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Peer Review

Review of: "Bioelectrical Impedance Devices in Clinical and Oncological Nutrition: Types, Physical Principles, and Integration with Biochemical and Pathological Biomarkers"

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The authors address a current topic of practical clinical importance in a framework including theory and application of the bioimpedance (BIA) method. The narrative would benefit from more rigor in describing the physical and technical principles and limitations of the method, coupled with additional examples of potential clinical uses to overcome deficits in the current literature and to advance the proper application of BIA to assess hydration status, malnutrition, and prognosis. The authors should consider the following comments.

For clarity, the authors should clearly state that their focus is on whole-body BIA rather than presume the readers understand it. This distinction is important because of the fascinating literature describing the novel use of localized BIA to identify and classify muscle injuries based on R, Xc, and PhA using MRI as the reference and to track recovery [Rev Endocr Metab Disord 2023; 24(3):415-428. doi: 10.1007/s11154-023-09790-9].

In the abstract, the authors state “..with BIS and MF-BIA offering superior discrimination between true tissue depletion and fluid overload..” This critical judgment should be amplified in the text with references and findings specifically demonstrating the superior performance of MF-BIA and BIS in agreement with tracer dilution measurement values compared to SF-BIA.

The manuscript could benefit from the addition of fundamental experimental findings supporting the interpretation of basic BIA measurements, R and Xc. As noted above, the classic work of Lexa Nescolarde

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and others provides fundamental information to improve the understanding of R, Xc, and PhA [Rev Endocr Metab Disord 2023; 24(3):367-370. doi: 10.1007/s11154-023-09799-0].

Add a clear discrimination of BIVA, as a qualitative method, compared to MF-BIA and BIS that attempt to quantify fluid volumes. What are the advantages and limitations of each approach?

Encourage the authors to emphasize that the BIA method principally and uniquely tracks fluid volumes and their distribution by measuring basic electrical conductivity parameters. Importantly, BIA measurements identify the consequences of physiological perturbations, such as hyperinflammation and tissue injury, directly as perturbations in fluid status, membrane integrity, and cell or tissue interface disruptions.

The authors should acknowledge that the focus of this review on BIA relies solely on series equivalent circuits that can limit interpretations of BIA measurements. Recall that physiological systems are universally accepted to be parallel-equivalent R-C systems that enable a broader understanding of fluid distribution and cells [Nutrients. 2019; 11(4):809. doi: 10.3390/nu11040809]. An important paper highlights the benefit of using the parallel, compared to the series, model to identify changes in fluid volumes measured with tracer dilutional fluid volumes in response to physical training [Nutrition 2024; 123:112414. doi: 10.1016/j.nut.2024.112414]. Discussion of the potential of this approach should be added to the manuscript.

Note that adipose tissue contains an appreciable amount of water (15-20%). Among adults with excess adiposity, this expansion of ECW [Am J Physiol. 1991; 261:E199-203. doi: 10.1152/ajpendo.1991.261.2.E199] can contribute to a significant overestimation of fat-free mass and an underestimation of body fat. Revise this sentence accordingly.

The discussion of the physiological interpretation of BIA measurements requires additional detail. Include references supporting that "..PhA is associated with BCM.." There is considerable information linking PhA with fluid distribution (E/I and ECW/TBW) in healthy adults. How do alterations in fluid status (hypohydration and fluid overload) affect the relationship between PhA and BCM?

Two additional technical concerns merit discussion. The type of contact electrode and instrument hardware directly affect BIA device measurements. This inconsistency emphasizes the lack of interchangeability of BIA measurement values within and between investigational locations.

Differentiate the roles of the Cole model and Hanai model in the BIS estimation of fluid volumes. Limitations of reliance on height, body weight, and BMI in the Cole model, as well as assumptions of

constancy of intra- and extracellular resistivities, should be discussed in relation to the validity of BIS-dependent fluid volume estimates.

Explanation of the process by which R and Xc are determined is critical. Are they measured directly or calculated? Is a phase-sensitive device required?

Inclusion of specific PhA (SPhA) is important. Is ethnicity a factor impacting the interpretation of sPhA?

The authors emphasize the potential value of BIA in the classification of the phenotype of an individual, specifically in the estimation of muscle mass. How is this approach affected by differences in hydration, considering that the method relies on the assumption of constant hydration of the fat-free mass? Include any evidence of agreement of the BIA estimates relative to a standard reference method (e.g., DXA or MRI)?

The proposal to include membrane capacitance (Cm) is novel and requires additional technical discussion. Is this limited to MF-BIA since Cm is frequency-dependent? Is there any clinical precedent for using Cm, and in what capacity?

The proposed tiered model for targeted applications of BIA is useful. Some additional clinical examples should include chronic kidney disease (estimation of fluid removal and nutritional status), cancer, infectious disease (e.g., COVID-19 as an example), sarcopenic obesity, and other current topics of interest.

An additional opportunity is the combination of PhA and BIVA to improve the assessment of fluid alterations with cell mass depletion. Malnutrition and certain clinical states experience concurrent fluid disturbances and loss of BCM that could be monitored in real time [Rev Endocr Metab Disord 2023; 24(3):563-583].

Declarations

Potential competing interests: No potential competing interests to declare.