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# Body fluid volumes measurements by impedance: A review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods

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#### **Abstract**

This paper reviews various bioimpedance methods permitting to measure non-invasively, extracellular, intracellular and total body water (TBW) and compares BIA methods based on empirical equations of the wrist-ankle resistance or impedance at 50 kHz, height and weight with BIS methods which rely on an electrical model of tissues and resistances measured at zero and infinite frequencies. In order to compare these methods, impedance measurements were made with a multifrequency Xitron 4200 impedancemeter on 57 healthy subjects which had undergone simultaneously a Dual X-ray absorptiometry examination (DXA), in order to estimate their TBW from their fat-free-mass. Extracellular (ECW) and TBW volumes were calculated for these subjects using the original BIS method and modifications of Matthie [Matthie JR. Second generation mixture theory equation for estimating intracellular water using bioimpedance spectroscopy. J Appl Physiol 2005;99:780-1], Jaffrin et al. [Jaffrin MY, Fenech M, Moreno MV, Kieffer R. Total body water measurement by a modification of the bioimpédance spectroscopy method. Med Bio Eng Comput 2006;44:873-82], Moissl et al. [Moissl UM, Wabel P, Chamney PW, Bosaeus I, Levin NW, et al. Body fluid volume determination via body composition spectroscopy in health and disease. Physiol Meas 2006;27:921–33] and their TBW resistivities were compared and discussed. ECW volumes were calculated by BIA methods of Sergi et al. [Sergi G, Bussolotto M, Perini P, Calliari I, et al. Accuracy of bioelectrical bioimpedance analysis for the assessment of extracellular space in healthy subjects and in fluid retention states. Ann Nutr Metab 1994;38(3):158-65] and Hannan et al. [Hannan WJ, Cowen SJ, Fearon KC, Plester CE, Falconer JS, Richardson RA. Evaluation of multi-frequency bio-impedance analysis for the assessment of extracellular and total body water in surgical patients. Clin Sci 1994;86:479-85] and TBW volumes by BIA methods of Kushner and Schoeller [Kushner RF, Schoeller DA. Estimation of total body water by bioelectrical impedance analysis. Am J Clin Nutr 1986;44(3):417–24], Lukaski et al. [Lukaski HC, Bolonchuk WW. Estimation of body fluid volumes using tetrapolar bioelectrical impedance measurements. Aviat Space Environ Med 1988;59:1163-9], Hannan et al. [Hannan WJ, Cowen SJ, Fearon KC, Plester CE, Falconer JS, Richardson RA. Evaluation of multi-frequency bio-impedance analysis for the assessment of extracellular and total body water in surgical patients. Clinical Science 1994;86:479–85], Deurenberg et al. [Deurenberg P, van der Koy K, Leenen R, Westrate JA, Seidell JC. Sex and age specific prediction formulas for estimating body composition from bioelectric impedance: a cross validation study. Int J Obesity 1991;15:17-25] These volumes were compared against those given by BIS method and, in the case of TBW, with those by DXA. For ECW, a good agreement was found between various BIS methods and that of Sergi while Hannan's values were higher. Both Matthie's and Moissl's methods gave mean TBW resistivities and volumes lower than those of Jaffrin's and DXA methods. Kushner et al. method gave values of TBW not significantly different from those of Jaffrin et al. and DXA, as Hannan's method in men, but Lukaski and Deurenberg methods led to an underestimation. © 2008 IPEM. Published by Elsevier Ltd. All rights reserved.

Keywords: Body fluid resistivity; Electrical modelling of tissues; Extracellular fluid; Total body water

#### 1. Introduction

The measurement of body fluid volumes, extracellular water (ECW), intracellular one (ICW) and their sum, total body water (TBW) is important in many pathologies. TBW

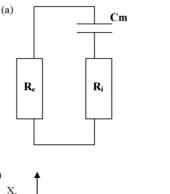
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#### Nomenclature body density (kg $L^{-1}$ ) $D_{\mathsf{h}}$ height (cm) Н shape factor $K_{\rm b}$ R resistance $(\Omega)$ Th hydration rate body volume (L) $V_{b}$ $V_{\rm e}, V_{\rm i}, V_{\rm t}$ ECW, ICW, TBW volume (L) weight (kg) Greek letter resistivity (Ω cm) Subscripts d DXA **ECW** e **ICW** i new method n **TBW** t infinite frequency $\infty$

is strongly related to fat-free-mass (FFM) which contains, in healthy individuals, an average of 73.2% of water [1]. Similarly, body cell mass (BCM), which is an important nutritional parameter, is also closely connected to ICW [2]. Independent measurements of FFM and TBW permit to detect dehydration, which is frequent in elderly persons or athletes after heavy training. Conversely, an overhydratation may indicate the presence of oedema in cardiac patients or of lymphoedema after a mastectomy [3]. The measurement of TBW is also useful for evaluation of diuretic therapy. Renal patients treated by hemodialysis accumulate fluid between treatments. It is important to evaluate their amount of excess fluid, in order to determine how much fluid they should loose by ultrafiltration and also how this fluid loss is distributed between ECW and ICW [4-6]. Measurements of BCM are also important for assessing the morbidity of patients infected by HIV [2].

Reference methods for measuring body fluid volumes are based on radio-isotopic dilution, of deuterium for TBW [7] and bromide for ECW [8]. ICW space can be measured by a radioactive potassium isotope, <sup>40</sup>K, included in body potassium [9]. These procedures described also in [10] are invasive as they require blood samples, and expensive due to dosage by mass spectrometry and cannot be repeated at short intervals. Thus, they cannot be used to measure volume variations over a short period of time.

These constraints have lead to the rapid development of bioimpedance methods for measuring body fluids, because they are non invasive, simple and inexpensive. However they are indirect and their accuracy is very much dependent upon the validity of the electrical model of tissues they use. Thomasset [11] was the first to propose to use two frequencies of 1 and 100 kHz to measure respectively ECW and TBW by



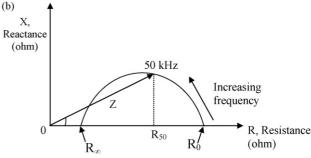


Fig. 1. (a) Equivalent electrical circuit of tissues with parallel resistances. (b) Variation of impedance with frequency. Resistances extrapolated at zero  $(R_r)$  and infinite  $(R_{\infty})$  frequencies.

an application of Cole model [12]. But in the period from 1985 to 1994, most methods proposed for measuring TBW were empirical and consisted in regression equations of the resistance index  $H^2/R_{50}$ , where H was the subject height and  $R_{50}$  his wrist-ankle resistance at 50 kHz which is usual for single frequency impedancemeters. An exhaustive compilation of such equations known as BIA (Bioimpedance analysis) is presented by Houtkouper et al. [13] and by Kyle et al. [14,15].

In 1992, a more elaborate method, bioimpedance spectroscopy (BIS), was proposed [16] to measure both ECW and ICW volumes using the equivalent electrical circuit of Fig. 1a and Hanai's mixture conductivity theory [17] to account for the presence of non conducting elements. This method and its validation by isotopic dilution measurements have been also described by Van Loan et al. [18].

# 2. Physical principles of body fluid measurements by bioimpedance

#### 2.1. Bioimpedance spectroscopy (BIS) method

Since ECW and ICW fluids contains ions, they are conducting and the measurements of their volume is based on their resistance or their impedance as cell membranes may act as capacitors at low and intermediate frequencies. The ionic composition of ECW, composed of plasma and interstitial fluid, is shown in Table 1, adapted from [19] and its resistivity is close to that of saline, about  $40~\Omega$  cm. The ionic composition of ICW depends upon the type of cells. Thus the ionic composition of the entire ICW is uncertain and its

Table 1 Ion concentrations in mequiv./L of ECW (plasma+interstitial) and ICW of muscle cells

Electrolyte	Na <sup>+</sup>	K <sup>+</sup>	Ca <sup>2+</sup>	Mg <sup>+</sup>	Cl-	HCO <sub>3</sub> <sup>-</sup>	PO <sub>4</sub> -	Protein	Org acid
Plasma	142	4	5	3	103	27	2	16	5
Interstitial	151	4.3	5.4	3.2	109.7	28.7	2.1	17	5.3
ICW muscle	10	160		35	2	8	140	55	

Adapted from Pitts [19].

mean resistivity cannot be measured directly. Table 1 shows the composition of ICW in muscle cells. Ions K<sup>++</sup> replace Na<sup>+</sup> as the most prevalent ion as potassium is pumped into the cells. The consequence of capacitive behavior of membrane cells is that ECW resistance must be measured at very low frequency, <1 kHz and that of ICW and ECW combined at very high frequency (>5 MHz). However, for technical reasons, impedance meters using surface electrodes are limited to a frequency range of 5-1000 kHz and the ECW resistance  $(R_{\rm e})$  and the TBW one  $(R_{\infty})$  must be calculated by extrapolation to zero and infinite frequencies, respectively. Even if measurements were possible at very low and very high frequencies, these limiting resistances would not be obtained because of relaxation mechanisms in living tissues which would prevent the impedance to reach the real axis. This extrapolation is facilitated by the observation that the locus of impedance data in the resistance-reactance plane lie on a semi circle with its center below the horizontal axis, according to the Cole model [12]. Then,  $R_0$  (at zero frequencies) and  $R_{\infty}$  are found as the intercepts of the circle with the resistance axis, as the reactance vanishes at these frequencies (Fig. 1b). This determination of  $R_e$ , assimilated to  $R_0$ , and  $R_{\infty}$  is the 1st step of the BIS method of body fluid volumes determination. The 2nd step is the approximation of the human body as a sum of 5 cylinders (limbs and trunk). This is done through a dimensionless shape factor  $K_b$  calculated from the length and perimeters of the limbs and the trunk in the resistance–volume relationship for a single cylinder as follows

$$R = \frac{K_{\rm b}\rho H^2}{V_{\rm b}} \tag{1}$$

where  $V_b$  is the body volume, H the height, and  $\rho$  is the fluid resistivity. Van Loan et al. [18] obtained a value of 4.3 for  $K_b$  from statistical anatomical measurements in adults. The third step is to take into account the effect of non conducting tissues imbedded in ECW and ICW which increases their "apparent resistivity"  $\rho_a$ . This is done by using (2) from Hanai's [17] "mixture" conductivity theory, where c is the volume fraction of non-conducting tissues

$$\rho_{\rm a} = \frac{\rho}{(1-c)^{3/2}} \tag{2}$$

This apparent resistivity must be substituted to  $\rho$  in (1). At low frequency, c is equal to  $1 - V_e/V_b$ , as only the ECW volume  $V_e$  is conducting and the above assumptions lead to

the following equation for ECW apparent resistivity  $\rho_{ae}$ 

$$\rho_{\rm ae} = \rho_{\rm e} \left(\frac{V_{\rm b}}{V_{\rm e}}\right)^{3/2} \tag{3}$$

Thus, using (1)–(3), the ECW resistance  $R_e$  may be written as

$$R_{\rm e} = K_{\rm b} H^2 V_{\rm b}^{1/2} \rho_{\rm e} V_{\rm e}^{-3/2} \tag{4}$$

After replacing  $V_b$  in (4) by  $W/D_b$  where W is the body weight and  $D_b$  its density, the ECW volume may be expressed as,

$$V_{\rm e} = k_{\rm e} \left(\frac{H^2 W^{1/2}}{R_{\rm e}}\right)^{2/3} \tag{5a}$$

with

$$k_{\rm e} = 10^{-2} \left(\frac{K_{\rm b}\rho_{\rm e}}{D_{\rm b}^{1/2}}\right)^{2/3}$$
 (5b)

From measurements of ECW volumes by bromide dilution technique, Van Loan et al. [18] suggested to take  $k_{\rm e}=0.306$  for men and 0.316 for women, when  $V_{\rm e}$  is in liter, H in cm, the body density  $D_{\rm b}=1.05$  kg/L and ECW resistivity  $\rho_{\rm e}$  is in  $\Omega$  cm. This resistivity is assumed to be uniform for each sex, unlike the apparent one which varies among individuals according to (3). When these values of  $k_{\rm e}$  are introduced in (5b), ECW resistivities  $\rho_{\rm e}$  are found equal to 40.3  $\Omega$  cm for men and 42.3  $\Omega$  cm for women, close to values of saline (40  $\Omega$  cm). De Lorenzo et al. [20] suggested to take  $\rho_{\rm e}$  equal to 39.0  $\Omega$  cm for women, giving  $k_{\rm e}=0.299$ .

To determine the ICW volume  $(V_i)$ , the BIS method first calculates the resistance  $R_i$ , assuming that  $R_e$  and  $R_i$  are in parallel as shown in Fig. 1b, so that the TBW resistance is given by

$$R_{\infty}^{-1} = R_{\rm e}^{-1} + R_{\rm i}^{-1} \tag{6}$$

Since the ICW compartment is represented by  $R_i$  and a capacitance,  $R_i$  cannot be considered as the ICW resistance unlike  $R_e$  for ECW. Then  $V_i$  is calculated by an equation given without derivation by De Lorenzo et al. [20]

$$\left(1 + \frac{V_{\rm i}}{V_{\rm e}}\right)^{5/2} = \frac{R_{\rm e} + R_{\rm i}}{R_{\rm i}} \left(1 + K_{\rm p} \frac{V_{\rm i}}{V_{\rm e}}\right) \tag{7}$$

where  $K_{\rho} = \rho_i/\rho_e$  is the ICW to ECW resistivity ratio and which must be solved numerically. From comparison of TBW given by the Xitron with measurements using deuterium

oxide dilution techniques, Van Loan et al. [18] have suggested values of  $K_{\rho}$  of 3.82 for men and 3.40 for women.

## 2.2. Bioimpedance analysis (BIA) methods

These methods rely only on the impedance  $(Z_{50})$  or the resistance  $(R_{50})$  measured at 50 kHz. They are empirical and generally express the TBW volume as a linear function of the resistance index  $H^2/R_{50}$  (or  $H^2/Z_{50}$ ) in accordance with (1), weight W, age A and sometimes sex. The coefficients of these parameters have been determined by comparison with deuterium dilution measurements. We list below some of these correlations.

Kushner et al. [21] used the following equation for men and women:

$$V_{\rm tk} = 0.5561 \frac{H^2}{R_{50}} + 0.0955 W + 1.726 \tag{8}$$

While Hannan et al. [22] proposed for men and women:

$$V_{\rm th} = 0.446 \frac{H^2}{R_{50}} + 0.126 W + 5.82 \tag{9}$$

The equation used by Deurenberg et al. [23] is different for men and women:

$$V_{\text{tde}} = 6.53 + 0.3674 \frac{H^2}{Z_{50}} + 0.1753 W - 0.11A$$
$$+ 2.83 \text{ sex}$$
 (10)

where *A* is the age in years, sex = 0 for men and 1 for women. In (8)–(13), *H* is in cm and *W* in kg. Lukaski et al. [24] have proposed a similar equation, but with  $R_{50}$  instead of  $Z_{50}$  and different coefficients

$$V_{\text{tL}} = 4.65 + 0.377 \frac{H^2}{R_{50}} + 0.14 W - 0.08A + 2.9 \text{ sex}$$
 (11)

Since a 50 kHz current will not penetrate completely into the cells, BIA methods actually do not measure the entire ICW volume, but their determination by comparison with dilution methods permit them to predict TBW with reasonable accuracy, at least in healthy subjects. The reason according to Hannan's et al. [22] and Matthie et al. [25] is due to the strong correlation existing between ECW and TBW, so that the ratio ECW/TBW is tightly regulated [10] and does not vary too much between healthy individuals. But BIA methods may not be as reliable in populations with abnormal ECW/TBW ratios, such as dialysed patients who have excess ECW before treatment.

Although the same procedure can be applied to ECW, there are fewer BIA methods proposed for these applications. Some examples are listed below

Hannan's et al. [22] have proposed

$$V_{\rm eh} = 0.0119 \frac{H^2}{X_{50}} + 0.123 \frac{H^2}{R_{50}} + 6.15 \tag{12}$$

where  $X_{50}$  is the reactance at 50 kHz. While Sergi's et al. [26] equation is

$$V_{\rm es} = -5.22 + 0.2 \frac{H^2}{R_{50}} + \frac{0.005}{X_{50}} + 0.08 W$$
$$+ 1.9 + 1.86 \,\text{sex}$$
(13)

where sex = 1 for women and 0 for men

### 2.3. Discussion of BIS method

While the determination of ECW by (5a,b) is fairly logical and straightforward and its predictions have been found satisfactory in healthy populations [10,20,25] and in dialysed patients [27], the validity of (7) for measuring ICW seems more questionable. First the determination of  $R_i$  from (6) is less accurate than for  $R_e$  since it cumulates the errors on  $R_e$  and  $R_{\infty}$ . Also the high resistivity of ICW, 3.4–3.8 higher than that of ECW is difficult to justify from ion composition difference between ECW and ICW. It also depends upon the validity of the parallel resistance model of (6). In addition the derivation of (7) is not readily found from the literature and the assumptions made are not clear. We indicate here the derivation by Fenech et al. [28].

# 2.3.1. Determination of intracellular volumes V<sub>iCW</sub>

Similarly as for ECW, Hanai's theory can be applied to impedance measurements at high frequency. In that case the volume concentration of non-conducting tissues is

$$c = 1 - \frac{V_{\rm e} + V_{\rm i}}{V_{\rm b}} \tag{14}$$

The apparent resistivity of total body water (TBW) is, from (2) and (14)

$$\rho_{\rm a\infty} = \rho_{\infty} \left( \frac{V_{\rm e} + V_{\rm i}}{V_{\rm b}} \right)^{-3/2} \tag{15}$$

We assume now that the mean total water resistivity  $\rho_{\infty}$  is related to ECW and ICW resistivities in proportion to their respective volumes by

$$\rho_{\infty}(V_e + V_i) = \rho_e V_e + \rho_i V_i \tag{16}$$

The TBW resistance  $R_{\infty}$  may be written, according to (1) and (6) as

$$R_{\infty} = \frac{R_{\rm e}R_{\rm i}}{R_{\rm e} + R_{\rm i}} = \frac{\rho_{\rm a\infty}K_{\rm b}H^2}{V_{\rm b}}$$
 (17)

Substitution of (15) and (16) into (17) yields

$$R_{\infty} = \frac{R_{\rm e}R_{\rm i}}{R_{\rm e} + R_{\rm i}} = \frac{\rho_{\rm e}V_{\rm e} + \rho_{\rm i}V_{\rm i}}{(V_{\rm i} + V_{\rm e})^{5/2}} V_{\rm b}^{1/2} K_{\rm b} H^2$$
 (18)

But, as seen earlier

$$R_{\rm e} = \frac{\rho_{\rm e}}{(V_{\rm e})^{3/2}} V_{\rm b}^{1/2} K_{\rm b} H^2 \tag{19}$$

Substituting this value of  $R_e$  into the left hand side of (18), we get after simplification

$$\frac{R_{\rm i}}{R_{\rm e} + R_{\rm i}} \frac{\rho_{\rm e}}{V_{\rm e}^{3/2}} = \frac{\rho_{\rm e} V_{\rm e} + \rho_{\rm i} V_{\rm i}}{(V_{\rm i} + V_{\rm e})^{5/2}}$$
(20)

and after some rearrangements, Eq. (7)

$$\left(1 + \frac{V_{\rm i}}{V_{\rm e}}\right)^{5/2} = \frac{R_{\rm e} + R_{\rm i}}{R_{\rm i}} \left(1 + K_{\rho} \frac{V_{\rm i}}{V_{\rm e}}\right) \tag{7}$$

The validity of (7) requires that the mean TBW resistivity is given by (16). However it will be shown in Appendix A that (16) contradicts the assumption that ICW and ECW resistances are in parallel since the application of (1)–(6) leads to the equation

$$\rho_{\infty}^{-1} = \rho_{\rm i}^{-1} + \rho_{\rm e}^{-1} \left(\frac{V_{\rm t}}{V_{\rm e}}\right)^{3/2} \tag{21}$$

which is not compatible with (16).

De Lorenzo et al. [20] have observed that the values of  $\rho_e$  and  $\rho_i$  supplied by Van Loan et al. [18] for (7) lead to an important underestimation of  $V_i$  by 3–4 L compared to their own measurements by deuterium dilution in 14 male subjects. For men, De Lorenzo et al. suggested to take  $\rho_e = 40.5 \Omega$  cm and  $\rho_i = 273.9 \Omega$  cm, a ratio  $K_\rho$  of 6.75 instead of 3.40 as in [16] and for women,  $\rho_e = 39.0 \Omega$  cm and  $\rho_i = 264.9 \Omega$  cm.

Ellis and Wong [10] have also compared the original BIS method of [18] with isotopic dilution measurements in various ethnic subgroups for a total of 248 men and 221 women and reported a mean underestimation of TBW of 2.7 L in men (3.35 L in Caucasians) and 2.4 L in women. This underestimation was mainly due to an underestimation of ICW. They suggested taking values of  $K_{\rho}$  of 3.032 in men and 2.694 in women, lower than those in [18].

# 2.4. Modifications of BIS method

With the discrepancies reported between the original BIS method and various reference methods for ICW and TBW [10,20] or during its application to dialysis [27], it is not surprising to find in the recent literature various modifications of this method.

Fenech et al. [29] and Jaffrin et al. [30] have proposed to calculate directly TBW using the same method as for ECW. This amounts to consider TBW as an electrically homogeneous fluid on a macroscopic scale. From (1) and (15) we have at infinite frequency, if  $V_{\rm tn}$  denotes the TBW volume and  $\rho_{\infty n}$  its resistivity

$$R_{\infty} = K_{\rm b} \left(\frac{H^2}{V_{\rm b}}\right) \rho_{\infty \rm n} \left(\frac{V_{\rm b}}{V_{\rm t}}\right)^{3/2} \tag{22}$$

and, solving for  $V_{\rm tn}$ , we obtain

$$V_{\rm tn} = k_{\rm t} \left(\frac{H^2 W^{1/2}}{R_{\infty}}\right)^{2/3} \tag{23a}$$

with

$$k_{\rm t} = \left(\frac{K_{\rm b}\rho_{\infty \rm n}}{D_{\rm b}^{1/2}}\right)^{2/3}.$$
 (23b)

It can be noted that Eqs. (23a) and (23b) are similar to (5a) and (5b), with  $\rho_{\infty}$  and  $R_{\infty}$  replacing, respectively  $\rho_{\rm e}$  and  $R_{\rm e}$ .

Individual values of resistivities ( $\rho_{\infty ni}$ ) were determined for each subject from comparison with values of TBW ( $V_{td}$ ), determined from fat-free-mass (FFM<sub>d</sub>) measured by DXA in a healthy population of 60 subjects, assuming a mean hydration rate of 73.2% [1] by

$$V_{\rm td} = 0.732 \, \text{FFM}_{\rm d} \tag{24}$$

TBW resistivities  $\rho_{\infty n}$  in (23b) were taken as the means of  $\rho_{\infty ni}$  in men and women and found to be 104.3  $\Omega$  cm for men and  $100.5 \Omega$  cm for women. When this method was applied to predict the water loss of 28 dialysed patients by ultrafiltration, the mean water loss predicted was 91% of mean ultrafiltered volume against 39% for the normal BIS method. Jaffrin et al. [30] showed that these TBW resistivities were close to those obtained from (16) with ECW and ICW resistivities given by [18] and listed in Section 2.1, and assuming standard  $V_e/V_i$ ratios of 0.403 for men and 0.43 for women, which gave respectively  $108.1 \Omega$  cm for men and  $100.2 \Omega$  cm for women. But (23a,b) led to higher values of TBW volumes than the original BIS method. When Eqs. (23a,b) were applied to a 2nd group of 21 subjects for an independent validation with same resistivities as of 1st group, the mean differences  $V_{\rm tn} - V_{\rm td}$ were  $0.79 \pm 1.48$  L for a mean hydration rate of 72.0%.

A 2nd generation BIS method, similar to the preceding approach as it is based on (23a,b), but with an individual TBW resistivity, has been proposed by Matthie [31] and implemented in the Xitron Hydra 4200 multifrequency impedancemeter (Xitron Tech., San Diego, USA). From another Hanai's equation for the mixture of two conducting fluids, ECW and ICW, he obtained the following expression for individual TBW resistivity  $\rho_{\infty mi}$  as

$$\rho_{\infty \text{mi}} = \rho_{\text{i}} - (\rho_{\text{i}} - \rho_{\text{e}}) \left(\frac{R_{\infty}}{R_{\text{e}}}\right)^{2/3}$$
(25)

The resistivity given by (25) varies with the ratio  $R_{\infty}/R_{\rm e}$  which is almost proportional to  $V_{\rm e}/V_{\rm t}$ . Thus (25) shows that  $\rho_{\infty {\rm mi}}$  decreases when the ratio  $V_{\rm e}/V_{\rm t}$  increases, which is logical as ECW is more conducting than ICW.

Matthie did not include any numerical application of his equation in [31], but Moissl et al. from Fresenius Medical Care [32] have said that the Xitron 4200 used  $\rho_i$  = 273.9  $\Omega$  cm and  $\rho_e$  = 40.5  $\Omega$  cm in men and 264.9  $\Omega$  cm and 39.0  $\Omega$  cm, respectively in women, values proposed by De Lorenzo et al. [20].

In the same paper Moissl et al. have proposed a modification of the BIS method denoted body composition spectroscopy (BCS) in which the coefficient  $k_e$  in (4) for

ECW calculation has been replaced by

$$k_{\rm ef} = \frac{a}{\rm BMI} + b \tag{26}$$

where BMI is the body mass index in order to better take into account the subject morphology, in particular his proportion of fat tissues. From cross validation with bromide dilution measurements in 120 healthy subjects and 32 renal failure patients, they obtained a = 0.188 and b = 0.2883 with the same units as those used in (5b).

For ICW, these authors use an analogy with (5a) for ECW as

$$V_{\rm if} = k_{\rm if} \left(\frac{H^2 W^{1/2}}{R_{\rm i}}\right)^{2/3} \tag{27}$$

with  $R_i$  replacing  $R_e$  and another coefficient  $k_{if} = c/BMI + d$ , replacing  $k_e$ . From cross validation with ICW measurements from potassium isotope in the same subjects and patients as for ECW, they chose c = 5.8758 and d = 0.4194. It can be observed that the BMI dependence decreases both  $k_{ef}$  and  $k_{if}$  for subjects with large BMI, but this correction is much larger for  $k_{if}$  (and  $V_{if}$ ) which varies from 0.7132 at a BMI of 20- to 0.5873 for a BMI of 35, than for  $k_{ef}$  which varies only from 0.2977 to 0.2936. Their TBW volume ( $V_{tf}$ ) is given as the sum of  $V_{ef} + V_{if}$ .

It must be noted that, apart from the BMI dependence of coefficients  $k_e$  and  $k_i$ , Moissl et al. method for calculating TBW is different from that of [31] as it leads to, using (4) and (27)

$$V_{\rm tf} = V_{\rm ef} + V_{\rm if} = (H^2 W^{1/2})^{1/3} \left(\frac{k_{\rm ef}}{R_{\rm e}^{2/3}} + \frac{k_{\rm if}}{R_{\rm i}^{2/3}}\right)$$
 (28)

$$V_{\rm tf} = \left(\frac{H^2 W^{1/2}}{R_{\infty}}\right)^{1/3} \left[ k_{\rm ef} \left(\frac{R_{\infty}}{R_{\rm e}}\right)^{2/3} + k_{\rm if} \left(\frac{R_{\infty}}{R_{\rm i}}\right)^{2/3} \right]$$
(29)

An equation similar to (23a) can be obtained from (29) as

$$V_{\rm tf} = k_{\rm tf} \left(\frac{H^2 W^{1/2}}{R_{\infty}}\right)^{1/3} \tag{30}$$

with

$$k_{\rm tf} = k_{\rm ef} \left(\frac{R_{\infty}}{R_{\rm e}}\right)^{2/3} + k_{\rm if} \left(\frac{R_{\infty}}{R_{\rm i}}\right)^{2/3} \tag{31}$$

For comparison with Matthie's and our method, Moissl's TBW resistivity  $\rho_{\infty f}$  can be obtained by similarity with (23b) as

$$k_{\rm tf} = \left(\frac{K_{\rm b}\rho_{\rm \infty f}}{D_{\rm b}^{1/2}}\right)^{2/3}$$
 (32)

giving

$$\rho_{\infty f} = \left(\frac{D_{\rm b}^{1/2}}{K_{\rm b}}\right) \left[ k_{\rm ef} \left(\frac{R_{\infty}}{R_{\rm e}}\right)^{2/3} + k_{\rm if} \left(\frac{R_{\infty}}{R_{\rm i}}\right)^{2/3} \right]^{3/2} \tag{33}$$

which shows that  $\rho_{\infty f}$  is a function of  $R_{\infty}$  and  $R_{e}$ , since  $R_{i}$  is related to the other two by (6).

# 3. Comparison of TBW calculated by various BIS and BIA methods

#### 3.1. Materials and methods

Whole body impedance data were recorded in a first group of 57 healthy volunteers (27 men and 30 women), aged from 18 to 71 years who gave informed consent and whose characteristics are summarized in Table 2. Their weight (W) was measured by a Bodymaster Vision scale (Tefal SA, Rumilly, France) to nearest 0.1 kg and their height by a wall mounted measuring tape to nearest 0.5 cm. A medical impedancemeter Xitron Hydra 4200 was used in supine position with four 7.5-cm × 1.9-cm gel electrodes placed on the dorsal surfaces of the right hand and foot, distal (current) ones being respectively proximal to metacarpal and metatarsal phalangeal joints, in accordance with standard tetra polar electrode placement [33]. Proximal (voltage) electrodes were separated by 5 cm from current ones. This device operates at 50 frequencies between 5 and 1000 kHz with a current of 50–700  $\mu$ A and calculates resistances at zero ( $R_e$ ) and infinite  $(R_{\infty})$  frequencies by extrapolation of its data to the real axis in the resistance-reactance plane. Mean values and standard deviations (S.D.) of these resistances together with resistances at 50 kHz ( $R_{50}$ ) are given in Table 2. These resistances are higher in women than in men, due to their smaller limb cross sections. The Xitron also calculates ECW volume  $V_e$  from  $R_e$  using (4) and ICW volume from  $R_{\infty}$  and  $R_{\rm e}$  using the Matthie's BIS method [31]. Simultaneously these subjects underwent a DXA examination at the Center for Advanced Medical Imaging (CIMA) of Compiegne using a Hologic Delphi WS/N 71224 (Hologic Inc., Waltham Ma, USA) equipped with a whole body Hologic software in order to measure their fat-free-mass (FFM<sub>d</sub>). Then the TBW volume ( $V_{\rm td}$ ) from DXA was calculated using (24).

This first group was used to determine values of  $\rho_{\infty n}$  for men and women necessary to calculate TBW volume by our method. For validation, this method was compared, using same resistivities against DXA measurements of  $V_{\rm td}$  in a second group of 16 healthy volunteers who had undergone the same protocol as the first group, which had been approved by the Picardy Regional Ethical Committee, and whose data had not been involved in the determination of  $\rho_{\infty n}$ .

#### 3.1.1. Statistical analysis

The comparisons between fluid volumes calculated by different methods were presented using linear regressions with

Table 2
Physical characteristics of subjects of 1st and 2nd groups

	Men, 1st group $(n = 27)$	Women, 1st group $(n=30)$	Men, 2nd group $(n = 15)$	Women, 2nd group $(n = 6)$
Height (m)	$1.78 \pm 0.054$	$1.64 \pm 0.042$	$1.79 \pm 0.06$	$1.629 \pm 0.042$
Age (year)	$33.33 \pm 16.86$	$35.0 \pm 15.47$	$28.2 \pm 10.93$	$24.05 \pm 10.17$
Weight (kg)	$75.42 \pm 14.53$	$62.66 \pm 9.32$	$78.78 \pm 12.7$	$57.42 \pm 14.26$
BMI ( $kg m^{-2}$ )	$23.83 \pm 4.46$	$23.40 \pm 3.08$	$24.7 \pm 3.68$	$21.82 \pm 6.12$
FFM <sub>d</sub> (kg)	$60.58 \pm 7.71$	$43.09 \pm 4.22$	$62.67 \pm 7.21$	$40.42 \pm 3.62$
$R_{\rm e} (\Omega)$	$523.43 \pm 68.07$	$741.59 \pm 69.75$	$523.6 \pm 67.76$	$707.60 \pm 66.77$
$R_{\infty}\left(\Omega\right)$	$407.74 \pm 46.26$	$505.61 \pm 55.91$	$403.1 \pm 52.5$	$482.5 \pm 65.6$
$R_{50}(\Omega)$	$501.67 \pm 55.97$	$618.29 \pm 63.58$	$498.6 \pm 58.0$	$598.4 \pm 74.5$

squared correlation coefficients ( $R^2$ ) and giving mean values and standard deviations (S.D.) of differences and results of paired Student tests (t-tests). Data compared are considered to be significatively different if P values are less than 0.05.

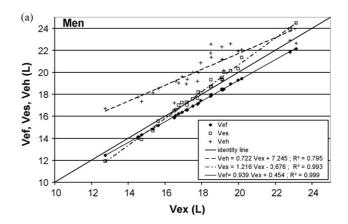
# 3.2. Comparison of ECW volumes calculated by different methods

Values of  $V_{\rm ex}$  from (5a,b),  $V_{\rm ef}$ , using (5a) and (26),  $V_{\rm eh}$ from (12), and  $V_{\rm es}$  using (13) are displayed in Table 4 for the 1st group. It can be seen that the mean values of  $V_{\rm ef}$  (modified BIS method of Moissl et al. [32] with  $k_{ef}$  depending upon BMI) are slightly lower than those of  $V_{\rm ex}$ . The BIA method of Sergi et al. [28] gives slightly larger mean values than those of  $V_{\rm ex}$  while Hannan's method overestimates ECW by 2.3 L in men and 3.16 L in women as compared to  $V_{\rm ex}$ . A detailed comparison of Moissl, Hannan and Sergi's ECW volumes with  $V_{\rm ex}$  in our subjects is shown in Fig. 2a for men and Fig. 2b for women. In men, values of  $V_{\rm ef}$  are slightly lower than those of  $V_{\rm ex}$ , while those of  $V_{\rm es}$  are slightly larger at large volumes. In women,  $V_{\rm ef}$  values are almost identical to those of  $V_{\rm ex}$  while Sergi's values overestimate it by up to 2 L at large volumes. Hannan's values overestimate  $V_{\rm ex}$  for both men and women, especially at small volumes.

# 3.3. Comparison of TBW resistivities calculated by different BIS methods

In order to further compare our method  $V_{tn}$  with that of Matthie [33] we have compared in Fig. 3 individual resistivities ( $\rho_{\infty mi}$ ) calculated by Matthie's method using (25), those ( $\rho_{\infty f}$ ) of Moissl calculated by (33) with those ( $\rho_{\infty ni}$ ) calculated from DXA. Matthie's resistivities for men were on the average 6% lower than those of DXA for men and 11% lower for women, while those of Moissl were 5.5% lower than  $\rho_{\infty mi}$  in men and 5% in women. Mean and S.D. values of TBW resistivities of various BIS methods are shown in Table 3.

Since it is logical that TBW resistivity increases with the proportion of ICW in TBW, we have plotted in Fig. 4 the variation of  $\rho_{\infty \rm ni}$  with  $V_{\rm in}/V_{\rm ex}$ , together with that of  $\rho_{\infty \rm mi}$  with  $V_{\rm im}/V_{\rm ex}$ . While  $\rho_{\infty \rm mi}$  resistivities increase with  $V_{\rm im}/V_{\rm ex}$  as expected from Eq. (25) with a higher rate for women than for men, it is not the case for  $\rho_{\infty \rm ni}$  in women resistivities



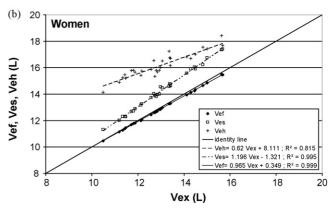


Fig. 2. (a) Comparison between ECW volumes calculated in male subjects of 1st group by methods of Moissl et al.  $(V_{\rm ef})$ , Sergi et al.  $(V_{\rm es})$ , Hannan et al.  $(V_{\rm eh})$  and measured by Xitron using BIS method  $(V_{\rm ex})$ . (b) Same as (a) for female subjects of 1st group.

which are not correlated with the ratio  $V_{\rm in}/V_{\rm ex}$ . For men,  $\rho_{\infty {\rm ni}}$  increases with  $V_{\rm in}/V_{\rm ex}$  but with a low correlation coefficient. This confirms that the determination of  $\rho_{\infty {\rm ni}}$  from FFM given by DXA is not sensitive to the ICW/ECW ratio as FFM is only related to TBW. In order to check if our individual resistivities

Table 3
Mean and S.D. of individual TBW resistivities of subjects of 1st group calculated by different methods

1st group	Men $(n = 27)$	Women $(n = 30)$
$\rho_{\infty \text{ni}}$ from DXA ( $\Omega$ cm)	$104.31 \pm 7.9$	$100.5 \pm 7.8$
$\rho_{\infty \rm mi}$ Matthie ( $\Omega  {\rm cm}$ )	$98.0 \pm 5.2$	$90.1 \pm 4.0$
$ ho_{\infty f}$ Moissl et al. ( $\Omega$ cm)	$98.4 \pm 5.7$	$95.8 \pm 4.5$

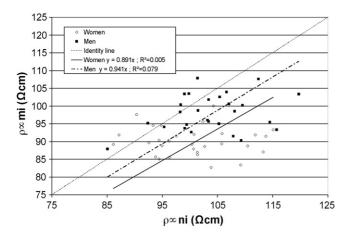


Fig. 3. Comparison between individual TBW resistivities calculated by Matthie  $(\rho_{\infty mi})$  and those calculated from DXA  $(\rho_{\infty ni})$  in 1st group of subjects.

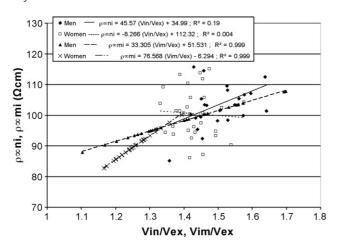


Fig. 4. Variation of individual TBW resistivities calculated by Matthie  $(\rho_{\infty mi})$  and those calculated from DXA  $(\rho_{\infty ni})$  with ICW/ECW ratio in 1st group of subjects.

 $ho_{\infty ni}$  increased with decreasing BMI as observed by Moissl et al. [34] for ECW and ICW, we have plotted them in Fig. 5 versus 1/BMI. This figure shows that it was the case, but with small correlation coefficients. Values of  $ho_{\infty mi}$  calculated

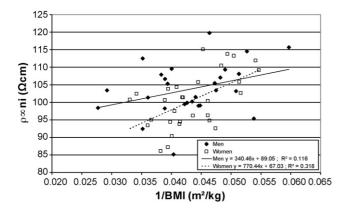


Fig. 5. Variation of individual TBW resistivities  $\rho_{\infty ni}$  from DXA with 1/BMI in 1st group of subjects.

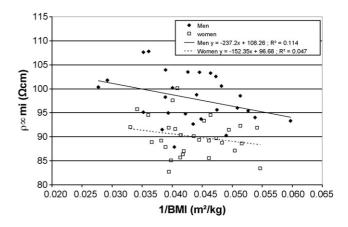


Fig. 6. Variation of Matthie individual TBW resistivities  $\rho_{\infty mi}$  with 1/BMI in 1st group of subjects.

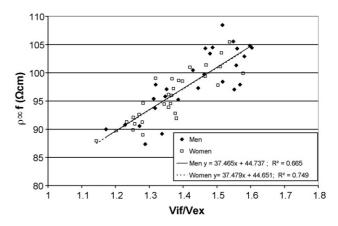


Fig. 7. Variation of Moissl et al. individual TBW resistivities  $\rho_{\infty f}$  with  $V_{if}/V_{ex}$  in 1st group of subjects.

by Matthie's method, shown in Fig. 6, decay when 1/BMI increases, in contrast to our method and that of Moissl et al.

Moissl et al. resistivities  $\rho_{\infty f}$  have been calculated using (33). Table 3 shows that their mean values are lower than these of  $\rho_{\infty ni}$ , but higher than those of Matthie in women. Fig. 7 shows that values of  $\rho_{\infty f}$  increase approximately linearly with  $V_{if}/V_{ex}$  like Matthie's resistivities.

# 3.4. Comparison of TBW volumes calculated by different methods

Table 5 shows that the BIS method of Matthie [31] gives mean values of TBW identical to those of the Xitron.

Table 4
ECW volumes in liters calculated by various BIS and BIA methods in 1st group of subjects

	Men, 1st group (	(n=27)	Women, 1st group $(n=30)$			
	Mean $\pm$ S.D.	P/V <sub>ex</sub>	Mean $\pm$ S.D.	P/V <sub>ex</sub>		
$\overline{V_{\mathrm{ex}}}$	$17.88 \pm 2.32$		$13.02 \pm 1.35$			
$V_{ m ef}$	$17.26 \pm 2.16$	4E - 18	$12.90 \pm 1.30$			
$V_{\rm es}$	$18.08 \pm 2.81$	0.086	$14.24 \pm 1.62$	2.0E - 20		
$V_{\mathrm{eh}}$	$20.16 \pm 1.86$	2E-11	$16.18 \pm 0.93$	1.3 E-6		

Table 5
TBW volumes in liters calculated by various BIS and BIA methods in 1st group of subjects with mean and S.D. of differences with  $V_{\rm td}$  and P-values of Student test with respect to  $V_{\rm td}$  and  $V_{\rm tn}$ 

	Men, 1st group $(n=27)$			Women, 1st group $(n=30)$			
	$\overline{\text{Mean} \pm \text{S.D.}}$	P/V <sub>td</sub>	P/V <sub>tn</sub>	$\overline{\text{Mean} \pm \text{S.D.}}$	$P/V_{ m td}$	P/V <sub>tn</sub>	
$\overline{V_{ m td}}$	$44.35 \pm 5.64$			$31.54 \pm 3.09$			
$V_{ m tn}$	$44.63 \pm 6$	0.474		$31.65 \pm 3.58$	0.709		
$V_{ m tf}$	$42.78 \pm 4.85$	4.33E-4	2.2E-5	$30.57 \pm 3.13$	9.0E-4	2.44E-6	
$V_{ m tm}$	$42.85 \pm 6.4$	6.6E - 04	1.1E-6	$29.46 \pm 3.85$	3.5E-7	4.14E-7	
$V_{ m tk}$	$44.46 \pm 5.45$	0.805	0.506	$31.99 \pm 3.19$	0.127	0.007	
$V_{ m th}$	$43.82 \pm 4.96$	0.231	0.002	$33.19 \pm 2.92$	1.2E-6	1.4E - 12	
$V_{ m tde}$	$39.38 \pm 5.14$	3.2E-12	8.9E-13	$32.43 \pm 3.28$	0.0325	0.0238	
$V_{ m tL}$	$36.63 \pm 4.71$	1.4E-16	1.7E-17	$29.98 \pm 4.71$	6.7E - 28	1.59E-6	
$V_{\rm tn} - V_{\rm td}$	$0.284 \pm 2.03$			$-0.11 \pm 1.63$			
$V_{ m tf} - V_{ m td}$	$-1.57 \pm 2.02$			$-0.968 \pm 1.44$			
$V_{ m tm}-V_{ m td}$	$-1.49 \pm 2.01$			$-2.084 \pm 1.76$			
$V_{\mathrm{tk}} - V_{\mathrm{td}}$	$0.118 \pm 2.45$			$0.447 \pm 1.56$			
$V_{ m th}-V_{ m td}$	$-0.52 \pm 2.2$			$1.645 \pm 1.48$			
$V_{ m de} - V_{ m td}$	$-4.97 \pm 2.13$			$0.892 \pm 2.174$			
$V_{ m tL}-V_{ m td}$	$-7.71 \pm 2.15$			$-1.56 \pm 1.87$			

Table 6 Comparison of TBW volumes calculated in the 2nd group by different BIS method and mean values and S.D. of their differences with  $V_{\rm td}$ 

	$V_{ m td}$	$V_{ m tn}$	$V_{ m tm}$	$V_{ m tf}$	$V_{ m tn}-V_{ m td}$	$V_{ m tm}-V_{ m td}$	$V_{ m tf}-V_{ m td}$
Men 2nd group, $n = 15$	$45.87 \pm 5.28$	$45.83 \pm 5.18$	$44.46 \pm 5.75$	$43.84 \pm 4.61$	$-0.033 \pm 2.58$	$-1.418 \pm 3.18$	$-2.025 \pm 3.34$
women 2nd group, $n = 6$	$29.59 \pm 2.65$	$31.53 \pm 4.74$	$29.48 \pm 5.49$	$31.31 \pm 3.85$	$1.94 \pm 2.97$	$-0.104 \pm 3.9$	$1.723 \pm 3.24$
$P/V_{\rm td}$ men	N A	0.958	0.107	0.034			
$P/V_{\rm td}$ , women	N A	0.17	0.95	0.249			

P values of student test relative to  $V_{\rm td}$ .

Although mean values of  $V_{\rm tm}$  and  $V_{\rm tf}$  were close in men, individual values were different. As expected, mean values of  $V_{\rm tn}$  were closest to mean values of  $V_{\rm td}$ , while mean values of  $V_{\rm tm}$  were lower by 1.48 L in men and by 2.08 L in women. Mean values of  $V_{\rm tf}$  were also lower than those of  $V_{\rm td}$  by 1.57 L in men and by 0.97 L in women.

We have represented the comparison of individual values of  $V_{\rm tn}$ ,  $V_{\rm tm}$  and  $V_{\rm tf}$  against corresponding values of  $V_{\rm td}$  in Fig. 8a for men and in Fig. 8b for women and in Table 6. In men, values of  $V_{\rm tf}$  are generally lower than those of  $V_{\rm tn}$  and  $V_{\rm td}$ , especially when  $V_{\rm td} > 45$  L, while those of  $V_{\rm tm}$  become close to those of  $V_{\rm td}$  above 45 L. In women, values of  $V_{\rm tn}$  are closer to those of  $V_{\rm td}$  than in men, while both values of  $V_{\rm tm}$  and  $V_{\rm tf}$  are generally lower than those of  $V_{\rm td}$ .

Table 5 shows that Kushner et al. [21] and Hannan et al. [22] BIA methods gave mean TBW values,  $V_{\rm tk}$  and  $V_{\rm th}$ , respectively, closer to those of  $V_{\rm td}$  and  $V_{\rm tn}$  than Matthie and Moissl et al. methods. Mean values of  $V_{\rm tk}$  were close to those of  $V_{\rm tn}$  and  $V_{\rm td}$  while Hannan's and Deurenberg methods ( $V_{\rm tde}$ ) overestimated TBW in comparison with other methods tested.

The comparison of individual values of  $V_{\rm tk}$ ,  $V_{\rm th}$  and  $V_{\rm tde}$  with those of  $V_{\rm td}$  is displayed in Fig. 9a for men and in Fig. 9b for women. For men, values of  $V_{\rm tk}$  and  $V_{\rm th}$  are not too different from those of  $V_{\rm td}$ , confirming the small differences in mean values of Table 3, 0.11 L for  $V_{\rm tk} - V_{\rm td}$  and -0.53 L for  $V_{\rm th} - V_{\rm td}$ . Deurenberg's method seems to underestimate TBW as compared to other methods with a mean value of

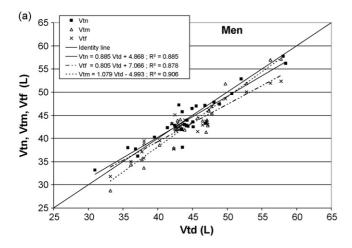
 $V_{\rm td} = V_{\rm td}$  of 5.25 L. In women, the three BIA methods gave larger mean values than  $V_{\rm td}$ , by 0.45 L for  $V_{\rm tk}$ , 1.65 L for  $V_{\rm th}$  and 0.89 L for  $V_{\rm tde}$ . This overestimation becomes less at volumes >33 L.

#### 4. Discussion

When comparing different impedance methods, BIS and BIA, one must keep in mind that their coefficients have been obtained from measurements taken with various instruments, single and multifrequency and different types of electrodes. This may account for some of the observed discrepancies. As our measurements were taken with a Xitron 4200 and Xitron electrodes, their comparison may be more legitimate with methods of Matthie [31] and Moissl [32] who have used the same equipment than with BIA methods.

#### 4.1. Measurements of ECW volumes

BIS methods, which compute ECW volumes from the resistance extrapolated at zero frequency  $R_{\rm e}$  should be, in principle, more accurate than BIA methods based on empirical relations of the resistance  $R_{50}$  or impedance at 50 kHz and weight, such as those of Hannan's et al. [22] and Sergi et al. [26] since  $R_{50}$  includes a contribution from ICW. The initial BIS method presented in [16,20] which has been validated by bromide dilution measurements has been generally



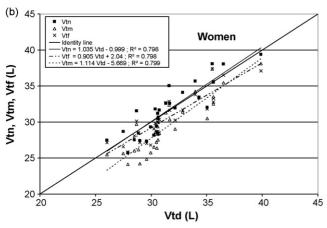
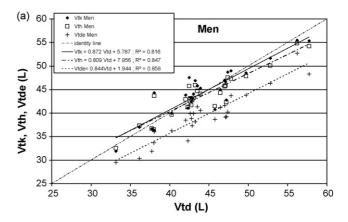


Fig. 8. (a) Variation of TBW volumes calculated by our method  $(V_{\rm tn})$  Matthie  $(V_{\rm tm})$  and Moissl et al.  $(V_{\rm tf})$  with those calculated from DXA in men of 1st group. (b) Same as (a) for women of 1st group.

found to be satisfactory, even in dialysed patients [27]. The modification proposed by Moissl et al. [32] of introducing a BMI dependence can be considered as a refinement of the initial method as it hardly changes ECW volumes in women and only a little in men as seen in Fig. 2. Since we did not have access to simultaneous measurements of bromide dilution and impedance data, we could compare the accuracy of these different methods. Among the two BIA methods tested, it is Sergi's method which is closest to values of  $V_{\rm ex}$  or  $V_{\rm ef}$ , while Hannan's method overestimates ECW, especially at low volumes.

## 4.2. Measurements of TBW volumes

Here again, BIS methods based on the resistance extrapolated to infinite frequency could be expected to be more accurate than BIA methods since a 50 kHz current only penetrates a fraction of ICW. However the situation is more complex and different from that of ECW, as the initial BIS method presented in [18] which calculated ICW by (7) was reported to give TBW volumes different from those deuterium dilution measurements, leading De Lorenzo et al. [20]



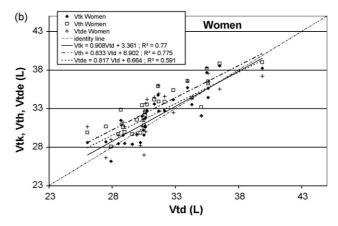


Fig. 9. (a) Variation of TBW volumes calculated by Kushner method ( $V_{\rm tk}$ ), Hannan's ( $V_{\rm th}$ ) and Deurenberg ( $V_{\rm tde}$ ) with those calculated from DXA in men of 1st group. (b) Same as (a) for women of 1st group.

to propose higher ICW resistivities than those of the initial BIS method. A first question which arises with the BIS method, is whether it is better to calculate ICW volume from ICW resistance  $R_i$  and then TBW as the sum of ECW and ICW volumes, or to calculate directly TBW, even though it is composed of two fluids with very different resistivities. The ICW resistance  $R_i$ , unlike  $R_e$  and  $R_\infty$  cannot be measured directly by extrapolation, but must be calculated from (6), which assumes that ECW and ICW behave as parallel resistances. The difference between Matthie's modified BIS method [31] and ours [30] is that he uses an individual TBW resistivity for each subject, function of the  $R_{\infty}/R_{\rm e}$  ratio, which increases linearly with the ratio  $V_i/V_e$ . This is logical as ICW is less conducting than ECW and his method should be more accurate than ours. But when Matthie's method was applied to our subjects, it gave a low mean resistivity, resulting in lower values of TBW, Measurements of TBW loss by ultrafiltration by the Xitron 4200 which uses Matthie's method in dialysed patients were also found to be underestimated [27].

Since we did not know ICW resistivity, we choose to compute the individual TBW resistivity  $\rho_{\infty ni}$  from  $V_{td}$  deducted from the FFM of our subjects assuming a hydration rate of 73.2%. This assumption is of course not true

Table 7
Mean and S.D. of hydration rates in %, using TBW volumes computed with different methods and FFM measured by DXA in 1st and 2nd groups

	$V_{\rm tn}/{\rm FFM}$	$V_{\rm tm}/{\rm FFM}$	$V_{ m tf}/{ m FFM}$	$V_{\rm tk}/{\rm FFM}$	$V_{\rm th}/{\rm FFM}$	$V_{\rm tde}$ /FFM	V <sub>tL</sub> /FFM
Men, 1st group	$73.7 \pm 3.6$	$70.6 \pm 3.5$	$70.8 \pm 3.1$	$73.5 \pm 4.2$	$72.5 \pm 3.7$	$65.0 \pm 3.2$	$60.5 \pm 2.9$
Women 1st group	$73.4 \pm 3.8$	$68.3 \pm 4.$	$71 \pm 3.3$	$74.3 \pm 3.6$	$77.2 \pm 3.6$	$75.4 \pm 5.1$	$69.7 \pm 4.2$
Men, 2nd group	$73.3 \pm 4.3$	$71 \pm 5.2$	$70.2 \pm 5.4$	$72.3 \pm 4.7$	$71.4 \pm 4.3$	$65.2 \pm 3.4$	$62.2 \pm 3.4$
Women 2nd group	$77.8 \pm 7.2$	$72.6 \pm 9.6$	$77.6 \pm 7.8$	$79.6 \pm 5.6$	$81.8 \pm 4.6$	$82.1 \pm 5$	$77.9 \pm 4.7$

for every person, but it should be statistically true for a healthy population as our subjects were. We then assumed, for simplicity, uniform resistivities in men and women equal to the average values for each sex. This method may, of course, become inaccurate in subjects with abnormal  $V_{\rm i}/V_{\rm e}$  ratios.

Moissl et al. [32] have chosen to compute directly ICW volumes from  $R_i$  using (27). But it is difficult to justify (27) from Hanai's mixture theory. Adapting (1) to ICW considered as an electrically homogeneous fluid gives

$$R_{\rm i} = \frac{K_{\rm b}\rho_{\rm ai}H^2}{V_{\rm b}} \tag{34}$$

To obtain (27) from (34) requires to assume that the apparent ICW resistivity  $\rho_{ai}$  is given by

$$\rho_{ai} = \rho_i \left(\frac{V_b}{V_i}\right)^{3/2} \tag{35}$$

or that the fraction of non conducting elements in the body volume  $V_b$  is  $c = 1 - V_i/V_b$  which is wrong as the ECW volume is also conducting. Moissl's method led also to an underestimation of  $V_{\rm tf}$  as compared to  $V_{\rm td}$ , but to a lesser extent than  $V_{\rm tm}$  in women.

We have included in Table 7 the mean values and S.D. of hydration rates of our subjects, calculated using (24) and values of FFM<sub>d</sub> measured by DXA with TBW volumes given by various methods. Hydration rates closest to the standard rate of 73.2% were those given by  $V_{\rm tn}$  (which could be expected, since its resistivity was determined from DXA), by  $V_{tk}$  and by  $V_{\rm th}$  in men. Mean hydration rates computed from  $V_{\rm tm}$ were only 70.6% in men and 68.3% in women. It is normal that individual hydration rate may vary among subjects, but it is surprising to find in a healthy population mean values below 70% as was the case for Matthie's method in women, Deurenberg's method in men and Lukaski et al. for both, or higher than 75% as was the case for Deurenberg's and Hannan's methods in women. An unbiased comparison of our new method  $V_s$  should be made on the 2nd group (validation group). Table 7 shows that, in men of 2nd group, the hydration rate based on our method is closer to 73.2% than those of other methods. However, in women, all methods, except that of Matthie give high hydration rates, but it may be because their number was only 6 and not representative of a normal population.

#### 5. Conclusion

Since we did not have access to isotopic dilution techniques, we could not evaluate with confidence the accuracy of each impedance method tested. However, mean hydration rates calculated from FFM by DXA and values of TBW by impedance in a healthy population constitute probably a good index of the absence or presence of a bias in methods for calculating TBW. Since the DXA used in our study was considered to be reliable for measuring FFM, a mean hydration rate within the range  $73.2 \pm 2\%$  should indicate that the impedance method used for TBW had probably no bias. On this basis, the best BIA method, among those tested, would be that of Kushner et al. [21] and the worst, those of Lukaski et al. [24] and Deurenberg et al. [23]. But this conclusion may only be valid for our population. Matthie's [31] and Moissl's [32] methods look conceptually good as they use an individual TBW resistivity which increases as the ratio of ICW/ECW rises. However, when applied to our population, these methods led to low resistivities resulting in an underestimation of TBW as compared to DXA or other impedance methods, especially in women. It is surprising that different BIS methods arrive at about the same TBW and ICW volumes with very different ICW resistivities, ranging in men from 154  $\Omega$  cm for the initial BIS method, around  $126 \Omega$  cm for Moissl 'method and 274  $\Omega$  cm for Matthie's method. These apparent discrepancies illustrate the difficulty of comparing the accuracy of different methods which have been conceived from data taken on different populations, including renal failure patients as for Moissl's method. No impedance method exists, which can measure accurately ECW or TBW in a diversified population. While for healthy populations, our method with a universal TBW resistivity or BIA methods such as that of Kushner et al. seem to be adequate, it is probable that, in patients with abnormal fluid distribution or a large amount of adipose tissue, BIS methods based on individual TBW resistivities may be more accurate.

Regarding ECW, we think that the BIS methods of the Xitron  $(V_{\rm ex})$  and that of Moissl et al.  $(V_{\rm ef})$  are as simple and more accurate than BIA methods tested, apart from the necessity of using a multifrequency impedancemeter which calculates  $R_{\rm e}$ .

There may be a way to reconcile BIS and BIA techniques. We have shown recently [34] that it is possible to combine the simplicity of BIA methods and single frequency impedancemeters with the formalism of BIS—Hanai methods, by extrapolating values of  $R_{\rm e}$  and  $R_{\infty}$ , not from several frequencies as in the Xitron, but from the resistance at 50 kHz

 $(R_{50})$  and to use BIS equations such as (5a,b) for ECW and (23a,b) for TBW. Due to the strong correlation existing between these three resistances [22,25], errors made when  $R_{\rm e}$  and  $R_{\infty}$  are determined from  $R_{50}$  are small and do not compromise the accuracy of BIS methods. No significant differences between TBW volumes calculated from  $R_{\infty}$  and  $R_{50}$  using a Xitron and (23a,b) were found in the 1st and 2nd groups of subjects [34]. A similar study for ECW will be reported shortly.

## Appendix A. Derivation of (21)

Using (2) for ICW with  $c = 1 - (V_i/V_b)$  gives, for the apparent ICW resistivity  $\rho_{ai}$ 

$$\rho_{\rm ai} = \rho_{\rm i} \left(\frac{V_{\rm b}}{V_{\rm t}}\right)^{3/2} \tag{A1}$$

where  $\rho_i$  is the ICW resistivity and from (1) and (A1)

$$R_{\rm i}^{-1} = \frac{V_{\rm t}^{3/2}}{(K_{\rm b}V_{\rm h}^{1/2}H^2\rho_{\rm i})} \tag{A2}$$

Similarly, from (5a,b), we can write

$$R_{\rm e}^{-1} = \frac{V_{\rm e}^{3/2}}{(K_{\rm h}V_{\rm h}^{1/2}H^2\rho_{\rm e})} \tag{A3}$$

And from (6), (23a) and (A2), (A3)

$$R_{\infty}^{-1} = (V_{b}^{1/2} K_{b} H^{2})^{-1} \left[ \frac{V_{t}^{3/2}}{\rho_{i}} + \frac{V_{e}^{3/2}}{\rho_{e}} \right]$$

$$= \frac{V_{t}^{3/2}}{(V_{b}^{1/2} K_{b} H^{2} \rho_{\infty})}$$
(A4)

And after simplification of the 2nd equation in (A4)

$$\rho_{\infty}^{-1} = \rho_{\rm i}^{-1} + \rho_{\rm e}^{-1} \left(\frac{V_{\rm t}}{V_{\rm e}}\right)^{3/2} \tag{A5}$$

### **Conflict of interest**

None.

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