women lie outside the limits of agreement.

3.2 Application to the BodyExplorer

This application was performed on the third group of subjects.

3.2.1 Comparison of resistances measured by BodyExplorer and Xitron

The first step was to verify that resistances R_{50b} and reactances X_{50b} at 50 kHz of the BodyExplorer were close to those of the Xitron. Mean values and SD of R_{50b} and X_{50b} are given in Table 4 while those of R_{50} and X_{50} from Xitron in third group are listed in Table 2. Mean values of $R_{50b}-R_{50}$ were 4.16 ± 2.73 Ω or +0.8% in men and 6.79 ± 2.14 in women or +1.07% as can be seen in Table 4.

3.2.2 Comparison of ECW volumes in the third group by BodyExplorer and Xitron with different methods

Mean values and SD of these volumes are shown in Table 3. Mean ECW volumes measured by the Xitron (V_{ex}) using R_e were 18.61 L in men and 13.89 L in women. Mean ECW volumes V_{e50} using Eq. (8) and the BodyExplorer resistance R_{50b} were 18.53 L for men and 13.73 L in women. Both were not significantly different from V_{ex} with respective p values of 0.545 and 0.096. When using Sergi's equation (9) and R_{50b}, ECW volumes V_{es} were, respectively, 18.7 L for men ($p/V_{ex} = 0.689$) and 15.14 L for women, an overestimation of 1.24 L relatively to the Xitron ($p = 8 \times 10^{-7}$). As with the first and second groups, Hannan's method with R_{50b} overestimated ECW by 1.8 L in men and by 2.4 L in women. Corresponding graphs of comparison of V_{e50} with V_{ex} are shown in Fig. 8 for men and in Fig. 9 for women together with linear regressions and correlation coefficients. Figure 8 shows that, in men, our method (V_{e50}) gives results almost identical to those of Xitron while Sergi's method slightly underestimates ECW as compared to Xitron below 16 L and overestimates it above 22 L by 0.5–1 L. In women, as seen in Fig. 9, values of V_{e50} are again very close to those of Xitron, with a slight underestimation of 0.08 L, while Sergi's method (V_{es}) overestimates V_{ex} by 1–1.3 L.

Table 3 Comparison of ECW volumes calculated by our 50 kHz-Bis method V_{e50}, Sergi's and Hannan's methods with those given by the Xitron V_{ex}, including values of p tests

	Men first group, $n = 27$	Women first group, $n = 30$	Men second group, $n = 15$	Women second group, $n = 16$	Men third group, $n = 11$	Women third group, $n = 10$
V_{ex} (L)	17.88 ± 2.3	13.01 ± 1.35	18.19 ± 1.97	13.52 ± 1.42	18.61 ± 3.04	13.89 ± 1.29
V_{e50} (L)	17.92 ± 2.39	13.01 ± 1.40	18.32 ± 2.02	13.45 ± 1.53	18.53 ± 3.11	13.73 ± 1.26
$V_{e50} - V_{ex}$ (L)	0.03 ± 0.38	0.005 ± 0.20	0.114 ± 0.39	−0.06 ± 0.29	−0.08 ± 0.44	−0.16 ± 0.27
pV_{e50}/V_{ex}			0.277	0.393	0.545	0.096
V_{es} Sergi (L)	18.08 ± 2.81	14.24 ± 1.61	18.44 ± 2.37	14.52 ± 1.83	18.69 ± 3.62	15.14 ± 1.55
$V_{es} - V_{ex}$ (L)	0.19 ± 0.55	1.23 ± 0.29	0.24 ± 0.49	0.998 ± 1.04	0.08 ± 0.66	1.25 ± 0.34
pV_{es}/V_{ex}	0.0859	2.0×10^{-20}	0.078	0.0016	0.689	1.1×10^{-6}
V_{eh} Hannan (L)	20.16 ± 1.86	16.18 ± 1.53	20.14 ± 1.42	16.37 ± 1.83	20.24 ± 1.88	16.3 ± 1.10
pV_{eh}/V_{ex}	2.07×10^{-11}	5.56×10^{-22}	9.64×10^{-8}	4.92×10^{-8}	0.002	5.16×10^{-6}

In third group, V_{e50}, V_{es} and V_{eh} were calculated using R_{50b} and X_{50b}

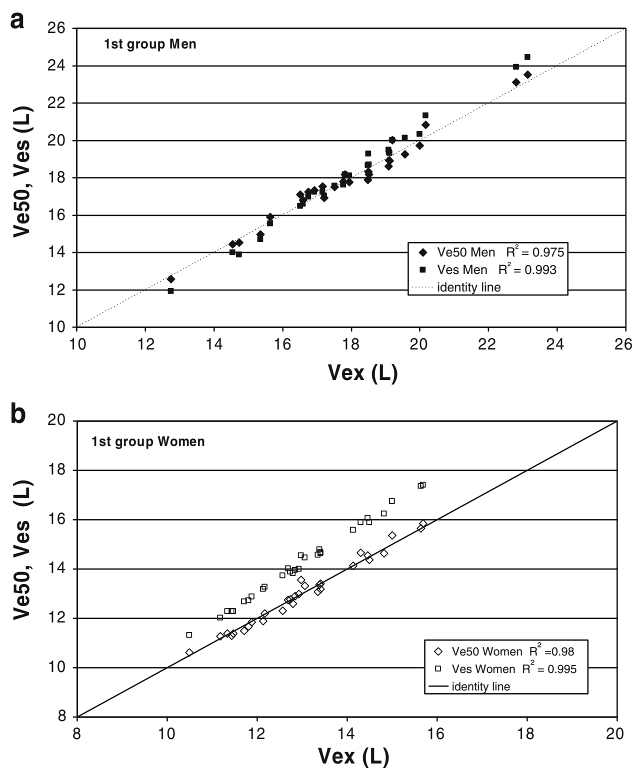

Fig. 5 **a** Comparison of V_{e50} and V_{es} with V_{ex} from Xitron in men of first group. **b** Comparison of V_{e50} and V_{es} with V_{ex} from Xitron in women of first group

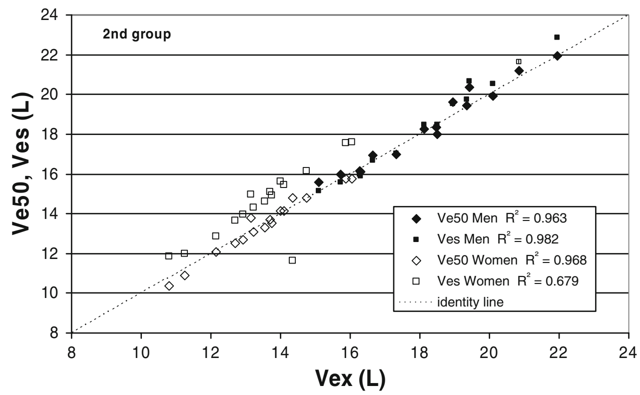

Fig. 6 Comparison of V_{e50} and V_{es} with V_{ex} from Xitron in second group

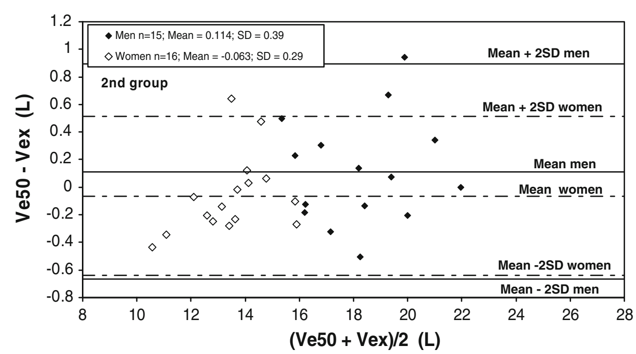

Fig. 7 Bland–Altman graph of comparison between ECW volumes V_{e50} and V_{ex} in the second group

4 Discussion and conclusion

Our results show that it seems possible to use the BIS-Hanai method of determination of ECW which, although it is not a gold standard, is often considered as the most accurate impedance method, with a 50 kHz impedancemeter. This was done by substituting to R_e, the resistance at 50 kHz divided by 0.806 for men and by 0.833 for women. No significant improvement in accuracy for R_{e50} was obtained by using the reactance at 50 kHz. Even in the validation group (second group), values of R_{e50} and V_{e50} were not significantly different from those given by the Xitron for R_e and V_{ex}. While our method gave ECW volumes closer to V_{ex} in second and third group than Sergi's method in women and than Hannan's method in men and women, Sergi's method was as close as ours to V_{ex} for men

Table 4 Mean and SD of resistances R_{50b} and reactances X_{50b} measured by BodyExplorer in the third group) and of ECW resistances R_{e50b} calculated from R_{50b}, comparison with corresponding resistances by the Xitron using p values of Student paired tests

	M = measured, C = calculated	Men, third group, $n = 11$	Women, third group, $n = 10$
R_{50b}, Ω	M	498.9 ± 48.2	633.7 ± 61.3
$R_{50b} - R_{50}$ Ω	C	4.2 ± 2.7	6.8 ± 2.1
X_{50b}, Ω	M	63.5 ± 8.2	71.2 ± 10.5
R_{e50b}, Ω	C from Eq. (8)	619.0 ± 59.8	760.7 ± 73.6
$R_{e50b} - R_e$	C	3.3 ± 22.6	11.3 ± 22.6
p(R_{e50b}/R_e)	C	0.647	0.149

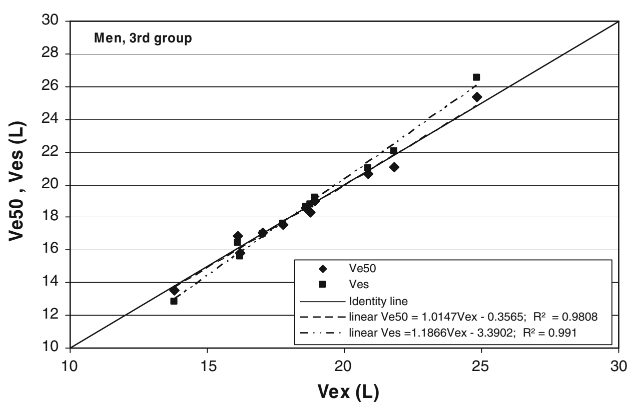

Fig. 8 Comparison between V_{e50} and V_{es} (from BodyExplorer) and V_{ex} (from Xitron) for men of third group

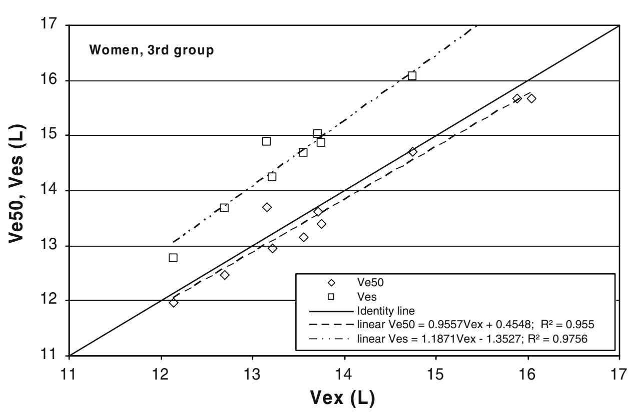

Fig. 9 Comparison between V_{e50} and V_{es} (from BodyExplorer) and V_{ex} (from Xitron) for women of third group

of second and third group. When our method was applied to the third group, using R_{e50b} from the BodyExplorer and Eq. (8), differences between ECW volumes of the BodyExplorer and Xitron, $V_{e50} - V_{ex}$, were very small -0.08 ± 0.44 L for men and -0.16 ± 0.27 L for women, even though our method has been established from a different group of subjects.

The success of our method is due to the fact that, in our population, the R_{50}/R_e ratio varied between narrow limits as its SD represented only 3.1% of its mean value in men and 2.2% in women, and also to the strong correlation which exists between ECW and TBW in healthy individuals as noted in [7, 14]. It would be interesting to verify whether our method would be applicable to a population with abnormal fluid distribution, such as dialysed patients.

Although the Xitron method for ECW cannot be considered as a reference method, it has been compared with bromide dilution data by various authors [3, 18] and more recently by Moissl et al. [15] who found a mean difference of -0.39 ± 1.44 L relatively to dilution data in a population of 120 healthy subjects and 32 renal failure patients.

This work shows that it is possible, in a normal population, to calculate resistances at zero (R_e), and at infinite frequency (R_∞) from R_{50}, as was shown in [16] with nearly the same accuracy as with a multifrequency impedancemeter. However, since our method for estimating TBW from R_{50} presented in [16] uses an equation similar to Eq. (8) with different coefficients k and b, a simultaneous use of these two methods would result in uniform ECW/TBW ratios of 0.403 in men and 0.412 in women, which correspond to mean ratios published in the literature [19] but would not be realistic for each individual. However, we feel that our new BIA method for ECW may be useful, as much less BIA correlations are available for ECW than for TBW and the two BIA correlations that we have tested gave results more different from those of the Xitron BIS method even in second and third groups than our method. If our ECW method was combined with a BIA linear correlation of H^2/R_{50} and W, such as that of Kushner and Schoeller [11] or Hannan et al. [7], it would give different values of the ECW/TBW ratio in each individual.

Thus, based on these data, our method seems to be an interesting alternative to previous BIA methods, as it combines the rationale of the BIS-Hanai method with the simplicity and low cost of 50 kHz impedancemetry.

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References

1. Bland J, Altman DG (1996) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1:307–313
2. Buchholz AC, Bartok C, Schoeller DA (2004) The validity of bioelectrical impedance models in clinical populations. Nutr Clin Pract 19:433–446. doi:10.1177/0115426504019005433
3. De Lorenzo A, Andreoli A, Matthie JR, Withers P (1997) Predicting cell mass with bio-impedance by using theoretical methods: a technological review. J Appl Physiol 82(5):1542–1558

4. Deurenberg P, van der Koy K, Leenen R, Westrate JA, Seidell JC (1991) Sex and age specific prediction formulas for estimating body composition from bioelectric impedance: a cross validation study. Int J Obes 15:17–25
5. Gudikawa R, Schoeller DA, Kushner RF, Bolt MJG (1999) Single and multifrequency models for bioelectrical impedance analysis of body water compartments. J Appl Physiol 87:1087–1096
6. Hanai T (1968) Electrical properties of emulsions. In: Sherman DH (ed) Emulsions science. Academic Press, London, pp 354–477
7. Hannan WJ, Cowen SJ, Fearon KC, Plester CE, Falconer JS, Richardson RA (1994) Evaluation of multi-frequency bio-impedance analysis for the assessment of extracellular and total body water in surgical patients. Clin Sci 86:479–485
8. Jaffrin MY, Fenech M, Moreno MV, Kieffer R (2006) Total body water measurement by a modification of the bioimpedance spectroscopy method. Med Biol Eng Comput 44:873–882. doi:10.1007/s11517-006-0099-0
9. Jaffrin MY, Kieffer R, Moreno MV (2005) Evaluation of a foot-to-foot impedancemeter measuring extracellular volume in addition to fat free mass and fat tissue mass. Nutrition 21:815–824. doi:10.1016/j.nut.2004.11.016
10. Kushner RF, Schoeller DA (1986) Estimation of total body water by bioelectrical impedance analysis. Am J Clin Nutr 44(3):417–424
11. Kushner RF, Schoeller DA, Fjeld CR, Danford L (1992) Is the impedance index (ht^2/R) significant in predicting total body water? Am J Clin Nutr 56:835–839
12. Kyle UG, Bosaeus I, De Lorenzo A, Daurenberg P, Elia M et al (2004) Bioelectrical impedance analysis. Part II: utilization in clinical practice. Clin Nutr 23:1430–1453. doi:10.1016/j.clnu.2004.09.012
13. Lukaski HC (1997) Validation of body composition techniques in the dialysis population. ASAIO J 43:251–255. doi:10.1097/00002480-199705000-00027
14. Matthie JR, Zarowitz B, De Lorenzo A, Andreoli A, Katzarski K, Pan G et al (1998) Analytic assessment of the various bioimpedance methods used to estimate body water. J Appl Physiol 84(5):1801–1816
15. Moissl U, Wabel P, Chamney PW, Bosaeus I et al (2006) Body fluid volume determination via body composition spectroscopy in health and disease. Physiol Meas 27:921–933. doi:10.1088/0967-3334/27/9/012
16. Morel H, Jaffrin MY (2008) A bridge from bioimpedance spectroscopy to 50 kHz bioimpedance analysis: application to total body water measurements. Physiol Meas 29:S465–S478. doi:10.1088/0967-3334/29/6/S39
17. Sergi G, Bussolotto M, Perini P, Calliari I et al (1994) Accuracy of bioelectrical bioimpedance analysis for the assessment of extracellular space in healthy subjects and in fluid retention states. Ann Nutr Metab 38(3):158–165
18. Van Loan MD, Withers PO, Matthie JR, Mayclin PL (1993) Use of bio-impedance spectroscopy to determine extracellular fluid, intracellular fluid, total body water and fat-free mass. In: Ellis KJ, Eastman JD (eds) Human Body Composition: in vivo methods, models and assessment. Plenum, New York, pp 67–70
19. Van Marken Lichtenbelt WD, Westerterp KR, Wouters L, Luijendik S (1994) Validation of bioelectric impedance measurements as a method to estimate body water compartments. Am J Clin Nutr 60:159–166
20. Wang Z, Shen W, Kotler DP, Heshka S et al (2003) Total body protein: a new cellular level mass and distribution prediction model. Am J Clin Nutr 78:979–984