Original article

Bioimpedance index for measurement of total body water in severely malnourished children: Assessing the effect of nutritional oedema

Tsinuel Girma [a, *], Pernille Kæstel [b], Netsanet Workeneh [a], Christian Mølgaard [b], Simon Eaton [d], Gregers S. Andersen [c], Kim F. Michaelsen [b], Henrik Friis [b], Jonathan C.K. Wells [d]

[a] Department of Pediatrics and Child Health, Jimma University, Ethiopia
[b] Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark
[c] Department of Clinical Epidemiology, Steno Diabetes Centre, Gentofte, Denmark
[d] Childhood Nutrition Research Centre, UCL Institute of Child Health, London, UK

ARTICLE INFO

SUMMARY

Background & objectives: Restoration of body composition indicates successful management of severe acute malnutrition (SAM). Bioimpedance (BI) index (height^2/resistance) is used to predict total body water (TBW) but its performance in SAM, especially with oedema, requires further investigation.
Subjects/Methods: Children with SAM (mid-arm circumference <11.0 cm or weight-for-height <70% of median of NCHS reference and/or nutritional oedema) admitted to Jimma University Hospital were included. Tetrapolar-whole-body impedance (Z), resistance (R) and reactance (Xc) were measured at 50 and 200 kHzs. Pre- and post-deuterium dose saliva samples were analysed using isotope-ratio mass spectrometry. TBW was regressed on H^2/Z. Xc and R were height (H)-indexed, and Xc/H plotted against R/H.
Results: Thirty five children (16 non-oedematous and 19 oedematous) with median (interquartile range) age of 42 (26–54) months were studied. Height-for-age z-score (mean ± SD) was low in both non-oedematous (−3.9 ± 2.8) and oedematous (−3.6 ± 1.7) children. Oedematous children had lower BI parameters than non-oedematous (p < 0.001) and hence higher H^2/Z for a given amount of TBW. At both 50 and 200 kHz, association between H^2/Z and TBW was stronger in non-oedematous children than oedematous (60% higher coefficient of determination and 20% lower standard error of estimate). Intercepts and regression estimates at 50 and 200 kHz were similar, in both oedematous and non-oedematous children.
Conclusions: In children with oedematous SAM, BI index was weak in predicting TBW. Moreover, predicted TBWs at 200 kHz and 50 kHz did not differ and hence BI measurement at 50 kHz is still practical for TBW estimation.

© 2015 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism.

1. Introduction

Restoration of body composition indicates successful management of severe acute malnutrition (SAM), but no easy and accurate method is available [1–3]. Bioimpedance method (BIM), whole-body [4] or segmental [5], is a safe, rapid and easy technique often used to predict total body water (TBW) and lean mass can in healthy individuals. However, its conventional application, commonly referred to as bioimpedance analysis (BIA), requires population-specific equations [6,7], and its accuracy is limited in general [8]. This is due in part to inter-individual variability in body proportions (e.g. limb lengths), as narrow cylinders such as limbs contribute disproportionately to total body impedance [9]. In healthy children, age or body size-to-age variation in impedance (Z in Ohm) could affect accuracy of TBW prediction [10]. Stunted children with some degree of wasting produce higher R compared with anthropometrically normal children [11] and thus reflects the influence of abnormal body composition and/or body proportion.

* Corresponding author. Department of Pediatrics and Child Health, Jimma University Specialized Hospital, Jimma, Ethiopia. PO box 384, Jimma, Ethiopia. Tel.: +251 917 24 0174; fax: +251 417 111457.
E-mail address: tsinuel.girma@ju.edu.et (T. Girma).

The poorer the ability of BIA to predict TBW, the less suitable it will be for clinical monitoring of body composition.

In most four-electrode (tetrapolar) measurements, Z is measured with 800 μA alternating current at 50 kHz passing through the body, between the wrist and ankle [12]. Two relationships between the Z of the body and its volume (V) are central to this method [4]. First, derived from Ohm's Law, V is inversely related to Z and directly to conductive distance, approximated by height or length (H):$V = \rho H^2/Z$. Tissue specific resistivity, ρ, is a frequency-dependent constant inversely related to the number of free ions per V [13]. Theoretically it is independent of body size, shape and age but could be affected by abnormal tissue hydration and/or osmolality [10—12]. Second, at low frequencies electric current flows around the cell without penetrating into the cell, whereas at high frequencies the membrane capacitance is no impediment to the current and it flows indiscriminately through both intracellular and extracellular space, and thus assumed to reflect TBW better [4].

Decreased total body potassium, increased total body sodium and increased TBW are well recognized and common features of SAM, and often indicate diminished body cell mass and expanded extracellular fluid [1,2,16]. Yet, how these abnormalities, particularly oedema, affect the performance of BIA is little studied. This study explores the performance of BIA in estimating TBW in children with SAM and the influence of oedema, using deuterium dilution method as a reference.

2. Subjects and methods

2.1. Study setting and subjects

Children 0.5—14 years of age with SAM (MUAC <11.0 cm or weight-for-height <70% of the median of the NCHS growth reference and/or nutritional oedema) admitted to Jimma University Hospital were included after informed consent. Children with life threatening conditions such as shock were excluded.

2.2. Data collection

Weight was measured to the nearest 10 g using a digital scale (Tanita BD 815 MA, Tokyo, Japan) and length to nearest 0.1 cm using a length board (SECA 416, Hamburg, Germany) for children less than 2 years of age. For older children, height was measured using stadiometer (SECA 214, Hamburg, Germany) to nearest 0.1 cm. Pitting oedema was checked by gentle pressure with the thumb on the feet for 3—5 s.

TBW was determined by deuterium dilution at a dose of 0·5 g of ^2H_2O (Sercon, Crewe, UK) per kg body weight diluted in 5 ml of sterile water. Older children drank the deuterium whereas for younger children it was dripped into the mouth using a plastic tube attached to a syringe. Any spillage was collected in a tissue, weighed and subtracted from the dose. Pre-dose, and 3-h post-dose samples of saliva were collected in all children. An additional 4-h post-dose sample was collected in 15 children. In two children (1 with oedema), samples were collected hourly till 8-h post-dose. Children were not given feeds 30 min before and 15 min after deuterium dosing. Saliva samples were kept at −20 °C before shipment to the UK for analysis. Though the dose used was based on Fourier transform infrared (FTIR) protocol, it was difficult to get the minimum (2 ml) saliva volume required for this method [17] and analysis was therefore undertaken at Institute of Child Health, UK using isotope-ratio mass spectrometry (Delta Plus XP; Thermofisher Scientific, Bremen, Germany). Samples were analysed in duplicate, with all enrichments normalized to values for international standard water samples, and the average value used in

subsequent calculations. The mean precision of ^2H analyses was, 9.4 deltas, inducing imprecision on TBW of 0·8%. For calculating TBW, it was assumed that ^2H dilution space overestimated TBW by a factor of 1·044 (Ref. [16]).

A tetrapolar portable bioimpedance (BI) analyser (BODYSTAT QuadScan 4000, British Isles, England), emitting 200 μA root mean square alternating current at 5, 50, 100 and 200 kHzs, was used to measure resistance (R), reactance (Xc) and Z. Self-adhesive disposable electrodes were attached at the right hand and foot, injecting leads were connected to the electrodes just behind the finger and toe and the measuring leads were then connected to the electrodes on the right wrist and right ankle. Measurement was done after deuterium dosing and in triplicate, 5 min apart, while children were calm and supine on stretcher with limbs abducted from the body. Triplicate values were averaged for each subject.

Among 7 oedematous children with TBW data at 3 and 4 h, there was an average increase in isotopic enrichment, which indicated a delayed deuterium equilibration time. The calculated TBW values therefore decreased during this period by 3.5% (95% CI: -10.6, 3.4). Among 7 non-oedematous children, there was no average change in TBW calculated from 3- and 4-h post dose samples (average difference −0.2%, 95%CI -5.4, 5.0). Data on deuterium enrichment up to 8 h in two children are shown in Fig. 1. In the non-oedematous child, enrichment declined from 3 h, indicating equilibration by 3 h and subsequent dilution of body water by fluid intakes. In the oedematous child, enrichment increased between 3 and 4 h, and then declined. This suggests that equilibration was complete by 4 h in this child. On this basis, we assumed that all oedematous children were equilibrated by 4 h. Therefore, 3-h TBW values were
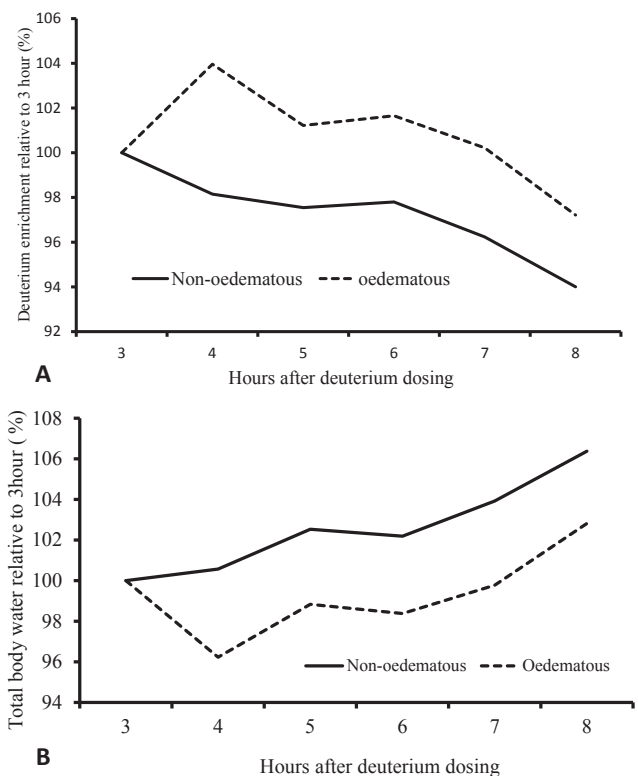

Fig. 1. Patterns of deuterium enrichment (A) and corresponding calculated total body water (B) in two children with severe acute malnutrition. In Fig. 1A, declines in enrichment can be attributed to post-equilibration fluid intake, whereas increases in enrichment indicate continuing isotopic equilibration. The data therefore indicate that the non-oedematous child was equilibrated by 3 h, and the oedematous child by 4 h.

reduced by 3.5% in all children with oedema, but no adjustment was made to the 3-h TBW values in the non-oedematous children.

The study was approved by the Research Ethical Review Committee, College of Public Health and Medical Sciences, Jimma University. Before giving consent, caretakers were given verbal and written information. All the data were collected by two research nurses. The study was conducted from December 2009 to October 2011.

2.3. Statistics and data handling

Data were double entered into EpiData version 3.1 (EpiData Association, Odense, Denmark) and analysed with Stata/IC 12.1 (StataCorp, Texas, USA). Anthropometric z-scores, based on WHO child growth standard, were calculated in Stata and WHO Anthro Plus v 1.0.3 (WHO, Geneva, Switzerland) [19]. BI index H^2/Z (cm^2/ohm) was calculated, where H is height or length. TBW from deuterium was regressed on BI index for SAM children as a single group, and separately for oedematous and non-oedematous. Then their regression coefficients and slopes were compared. Data were also expressed graphically, using the bioimpedance vector analysis (BIVA) approach of Piccoli [20]. This approach, through RXc plot, allows axes of variability in the magnitude and hydration of lean tissue to be visualized. Xc and R were height-indexed (Xc/H, ohm/m and R/H, ohm/m), and Xc/H plotted against R/H.

3. Results

The study comprised 16 non-oedematous and 19 oedematous children with SAM and having median (interquartile range) age of 42 (26–54) months 48 (26–60) and 36 (30–48) months, respectively (Table 1). The minimum and maximum ages of the children were 10 month and 144 months, respectively. Both non-oedematous and oedematous children were severely stunted (p = 0.70), but the latter had higher BMI-for-age (p < 0.001). As shown in Table 2, the primary BI parameters (Z, R and Xc) were lower among oedematous children compared with non-oedematous, even when adjusted for height (p < 0.001) whereas the BI indices at the two frequencies were not different between the two groups (p > 0.086).

Results of the regression of TBW on BI indices for SAM children as a single group and separately for oedematous and non-oedematous are shown in Table 3. In the single group, there were marginal differences in the estimates between the two frequencies. In each separate group, all the regression estimates were similar for the two frequencies, and the intercepts were also comparable. This indicates that little is gained by using 200 kHz, and further analyses described below were therefore undertaken using Z50 only. The non-oedematous children had about 60% higher coefficient of determination (R^2) and 20% lower standard

Table 1
Selected characteristics of children with severe acute malnutrition admitted to Jimma University Hospital by nutritional oedema[a].

	Non-oedematous (n = 16)	Oedematous (n = 19)	P-value
Age, month	48 (26–60)	36 (30–48)	0.01[b]
Sex, female	10 (62.5)	8 (42.1)	0.23[c]
Z- score			
Height-for-age	−3.9 ± 2.8	−3.6 ± 1.7	0.70
Body mass index-for age	−4.3 ± 1.4	−1.5 ± 1.4	<0.001
Weight-for-age	−5.3 ± 1.5	−3.3 ± 1.6	<0.001

[a] Mean ± SD or median (interquartile range) or n(%).
[b] Kruskal−Wallis rank.
[c] Chi-square and independent *t*-test.

Table 2
Bioimpedance parameters and total body water of children with severe acute malnutrition by nutritional oedema[a].

	Non-oedematous n = 16	Oedematous n = 19	P − value
Impedance at 50 kHz, Z50 (Ohm)	1128.9 ± 222.8	792.9 ± 197.8	<0.001
Impedance at 200khz, Z200 (Ohm)	1040.4 ± 199.2	752.1 ± 185.1	<0.001
Resistance, R50 (Ohm)	1117.5 ± 218.4	738.5 ± 215.2	<0.001
Reactance, Xc50 (Ohm)	56.0 ± 17.4	33.6 ± 14.9	<0.001
R50/H (Ohm/m)	1354.6 ± 374.6	872.6 ± 233.9	<0.001
Xc50/H (Ohm/m)[b]	66.6 ± 22.1	40.0 ± 18.1	<0.001
H^2/Z50 (cm^2/Ohm)	7.4 ± 4.5	9.6 ± 2.6	0.09
H^2/Z200 (cm^2/Ohm)	7.9 ± 5.0	10.0 ± 2.6	0.11
Total body water (L)	7.9 ± 3.2	8.2 ± 1.5	0.75

[a]Mean ± SD, total body water (TBW) using deuterium dilution and, [b]Height or length (H).

error of estimate (SEE) than oedematous children, indicating a much tighter association between BI indices and TBW than in oedematous children.

Although the difference in slopes between oedematous and non-oedematous group was not significant (Table 3), for a given amount of TBW, oedematous children had a lower Z value and hence higher index (Fig. 2). Additionally, in Fig. 3 it is evident that the contrast in the slopes between oedema and non-oedema declines slightly at Z200 compared to Z50. So, there is a weak indication that at higher frequencies, where the current passes through both extracellular and intracellular space, the impedance-TBW association is not quite so different as when the current mainly passes through ECW. Using BIVA approach, the oedematous and non-oedematous children showed contrasting association between height-adjusted Xc and R (Fig. 3).

4. Discussion

In this study the poor agreement between TBW and the BI index showed the complexity of assessing TBW in SAM patients, particularly among oedematous children. Fluid and electrolyte abnormalities in SAM might alter tissue electrical properties and thus make prediction of TBW using the BI index invalid.

Deuterium equilibration was delayed in oedematous (4hr) but not in non-oedematous children (3hr). This reflects and confirms the hemodynamic abnormality in children with SAM; analogous to hypothyroidism, they are characterized by significant prolongation of circulation time and expanded extracellular water [21]. The longer equilibration duration among oedematous children could be explained by their excess ECW, which is clinically evident as oedema. This is a methodological issue which can thus be resolved

Table 3
Regressions of total body water using deuterium dilution on bioimpedance index (H^2/Z) by nutritional oedema of children (n = 35) with severe acute malnutrition[a].

	Intercept	β(95%CI)	SEE	R^2
H^2/Z50 (cm^2/ohm)				
Both groups	2.70	0.50 (0.35−0.64)	0.07	0.59
Oedematous	3.72	0.35 (0.11−0.60)	0.12	0.37
Non-oedematous	2.33	0.60 (0.39−0.81)	0.10	0.73
H^2/Z200 (cm^2/ohm)				
Both groups	2.50	0.48 (0.35−0.61)	0.06	0.65
Oedematous	3.43	0.36 (0.14−0.60)	0.11	0.38
Non-oedematous	2.27	0.55 (0.37−0.74)	0.09	0.76

[a] Height or length (H)/impedance (Z at 50 or 200 kHz), standard error of estimate (SEE) and coefficient of estimate (R^2). Intercepts and β (slopes) for oedematous and non-oedematous are not different between 50 kHz and 200 kHz, p > 0.05.
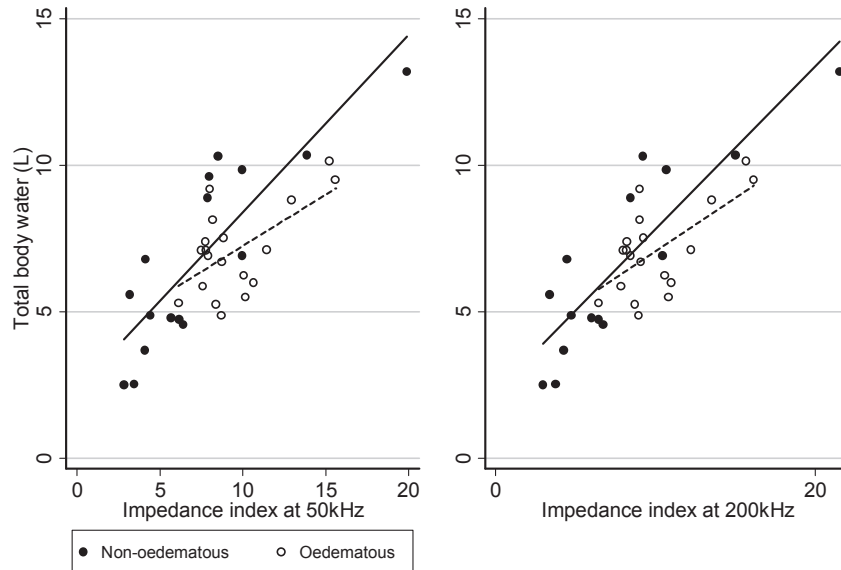
Fig. 2. Linear regressions of total body water using deuterium dilution on BI index (H^2/Z, cm^2/Ohm) of children with severe acute malnutrition, where H is height or length and Z impedance. The contrast in the slopes between oedema and non-oedema declines slightly at Z200 compared to Z50. The solid (non-oedematous) and broken (oedematous) lines represent the fitted values.

by adapting the protocol; a separate issue is whether the association between the BI index and TBW is also affected by oedema.

In this study, oedematous children were found to produce lower impedance per unit of height, although they were as severely stunted as the non-oedematous children. Walker el al [11] showed that stunted Jamaican children have higher R than the non-stunted despite having the same TBW%. However, in the current study stunted children with oedema had lower BI parameters. The lower ρ , as estimated from the regression coefficients, may explain this difference. Theoretically ρ varies with frequency but not the size and shape of individuals [13]. Alterations in the amount and composition of extracellular fluids, expected to be extreme in oedematous children, influence tissue-specific resistivity [22]. The variations in the RXc plot between oedematous and non-oedematous may further support difference in their lean tissue hydration.

Regressing of TBW on H^2/Z appears to give weak predictive power generally for SAM. However, when the oedematous and non-oedematous children are analysed separately, the poor overall accuracy can be attributed primarily to a much looser fit between TBW and H^2/Z in the oedematous group (lower R^2 and higher SEE). The predictive power was similar between 200 kHzs and 50 kHzs.
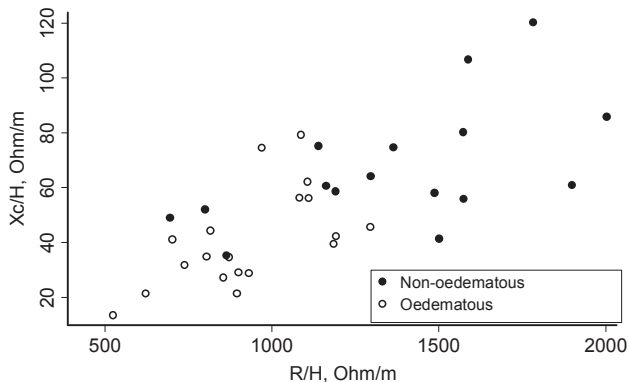
The criteria for deciding on equations however is somehow empiric and also relies on the assumption that impedance has been measured equally well at each frequency [23]. Our study suggests that BIA might help monitor TBW of non-oedematous children through treatment, but would be of less use in oedematous children. However, the hydration of lean tissue in non-oedematous SAM children is unknown [24] hence at present there is insufficient information to convert TBW to lean mass.

In conclusion, this study demonstrated that BI parameters were lower in oedematous compared with non-oedematous. Prediction of TBW using the BI index was unsatisfactory mainly among oedematous SAM, but performed better in non-oedematous patients. Predictions of TBW at 200 kHz and 50 kHz didn't differ. The study also showed that isotope equilibration in children with oedematous SAM is delayed. Larger sample size and narrower age range could have demonstrated the variation in BIA prediction better. The potential utility of the BI index for monitoring changes in body composition in SAM patients therefore varies substantially between oedematous and non-oedematous children. Further work is required to develop BIA technology for clinical monitoring of these patients; in the meantime our equation for non-oedematous children may be valuable for research studies, but should not be applied in clinical practice.

Conflicts of interest

None declared.

Source of funding

Fig. 3. RXc plot of reactance (Xc) on resistance (R) of children with severe acute malnutrition by oedema. Height or length (H).

Acknowledgements

References

[1] Garrow JS, Fletcher K, Halliday D. Body composition in severe infantile malnutrition. J Clin Invest 1965 Mar 1;44(3):417–25.

[2] Kerpel-Fronius E. Volume and composition of the body fluid compartments in severe infantile malnutrition. J Pediatr 1960 Jun;56(6):826–33.

[3] Guideline WHO. Updates on the management of severe acute malnutrition in infants and children. World Health Organization; 2013.

[4] Foster KR, Lukaski HC. Whole-body impedance—what does it measure? Am J Clin Nutr 1996 Sep;64(3 Suppl). 388S–396S.

[5] Segal KR, Burastero S, Chun A, Coronel P, Pierson Jr RN, Wang J. Estimation of extracellular and total body water by multiple-frequency bioelectrical-impedance measurement. Am J Clin Nutr 1991 Jul;54(1):26–9.

[6] Jaffrin MY, Morel H. Body fluid volumes measurements by impedance: a review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. Med Eng Phys 2008 Dec;30(10):1257–69.

[7] Dehghan M, Merchant AT. Is bioelectrical impedance accurate for use in large epidemiological studies? Nutr J 2008;7(1):26.

[8] Baumgartner RN, Chumlea WC, Roche AF. Estimation of body composition from bioelectric impedance of body segments. Am J Clin Nutr 1989 Aug;50(2):221–6.

[9] Fuller NJ, Fewtrell MS, Dewit O, Elia M, Wells JCK. Segmental bioelectrical impedance analysis in children aged 8-12 y: 1. The assessment of whole-body composition. Int J Obes Relat Metab Disord J Int Assoc Study Obes 2002 May;26(5):684–91.

[10] Bosy-Westphal A, Danielzik S, Dörhöfer R-P, Piccoli A, Müller MJ. Patterns of bioelectrical impedance vector distribution by body mass index and age: implications for body-composition analysis. Am J Clin Nutr 2005 Jul;82(1):60–8.

[11] Walker SP, Grantham-McGregor S, Powell C, Fletcher P, Himes JH. Bioelectrical impedance, anthropometry and body composition in stunted and non-stunted children. Eur J Clin Nutr 1990 Oct;44(10):763–8.

[12] Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, et al. Bioelectrical impedance analysis–part I: review of principles and methods. Clin Nutr Edinb Scotl 2004 Oct;23(5):1226–43.

[13] Abu Khaled M, McCutcheon MJ, Reddy S, Pearman PL, Hunter GR, Weinsier RL. Electrical impedance in assessing human body composition: the BIA method. Am J Clin Nutr 1988 May;47(5):789–92.

[16] Dempsey DT, Crosby LO, Lusk E, Oberlander JL, Pertschuk MJ, Mullen JL. Total body water and total body potassium in anorexia nervosa. Am J Clin Nutr 1984 Aug;40(2):260–9.

[17] International atomic Energy Agency. IAEA human health series. Introd Body Compos Assess Using Deuterium Dilution Tech Analysis Saliva Samples by Fourier Transform Infrared Spectrom 2010;(12). Viena:IAEA.

[19] Leroy JL. Zscore06: stata command for the calculation of anthropometric z-scores using the 2006 WHO child growth standards. 2011.

[20] Piccoli A, Rossi B, Pillon L, Bucciante G. A new method for monitoring body fluid variation by bioimpedance analysis: the RXc graph. Kidney Int 1994;46(2):534–9.

[21] Viart P. Hemodynamic findings during treatment of protein-calorie malnutrition. Am J Clin Nutr 1978 Jun;31(6):911–26.

[22] Roos AN, Westendorp RG, Frölich M, Meinders AE. Tetrapolar body impedance is influenced by body posture and plasma sodium concentration. Eur J Clin Nutr 1992 Jan;46(1):53–60.

[23] Thomas BJ, Ward LC, Cornish BH. Bioimpedance spectrometry in the determination of body water compartments: accuracy and clinical significance. Appl Radiat Isot 1998;49(5):447–55.

[24] Wang Z, Deurenberg P, Wang W, Pietrobelli A, Baumgartner RN, Heymsfield SB. Hydration of fat-free body mass: review and critique of a classic body-composition constant. Am J Clin Nutr 1999;69(5):833–41.