European Journal of Clinical Nutrition (1994) 48, 425–432 , n° 6
Received 19 January 1993; accepted 12 January 1993

ISSN 0954-3007

Bioelectrical impedance analysis in small- and appropriate-for-gestational-age newborn infants

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Objective: To determine the reliability of bioelectrical impedance analysis, and to compare and contrast the anthropometric and BIA status of newborns.
Design: BIA and anthropometric parameters were compared in the few days after birth and at about 3 weeks of age.
Setting: At the maternity hospital or in a paediatric care unit.
Subjects: Small- or appropriate-for-gestational-age newborns, with birth weight below or above the 10th percentile of the reference value, respectively. Measurements were performed on 36 and 47 newborns at birth, and for a subgroup (21 and 11) again about 3 weeks later, respectively.
Results: At birth, length^2/resistance was 4.3 ± 0.6 and 6.1 ± 1.2 cm^2/Ω ($P = 10^{-7}$), and at 3 weeks of age length^2/resistance was 5.0 ± 0.6 and 5.7 ± 0.8 cm^2/Ω ($P =$ 0.11), for small- and appropriate-for-gestational-age newborns, respectively. Percentage reliability was 2.2% and 2.6% for intra- and inter-observer measurements of resistance. Importance of a correct placement of the sensor electrode was demonstrated.
Conclusions: Ease of measurement and reliability of BIA in neonates were shown. Evolution of BIA values is in agreement with the known increase in total body water linked to regrowth of cell mass in small-for-gestational-age infants. Additional study is required before BIA should be used in usual clinical setting in newborns due to the lack of prediction equation.
Sponsorship: Languedoc–Roussillon regional research and development program on nutrition.
Descriptors: body composition, growth, infant, newborn, reproducibility of results, small-for-gestational-age

Introduction

Rapid growth occurs during fetal and neonatal development. The duration and quality of intrauterine development affect neonate body composition. Weight is routinely used to assess and monitor the nutritional status of newborns. Any weight loss or gain in hospitalized newborn infants may reflect shifts in water balance rather than changes in body composition, and have strong implications for investigating the nutritional status of newborns. It is, however, difficult to measure the body composition of newborns.

Bioelectrical impedance analysis (BIA) is a relatively new technique for estimating body composition. It is based on the fact that the conduction of an applied electrical signal is far greater in fat-free tissues (because of water and electrolyte content) than in fat. Impedance

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measurements were first suggested by Thomasset (1962). Assessment of fat-free mass from measurement of electrical impedance was introduced by Lukaski *et al.* (1985), based on the original studies of Hoffer, Meador & Simpson (1969) who showed that the resistance of the human body to the conduction of an alternating electrical current is inversely related to the volume of fluid within the body and to the body dimensions. BIA gained wide usage for the estimation of body composition in adults (Lukaski *et al.*, 1986; Kushner & Schoeller, 1986; Van Loan & Mayclin, 1987; Segal *et al.*, 1988) and should be a very suitable method for children because of its non-invasiveness, simplicity and reliability.

Body compartments (lean, fat, water . . .) are altered by many factors such as nutritional status and disease. In children, the additional factor of changes in body composition that take place during growth and development must also be considered. Few studies using BIA have been performed in young children. Fjeld, Freundt-Thurne & Schoeller (1990) and Walker *et al.* (1990) showed the interest of using BIA in well- and malnourished young children. No mathematical equation can be applied to young infants to transform BIA results into body composition variables. Calculation of the lean and fat content from measurement of body weight and BIA implies a constant relation between body water and lean body mass, but present measurements in neonates do not support this assertion. The first step would therefore be to determine whether BIA values reflect predictable and appropriate variations in childrens' total water. Vettorazzi *et al.* (1990) demonstrated that the expected responses to differential changes in body water are clearly detectable and demonstrable in the acute stage of clinical protein-energy malnutrition. Molina *et al.* (1987) reported a relationship between rehydration of diarrhoeal children and a decrease in resistance. To date, few studies in newborn infants have been conducted. Grazioso *et al.* (1990) showed that measurements of BIA indices can be made in low-birth-weight infants with intrauterine growth retardation despite their small body size, and that results are sufficiently reliable for differences between the two groups (chronic and acute intrauterine growth retardation) to be compatible with the distinct biological processes of each *in utero* type of malnutrition. Muthappa *et al.* (1990) showed that height^2/impedance correlated positively with the size of the body fluid compartments, measured with reference methods, and with body fat and lean body mass, thus suggesting that BIA can be useful for the assessment of preterm infant body composition. In a study with low-birth-weight newborns Mayfield, Uauy & Waidelich (1991) concluded that bioelectrical resistance and reactance are good indices of total body water and extracellular water, respectively. The purposes of our study were to determine the reliability of the method, to compare and contrast the anthropometric and BIA status of small- or appropriate-for-gestational-age newborns at birth and at 3 weeks of age. The need for standardization of BIA in young children has been reported previously (Gartner *et al.*, 1992) and is an essential stage before further validations with reference methods.

Subjects and methods

Subjects

BIA and anthropometric measurements were performed at the maternity hospital or in a paediatric care unit on newborns hospitalized at birth. Gestational age was calculated in terms of completed weeks of gestation from the first day of the mother's last menstrual period, and confirmed with early fetal echography. A gestation of less than 37 weeks defined prematurity. The newborns were divided into two groups: small-for-gestational-age (SGA) or appropriate-for-gestational-age (AGA), with birth weight below or above the 10th percentile of the reference value (Leroy & Lefort, 1971), respectively. Measurements were performed on 36 SGA and 47 AGA in the first few days after birth, and for a subgroup (21 SGA and 11 AGA) again about 3 weeks later. BIA, skinfold and circumference measurements were taken by the same person. Measurements were always performed early in the morning on infants lengthened inside the incubator or lengthened on a table with mattress. Although the measurements performed were safe and non-invasive, parent consent was requested.

Anthropometry

Nude weight was reported to the nearest 0.01 kg and crown–heel length was measured in supine position, to the nearest 0.5 cm. Thigh circumference (TC) and mid-upper arm circumference (MUAC) were recorded on the right limb, as the mean of two successive measurements and rounded to the nearest 0.1 cm. Subscapular skinfold (SSF) and triceps skinfold (TSF) measurements were performed with a Harpenden caliper (John Bull, British Indicators, UK). Skinfolds were recorded as the mean of two successive measurements and rounded to the nearest 0.1 mm.

Bioelectrical impedance analysis

BIA measurements [resistance (R) and reactance (Xc)] were recorded using a BIA/101S unit (Akern, Florence, Italy; RJL System licensee) which uses a tetrapolar electrode configuration, applying an imperceptible current of 800 μA at a frequency of 50 kHz at the distal electrodes. Voltage was detected by the proximal electrodes. Measurements were made without concurrent use of a cardiorespiratory monitor. Preliminary assays showed that BIA measurements did not vary with concurrent use of the cardiac monitor as reported recently (Mayfield *et al.*, 1991), but we made the measurements with the cardiac monitor off and the electrodes disconnected in order to avoid current loss. BIA measurements were taken with the subject lying down, legs slightly apart to avoid contact, and arms held away from the body. The disposable adhesive-backed electrodes were placed on the right-hand side of the body, except when catheters were inserted into the dorsal surfaces of the right hand or foot. In this case electrodes were placed on the left side. Mayfield *et al.* (1991) observed no difference when measurements were made on the right or left side in low-birth-weight newborns. We chose to place the signal electrode on the dorsal side of the wrist and the sensor electrode 6 cm along the forearm; the leg signal electrode was placed on the dorsal side of the ankle and the sensor electrode 6 cm away in the pre-tibial region (Gartner *et al.*, 1992). By connecting the analyser clips to the electrodes, electrical current was passed through the whole body. The child was comforted and pacified, if necessary, the arm or leg being held using a cloth to avoid operator's skin contact that led to a reduction in R (data not shown). When a consistent, unvarying reading for R and Xc was registered on the digital meter, it was recorded. R was also expressed in the form $length^2/R$ because that is a function of total body water volume conventionally used to express impedance measurements.

Reliability study

A first test–retest study, with electrodes kept in place, was performed by the same observer on subsamples of 67 newborns (33 SGA and 34 AGA) between 1 and 64 days of age. Replicate measurements of R and Xc were made within a 30-min period, during which subjects were of course depositioned and repositioned. A second test–retest study was performed by the same observer by repositioning the four electrodes between the replicate measurements using the usual 6 cm, and also 5 cm between the electrodes; this distance of 5 cm was used to demonstrate the importance of the position of the sensor electrode. Subsamples of 22 newborns (13 SGA and 9 AGA) between 2 and 54 days of age were assessed in a space of 30 min. R and Xc were recorded as the mean of two successive measurements performed alternatively at each distance (5 or 6 cm). For the evaluation of inter-observer reliability, 15 newborns (7 AGA and 8 SGA) were assessed by both observers on the same occasion. The formula used for estimating technical error of measurement is $\sqrt{\Sigma d^2/2n}$ where d is the difference between two observations, n is the number of pairs of observations, and percentage reliability is the technical error × 100/overall mean of the measurements (Cameron, 1986).

Statistical analysis

All results are expressed as mean ± SD. To compare the mean results in the two groups, statistical analysis was performed using Student's t-test. A value of $P < 0.05$ was considered statistically significant.

Results

The technical error of measurement and percentage reliability were calculated for all reliability studies of BIA (Table 1), even when the sensor electrode was intentionally moved by 1 cm on each limb. In the reliability study with electrodes kept in place, values for R and Xc ranged from 286 to 640 Ω (462 ± 67) and from 12 to 42 Ω (24 ± 6), respectively. Absolute value

Table 1. Reliability tests and comparison of two positions of the sensor electrode

Reliability test	*n*	*Mean difference*[a] ± *SD* *R* (Ω)	*Mean difference*[a] ± *SD* *Xc* (Ω)	*Technical error of measurement*[b] *R* (Ω)	*Technical error of measurement*[b] *Xc* (Ω)	*Percentage reliability*[c] *R* (%)	*Percentage reliability*[c] *Xc* (%)
Duplicate with electrodes kept in place	67	10.8 ± 9.5	1.8 ± 1.6	10.1	1.7	2.2	7.1
Duplicate with repositioning the 4 electrodes (6 cm)	22	13.0 ± 8.4	2.9 ± 2.4	10.9	2.6	2.3	9.1
Duplicate with repositioning the 4 electrodes (5 cm)	22	13.5 ± 9.3	2.8 ± 2.1	11.5	2.4	2.2	7.9
Duplicate with two observers	15	11.8 ± 13.3	2.1 ± 1.5	12.4	1.8	2.6	6.5
Sensor electrode 6 or 5 cm from the signal electrode	22	62.2 ± 14.6	3.2 ± 1.7	45.1	2.5	9.1	8.5

[a] Differences are absolute values.
[b] $\sqrt{\Sigma d^2/2n}$; d = difference between two observations; n = number of pairs of observations.
[c] Technical error of measurement × 100/overall mean of the measurements.
R = resistance; Xc = reactance.

of the difference between replicates ranged from 0 to 49 Ω for R and from 0 to 8 Ω for Xc. In the reliability study with repositioning of the four electrodes (distance of 6 cm), values for R and Xc ranged from 324 to 601 Ω (465 ± 72) and from 16 to 42 Ω (29 ± 6), respectively. Absolute value of the difference between replicates ranged from 1 to 28 Ω for R and from 0 to 10 Ω for Xc. In the reliability study with repositioning of the four electrodes (sensor 5 cm from the fixed signal electrode), values for R and Xc ranged from 379 to 666 Ω (527 ± 84)

Table 2. Anthropometric and BIA measurements (mean ± SD) of small (SGA) or appropriate-for-gestational-age (AGA) newborn infants with birth weight below or above the 10th percentile, respectively

	SGA (n = 36)	*AGA (n = 47)*
Age (days)	3.3 ± 1.7	3.2 ± 1.3[NS]
Gestational age at birth (weeks)	36.2 ± 1.9	37.1 ± 3.0[NS]
Weight (kg)	1.840 ± 0.277	2.833 ± 0.709[c]
Length (cm)	43.4 ± 2.1	47.9 ± 3.5[c]
Arm circumference (cm)	7.8 ± 0.6	9.6 ± 1.2[c]
Thigh circumference (cm)	10.9 ± 1.0	13.6 ± 1.8[c]
Triceps skinfold (mm)	2.6 ± 0.4	3.5 ± 0.7[c]
Subscapular skinfold (mm)	2.9 ± 0.6	4.0 ± 0.9[c]
Resistance (Ω)	439 ± 53	388 ± 69[c]
Length^2/R (cm^2/Ω)	4.3 ± 0.6	6.1 ± 1.2[c]

	SGA Mature (n = 13)	*SGA Premature (n = 23)*	*AGA Mature (n = 28)*	*AGA Premature (n = 19)*
Age (days)	3.3 ± 1.4	3.3 ± 1.9	3.6 ± 1.2	2.4 ± 1.2
Gestational age at birth (weeks)	38.4 ± 1.2	35.0 ± 1.0	39.3 ± 1.2	33.9 ± 1.4
Weight (kg)	2.011 ± 0.287	1.747 ± 0.227	3.320 ± 0.281	2.115 ± 0.391
Length (cm)	44.1 ± 1.6	43.1 ± 2.2	50.3 ± 1.7	44.7 ± 2.5
Length^2/R (cm^2/Ω)	4.5 ± 0.4	4.3 ± 0.6	6.3 ± 1.0	5.9 ± 1.3

[a] $P < 0.05$. [b] $P < 0.01$. [c] $P < 0.001$ versus the SGA group; [NS] non significant.

and from 16 to 46 Ω (31 ± 7), respectively. Absolute value of the difference ranged from 2 to 31 Ω for R and from 1 to 9 Ω for Xc.

The absolute value of the difference between BIA results observed with 6 and 5 cm between the electrodes ranged from 35 to 87 Ω for R and from 0 to 6 Ω for Xc. The mean proportion of this difference, as compared with basic BIA measurement (distance of 6 cm between the electrodes), was 13.3 ± 2.2% and 10.6 ± 5.6% for R and Xc, respectively.

In the inter-observer reliability study, values for R and Xc ranged from 321 to 597 Ω (482 ± 85) and from 15 to 39 Ω (28 ± 7), respectively. Absolute value of the difference ranged from 2 to 56 Ω for R and from 0 to 5 Ω for Xc.

The two groups studied at birth (Table 2) had similar mean age and mean gestational age at birth. There was a significant difference between the two groups as regards all anthropometric parameters reported (Table 2), with higher values in the AGA group.

Values for length^2/R (Table 2) were significantly different between the two groups in the first days of life with lower length^2/R values in SGA newborns. Moreover, value of the index length^2/R was affected by impaired intrauterine growth and was not related to duration of gestation, the values not being different between mature and premature newborns in each of the AGA and SGA group (see repartition in four groups in Table 2).

Whereas anthropometric parameters during the 3 weeks increased concomitantly (Table 3), BIA values showed a different evolution in the 2 groups, BIA values being similar for the two groups at 3 weeks of age.

Discussion

The composition of weight at birth and of weight variations during post-natal growth is of particular interest for investigating the nutritional status of the newborn. In this study we used BIA measurements in parallel to anthropometry in SGA or AGA newborns at birth and at 3 weeks of age, i.e. in situations where body composition changes are of interest.

In the reliability studies, BIA results gave a coverage of the whole range of measurements. Test–retest trials for the single observer in this study showed a good reliability of about 2.2% for the R measurements in the population of newborns studied, as did tests when electrodes were kept in place, when electrodes were repositioned and when two observers were used. Xc measurements in the same cases produced reliability of between 7.1% and 9.1%. Moreover, our results showed the importance of a correct electrode positioning, as an error of 1 cm on the arm and the leg of a newborn leads to an error of about 13% in the basic measurement of R. The correct placement of the sensor electrode represents a high source of error in the BIA method (Gartner *et al.*, 1992).

Length^2/R was significantly different between the groups at birth. The use of the index length^2/R allowed us to show that the

Table 3. Anthropometric and BIA measurements (mean ± SD) of small (SGA) or appropriate-for-gestational-age (AGA) newborn infants with birth weight below or above the 10th percentile, respectively

	Birth		*Age 3 weeks*	
	SGA (n = 21)	*AGA (n = 11)*	*SGA (n = 21)*	*AGA (n = 11)*
Age (days)	3.2 ± 1.7	2.5 ± 1.3^{NS}	18.6 ± 6.5	19.0 ± 7.6^{NS}
Weight (kg)	1.767 ± 0.231	2.183 ± 0.512^a	2.111 ± 0.158	2.497 ± 0.456^b
Length (cm)	43.0 ± 2.0	44.2 ± 2.8^{NS}	45.2 ± 1.4	47.2 ± 1.7^a
Arm circumference (cm)	7.6 ± 0.5	8.7 ± 1.1^b	8.3 ± 0.4	9.0 ± 0.8^a
Thigh circumference (cm)	10.7 ± 0.8	12.4 ± 1.8^b	11.5 ± 0.7	12.5 ± 1.1^a
Triceps skinfold (mm)	2.5 ± 0.4	2.9 ± 0.4^a	3.1 ± 0.5	3.4 ± 0.6^{NS}
Subscapular skinfold (mm)	2.8 ± 0.5	3.2 ± 0.6^{NS}	3.4 ± 0.4	3.7 ± 0.8^{NS}
Resistance (Ω)	444 ± 46	357 ± 85^b	432 ± 51	419 ± 60^{NS}
Length^2/R (cm^2/Ω)	4.2 ± 0.6	5.8 ± 1.5^c	5.0 ± 0.6	5.7 ± 0.8^{NS}

^{a} $P < 0.05$, $^b P < 0.01$, $^c P < 0.001$ versus the SGA group; ^{NS}non significant.

Table 4. Bioelectrical impedance analysis parameters reported in the few studies on newborns or young infants

			R		*Xc*		*Z*		
Group	*Age*	*Electrode placement*	*Mean ± SD*	*Range*	*Mean ± SD*	*Range*	*Mean ± SD*	*Range*	*Reference*
SGA newborns	3 days	6 cm[a]	439 ± 53	360–565	24 ± 6	15–40	439 ± 55		This study
AGA newborns	3 days	6 cm[a]	388 ± 69	236–515	16 ± 7	8–34	365 ± 62		
SGA newborns	19 days	6 cm[a]	432 ± 51	320–548	24 ± 6	13–30	428 ± 61		
AGA newborns	19 days	6 cm[a]	419 ± 60	318–511	21 ± 6	12–28	416 ± 62		
Preterm newborns	9 days	?					556 ± 80		Muthappa *et al.* (1990)
Preterm newborns	<24 h	[b]	778 ± 76	668–1288	40 ± 10				Mayfield *et al.* (1991)
	4–7 days	[b]	957 ± 109		43 ± 5				
SGA term newborns (total)	<24 h	6 cm[a]	448 ± 51	295–630	43 ± 8	22–71			Grazioso *et al.* (1990)
acute IUGR	<24 h	6 cm[a]	494 ± 53	295–630	43				
chronic IUGR	<24 h	6 cm[a]	442 ± 48	295–630	43				
Kwashiorkor	2–6 months	6 cm[a]	388 ± 94		31 ± 6				Vettorazzi *et al.* (1990)
after treatment	2–6 months	6 cm[a]	568 ± 105		36 ± 9				
Marasmus	2–6 months	6 cm[a]	553 ± 3		38 ± 5				
after treatment	2–6 months	6 cm[a]	511 ± 87		39 ± 5				
Mixed form	2–6 months	6 cm[a]	519 ± 120		31 ± 11				
after treatment	2–6 months	6 cm[a]	633 ± 141		42 ± 11				
Dehydrated infants	3–20 months	?	772 ± 159		48 ± 19				Molina *et al.* (1987)
after treatment	3–20 months	?	684 ± 133		37 ± 13				
Well- and malnourished	3–36 months	3 cm[c]					777 ± 74	650–907	Fjeld *et al.* (1990)
(2 groups)	3–36 months	3 cm[c]					831 ± 98	681–981	
Stunted	9–24 months	hand 3 cm[c]	756 ± 92		55 ± 10				Walker *et al.* (1990)
Non-stunted	9–24 months	foot 4 cm[c]	714 ± 76		56 ± 10				
Total sample	9–24 months	foot 4 cm[c]	747						

[a] Signal electrode at wrist or ankle.
[b] Electrode placement as for adult.
[c] Signal electrode at phalanges.
R = resistance; Xc = reactance; SGA = small-for-gestational-age; AGA = appropriate-for-gestational-age; IUGR = intrauterine growth retardation.

difference in R was not due to the difference in length only. There was no influence of prematurity on the difference in BIA parameter values. Although there is so far no nomogramic relationship between BIA indices and body composition in newborn infants, the expected response to change in body water that occurs after birth in healthy newborns is detectable and demonstrable by the decrease in length^2/R in the AGA newborns. The evolution of BIA measurements in SGA newborns was different from that in AGA infants. Our results show a very clear-cut difference of initial BIA values between our SGA and AGA infants, so that it was possible to classify them on the basis of these measurements alone. Intrauterine and postnatal malnutrition are followed by a decrease in tissue mass and intracellular fluid (Friis-Hansen, 1982). Most SGA infants have experienced intrauterine malnutrition and normally exhibit decreased total body water and fat deposition. During the week after delivery, infants may show weight loss due to catabolism (Heimler *et al.*, 1993) or extracellular water contraction (Bauer *et al.*, 1993), depending on gestational age, birth weight and diet. Thereafter weight gain normally occurs at the same rate on an adequate diet. For the next 3 weeks, weight gain in our infants, and fat accretion, as ascertained by skinfolds, follow a parallel evolution in both groups. The differences in BIA parameters disappeared during early postnatal growth even when anthropometric variables remained different: mean BIA values increase in SGA infants, not in AGA infants, and are similar in both groups at 3 weeks. This increase in total body water is in favour of an expansion of the intracellular compartment indicating regrowth of cell mass in SGA infants.

The assessment of newborn body composition is a key component in the monitoring of their development. The potential usefulness of these measurements in newborns is twofold: follow-up of infants affected by impaired intrauterine growth who are at risk of metabolic disorders in the neonatal period, and non-invasive assessment of the adequacy of early postnatal nutritional status in newborns when changes in anthropometric parameters alone may not accurately reflect real growth status. A weight change in infants is difficult to interpret because it represents a change in both the adipose and the lean tissues. Tetrapolar BIA offers great potential for non-invasive assessment of infant body composition because it is safe and easy to use. BIA variables, being dependent upon both electrolyte concentration and fluid volume, give an estimate of body water, an essential component which is subjected to variations during pre- and postnatal evolution. This technique has not been studied systematically in the very young infant, but holds promise for paediatric studies.

Nevertheless, extending the use of BIA still needs a standardization of the technique. Indeed, standard electrode application sites established in adults (RJL manual) are too close together when used on the hand and foot of newborns or young infants. Electrodes proximity could result in measurement error due to electrode interaction. A minimal distance must therefore separate the electrodes. Barillas-Mury *et al.* (1987) showed that after an initial decrease in R values as the inter-electrode separation was increased by moving the signal electrode, a stable plateau in the R values was reached. A distance of 3 cm (Fjeld *et al.*, 1990) or 5.5 cm (Barillas-Mury *et al.*, 1987) has been found to be the minimum required for sufficient separation of the electrodes in young children. In our study we used the same placement as Grazioso *et al.* (1990) in newborns, with electrodes 6 cm apart from signal on wrist and ankle. The few studies in young children or newborns were either not performed with same electrode application sites or with the same distance between them, or this information is not always mentioned. The lack of standardization could explain the differences in values of R, Xc, or impedance (Z) reported (Table 4), and prevents comparison. Hence it is necessary to harmonize the placement of the two pairs of electrodes when BIA studies are performed on normal, sick and malnourished young children in view of obtaining standard values (Gartner *et al.*, 1992) and useful validation studies.

The ability to predict total body water in a wide range of conditions coupled with the ease of measurement, even in neonates as shown in this study, make the BIA technique especially attractive for clinical applications. A relation between length^2/R and the volume of body water in the newborn has been postulated (Muthappa *et al.*, 1990; Mayfield *et al.*, 1991; Kushner *et al.*, 1992). Assuming this relation to be true, BIA measurements provide a useful tool in perinatal body water and nutrition studies. There is still much to be learnt as regards the effect of the influence of the body composition abnormalities in early life on subsequent growth and development. The recent introduction of multifrequency materials being able to differentiate more accurately between intra- and extracellular water compartments may help follow closely the evolution of at-risk infants. A precise standardization should help to define reference values for this age group.

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