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Equivalence of information from single versus multiple frequency bioimpedance vector analysis in hemodialysis

ANTONIO PICCOLI, GIORDANO PASTORI, MARTA GUIZZO, MIRCA REBESCHINI, AGOSTINO NASO, and CARMELO CASCONE

Department Scienze Mediche e Chirurgiche, University of Padova, Padova, Italy; and Division of Nephrology, University Hospital of Padova, Italy

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Background. In suspended cells, low-frequency current only passes through extracellular fluids, while current at higher frequencies passes through extra- and intracellular fluids. Cells in soft tissues are in contact with each other, which causes tissue anisotropy, meaning that impedance changes along different cell directions, with part of low-frequency current also passing through cells. Hence, equivalent information on body impedance change is expected at all frequencies, which we proved in a dynamic condition of fluid removal with hemodialysis.

Methods. We performed whole-body impedance spectroscopy (496 frequencies from 4 to 1024 kHz, SEAC SFB3 analyzer; Brisbane, Australia) before and during fluid removal (0, 60, 120, 180 min, 2.5 kg) in 67 hemodialysis patients. With increasing current frequency, resistance (R) decreases and reactance (Xc) moves along the Cole's semicircle on the R-Xc plane.

Results. The Cole's semicircles progressively enlarged and moved to the right on the R-Xc plane following fluid removal (increase in both R and Xc values at any given frequency). Xc values at 5 kHz (expected values close to 0 Ohm) were 70% of the maximun Xc, indicating an intracellular current flows at low frequencies. The correlation coefficient between R at 50 kHz (standard frequency) and R at other frequencies ranged from 0.96 to 0.99, and the correlation coefficient between Xc at 50 kHz and Xc at other frequencies at any time point ranged from 0.65 to 0.99.

Conclusion. From high Xc values at low frequency, tissue anisotropy is inferred. Intra- and extracellular current flow causes equivalence of information based on functions of R and Xc measurements made at 50 kHz versus other frequencies.

Bioelectrical impedance analysis (BIA) is a noninvasive method of body composition analysis. Impedance is represented with a complex number (a point) in the real-imaginary plane (Z vector), that is a combination of resistance, R (i.e., the opposition to flow of an alternating current through intra- and extracellular ionic solutions, representing the real part of Z) and reactance, Xc (i.e., the capacitative component of cell membranes and organelles, and tissue interfaces, representing the imaginary part of Z) [1–4].

Key words: bioimpedance, bioimpedance spectroscopy, multifrequency bioimpedance, total body water, intracellular water, extracellular water, hemodialysis, Cole model.

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BIA methods for body composition analysis

Although impedance is an electrical property of tissues that can be directly utilized in body composition analysis, it is commonly embedded in predictive equations that are derived by correlation with criterion measures of body compartments. Literature is divided along 4 methods of body composition analysis based on impedance. The first and the most validated is prediction of total body water (TBW) with functions of 50-kHz single-frequency impedance (either series measures or their parallel equivalents, mostly neglecting the Xc component) [4–9]. The second is prediction of extracellular water (ECW) and TBW with functions of low (1–5 kHz)- and high (100–500 kHz)-frequency impedance (dual- or multiple-frequency BIA), with the intracellular water (ICW) calculated by difference [10–12]. The third is use of many impedance measurements (1 to 1000 kHz) through bioimpedance spectroscopy (BIS) following the Cole's model approach (i.e., extrapolating R values at limit frequencies) for prediction of TBW, ECW, and ICW [13–17] (Figs. 1 and 2). The fourth is use of the direct impedance vector measurement (both R and Xc component) at 50 kHz in a probabilistic graph (vector BIA with the *RXc graph*). Vector BIA is a stand-alone method of body composition analysis, where the continuous, bivariate, random vector of impedance is evaluated through an ordinal scale (tolerance interval percentiles) of the deviation from a reference population. Body composition is then evaluated through patterns of vector distribution with respect to the reference percentiles [18–21].

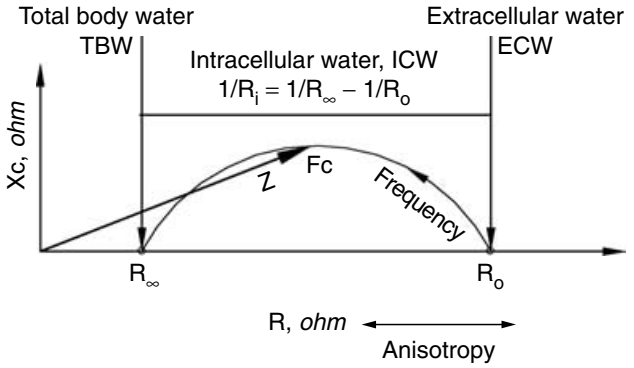

Fig. 1. The semicircle of the Cole's model for cell suspension is utilized in body composition analysis. The curve formed by Z vectors on the R-Xc plane (impedance locus) is a semicircle with a depressed center (see Fig. 2). At the extrapolated zero frequency limit resistance, R_0, current would only flow through the extracellular water solution. The current frequency at which Xc reaches the maximum is the characteristic frequency (Fc). At the extrapolated infinite frequency limit resistance, R_∞, the current would flow through both intra- and extracellular water solution (total body water compartment). The model is not appropriate for human tissues due to their anisotropy (longitudinal conduction of part of low frequency current through muscle cells), which transforms R_0 into a random sum of extra- plus intracellular resistance. R, resistance; Ri, intracellular R; Xc, reactance.

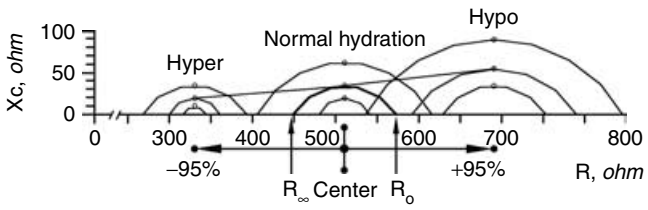

Fig. 2. Effect of between-subject variability of R and Xc on both position and size of an individual Cole's semicircle. In literature, R_0 and R_∞ are derived "without error" from an individual semicircle (e.g., the thick semicircle). Considering independent random errors for both R (horizontal shift of the center, mean R ± 2SD, 95% interval) and Xc component (vertical shift of the center, mean Xc ± 2SD, 95% interval), both circle position and extension dramatically change on the R-Xc plane. Xc at the characteristic frequency (Fc) is represented with an open dot in the vault of each arc. As circles enlarge due to circle migration from left to right, the migration trajectory of individual vectors on the semicircles is linear. Smaller versus larger circles correspond to a more versus less hydrated status as a progressive tissue dehydration increases tissue impedance (real data in Fig. 4). R, resistance; R_0, resistance at 0 frequency; R_∞ at infinity; Xc, reactance.

Errors in BIA and BIS equations

The prediction error of BIA and BIS equations is the sum of 5 errors, namely the impedance measurement error, the regression error (standard error of the estimate against the reference method), the intrinsic error of the reference method (assumptions and measurement error of dilution reference methods and models), the electric-volume model error (anisotropy of tissues and human body geometry other than one cylinder), and the biological variability among subjects (different body composition and body geometry) [3, 9].

In contrast, measurement validity is only required for vector BIA that needs to take care of the measurement error and of the biological variability of subjects [20].

Impedance measurements are made with a 2% to 3% precision error [3, 4, 8, 16, 17]. BIA and BIS equations are validated against dilution methods that have their relevant error, dependent on isotope and compartment, but greater than 3% to 6% [3, 15–17]. For instance, the ratio of ECW/TBW ranged from absurd values of −0.3 to 2.1 following infusion of lactated Ringer's solution [16]. Hence, in addition to costs, low precision prevents clinical utilization of dilution reference methods and models [3, 16, 17].

Although tissue anisotropy (current conduction is not constant in different direction; see Appendix) [1–3, 22] severely impairs validity of BIS in the clinical setting, a panel of BIA experts recommended the utilization of BIS in estimating TBW, ECW, and ICW also in altered fluid distribution. The panel discouraged doctors from using 50 kHz, single-frequency BIA [23].

In this study, using tissue anisotropy as working hypothesis, we wanted to prove that single-frequency 50 kHz-impedance measurements provide the same information as BIS and multifrequency BIA during fluid removal with hemodialysis (HD). To this end, we assessed measurement validity (construct and content validity) of impedance vector at 50-kHz frequency versus other frequencies during fluid removal with HD.

METHODS

Hypothesis

In principle, tissue anisotropy leads to equivalence (meaning similar predictive accuracy) between information provided by single-frequency 50-kHz impedance measurements versus other frequencies, as part of the current at any frequency flows through extra- and intracellular ionic solutions of soft tissues. We tested this hypothesis of equivalence assessing measurement validity (construct and content validity) of BIS versus 50-kHz frequency impedance, considering both steady state and fluid removal with HD (Fig. 2).

Construct validity of BIS (the measurement corresponds to theoretical expectations) was checked by looking at the distribution of Xc at the lowest frequencies, where Xc values were expected both to approach zero (where current flow would only be extracellular), and to be lower than Xc values at the highest frequencies (where impedance becomes progressively independent on cell membrane capacitance). Also, conflicting indications about ICW and ECW changes during dialysis were analyzed.

Content validity (the measurement incorporates the domain of the phenomenon under study) was checked by comparing the amount of information provided by BIS with respect to 50-kHz measurements (correlation