Body composition during growth in children: limitations and perspectives of bioelectrical impedance analysis

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There are a number of differences between the body composition of children and adults. Body composition measurements in children are inherently challenging, because of the rapid growth-related changes in height, weight, fat-free mass (FFM) and fat mass (FM), but they are fundamental for the quality of the clinical follow-up. All body composition measurements for clinical use are 'indirect' methods based on assumptions that do not hold true in all situations or subjects. The clinician must primarily rely on two-compartment models (that is, FM and FFM) for routine determination of body composition of children. Bioelectrical impedance analysis (BIA) is promising as a bedside method, because of its low cost and ease of use. This paper gives an overview of the differences in body composition between adults and children in order to understand and appreciate the difference in body composition during growth. It further discusses the use and limitations of BIA/bioelectrical spectroscopy (BIA/BIS) in children. Single-frequency and multi-frequency BIA equations must be refined to better reflect the body composition of children of specific ethnicities and ages but will require development and cross-validation. In conclusion, recent studies suggest that BIA-derived body composition and phase angle measurements are valuable to assess nutritional status and growth in children, and may be useful to determine baseline measurements at hospital admission, and to monitor progress of nutrition treatment or change in nutritional status during hospitalization.

INTRODUCTION

Body composition measurements can be useful to predict clinical outcomes and nutritional status, but it is still an evolving field, particularly in children. Earlier studies have clearly illustrated the shortcomings of using body mass index for these purposes, because body mass index does not distinguish between fat-free mass (FFM) and fat mass (FM).5 and excess FM may conceal FFM deficits. However, body composition has been shown to affect clinical function and outcome. Malnutrition is also associated with more frequent hospitalizations and increased mortality in children with chronic kidney disease.6 In adults, a low FFM was significantly associated with longer length of hospital stay.8 Both depletion of FFM and excess FM negatively affected length of hospital stay.8 In adult cystic fibrosis patients, apparent or hidden loss of FFM, rather than weight loss, was related to the overall disease severity and systemic inflammatory activity.6 Reduced accretion of body cell mass in children with cystic fibrosis predicted a decline in FEV₁, suggesting that body composition changes that are undetectable with weight measurement may be a subtle predictor of declining pulmonary function.7 Loss of body mass index and FFM decreased overall survival in children with cancer.8 Thus, measurement of body composition, including FFM and FM determination, can provide valuable information for patient assessment.

This review highlights the main differences in body composition between adults and children in order to understand and appreciate the difference in body composition during growth. Furthermore, the purpose of the review is to discuss the field of bioelectrical impedance analysis (BIA)/bioelectrical spectroscopy (BIS) including all relevant issues/points specific to BIA in children. A detailed discussion of body composition measurement in general is beyond the scope of this review paper.

MATERIALS AND METHODS

A computer database search was undertaken using Medline and PubMed. We recovered 254 references and reviewed all references with the term 'bioelectrical impedance analysis', with filters for 'human, English and child'. We manually deleted those references that did not pertain to children or pertained to children below 2 years of age (total of 80). We also deleted 52 references that did not apply to healthy children (various diseases).

We included 39 papers that give specific BIA equations in children (Supplementary Material). We included 97 references that pertain to body composition methods in general, differences in body composition between children and adults and publications that evaluated specific BIA equations in children.

Body composition differs fundamentally in children compared with adults

Body composition has been extensively studied in adults. Our understanding of body composition in children is limited by fundamental differences between children and adults. These differences present additional challenges in determining the body compartments of children. It has been shown that the proportion of water and bone mineral content of the FFM changes during...
growth. Fomon et al.\textsuperscript{9} showed that total body water (TBW) decreases from 80.6% of FFM at birth to 75.1% at age 10 years in boys and to 76.9% in girls. Percent of body fat increased in males from 13.7% in infancy to 25.4% at 6 months and then decreased to 13.7% at 10 years.\textsuperscript{9} Similar FFM hydration values were reported by Boileau et al.\textsuperscript{10} (75.1 ± 2.8% (s.d.) for boys and 76.0 ± 3.7% for girls, mean age 10 years) and by Wells et al.\textsuperscript{11} (75.1 ± 2.5% and 75.5 ± 1.8%, for boys and girls, respectively). Percent body fat increased in females from 14.9% in infancy to 26.4% at 6 months and then decreased to 19.4% at 10 years of age.\textsuperscript{9}

Wells et al.\textsuperscript{11} also found that the FFM density value of 1.0864 kg/l is significantly lower compared with the value of 1.1 kg/l for adults.\textsuperscript{12} In addition, children, compared with adults, have a relatively higher amount of extracellular tissue, which has a higher electrolyte content compared with intracellular tissue and consequently a lower resistivity.\textsuperscript{13,14}

Furthermore, racial and ethnic differences also affect body composition results in children.\textsuperscript{15,16} Chinese boys and girls (5–18 years) were found to have higher weight and FM compared with white females and Japanese boys and girls of similar age. Young African American females (age 9–19 years) have higher FFM compared with age- or size-matched white or Hispanic females.\textsuperscript{17} African American prepubertal children (9–12 years) had lower amounts of total body visceral and subcutaneous fat compared with Caucasian prepubertal children\textsuperscript{18} but had a greater percentage of FM as they grew older. These differences would affect the BIA results in children.

Body composition measurements in children

All available body composition methods in children are indirect. A summary of advantages and limitations of most commonly used two- and four-compartment body composition methods is shown in Table 1. The gold standard for body composition is the four-compartment (4-C) model, which uses body weight or mass, total body volume, TBW and bone mineral. However, the 4-C model is generally not available to clinicians, because of the need for specialized equipment and technicians and may expose children to radiation (for example, neutron activation, computerized tomography scan).\textsuperscript{19} Furthermore, all reference methods are based on assumptions that convert raw data into measures of TBW, FFM, BF or % BF, and constants needed for these calculations vary depending on the method, age, gender and health condition of the subjects.\textsuperscript{20}

Thus, the clinician must primarily rely on techniques that are based on the two-compartment model for routine determination of body composition in children, including dual-energy X-ray absorptiometry (DXA), dilution techniques, hydrodensitometry (also known as underwater weighing) and air displacement plethysmography, single- and multi-frequency BIA and BIS.

Bioimpedance techniques are typically developed and validated against DXA, dilution and/or hydrodensitometry techniques, which serve as reference methods for that purpose. However, it is important to understand that these ‘reference’ methods may not themselves provide the most accurate measurements in children because of potential violations of underlying assumptions. Algorithms used in these methods are based on adult proportions and therefore may be less accurate in children. FFM hydration and body density change throughout childhood, and the relative amount of muscle and bone also changes substantially during growth. In children, the FFM contains relatively more water, less protein and mineral than adults.\textsuperscript{10,21} This implies that the body density is lower in children than in adults.\textsuperscript{10,21}

The differences in the body proportion between adults and children violate the underlying assumption of the 2-C model, because there is a gradual change in chemical composition of the FFM as children grow. The 2-C model will lead to significant errors in the estimation of FFM and % body fat,\textsuperscript{22,23} unless age-specific constants are developed for the estimation of FM and FFM during childhood. The use of age- and sex-specific conversion factors is a viable alternative, but its validity rests on the quality and completeness of the original data from which the constants are derived.\textsuperscript{24}

Wells et al.\textsuperscript{11} found deuterium dilution and DXA to produce acceptable 2-C models for children 8–12 years, but bedside techniques (BIA, skinfolds) were not satisfactory. Hydrodensitometry or underwater weighing was found to show systematic errors relative to the 4-C model. Wells et al.\textsuperscript{11} estimated that half of the variability in the water and protein content and ratio of mineral to protein may be due to biological variations. They suggested that the precision of the three- and four-C models is about 0.5 kg of FFM and FM. Both measurement error and choice of values for FFM density substantially influence the relation between fatness by hydrodensitometry and alternative techniques, thereby increasing predictive errors in both groups and individuals. Thus, hydrodensitometry and air displacement plethysmography should be used with caution to validate BIA and other bedside techniques. Although BIA was the technique most susceptible to imprecision when compared with the 4-C model,\textsuperscript{11} it is the most logical bedside method to apply in children owing to its low cost, noninvasiveness, lack of radiation exposure and ease of use and better reproducibility compared with other bedside techniques, such as skinfold measurements.

Bioelectrical impedance analysis/bioelectrical impedance spectroscopy

For a detailed description of the method, please refer to Lukaski et al.,\textsuperscript{25} Kyle et al.\textsuperscript{26,27} or Moon et al.\textsuperscript{28} Using a 2-C model, single-frequency BIA (SF-BIA) measures the impedance (Z) or resistance (R) and reactance (X) to a small electrical current as it travels through the body’s water pool. BIA measures the water content of the body. However, as clinicians are primarily interested in FFM, except for abnormal hydration status when TBW matters, most studies have focused on FFM. The FFM is calculated from the TBW, using the assumption that 73% of the FFM is water in adults. However, the 73.2% reference factor for the water content of FFM results in an overestimation of FFM and underestimation of FM in children who have 75–76% water for the FFM.\textsuperscript{29} Regardless of whether TBW is determined by a reference method such as deuterium depletion and then used to estimate FFM or if FFM is determined by DXA or some other reference method, there always remains the unknown (or imprecise) hydration status that is likely to be responsible for some of the differences encountered in body composition research in children.

Typically, whole-body BIA measures are obtained using standard tetrapolar placement of electrodes (two electrodes on the hand and two on the foot). Newer methods of foot-to-foot BIA offer the advantages of requiring less time but have limitations because they only ‘measure’ the lower body part (legs/lower trunks versus arms and whole trunk). Kriemler et al.\textsuperscript{30} developed BIA algorithms (not shown) using eight-point tactile electrode impedance for FFM and segmental arm and leg lean tissue mass in children 6–13 years and suggested that eight-point BIA is superior to four-electrode BIA. Further validation of this method is necessary.

Single-frequency BIA (SF-BIA) is used for assessing FFM and TBW but is not able to distinguish between the intracellular and extracellular compartments of TBW. BIS or multi-frequency BIA
<table>
<thead>
<tr>
<th>Method</th>
<th>Body compartment measured</th>
<th>Assumptions</th>
<th>Advantages</th>
<th>Causes of error</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-C</td>
<td>Oxygen, carbon, hydrogen, nitrogen, calcium, phosphorus, potassium, sodium, chloride by neutron activation analysis</td>
<td>Steady-state proportions between known and unknown components (oxygen, carbon, calcium, phosphorus and so on)</td>
<td>Considered gold standard, reduces errors</td>
<td>Multiple methods perpetuate errors</td>
<td>Radiation exposure with neutron activation analysis; limited equipment availability worldwide; technical requirements; high cost; research purposes only</td>
</tr>
<tr>
<td>4-C</td>
<td>Total body volume from ADP or HD, TBW from dilution method, BMC from DXA</td>
<td>Constant tissue hydration and body density</td>
<td>Reliance on constants for proportions and densities is eliminated</td>
<td>Biological variability in density and FFM hydration with growth; multiple methods perpetuate errors</td>
<td>Limited availability of equipment, not feasible for clinical routine; high cost</td>
</tr>
<tr>
<td>MRI</td>
<td>Organ, muscle, visceral and subcutaneous volume and density</td>
<td>Assumptions about tissue hydration</td>
<td>Distinguish tissue type with « chemical shift » imaging techniques</td>
<td>Patient positioning; movement; slice selection and image interpretation</td>
<td>Equipment mostly used for medical diagnosis; mostly for research use; cost; accessibility to researchers and clinicians; lack of providing relevant information to clinicians (e.g., percentiles or diagnosis of sarcopenia); current development for routine use</td>
</tr>
<tr>
<td>CT</td>
<td>Organ, muscle, visceral and subcutaneous volume and density</td>
<td>Assumptions about tissue hydration</td>
<td>Distinguishes tissue type (lipid content in muscle)</td>
<td>Patient positioning; slice selection and image interpretation</td>
<td>Equipment mostly used for medical diagnosis; exposure to radiation; accessibility to researchers and clinicians; lack of providing relevant information to clinicians (e.g., percentiles or diagnosis of sarcopenia); current development for routine use</td>
</tr>
<tr>
<td>DXA</td>
<td>Bone mineral density, FFM, FM</td>
<td>Hydration 73.2% of FFM; fat content of analyzed (non-bone-containing) area is comparable to unanalyzed (bone-containing) area</td>
<td>Whole-body and regional estimates of FFM, FM and bone; wide availability of equipment; ease of use; little cooperation from subject</td>
<td>Differences between instruments of different manufacturers; for children need correction factor by Pintauro et al.</td>
<td>Equipment mostly used for medical diagnosis; equipment mostly used for medical diagnosis; exposure to radiation; accessibility to researchers and clinicians; lack of providing relevant information to clinicians (e.g., percentiles or diagnosis of sarcopenia); current development for routine use</td>
</tr>
<tr>
<td>Dilution (TBW)</td>
<td>Total body water</td>
<td>Constant hydration</td>
<td>Acceptable for all ages, easy to administer isotopes</td>
<td>Precision, isotope equilibration within the body, corrections for exchange of label with nonaqueous hydrogen or oxygen, and estimation of the hydration of FFM.</td>
<td>Exposure to small amount of radiation; lack of agreement between software versions and manufacturers; underestimates FM in leaner subjects and overestimates in heavier subjects; impractical for large-scale studies and very small children or routine use; high cost</td>
</tr>
<tr>
<td>TBK</td>
<td>Total body potassium</td>
<td>Constant TBK/FFM</td>
<td>Noninvasive, high accuracy to determine body cell mass</td>
<td>TBK not constant during growth</td>
<td>Limited availability of equipment</td>
</tr>
<tr>
<td>HD</td>
<td>Body density</td>
<td>Constant density</td>
<td>Noninvasive</td>
<td>Biological variability in density and FFM hydration with growth</td>
<td>Measurement difficult in young children due to need to submerge head while exhaling; unable to use in sick children; child needs to stay still; instrument less readily available because of cost of instrument; reduced accuracy if used in disease states</td>
</tr>
<tr>
<td>ADP</td>
<td>Body volume by air displacement, body density</td>
<td>Constant density</td>
<td>Ease of use; noninvasive; does not require water displacement; does not expose to radiation</td>
<td>Biological variability in density and FFM hydration with growth; temperature, pressure and relative humidity; clothing can affect the measurement</td>
<td>Limited availability of equipment</td>
</tr>
</tbody>
</table>

Abbreviations: ADP, air displacement plethysmography; BMC, bone mineral content; CT, computer tomography; DXA, dual-energy X-ray absorptiometry; FM, fat mass; FFM, fat-free mass; HD, hydrodensitometry or underwater weighing; MRI, magnetic resonance imaging; multi-C, multi-compartment; TBK, total body potassium; TBW, total body water; 4-C, 4-compartment model. *Pintauro et al.*: \[ FM = (0.78 \times \text{DXA lean}) + (0.16 \times \text{body weight}) + 0.34 \]
Table 2. Bioelectrical impedance analysis in children: specific considerations

| Validation against reference method (multi-compartment, DXA, densitometry, dilution method) is essential in children and must be age- and gender specific |
| Age and gender adjustment of hydration fraction in reference method and BIA equation |
| Racial/ethnic differences |
| Standardization of measurement conditions |
| Fasting 2–3 h |
| Voiding before measurement |
| Physical exercise restriction |
| Abduction of arm ≈30° from trunk and legs separated by 45°; position consistent |
| Electrodes > 4 cm² and well preserved |
| Standardized time subject is in supine position |
| Hand-and-foot or foot-to-foot, follow written manufacturers protocol |
| Clean skin with alcohol; no skin lesions or significant edema at the site of electrodes |
| BIA analyzer—monthly calibration; cross-calibration between instruments by different manufacturers |

Abbreviations: BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry.

(MF-BIA) offer the advantage of differentiating between the intracellular and extracellular compartments. Previous studies have shown that % body fat by BIS was correlated with the 4-C model in adults. It is not known or unclear at this time how the resistivity constants used in BIS modeling equations derived from the Hanai mixture theory change across the neonatal period and throughout growth, as well as in pathological states. The most widely utilized and studied BIA method in children is SF-BIA, because BIS and MF-BIA devices have been less commercially available until recently.

There are several potential technical sources of error in BIA measurements that could account for discrepancies in findings between studies, including protocol variations, interdevice variability and electrode sizing and positioning. Calibrations and cross-validations are needed if different analyzers are used in the same study and when measuring the same patients longitudinally, as the technical characteristics are different among manufacturers. Warner et al. found significantly lower impedance readings with a Holtain analyzer (Holtain Ltd, Crosswell, Crymych, Pembs., Wales, UK; 488 ± 65 ohm) than with an RJL instrument (RJL Systems Inc., Clinton Twp, MI; 586 ± 84 ohm) in children, with greater differences noted between the two analyzers at higher impedance values. Kyle et al. found nonsignificant differences between RJL and Xitron instruments. Guidelines for BIA measurements are shown in Table 2.

BIA in children

The validation process of SF-BIA equations is more difficult in children than in adults, because the hydration fraction changes throughout childhood. Changes in the relative length of limbs and trunk during growth may influence the relation between TBW and FFM and height²/R or Z. Furthermore, variations in the relative body geometry between ethnic groups confound the relative distribution between weight and resistance/impedance among limb and trunk in the BIA model. In adults, the trunk accounts for 75% of the body mass but only about 9% of the total impedance. On the other hand, the upper and lower limbs contain 25% of the body mass but are responsible for 91% of the total Z. A higher relative leg/arm length will have higher R/Z and thus will yield a lower R/height² index at a given FFM and an underestimation of TBW and FFM. SF-BIA equations must, therefore, reflect the changes relating to lean mass ratio to Ht²/R in the slope and intercept that occur with age between younger and older children.

The SF-BIA equations reported in the literature in children are shown in Supplementary Material, with specific references, comments and ratings: Supplementary Table S1—TBW; Supplementary Table S2—FFM. An equation to estimate % FM was developed by Lohman et al. in native American children.

A number of studies have evaluated BIA equations from the literature in various pediatric populations. Wells et al. found that there were large bias and limits of agreement for FFM and % body fat in children aged 8–12 years by BIA equations previously published compared with the 4-C model. Loveday et al. tested other equations in Down’s syndrome children and found that the Schaefer equation was the most accurate equation to predict % BF compared with the 4-C model and DXA. They found that BIA underestimated the % body fat in girls compared with DXA. Houtkooper et al. found that, compared with the multi-compartment model, the best-fitting equations included anthropometric (chest circumference, abdomen circumference) and skinfold measurement. Furthermore, the prediction of % BF from height²/R and weight was lower than the prediction of FFM. Houtkooper et al. also found that the adult equations by Lukasi et al. had good agreement with a multi-compartment model in boys and girls aged 10–14 years.

Trell et al. found that, compared with DXA, foot-to-foot BIA correlated better than anthropometric indices in the estimation of FFM in children 4.9–10.9 years, but limits of agreement were large for % body fat (–4.29 to 9.36%). Palchetti et al. found that the equation of Houtkooper yielded strong sensitivity and specificity for total BF compared with DXA in HIV (human immunodeficiency virus)-infected children (9.8 ± 1.2 years). Kehoe et al. found that, compared with DXA, there were wide limits of agreement when the manufacturer’s equation from the Bodystat SF-BIA device was used in Indian children aged 6–9 years.

Reilly et al. found that a BIA equation (using a Holtain SF-BIA analyzer) by Houtkooper predicted FFM with negligible bias and had narrower limits of agreement relative to hydrodensitometry (underwater weighing), using the model described by Weststrate and Deurenberg than prediction equations by others in 98 Caucasian children with a mean age of 8.9 ± 1.6 years. They suggested that ‘chemical immaturity’ of children presents a problem because FFM does not have a constant composition in childhood but shows systematic variations during development and results in interindividual variability in FFM composition in children of similar age. Eisenkolbl et al. found that the equation by Kushner et al. underestimated % BF by 10.6% in a sample of obese children with higher underestimation in boys than girls; and they suggested that this was due to false assumptions of the hydration fraction of the FFM in children and obese. Bandini et al. found that the Kushner equations accurately estimated FFM in Tanner Stage 1 girls, and the Kushner equation with height²/R only and height²/R plus weight as well as the Houtkooper equation accurately predicted the FFM in Tanner stage 2 and 3 girls compared with the dilution method.

Cleary et al. found that the Schaefer equation was most valid in 5–9-year-old overweight and obese white children,
whereas three other equations,\textsuperscript{13,50,62} showed large differences possibly due to the exclusion of age as a variable. Warner \textit{et al.}\textsuperscript{33} found that SF-BIA TBW equations by RUL analyzer significantly underestimated the measured values compared with the dilution method in children treated for acute lymphoblastic leukemia but not by Holtain analyzer. Bell \textit{et al.}\textsuperscript{53} found that the Fjeld equation\textsuperscript{64} for TBW by the dilution method gave the least bias in cerebral palsy children with bilateral and unilateral impairment using a SF-device. Bodystat (Isle of Man, UK) \textit{et al.}\textsuperscript{99} found a nonsignificant difference between TBW estimated by the Kushner \textit{et al.}\textsuperscript{60} equation compared with the dilution method in children aged 4–6 years ($R^2 = 0.88$, SEE 0.63 kg). Large differences for TBW, extracellular and intracellular compartments were noted between BIS (Xitron 4000B) and DXA for children, which might be improved with age- and sex-specific calibration constants.\textsuperscript{56}

Proprietary equations/algorithms

Many devices have BIA equations developed by manufacturers for their specific instrument that remain unpublished and undisclosed by the company and are programmed into their software that is considered by the manufacturer to be proprietary (i.e., the equations are not provided in the written materials accompanying the device), and thus it is not known how FFM or FM is derived from the raw measurement of BIA. Proprietary equations have an important disadvantage to the clinician. They are population specific, having been previously developed based on reference data in a particular population (for example, adults), and thus are often maladapted to specific subjects being studied, leading to significant error. Large limits of agreement were found by an RUL 101 SF-BIA.\textsuperscript{57} BIA overestimated BF in lean and underestimated BF in overweight subjects.\textsuperscript{67} RUL-103 performed adequately for %BF compared with hydrodensitometry in Afro-Jamaican 8–18 years of subjects\textsuperscript{68} and for FFM in 8–20-year-old Caucasian children and adolescents.\textsuperscript{56} MF-BIA by Bodystat 1500, compared with the deuterium dilution method, in children 6–17 years overestimated FFM, and TBW underestimated FM in obese Brazilian adolescents.\textsuperscript{70} Tanita-300A-derived prediction equations are for subjects from 7 to 99 years with option for standard or athletic subjects.\textsuperscript{71} Previous validation of foot-to-foot BIA (Tanita TBF-300) underestimated lean mass and overestimated BF in overweight children compared with DXA.\textsuperscript{46,72,73} and overestimated FFM and underestimated %BF in children 4–9 years.\textsuperscript{73} Tanita BC-418 underestimated FFM compared with the dilution method in healthy Gambian children aged 5–16 years.\textsuperscript{74} Proprietary equations (MF-BIA Human-IM Scan, Dietsysystem, Milan, Italy) overestimated %BF in 11–15-year-old Indonesian girls.\textsuperscript{75} There were no differences between %BF by Stayhealthy handheld BCI BIA analyzer (Stayhealthy Inc., Monrovia, CA, USA) and DXA and hydrostatic weighing in children 10–17 years.\textsuperscript{76}

Many of the equations do not apply age- and gender-specific hydration factors. Hydration factors should be age- and sex specific in children. Segmental BIA, suggested by some authors,\textsuperscript{36,77–79} has been shown to complicate the method, and the sum of the errors of the segments tends to yield greater differences between whole-body BIA and reference methods.

Talma \textit{et al.}\textsuperscript{20} found good reliability of BIA in children. However, the test–retest mean differences for %BF were rather large and suggested that BIA is susceptible to measurements errors. Talma \textit{et al.}\textsuperscript{20} also stated that important details about test–retest procedures were lacking in most studies, leading to lower methodological quality. They noted that the responsiveness of BIA is unknown, and they do not recommend the use of BIA to follow within-person changes in FFM and FM in children.

In summary, despite some discrepancies, these studies suggest that the BIA and BIS method may be used to determine FFM and BF in children, but the BIA/BIS method must be cross-validated against a reference method in order to determine the most suitable equations for children at different ages. Furthermore, BIA equations to estimate FFM, TBW or FM in children must take the child's age and gender into consideration either by adding an age- and gender factor or by using separate equations for infants and children of pre- or post-pubertal age. Electrode position is a further consideration in small children. Written methodologies are needed when measuring children, especially infants, to avoid differences in results because of changes in position of the electrodes. It is important that the anatomic position remains the same for longitudinal measurements. Ethnic differences may also require specific factors or separate equations. When validating BIA equations, the changes in hydration ratio that occur throughout childhood must also be accounted for.

'Raw' BIA parameters

More recently, in order to avoid problems of disturbances in fluid distribution in subjects with abnormal hydration, several studies\textsuperscript{80,81} suggested the use of raw BIA measurements such as $R$, $X_c$ and PhA. The $R$ and $X_c$ components at 50 kHz can be used directly in a $R_X$ vector BIA graph. The body composition is then evaluated through patterns of vector distribution with respect to the reference population.\textsuperscript{82} This method may be useful in determining before and after hydration changes in hemodialysis patients.\textsuperscript{83} Although vector analysis does not provide quantitative estimations of body fluid volumes, it does allow for the discrimination of differing fluid volumes (over and underhydration) and between obese and edematous subjects in adults.\textsuperscript{84}

Phase angle (PhA) is not a measurement of body composition. However, PhA has been shown in adults to be predictive of prognosis and mortality in hemodialysis,\textsuperscript{85} cancer,\textsuperscript{86} human immunodeficiency virus syndrome,\textsuperscript{87} liver disease\textsuperscript{88} and geriatric subjects.\textsuperscript{89} It can be calculated directly from $R$ and $X_c$ as the arc-tangent ($X_c/R \times 180^\circ$/m). The PhA represents, on one hand, the capacitance behavior of tissues ($X_c$) and is associated with cellularity, cell size and integrity of the cell membrane and on the other hand the pure resistive behavior ($R$) of tissues, which is dependent on lean tissue mass and tissue hydration.\textsuperscript{80,81} Thus, PhA is associated with cell mass, nutritional risk and general health\textsuperscript{90} in both adults and children.\textsuperscript{81}

Clinical implications of body composition measurements

Few studies have reported clinical outcomes as they relate to body composition in children, in part, because body composition methods have only recently been available for clinical studies. Shime \textit{et al.}\textsuperscript{91} found that the relative changes in BIA reflecting postoperative alterations in body composition provided a quantitative estimation of critical illness in pediatric patients after heart surgery. Azevedo \textit{et al.}\textsuperscript{92} found an association between low values of $X_c$/height and $R$/height on admission with multiple organ failure greater than four organs. Both $R$/height and $X_c$/height increased between admission and discharge in survivors, whereas among nonsurvivors there was a trend toward a decrease between admission and last measurement before death. Farias \textit{et al.}\textsuperscript{93} found that children and adolescents who developed chronic graft-versus-host disease after hematopoietic stem cell transplantation had lower levels of standardized (for age and sex) PhA compared with patients who did not lose weight.

These studies suggest that body composition measurement and BIA-derived PhA are valuable and should be used to assess nutritional status and growth in children, as well as to determine baseline measurements at hospital admission and to monitor progress of nutrition treatment or change in nutritional status during hospitalization.
Future directions
It is difficult to incorporate growth velocity changes into BIA equations for application to growing children. We believe it is important to focus further research on this issue. Use of BIA prediction equations is inherently limited by potential violations of underlying theory to the BIA method; their use in children in particular requires age- and ethnicity-specific modifications. Further research should thus be directed toward further refinement of appropriate electrode positioning in children. There are many in the body composition field who believe that the best direction for future applications of bioelectrical impedance is the BIS approach given recent developments in adults, particularly in individuals on dialysis. Wide limits of agreement have, however, been reported for BIS in nearly all validation studies. Therefore, the method, including the use of constants in the BIS equations, needs further refinement for adults, and there has been little work conducted in children to tailor the methods to their physiologic characteristics.

CONCLUSIONS
Body composition measurements are important for assessing nutritional status and monitoring clinical outcomes both in children and adults. Rapid change in height, weight, FFM, and FM during growth requires tailoring of methods to children. The best candidate method for bedside assessment is bioimpedance. Although the SF-BIA method has limitations, the use of raw BIA parameters has recently gained some interest. The use of BIS for fluid management in adults holds promise, if it can be refined for application in children. Further development of body composition methods is vital in children, and bioimpedance remains promising as a simple and easy to use bedside method.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS
UGK conceived and carried out the review of literature and drafted the manuscript. JAC-B, CPE and CP participated in the drafting of the manuscript. All authors read and approved the final manuscript.

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