impedance in different (ethnic) groups and to relate the bias of predicted values to body water distribution and measures of body build.

Subjects and methods.

In total, 172 healthy subjects, 89 males and 83 females participated in the study. They were recruited in four countries (cities), Ethiopia (Addis Ababa), China (Beijing), Italy (Pavia) and The Netherlands (Wageningen). The subjects cannot be regarded as representative for their country, however they were not specially selected. The aim of the study was explained to the subjects. The study protocol was in accord with the guidelines of the Declaration of Helsinki of the World Medical Association (1989) and was approved by the Medical Ethical Committee of the Department of Human Nutrition, Wageningen, The Netherlands. In each centre the same study protocol was used.

All measurements were performed in the morning, in the fasting state after emptying the bladder. Body weight in underwear or swimsuit was measured to the nearest 0.1 or 0.5kg (Ethiopia) and body height without shoes to the nearest 0.1 or 0.5cm (Ethiopia). Body mass index was calculated as weight/height squared (W/H^2, kg/m^2). After that, body impedances at 1 and 100kHz were measured on the left side of the body immediately after lying supine using a HUMANIM SCAN (Dietosystem, Milan, Italy) multi-frequency impedance analyser. The self-adhesive electrodes (Littman 3M, 2325 VP, St. Paul MN, USA) with a surface area of about $5cm^2$ were attached as described by Lukaski et al[14]. From impedance, the impedance index was calculated as height squared/impedance at frequency f (H^2/Z_f, cm^2/Ω). From impedance index at 1kHz and at 100kHz, extracellular water (ECW) and total body water (TBW) were predicted with the respectively formulas[6]:

$$ECW\ (kg) = 0.24253*H^2/Z_1 + 4.1 \text{ and}$$

$$TBW\ (kg) = 0.51303*H^2/Z_{100} + 6.3$$

In addition, ECW and TBW were calculated with prediction formulas that included not only impedance index but also weight and age, and, for TBW, also sex[6].

Total body water and extracellular water were determined by dilution techniques. A cocktail of an accurately weighed dose of about 15g deuterium oxide and 900mg bromide (1.34g as potassium bromide) was taken orally by the subjects. After 2.5 to 3 hours dilution time a venous blood sample was taken, plasma was separated and stored at -80°C until analysis. Deuterium in plasma was determined after sublimation by infrared spectroscopy[15]. TBW was calculated using a correction factor of 0.95 for non aqueous dilution[1]. Bromide in plasma was determined by HPLC after ultra filtration[16]. ECW was calculated using a correction factor of 0.9 for non-extracellular distribution[1] and a correction factor of 0.95 for the DONNAN effect[1]. All analyses were done in the same laboratory (Wageningen).

As a crude measure of body build, TBW/height and ECW/height were calculated. A slender subject will have lower values of these parameters compared to a more plump subject. Body water distribution and measures of body build in the country groups were compared with the values of these parameters of the population in which the prediction formulas were developed (reference population). The bias of predicted values of TBW and ECW was corrected for differences in body build and body water distribution compared to the reference population.

The SPSS program[17] was used for statistical analysis. Differences between measured and predicted values (bias) were tested for significance with the paired t-test. Correlations are Pearson's product moment correlations. Differences in variables between groups (countries) were tested with ANOVA or ANCOVA (analysis of co-variance). Multiple regression analyses were performed using country as a dummy variable. Regression equations were tested for differences in slope and/or intercept with the technique described by Kleinbaum and Kupper[18]. The validity of predicted values is described according to Bland and Altman[19]. Values are expressed as mean ± standard deviation (SD) except for regression coefficients for which the standard error of the mean (SE) is shown

Results

Table 1 provides characteristics of the subjects of the four countries. The sex distribution was comparable between the countries. Most pronounced differences between the groups were the lower age of the Italians, the low values of body water compartments in the Ethiopians and the high body weight, body height and body mass index of the Dutch subjects.

Table 1. Characteristics of the study groups.

	Ethiopia		China		Italy		Netherlands	
	mean	SD	mean	SD	mean	SD	mean	SD
Males	24		22		20		23	
Females	20		23		20		20	
Age (years)	34.2	6.3	31.5	6.4	22.0	2.0	31.4	4.5
Weight (kg)	56.4	10.1	58.3	10.2	64.6	11.1	74.4	13.5
Height (cm)	163	9	165	7	170	10	176	10
BMI (kg/m^2)	21.3	3.4	21.3	2.6	22.2	2.5	24.1	4.8
TBW (kg)	26.9	5.2	34.7	5.9	35.6	7.4	39.7	7.0
ECW (kg)	11.7	1.6	13.9	2.3	14.1	2.5	16.2	2.4

Abbreviations: BMI = body mass index; TBW = total body water; ECW = extracellular water

Table 2. Regression coefficients for total body water and extra cellular water against impedance index.

	Total body water				Extracellular water			
	H^2/Z_{100}		intercept		H^2/Z_1		intercept	
	mean	SE	mean	SE	mean	SE	mean	SE
Ethiopia	0.523	0.010	5.6	0.6	0.258	0.007	3.1	0.4
China	0.526	0.011	6.0	0.7	0.253	0.009	3.4	0.5
Italy	0.522	0.011	5.7	0.8	0.255	0.008	3.3	0.4
Netherlands	0.526	0.011	5.9	0.8	0.244	0.008	4.0	0.4

Abbreviations: H = body height; Z_{100} = impedance at 100 kHz, Z_1 = impedance at 1 kHz

In Table 2 the coefficients of the regression equations between TBW and H^2/Z_{100} and ECW and H^2/Z_1 are given for the four groups. The four regression equations for TBW and the four regression equations for ECW did not differ in slope and intercept. Figure 1 and Figure 2 show the relationship between TBW and H^2/Z_{100} and ECW and H^2/Z_1 respectively for all subjects combined.

In Table 3 the differences between measured and predicted TBW and ECW (bias) from impedance index alone, using prediction equations from the literature, are given. Although the bias for ECW was significantly different from zero in all groups it was relatively small and did not differ between the countries. The bias of ECW and TBW correlated with body water distribution (ECW/TBW) and with body build (TBW/height and ECW/height).

Figure 1. Relation between total body water and impedance index at 100kHz.

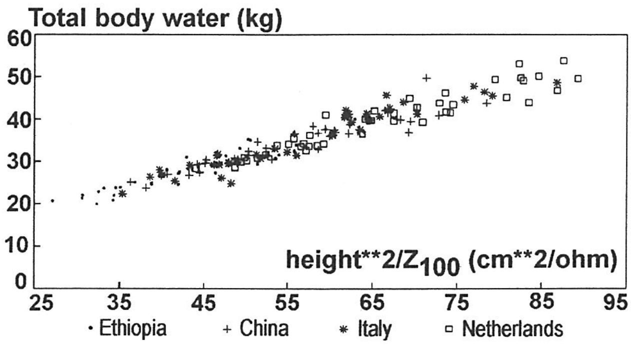

Figure 2. Relation between extracellular water and impedance index at 1kHz.

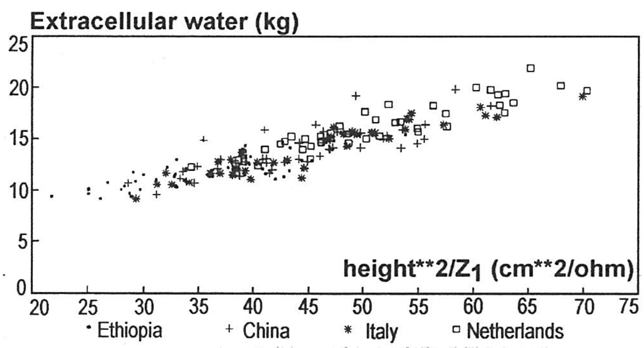

Table 3. Differences between measured and predicted total body water and extracellular water.

	Ethiopia		China		Italy		Netherlands	
	mean	SD	mean	SD	mean	SD	mean	SD
δ TBW (kg)	-0.5	1.7	-0.3	1.8	-0.1	1.8	-0.6*	1.8
δ ECW (kg)	-1.0*	1.0	-0.9*	1.1	-1.1*	0.9	-0.3*	0.9

* $p<0.05$ from zero; Abbreviations: δ TBW = measured minus predicted total body water; δ ECW = measured minus predicted extracellular water

Table 4. Correlation of the bias of predicted total body water and extracellular water with body water distribution and measures of body build.

	Ethiopia	China	Italy	Netherlands
δ TBW with:				
mean TBW	0.25	0.19	0.40*	0.27
ECW/TBW	-0.22	0.09	-0.51*	-0.38*
TBW/H	0.38*	0.33*	0.56*	0.47*
δ ECW with:				
mean ECW	-0.18	0.29	0.28	0.26
ECW/TBW	0.62*	0.73*	0.23	0.18
ECW/H	0.23	0.63*	0.52*	0.58*

* $p<0.05$ Abbreviations: TBW = total body water; mean TBW = mean of measured and predicted TBW; δ TBW = measured minus predicted TBW; ECW = extracellular water; mean ECW = mean of measured and predicted ECW; δ ECW = measured minus predicted ECW; H = body height;

The correlation coefficients are given in Table 4 for the separate countries. As can be read from the table both TBW and ECW were slightly over predicted at higher levels of the body water compartment. The bias was correlated with body water distribution in most country groups and with measures of body build in all country groups. The positive correlation of the bias with body build means that in slender subjects, thus in subjects with a relatively low value of TBW/height or ECW/height, the prediction formulas tend to overestimate total body water and extracellular water.

Table 5. Body water distribution and body build in the four studied groups and in the reference group.

	Ethiopia		China		Italy		Netherlands		Reference[a]	
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
ECW/ TBW	0.41	0.03	0.40*	0.03	0.40*	0.02	0.41	0.02	0.42	0.03
TBW/H (kg/cm)	0.18*	0.03	0.21*	0.03	0.21*	0.03	0.22	0.03	0.22	0.03
ECW/H (kg/cm)	0.07*	0.01	0.08*	0.01	0.08*	0.01	0.09	0.01	0.09	0.01

a) reference: Dutch group in which the prediction formulas were developed; * $p<0.05$ compared to reference population

Table 5 shows body water distribution and body build in the four groups in comparison with the population in which the prediction formulas were developed (reference population). In some population groups, body water distribution and body build were different compared to the reference group. These differences were apparent in both males and females (data not shown). Table 6 shows the bias of TBW and ECW in each group corrected for differences in body water distribution and/or measures of body build compared to the reference population. In most groups the mean bias in predicted values decreased, sometimes markedly, after correction for these parameters. Also the individual error, which is indicated by the SD of the bias, lowered.

Table 6. Mean bias of total body water and extracellular water corrected for body water distribution and body build[a].

	Ethiopia		China		Italy		Netherlands	
	mean	SD	mean	SD	mean	SD	mean	SD
δ TBW corrected for:								
-	-0.5*	1.7	-0.3	1.8	-0.1	1.8	-0.6*	1.8
ECW/TBW	-0.5*	1.7	-0.3	1.8	-0.3	1.8	-0.7*	1.7
TBW/H	0.0	1.6	-0.1	1.7	0.1	1.7	-0.6*	1.8
ECW/TBW and TBW/H	0.0	1.6	0.0	1.7	0.0	1.7	-0.5	1.7
δ ECW corrected for:								
-	-1.0*	1.0	-0.9*	1.1	-1.1*	0.9	-0.3	0.9
ECW/TBW	-0.9*	0.8	-0.6*	0.9	-0.9*	0.9	-0.2	0.9
ECW/H	-0.4	0.9	-0.6*	0.9	-0.8*	0.9	-0.3	0.9
ECW/TBW and ECW/H	-0.2	0.7	-0.4	0.8	-0.5*	0.7	-0.2	0.7

a) corrected for differences in indicated parameters compared to the reference group in which the prediction formulas were developed * $p<0.05$

When prediction formulas not only containing the impedance index but also weight, age and sex[6] were applied to the subjects, the bias of ECW was -0.8 ± 1.0kg, -0.4 ± 1.1kg, -1.2 ± 0.8kg and -0.6 ± 0.7kg and for TBW -0.7 ± 1.5kg, 1.0 ± 1.8kg, -0.9 ± 1.5kg and -0.6 ± 1.5kg for Ethiopian, Chinese, Italian and Dutch subjects respectively. The bias of ECW showed comparable correlations with body water distribution as in Table 4, but was only in the Chinese group correlated with ECW/height. The bias of TBW was not correlated with body water distribution, nor with TBW/height in either group.

Discussion

In this study, prediction formulas for TBW and ECW developed in a Caucasian population were validated in several independently measured groups, partly with a different ethnic background. These groups cannot be regarded as representative for the entire population of that country, but they were not specially selected. The study design and the methodology used in this study was equal for all groups and the chemical analysis to obtain reference values for ECW and TBW were performed in the same laboratory. The impedance instruments used were from the same manufacturer. It is known from the literature[20,21] that different impedance instruments can give different readings, even when the same subject is measured. In three out of four groups (Ethiopia, China, The Netherlands) impedance was measured by the same investigator. Thus it is likely that differences found between groups are not due to differences in methodology and/or standardisation.

The inclusion of other independent variables than impedance index in a prediction formula generally lowers the prediction error. However, it also makes a prediction equation more population specific[7]. Therefore the main statistical analyses were performed using prediction equations containing only the impedance index as independent variable. The results show (Table 3) that the mean bias, in all four groups, was relatively small and comparable, for TBW as well as for ECW. This was to be expected as the regression equations for TBW and ECW did not differ between the groups (Table 2). The bias for TBW and ECW was not correlated with the mean value of predicted and measured ECW and TBW respectively, except for the Italian subjects for TBW. This is an important condition for a valid prediction[19]. However, generally the bias of ECW was positively correlated with body water distribution and the bias of TBW was negatively correlated with body water distribution. This was found by us in earlier studies[6,22,23]. For ECW it can be explained that, at low frequency, the current is partly conducted along the cell membrane[24], resulting in biased (lower) impedance values and hence causing an over prediction of ECW. For TBW it is likely that body impedance is influenced by the different specific resistivities of intra and extracellular fluid[6,10]. The phenomenon is discussed in detail elsewhere[23]. The bias of predicted TBW and ECW was also correlated with measures of body build. From a theoretical point of view, slender subjects have higher impedance values compared to subjects with a plumper body build[7]. As most of the water is located in the trunk which only shows a minor contribution to total body impedance[8,9], plump subjects will have relatively high impedance values compared to their amount of water. Hence, prediction formulas developed in plump subjects will overestimate body water in more slender subjects. This is confirmed by the positive correlation between bias and TBW/height or ECW/height.

After correction for differences in body water distribution (ECW/TBW) and/or for differences in body build (TBW/height and ECW/height) between the groups under study and the group in which the prediction formulas were developed, the bias decreased and was not statistically significant any more. This clearly confirms the dependency of body impedance on body build and shows that ideally population specific prediction formulas have to be used. The fact that, also in the Dutch group, the validity of the prediction was affected by body water distribution and body build, shows that even in a very comparable group these effects have an impact. The comparison in the four different groups confirms an earlier statistical analysis of the Italian and Dutch groups[25] where the differences in the relationship between body water compartments and impedance were studied in relation to a number of anthropometric variables.

When prediction formulas for TBW and ECW were used that also contained body weight, age and (for TBW) sex, the bias in predicted ECW generally decreased, but the bias for TBW slightly increased. With these prediction formulas, however, there was no effect of body build any more. It seems likely that including other parameters in the regression equation, especially weight, the effect of body build is taken into account.

Summary

Prediction formulas for TBW and ECW, developed in a Dutch Caucasian population, showed generally valid values in Ethiopian, Chinese and Italian subjects as well as in another group of Dutch subjects. The small bias was generally dependent on body water distribution and measures of body build, and decreased after correction for differences in body water distribution and body build.

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Multi-frequency bioelectrical impedance for the prediction of body water compartments: validation in different ethnic groups

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多頻生物電阻抗對身體水份的測定：應用在不同的種族人群

摘要

作者測定了埃塞俄比亞、中國、意大利和荷蘭成年男、女空腹時身高、體重和1kHz和100kHz的電阻抗。總體水份(TBW)和細胞外液(ECW)分别用重水和溴稀釋法測定，同時計算了$\frac{TBW}{身高}$和$\frac{ECW}{身高}$的比值作爲身體結構的測量。

分别用稀釋法和阻抗指數$\left(\frac{身高^2}{阻抗}\right)$測量TBW與ECW的關係，在4個民族之間沒有差異。如果從其它人群（荷蘭）建立起測定TBW和ECW的公式應用在四個國家的人群，TBW稍爲估計過高。應用在意大利人群估計過高爲0.1±1.8公斤，而應用在荷蘭人估計過高爲0.6±1.8公斤。同時ECW亦明顯估計過高，荷蘭人群爲0.3±0.9公斤，而意大利人群爲1.1±0.9公斤。在所有國家中，TBW與$\frac{TBW}{身高}$相關，（相關係數從0.33-0.56, $p < 0.05$）。除埃塞俄比亞外，其它國家的ECW與$\frac{ECW}{身高}$相關（相關係數從0.52-0.83, $p < 0.05$）。此外，在兩個人群中，TBW和ECW與身體水份分佈$\frac{ECW}{TBW}$相關。

作者得出結論，多頻生物電阻抗是一種測定人群身體水份的適當技術。不同種族間的差異部份由於身體結構不同所致。

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