Bioelectrical Impedance Methods in Clinical Research: A Follow-Up to the NIH Technology Assessment Conference

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ABSTRACT

In 1994, the National Institutes of Health (NIH) convened a Technology Assessment Conference “to provide physicians with a responsible assessment of bioelectrical impedance analysis (BIA) technology for body composition measurement.” In 1997, Serono Symposia USA, Inc., organized an invited panel of scientists and clinicians, with extensive research and clinical experience with BIA, to provide an update. Panel members presented reviews based on their own work and published studies for the intervening years. Updates were provided on the single and multifrequency BIA methods and models; continued clinical research experiences; efforts toward establishing population reference norms; and the feasibility of establishing guidelines for potential diagnostic use of BIA in a clinical setting. This report provides a summary of the panel’s findings including a consensus on several technical and clinical issues related to the research use of BIA, and those areas that are still in need of additional study. Nutrition 1999;15:874–880. ©Elsevier Science Inc. 1999

Key words: bioelectrical impedance, total body water, extracellular water, intracellular water, aging, growth

INTRODUCTION

Bioelectrical impedance analysis (BIA) measures the opposition of body cells and tissues to the flow of a radiofrequency alternating electric current. The voltage drop between electrodes provides a measure of impedance, which is low in lean tissue and high in fat tissue and bone. Impedance is the vector sum of the resistance or conductive characteristics of body tissues and the reactance or additional opposition due to the capacitance of cell membranes, tissue interfaces, and non-ionic substances. Many studies have applied the basic technique of BIA to estimate body composition in various clinical and research settings.

In December 1994, the National Institutes of Health (NIH) convened a technology assessment conference to evaluate the validity and interpretation of data derived by single frequency BIA for the estimation of body composition, noting the need for a consensus among experts on the appropriate conditions of use and
appropriate applications of BIA.$^4$ A summary of the NIH findings for the single frequency BIA technology were published$^{2,3}$ and a complete text of the draft conference statement is available on the Internet as well.\textsuperscript{4}

In October 1997, Serono Symposia USA, Inc., organized a 1-d conference (Bioelectrical Impedance Methods in Clinical Research) and invited eight research scientists and clinicians, with extensive BIA experience, to examine the progress made on single frequency BIA issues raised 3 y earlier at the NIH conference. In part, this meeting met the NIH's suggestion for periodic reviews of BIA technology and its use. In addition, the participants reviewed recent technologic advances in the field and how these have and will continue to affect the use of BIA in clinical research. A summary of these findings, presented in response to the questions raised at the NIH conference, are presented in Table I (see refs. 5–7). In addition, new issues related to BIA measurements, both for the individual and for population studies, that have arisen since 1994 are included in Table I (see refs. 5–7).

**CURRENT METHODS AND MODELS**

In 1994, BIA measurements at a single-frequency (typically, 50 kHz) were the "industry standard" and this approach continues to be the most frequently used, despite a number of shortcomings noted over the last 3 y. At the NIH technology conference, it was concluded that resistance, adjusted for height, measured at a single-frequency, was related to total body water (TBW) volume. Unfortunately, a number of biophysical assumptions are needed to translate the resistance value to TBW. Among these are: the human body can be represented as a single uniformly shaped cylinder; that the intracellular/extracellular water ratio remains constant (thus providing uniform conductance); that hydration of body tissues remains constant; that a 30 kHz frequency will penetrate all cells equally; and that impedance equals resistance (i.e., reactance, which is very small in magnitude relative to resistance, can be ignored). None of these assumptions is entirely valid and may be significantly altered in the clinical state, which can account for the variable results often obtained when the single frequency BIA method is used.\textsuperscript{8,9} These problems led the NIH panel to conclude that BIA was not yet useful for clinical studies of body composition, especially if the patient was suspected of having an altered body water distribution.

However, since 1994 two notable advances in BIA technology and modeling have been made which appear to have increased the utility of this technique for clinical research. Both advances focus on the need to differentiate between TBW and its extracellular water (ECW) and intracellular water (ICW) subcompartments. In one case, it has involved the replacement of the original series resistance model with a parallel resistance model. Preliminary applications of this model appear promising and may provide more acceptable estimates of fat-free mass (FFM) and body cell mass (BCM) in different clinical populations than with the older series model.\textsuperscript{10,11} The parallel model is more consistent with human physiology (i.e., the ECW is an independent resistive component in parallel with the ICW compartment which also has a capacitance property). With the parallel model, estimates of TBW and ICW are obtained from the body impedance measurement.\textsuperscript{10,12}

A second, highly significant refinement of the BIA technology involves the advancement of multifrequency measurement, which theoretically may provide the estimates of ECW, ICW, and TBW.\textsuperscript{13,14,15} At the 1994 NIH conference, it was noted that preliminary research in this direction was being performed, but that it was too preliminary to confirm that altered ECW/ICW ratios could be accurately detected. At that time, measurements were mainly being performed at two (high and low) fixed frequencies and, therefore, were not truly multifrequency. The theory is that at a low frequency, current flows primarily around cells (i.e., through extracellular fluids) and encounters few if any capacitance effects, while at a high frequency, the applied current uniformly penetrates all lean tissues. However, using only two fixed frequencies may provide an incomplete picture of the underlying physiologic response and can result in an erroneous estimate of fluid volume and distribution.\textsuperscript{16} In addition, there is the problem of deciding what is the correct pair of frequencies to use that would work accurately for all cases.

Various anthropometric measurements (e.g., height, weight, body mass indices, circumferences, sex, age, race, etc.) are often used in many of the BIA prediction equations. These parameters are included to reduce the effects of interindividual variance in resistance and impedance values, presumably related to differences in body size and shape. These parameters are included solely to increase the prediction accuracy of body composition estimates.\textsuperscript{17} These equations, however, describe the statistical relationships for a particular calibration population and, hence, the results for the prediction equations are often population-specific. That is, most published equations that incorporate these descriptive anthropometric parameters into the single-frequency, series-resistance prediction model, have been less than ideal for the purpose of estimating body composition in other populations. It remains uncertain if this limitation can be removed when the parallel, single-frequency model is used. It is clear, however, that improved prediction equations that will reduce individual errors are needed for patients in various disease states (e.g., acute, chronic, and critical illness), especially those with altered fluid status. Cross-validation of prediction equations remains a problem in that their accuracy must be clearly demonstrated in a population other than that from which the equation was derived.

Whether additional advances can be made with single frequency (50 kHz) BIA measurements that will have a significant impact on routine clinical use appears less likely than that for multifrequency BIA measurements. A summary of the comparison between methods is provided in Table II (see refs. 18 and 19). Each of the available models/methods used in estimating body composition from single frequency to multifrequency are presented, along with their limitations and some of the potential clinical applications.\textsuperscript{20} Unfortunately, dozens of bioimpedance machines are commercially available, each using different (and often, proprietary) prediction equations for converting the impedance, resistance, or reactance data to estimates of body composition.\textsuperscript{21}

Our basic understanding of the physiologic model that best describes the body's bioelectrical impedance response has not advanced significantly since 1994, and remains relatively unknown.\textsuperscript{9} Recent publications have examined the mathematical relations that result for various models (series versus parallel and multifrequency).\textsuperscript{22,23} One research group has illustrated the limitations associated with the mixture theory model,\textsuperscript{24} while others have explored the development of several electric circuit models.\textsuperscript{25} The BIA approach measures the general electric properties of the whole body. However, several sources of variance (e.g., blood viscosity, skin temperature, electrode placement, hydration status, recent meal, exercise, posture, etc.) still have not been adequately identified, characterized, or quantitated in relation to whole-body impedance measurements.\textsuperscript{26} From in vitro studies, it is also known that variations in blood viscosity, albumin concentration, and hematocrit (serum biomarkers associated with various clinical disorders) may affect the total body impedance values. Future clinical applications, as well as applied research studies, should include comparison of variations in BIA measurements with biochemical parameters.

A continuing concern with the BIA measurement is the impact of body geometry. Over the last 3 y, this issue has not been addressed. However, it is well established that the shape and size
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<tr>
<td>What does BIA measure in terms of electric and biological parameters?</td>
<td>No unique physiologic data provided. Statistical rather than biophysical</td>
<td>No additional studies in this important area</td>
<td>Need data on biochemical and hematologic effects (e.g., albumin, hematocrit, viscosity, etc.)</td>
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<td>principles apply</td>
<td>No change—statistical models still used</td>
<td>Need data on correlation between BIA measurements and biochemical markers of health or disease</td>
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<td>How safe is BIA?</td>
<td>Safety concerns related to implanted defibrillators</td>
<td>No additional data has been used in pregnancy (see Ref. 5)</td>
<td>Unlikely additional data will be found unless a significant incident occurs.</td>
</tr>
<tr>
<td>How should BIA be performed, and/or how can BIA measurements be standardized?</td>
<td>Standard methods and calibration needed</td>
<td>No standardization continues to be a problem</td>
<td>Distal electrode placement has become the ‘standard.’ Proximal placement may offer small advantages in reproducibility (see Ref. 6)</td>
</tr>
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<td>Data on primary resistance and reactance values and frequency(s) needed in</td>
<td>These data are still not provided. Improved reports per instrument are still needed</td>
<td>Serial single-frequency measurements require normal fluid distribution</td>
</tr>
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<td></td>
<td>printed reports</td>
<td></td>
<td>Segmental measurement useful in some altered fluid distribution, specific clinical settings (e.g., burns, paralysis, ascites), and regional body composition estimates (see Ref. 7).</td>
</tr>
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<td>Measurements affected by body position, hydration, status, consumption of food</td>
<td>Additional data now confirms these concerns (see Refs. 22–25)</td>
<td>Dew (high-low) frequency not as accurate as multifrequency</td>
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<td></td>
<td>and beverages, ambient air and skin temperature, recent physical activity, and</td>
<td>Multifrequency Cole-Cole models are more useful in altered fluid distribution</td>
<td>No clear benefits demonstrated to date for use of Hanai mixture models</td>
</tr>
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<td></td>
<td>conductance of the examining table</td>
<td>Parallel single-frequency BIA appears useful for BCM monitoring only</td>
<td>No comparisons reported between parallel model and multifrequency model for BCM estimates</td>
</tr>
<tr>
<td>How valid is the BIA technology in the estimation of total body water, fat-free</td>
<td>Fat mass estimates vary, highly instrument dependent</td>
<td>BIA does not measure fat mass, hence it has limited use</td>
<td>Additional validation studies need to identify sex-specific, age-specific (at age extremes, preadolescent and adults over 65 y), and race-specific differences exist.</td>
</tr>
<tr>
<td>mass, and/or adiposity?</td>
<td>Fat-free mass estimates vary</td>
<td>Fat-free mass estimates appear acceptable only when fluid status is normal</td>
<td>Additional validation studies needed for use in populations with altered fluid status—may indicate that disease-specific calibrations are needed.</td>
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<td>TBW estimates reliable under most conditions</td>
<td>BCM estimates appear acceptable only for the parallel model</td>
<td>Correlation analysis limited by colinearity among ECW, ICW, and TBW; by precision of “gold standard” techniques (e.g., D₂O, NaD₂O, DXA, anthropometry, etc.) Multiple datasets need to be combined to establish more general prediction equations and to minimize the population-specific aspects of equations developed for smaller population groups.</td>
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<td></td>
<td>Need population-specific equations and data for the standard errors of the</td>
<td>TBW estimates with BIA validated in healthy and some clinical populations</td>
<td>Usefulness in monitoring to treatment in some clinical population studies</td>
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<td></td>
<td>estimate</td>
<td>Limited studies (unpublished data) for selected populations have been completed</td>
<td>Use useful for monitoring clinical setting, i.e., individual patients, is limited by lack of reference norms.</td>
</tr>
<tr>
<td>What are the appropriate clinical uses of BIA technology, and what are the</td>
<td>Useful in healthy adult populations and in some patient studies with chronic</td>
<td>Has been shown to be useful in population studies to monitor effects of disease and/or treatment on body composition</td>
<td>More information is needed related to changes in hydration of FFM during growth and aging.</td>
</tr>
<tr>
<td>limitations?</td>
<td>conditions without major disturbances of water distribution</td>
<td>Has potential prognostic value in patients with renal disease</td>
<td>Monitoring of acute disturbance of body fluid distribution limited, in part, by accuracy of available ‘reference’ methods such as isotope dilution</td>
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<td>May be useful in assessing TBW in the dialysis patient</td>
<td>May be useful for monitoring BCM in AIDS patients</td>
<td>Need to examine more fully the clinical utility of (1) phase angle, (2) the ECW(ICW or ECW/BCM) ratios, and (3) resistance values directly. Need verification in various clinical conditions for multifrequency BIA, especially those with altered water distributions. Single-frequency BIA should be limited to studies in healthy subjects or for diseases in which ECW/ICW ratio is not abnormal. Single-frequency, series model BIA should be discontinued.</td>
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<td>No established role in the critical care setting</td>
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<td>What are the future directions for basic science, clinical research, and</td>
<td>What does BIA measure? Basic science of impedance measurements</td>
<td>Basically, remains a “black box.” Need to continue to explore new ways of expressing results to improve clinical utility</td>
<td></td>
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<tr>
<td>epidemiologic evaluation of body composition measurements?</td>
<td>Determinations of intracellular and extracellular water</td>
<td>Clear improvements made with use of multifrequency instruments</td>
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<td></td>
<td>Correlations with clinical outcome in specific patient populations</td>
<td>To date, limited to data for renal and AIDS patients</td>
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<td>Longitudinal clinical follow-up of the NHANES III subjects</td>
<td>Need follow-up of patient populations. Also newer NHANES IV data may help to better define population reference norms</td>
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BCM, body cell mass; BIA, bioelectric impedance analysis; DXA, dual-energy x-ray absorptiometry; ECW, extracellular water; ICW, intracellular water; TBW, total body water.
<table>
<thead>
<tr>
<th>Method/Model</th>
<th>Frequency(s)</th>
<th>Theory</th>
<th>Clinical uses and limitations</th>
</tr>
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<tbody>
<tr>
<td>Series</td>
<td>50 kHz</td>
<td>Body represents resistors in series (only one conducting path)</td>
<td>Not useful in estimating body composition (single measurement)</td>
</tr>
<tr>
<td>Parallel</td>
<td>50 kHz</td>
<td>Body represents resistors in parallel</td>
<td>Not useful in estimating ICW</td>
</tr>
<tr>
<td>High-low (dual frequency)</td>
<td>5 kHz, 500 kHz</td>
<td>Low-frequency current remains completely extracellular</td>
<td>Useful in estimating BCM (population studies only)</td>
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<td></td>
<td></td>
<td>High-frequency current penetrates all tissues, membranes, interfaces, etc. completely</td>
<td>Useful in estimating BCW and TBW (population studies only)</td>
</tr>
<tr>
<td>Cole-Cole (see ref. 18)</td>
<td>Multiple</td>
<td>Plot of reactance versus resistance to identify theoretical values of R&lt;sub&gt;C&lt;/sub&gt; and R&lt;sub&gt;o&lt;/sub&gt; at zero and infinite frequency.</td>
<td>Fixed frequencies limit model for use in all diseases</td>
</tr>
<tr>
<td>Hazai Mixture Model (see ref. 19)</td>
<td>Multiple</td>
<td>Tissue resistivity and body geometry alter relationships in the basic Cole-Cole model water volumes</td>
<td>Useful in estimating ECW, ICW, and TBW Phase angle spectrum has been useful in selected diseases (population studies only)</td>
</tr>
<tr>
<td>Segmental</td>
<td>Single or multiple</td>
<td>Body represented by up to five cylinders (versus one for whole-body approach) Resistance for each segment must be measured separately</td>
<td>No clearly demonstrated advantages over Cole-Cole model</td>
</tr>
</tbody>
</table>

BCM, body cell mass; ECW, extracellular water; ICW, intracellular water; TBW, total body water.

of various body segments affect the measured impedance values. For example, the body’s trunk region represents about 50% of the body’s FFM, but contributes only about 9% to the whole-body resistance. Conversely, one arm and one leg combine for about 24% of FFM, but contribute at least 92% of the measured whole-body resistance. These proportions are explained by the nature of the derived BIA equations, where the body parts with the smaller cross-sectional area produce the dominant effect on the resistance. Hence, changes in the trunk region are relatively insensitive to detection by BIA, independent of the choice of frequencies.

Some of these difficulties with the whole-body measurement can be reduced by using regional impedance measurements. For example, fluid status has been assessed by using impedance measurements of only the lower leg in end-stage renal disease (ESRD) patients. Upper arm skeletal muscle, extravascular lung water, and TBW changes during hemodialysis have also been monitored with electrode placements on discrete regions of the body. Thus, the use of regional or segmental BIA measurements may facilitate assessment of regional body composition and fluid accumulation. However, if multiple electrodes are used because several body segments must be measured, this basically defeats one major clinical reason for use of BIA, i.e., a relatively quick and easy measurement that requires minimum cooperation from the patient.

ROLE IN CLINICAL RESEARCH

The 1994 NIH conference focused considerable attention on the most common use of BIA at the time, i.e., mainly the (indirect) estimation of body fat. Although far easier to perform and less expensive than, for example, hydrodensitometry, single-frequency BIA was and should continue to be viewed with caution as a surrogate technique to estimate body fat. The bioimpedance method is related to the conducting volume (or mass) in the body. Body fat per se, because it is nonconductive, is not measured by BIA, but is calculated as the difference between body weight and the derived estimate for FFM. Hence, any BIA-based estimate of body fat is subject to cumulative errors associated with the prediction of FFM (i.e., the error in mass units for the prediction of FFM is directly transferred to the smaller fat mass, such that the percentage error for fat is amplified). This is a limitation of all two-compartment models (Wt = FFM + Fat) where fat is defined as the difference between body weight and FFM.

Furthermore, it remains unknown if there are effects related to variations in body fat distribution, such as central versus gynoid obesity (factors that are clinically significant and have been associated with mortality risk). Thus, the use of a baseline value in fat mass, obtained using single-frequency BIA, especially with the series model predictions, does not represent a promising or reliable application of this technology. That is, since series BIA requires the use of prediction equations to estimate body composition, its ability to accurately monitor changes in body fat is very limited.

In contrast, the single-frequency parallel transformed model and the multifrequency BIA approach may provide more acceptable estimates of BCM and FFM, respectively, even for those patients undergoing significant weight loss.

Clinical research studies have continued to search for a more meaningful role for BIA measurements other than that of body fat estimation. It is now known that single-frequency BIA primarily reflects the ECW space, which is normally a constant proportion of TBW. However, during normal growth and aging, and for many metabolic diseases, the constancy of this proportionally can be affected, thus reducing the validity of the basic BIA assumption. An increase in ECW or in the ECW/TBW ratio may indicate edema and/or protein malnutrition. Multifrequency BIA appears to be sensitive to such changes, even if there are no significant changes in body weight or the body mass index. The parallel-transformed, single-frequency BIA model appears to be sensitive to changes in ICW (or BCM), but not to changes in ECW. Therefore, this model may have limited use for estimating FFM or body fat when there is an abnormal hydration state.

Preliminary studies in patients with AIDS and human immu-
nodeficiency virus (HIV) infection have reported the value of the parallel-transformed single-frequency BIA measurements. Researchers in Germany have noted the sensitivity of BIA in identifying BCM depletion in otherwise symptom-free HIV patients. The prognostic value of BIA estimates of BCM and the ECW/BCM ratio in predicting short-term survival in AIDS patients has been shown. These findings were recently confirmed by Bell et al., which would suggest that the ECW/BCM ratio obtained by BIA accurately reflects malnutrition, once there has been a significant loss of weight. An elevated ECW/BCM ratio, on the other hand, has also been shown to be a sensitive marker for hyperthyroidism. It is clear that the clinical advantage to monitoring both ECW and ICW (or BCM) makes this the preferred technique for future clinical research.

The role of the parallel-transformed single-frequency BIA technique to monitor only the BCM in various disease states may lead to expansion of this method and to the availability of newer predictive equations. These models, however, will need to be validated in a series of separate clinical populations. Studies supporting the ability of BIA to monitor longitudinal changes in BCM are in progress (D. Kotler, MD, unpublished data, 1998). This confirmation of the single-frequency, parallel model to accurately predict changes in body composition reliably is critical to establishing its use in clinical research and possibly for inpatient and ambulatory practice. Proponents of the multifrequency technique, however, have questioned where any single frequency approach will be appropriate or adequate for this task.

An alternate approach that has been used with bioelectrical impedance analysis is the measurement known as the phase angle, which is based on the ratio of resistance to reactance without needing to know the subject’s height. Most published results using the phase angle approach have employed the resistance and reactance values obtained for the series model. It is not known how the phase angle calculation would work for the parallel model. Nevertheless, the phase angle may be clinically useful because it should respond to changes in the ICW/ECW ratio, which is a more sensitive measure of malnutrition and illness than either ICW or ECW alone.

For example, in a study of more than 3000 hemodialysis patients, the range of the mean phase angle (determined at 50 kHz, series model) was much narrower than that for a healthy population. After adjusting for age, sex, race, and several biochemical indicators of nutritional status, dialysis patients with a phase angle <3° had a threefold increase in mortality. It has been proposed that a narrower phase angle may be a marker for various processes related to cell membrane dysfunction (e.g., malnutrition, inflammation, death) and, ultimately, may be predictive for clinical outcome. Similarly, among HIV-infected patients, the phase angle was shown to be the best single predictive factor for survival among 12 clinical and BIA parameters examined.

Additional clinical uses of BIA have been reported as well. In dialysis patients, BIA may offer a reliable and valid method of assessing nutritional status, the degree of overall hydration, and possibly the adequacy of dialysis treatment for the individual patient. In patients with liver disease, use of segmental, but not whole-body, BIA may prove useful for accurately estimating ascites fluid volumes. Serial BIA measurements have been used to monitor the nutritional status of patients with cystic fibrosis. Research in each of these clinical areas is ongoing, including application of the parallel model with single-frequency BIA and the multifrequency methods.

**ESTABLISHING POPULATION REFERENCE NORMS**

The vast majority of BIA validation studies are in healthy populations and have used series BIA techniques, and have often included additional anthropometric parameters besides height to establish the prediction equations. It has been shown that sex- and age-specific equations are needed, particularly for younger populations (age <18 y) and older adults (age >65 y). Recently, multifrequency BIA data obtained from 500 children aged 3–18 y indicated that the assumed constants used to calculate ECW and ICW, were not constant with age (KJ Ellis, unpublished data, 1998). Unfortunately, the age-specific BIA equations derived for older adults from the Framingham Heart Study have also not proved accurate when applied to a second population of age-matched adults, but with a lower mean BMI. These discrepancies raise the issue of sample-dependency or population-specificity when developing prediction equations, especially those that include anthropometric parameters.

Not enough data for various ethnic groups have been published to determine whether ethnic-specific equations are required. Some research groups have not identified significant differences, while others report racial variation in the validity of BIA estimates. For example, have shown acceptable results with the Segal fatness-specific equations in heterogeneous adult populations that included Native Americans, Hispanics, and Caucasians. However, when this same group assessed the predictive accuracy of BIA equations for estimating FFM in African-American adults, it was concluded that modified Segal fatness-specific equations were needed. In a study of African-American, Mexican-American, and Caucasian children, Ellis et al. found no ethnic differences in the BIA relationships with the dilution-based estimated for body water volumes, although gender differences were observed.

Although all BIA equations have been derived against other body composition techniques, only a few have been crossvalidated in independent target populations. That is, the single-frequency (series and parallel models), the multifrequency or Cole-Cole model, and the Hanai mixture model have not been rigorously evaluated in large population studies for accuracy and sensitivity. A confounding problem with such studies is that the "reference" methods [e.g., isotopic dilution, dual-energy x-ray absorptiometry (DXA), anthropometry, etc.] are not without their own errors and, therefore, restrict the degree of precision and accuracy that can be achieved. Nevertheless, BIA models must be evaluated to determine their concurrence with established reference methods/models and to ascertain their degree of sensitivity and specificity for monitoring changes in body composition for the individual.

A number of studies in the US have collected large datasets using the series-model, single-frequency BIA method that are being collectively analyzed (S. Guo, W.C. Chumlea, unpublished data, 1998). These data include the 3rd National Health and Nutrition Examination Survey (NHANES-III) conducted between 1988 and 1994, which includes more than 17,000 BIA measurements as well as various anthropometric data (weight, height, circumferences, skinfolds) in subjects aged 12 y or older. The future NHANES-IV survey is expected to add DXA and to replace the single-frequency BIA measurement with a multifrequency technique for the assessment of body composition. It is anticipated that the NHANES-III data for BIA (resistance, reactance, phase angle) will be compared directly with such physiologic variables as blood pressure, blood lipid profiles, and glucose intolerance results to possibly improve prediction for clinical outcomes, without the intermediate step of calculating body composition values.

**ESTABLISHING GUIDELINES FOR CLINICAL USE**

For BIA to extend beyond research applications in the healthy population, standardization of the procedures is essential. The optimal method, though not always practical (in a clinical setting), for obtaining impedance measurements involves having the subject (preferably fasted, but not dehydrated) lie supine for at least
10 min. Despite this requirement, several low-cost instruments, apparently targeted for the general public, have been marketed that require the subject be in a standing position. In any case, the subject should have abstained from strenuous exercise, excess alcohol consumption, and use of diuretic substances prior to the exam. In addition, the ambient conditions should help ensure a constant skin and normal body temperature. An accurate value for height (and often, weight and age) is required for use in many of the prediction equations. For longitudinal studies, it is advisable to use a single height estimate for all the measurements of an individual, unless there is clear evidence for a change in stature.

Research studies over the last 3-4 y continue to support the use of the wrist and ankle placement of electrodes, though proximal placement (i.e., elbow and knee) may offer small advantages in reproducibility. Wrist and ankle skin surfaces should be cleaned with alcohol, and electrodes must be accurately placed since displacement by as little as 1.0 cm can easily result in a 2% or greater change in the resistance value. Segmental measurements may be required in certain clinical settings, such as burn units; in patients with significantly abnormal fluid distributions; in cases of paralysis; and when there are patients with amputated limbs.

No new safety concerns with BIA measurements have been expressed since the 1994 NIH conference. No additional data on the potential risk of using high-frequency current in patients with an implanted defibrillator have been reported, despite the specific recommendation by the NIH panel that this issue be examined. However, multifrequency BIA measurements have been performed in several studies involving pregnancy without incident.5 Again, we cannot overemphasize the importance for standardization of equipment, prediction equations, and body composition information that is provided if BIA is to be considered for routine clinical use. Currently, the BIA measurement can give a false sense of security with regard to specific results.2 The equations used by various manufacturers (and the reference populations from which they were derived) often poorly match their clinical applications. We recommend that all instruments should report not only the calculated body composition values, but also the appropriate resistance, reactance, phase angle values, and the prediction equations that are used. In addition, to ensure uniformity among research studies, access to the BIA instrument’s ‘raw data’ (e.g., source current, frequency, waveform, dynamic range, resolution, and accuracy) would be helpful. Without such information, meaningful guidelines for routine clinical use cannot be established or implemented.

CONCLUSIONS

In 1994, the NIH panel “recommend(ed) that a committee of appropriate scientific experts and instrument manufacturers be formed with the goal of developing instrument standards and procedural methods.” Unfortunately, in the 4 y since that conference reached this conclusion, no such panel (officially or otherwise) has been formed, hence no standard methodology exists among the many instruments that are used. The present panel was convened to start to address these issues. Given the range of equipment currently in use, such standardization may realistically be limited to the provision of directly measured data (resistance, reactance, impedance, phase angle) by all machines. In addition, we recommend that all instruments be provided with the complete calibration equations that are used to convert these data to body composition values. We also strongly advocate the immediate implementation of two recommendations by the NIH panel: 1) the creation of an expert committee to set instrument standards and procedural methods, and 2) the revision of access to “raw” data with available and future BIA devices.

Our updated assessment of the clinical utility of BIA has, in some ways, not changed appreciably since the 1994 NIH conference. This technology seems most useful in estimating TBW in healthy population studies. We did confirm one technical expectation of the NIH panel and that is the development of multifrequency BIA measurements for clinical research. We also conclude that the parallel-transformed, single-frequency BIA model holds promise, but needs to be systematically tested in various clinical conditions where the BCM is known to be altered. It is unclear how useful the phase angle approach will be for predicting mortality or morbidity in various clinical conditions, although this application has had some success with patient populations with end-stage renal disease and AIDS.

In the hospital setting, particularly among the acutely or critically ill, the role of BIA has not been clearly defined. Disturbances of intracellular and extracellular water, for example, often accompany organ dysfunction (liver, kidney, heart), severe malnutrition, injury, and/or inflammation. Use of multifrequency BIA to monitor changes in ECW or the ECW/BCM ratio may prove useful in these situations, but more clinical research is clearly needed to clarify and validate the appropriate applications. Another application that is emerging is the use of BIA to customize drug dosage more accurately for the individual patient. As our understanding of what BIA measures advance, more useful clinical applications may be developed for acute or inpatient care. It may be that BIA will need to be coupled with another body composition technique, such as DXA, to obtain an accurate overall assessment for the individual patient.

Perhaps the highest research priority still lies with identifying the biophysical characteristics and variables that comprise, contribute to, or affect the basic BIA measurement. Recent studies have addressed the theoretical and technical aspects of the BIA principle,22-25 but clearly additional information is needed. Studies before and after blood transfusion, for example, may shed light on the role of viscosity and osmolality in bioimpedance. More data on the relationships between changes in whole-body BIA measurements and hematocrit, electrolyte profile, albumin, creatinine, insulin, glucose, and other blood chemistry values are likewise needed. Until such questions are answered, we cannot fully distinguish between contributing and confounding factors, nor can we ensure a clinically meaningful interpretation of BIA results in various diseases. In the meantime, we remain encouraged that BIA can become a clinically useful tool in many disease states, assisting in diagnosis, assessing prognosis, and monitoring the efficacy of therapy.

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