SCIENTIFIC REVIEW



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Principles of Bioelectrical Impedance Analysis (BIA)

BIA is a non-invasive and painless technique for analyzing body composition.

It consists of delivering one or more very low intensity currents to measure the resistance of tissues to the passage of the current.

These measurements make it possible to obtain values of resistance, reactance, and impedance.

More precisely:

- resistance is related to the state of hydration (transitive resistance)
- reactance is related to the quantity and integrity of the cell membrane (capacitive resistance)[1]
- impedance, as for it, is calculated from these two parameters according to the following formula:

$$Z(\omega)=R(\omega)+j\times Xc(\omega)$$

Where **Z** represents impedance, **R** resistance, **Xc** reactance, **j** lthe imaginary component of the signal, and **ω** the current frequency.

It is then used within predictive equations to evaluate body composition, including, for example, hydration, skeletal muscle mass, or fat mass.

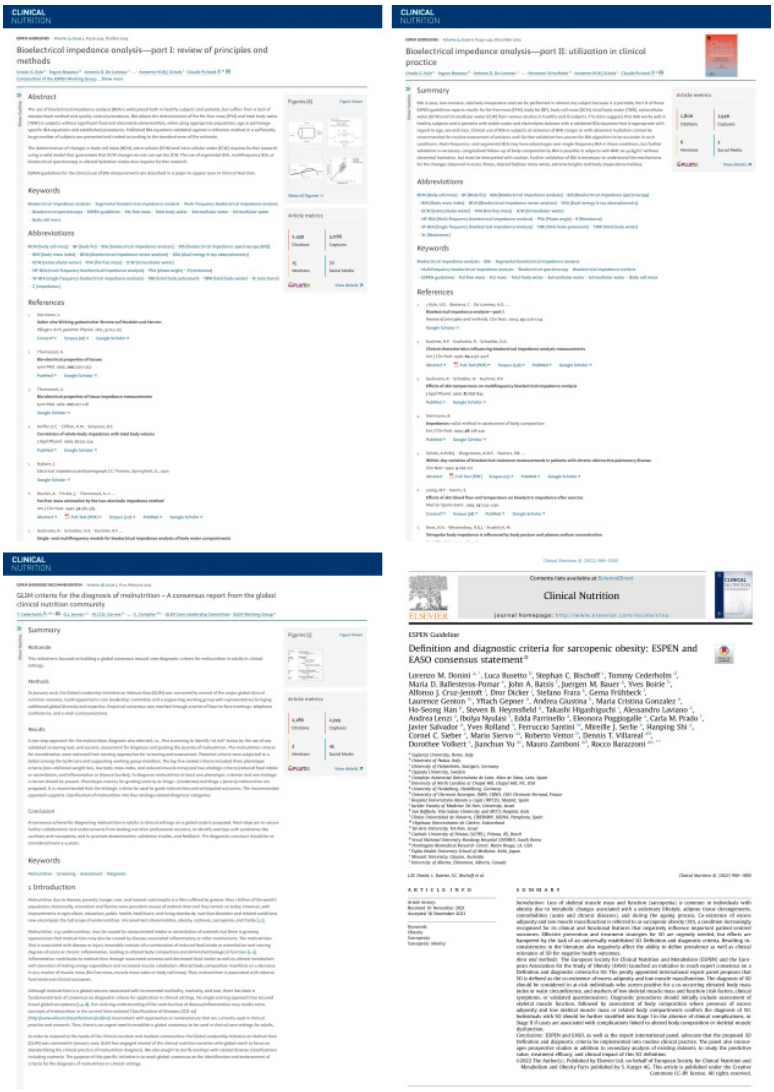
In addition to body composition parameters, BIA also allows obtaining raw parameters related to overall health status and systemic inflammation level, such as phase angle and impedance ratio[2,3].

From a technical point of view, these bioelectrical data can be obtained by two measurement modes using 4 electrodes (tetrapolar) or 8 electrodes (octopolar), which will be connected to the hand and foot.

Application domains of bioelectrical impedance analysis

Currently, BIA is used during clinical management, health status monitoring, or during physical preparation of athletes to:

- detect possible pathological imbalances in body composition or situations at risk of developing these imbalances,
- guide clinical, nutritional and/or sports management targeting body composition,
- evaluate the effectiveness of this management to reorient it if necessary.



In 2004, the European Society for Clinical Nutrition (ESPEN) issued recommendations for the use of BIA in healthy subjects and patients with chronic pathologies, according to a tetrapolar mode and the equations developed for it, for routine clinical use[4, 5].

It is notably recommended for the detection of undernutrition[6] and sarcopenia[7], as well as in the diagnosis of obesity[8] and sarcopenic obesity[9].

In a sports context, it is also used for monitoring body composition during physical preparation, and in prevention of chronic energy restriction syndrome (RED-S)[10].

Generally, the parameters used during management include fat-free mass, fat mass, skeletal muscle mass (total and segmental), as well as body hydration and the balance between intra- and extracellular compartments.

Compared to other techniques, BIA stands out for its ease of use, speed of measurement, convenience for the subject, and low cost[11].

Like any method, however, it presents certain limitations, particularly in clinical contexts where the hydration status is strongly disturbed. These specific situations require an adapted interpretation, by cross-referencing clinical data with the results obtained.

Technological choices of Biody Xpert^{ZM}3 with tetrapolar measurement

Tetrapolar measurement consists of placing two pairs of electrodes on the hand and foot: one emits a low-intensity electric current, the other measures the generated voltage. This allows obtaining the bioelectrical data necessary for evaluating body composition.

As indicated in part 1, this measurement mode is recommended in the literature for clinical management, as the equations used and validated are specifically adapted to tetrapolar measurement. In this context, Aminogram has chosen to use predictive equations from the scientific literature, validated against reference methods:

- An equation modified from that of Kyle et al.[12] for fat-free mass;
- The Kushner & Schoeller[13] equation for total body water volume;
- The Deurenberg et al. equation for extracellular water volume;
- The Kyle et al.[15] equation for appendicular skeletal muscle mass.

Bone mineral content is estimated from an internally developed algorithm. Other body compartments are deduced from compartmental modeling. For example, if total water and extracellular water are known, intracellular water can be calculated using the formula:

Intracellular water = Total water - Extracellular water.





When a measurement is performed in a supine position, one limitation of this measurement mode is the necessity to maintain a minimum time of several minutes in this position before performing the measurement, in order to allow for a balance of body fluids following the change in posture, and thus obtain optimal results. This waiting time can limit the use of the technique in a routine care context, due to a measurement duration that may conflict with the available consultation time.

Furthermore, the use of self-adhesive electrodes in the form of consumables implies a significant financial cost, particularly for hospital structures performing a large number of measurements, which can also limit the use of the technique. Based on this observation, Aminogram chose to develop a device offering two possibilities: a supine measurement with cables and self-adhesive electrodes, or a seated measurement with integrated electrodes, allowing for the avoidance of consumables and reducing measurement time. The result of this development is the Biody Xpert™ range, designed to adapt to clinical constraints while guaranteeing data quality.

Validation of seated and supine measurement versus DEXA

inefc Barcelona Generalitat de Catalunya

Key data from the INEFC study (2024):

Only 3.7 Ω average impedance difference between seated and supine positions.
Average deviation from DEXA: 0.3 to 0.8 kg depending on the parameters.

The measurement position and electrode placement are determining parameters in bioelectrical impedance analysis. If the measured bioelectrical data (resistance, reactance, impedance) do not vary depending on the position, the body composition results can be considered comparable.

A study conducted by the National Institute of Physical Education of Catalonia (INEFc) on 30 healthy subjects evaluated the precision of the Biody Xpert^{ZM}3[16] in seated and supine positions (published in Measurement (IF: 5,6)). The 50 kHz measurements were very close:

	Seated	Supine
Resistance	486,2 ± 51,5 Ω	489,5 ± 49,7 Ω
Reactance	60,9 ± 6,3 Ω	64,3 ± 7,5 Ω
Impedance	493,7 ± 50,0 Ω	490,0 ± 51,7 Ω

Bland-Altman analysis indicates a mean difference of:

- 3,3 Ω for resistance
- 3,3 Ω for reactance
- 3,7 Ω for impedance

Lin's concordance coefficient confirms very good consistency:

- 0,92 for resistance
- 0,79 for reactance
- 0,92 for impedance

Body composition data were also compared with those obtained by DEXA:

	Fat-free mass	Lean mass	Fat mass
Supine	62,8 ± 4,7 kg	59,9 ± 4,5 kg	16,3 ± 5,2 kg
Seated	62,9 ± 5,5 kg	60,0 ± 5,3 kg	16,3 ± 4,6 kg

The deviations from DEXA were small:

- Fat-free mass: 0.6 kg (supine), 0.8 kg (seated)
- Lean mass: 0,8 kg / –0,1 kg
- Fat mass: 0,3 kg / 0,4 kg

These results confirm the equivalence of measurements between seated and supine positions, as well as good agreement with DEXA. Although the data concern a limited sample, they provide solid evidence supporting the reliability of the method, and open the way for further studies on larger populations.

Comparison of results obtained between Biody Xpert^{ZM} and DEXA

To reinforce these results and broaden their scope, Aminogram compiled data from 234 subjects representative of the general population. These comparisons between the Biody Xpert II and DEXA were carried out as part of the Post-Marketing Clinical Follow-up (SCAC).

The concordance between the two techniques was evaluated according to recognized statistical methods: mean bias (mean difference) according to Bland-Altman, and intraclass correlation coefficient (ICC).

The results obtained confirm strong consistency between the two approaches for the four parameters analyzed: fat-free mass, fat mass, appendicular skeletal muscle mass, and bone mineral content (see figure below).

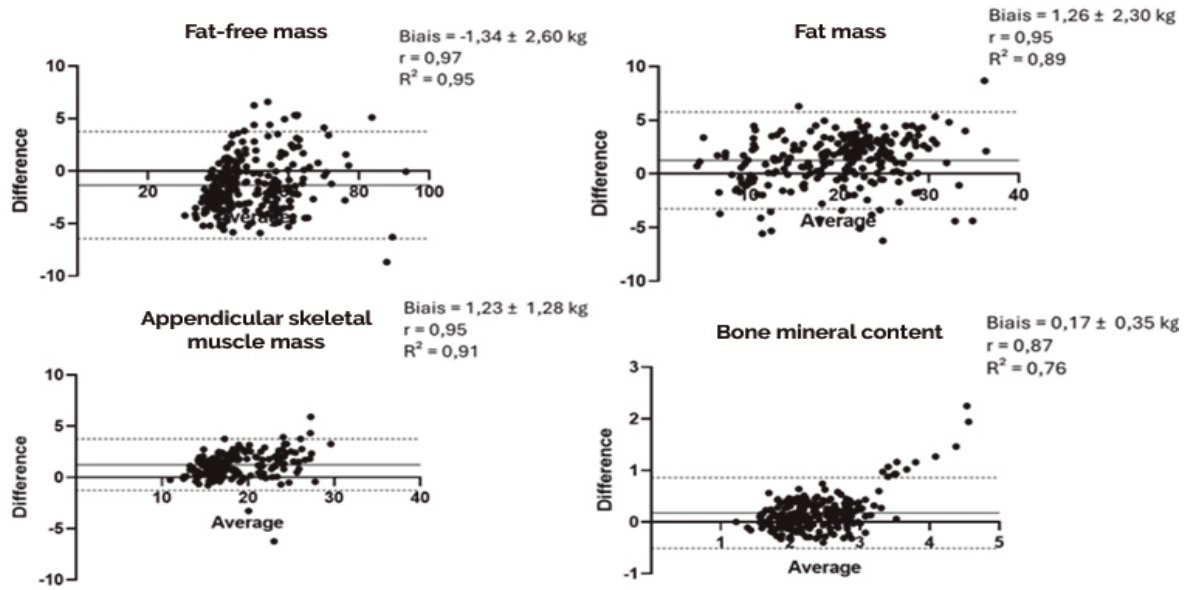


Figure: Bland-Altman plot of results obtained by the Biody XpertZMII and DEXA for fat-free mass, fat mass, appendicular skeletal muscle mass and bone mineral content. The intraclass correlation coefficient r and regression coefficient R^2 are also given for each parameter.

The mean difference for fat-free mass, fat mass, and appendicular skeletal muscle mass is slightly greater than 1 kg with r values much higher than 0.90, indicating excellent concordance between the two techniques. For bone mineral content, the mean bias obtained is 170 grams with an r slightly lower than that of the other three parameters but which, nevertheless, indicates very good concordance between the two techniques for this parameter. It is interesting to observe that about ten points are outside the limits of the 95% confidence interval, i.e., the dashed lines, indicating a significant difference between the two techniques for these individuals. These correspond to rugby players who are characterized by extremely high bone density, caused by the stresses of their sport. As a technique, DEXA is sensitive to bone mineral density, unlike BIA, thus explaining the observed differences for these individuals.

In conclusion, these data show that for these 4 parameters, the Biody Xpert^{ZM}II, and the Biody Xpert^{ZM}3 by extension, demonstrate equivalence in the results obtained compared to DEXA in the general population.

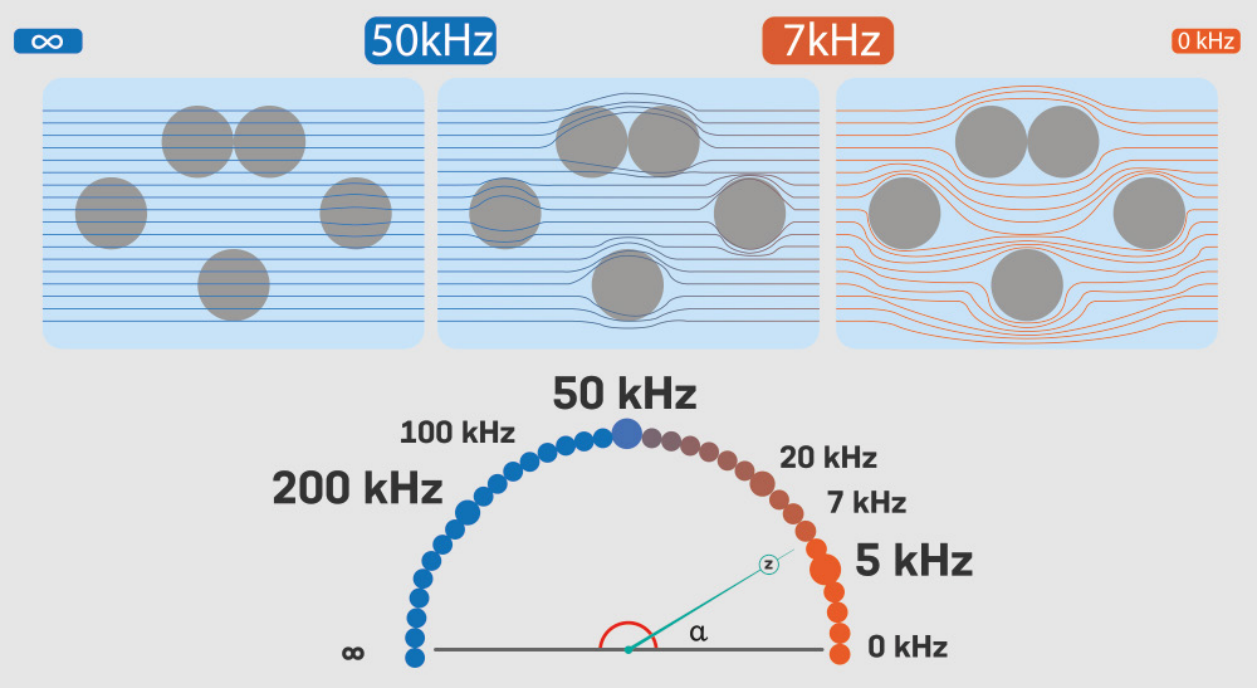
Single-frequency BIA (SF), multi-frequency BIA (MF-BIA) and spectroscopy BIA (BIS)

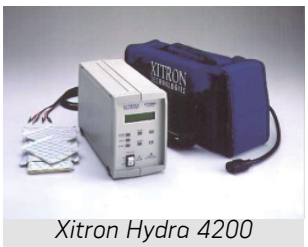
The first BIA devices were single-frequency, meaning they used a single current at a frequency of 50 kHz. They relied on prediction equations and reference values based on resistance, reactance, or impedance. The main limitation of this approach lies in its inability to precisely evaluate extracellular water volume and therefore the distribution between intra- and extracellular compartments. Indeed, at 50 kHz, the current passes through cell membranes, which prevents specifically targeting the extracellular compartment. This type of measurement has notably been used in early devices such as the RJL Systems Quantum II, considered a historical reference in the development of prediction equations.



RJL Systems Quantum II

The evaluation of the extracellular compartment is made possible by using low-frequency currents (below 7 kHz), which are unable to cross cell membranes[17]. SOn this basis, multi-frequency devices have been developed, using at least three frequencies: a low one (generally 5 kHz), an intermediate one (50 kHz) and a high one (100 or 200 kHz). Their main advantage is to allow a distinct estimation of total water and extracellular water, via algorithms combining the data obtained at 5 and 50 kHz. These devices also provide access to equations validated in the literature, usable at 50 kHz. The introduction of a third frequency also makes it possible to calculate the impedance ratio (impedance at 200 kHz / impedance at 5 kHz), a marker associated with systemic inflammation[3, 18].





Xitron Hydra 4200

The most advanced reference devices, such as the Xitron Hydra 4200, rely on a spectroscopic approach. This consists of scanning a wide spectrum of frequencies—from very low to very high—to finely analyze the electrical properties of body tissues. The Biody Xpert ZM3 fully aligns with this approach, with an analysis across 54 frequencies ranging from 1 kHz to 1000 kHz, including the lowest frequencies (1, 2, 3, and 4 kHz). This specificity makes it the only portable bio-impedancemetry device with spectroscopy to provide

measurements at these frequencies, which are particularly sensitive to extracellular compartments.

Processing this data allows for the generation of a Cole-Cole curve, shown below, whose consistency between theoretical modeling (curve) and measured points guarantees the quality of the measurement.

Thanks to this analytical precision, it becomes possible to estimate three fundamental resistances associated with the body's water compartments:

Estimated parameter	Physiological meaning
Resistance at 0 Hz (R_0)	Corresponds to extracellular water (outside cells)
Intracellular resistance	Reflects fluids contained inside cells
Resistance at infinity (R∞)	Estimation of total body water (intra + extracellular)

These data make it possible to feed more reliable body composition prediction equations than those based on a single frequency at 50 kHz, and adapted to a diversity of populations[19].

Furthermore, several recent studies show that certain parameters extracted from spectroscopic analysis are correlated with major clinical indicators, notably:

- insulin resistance[20],
- membrane permeability and exchanges[21],
- or the functional and architectural quality of skeletal muscle[22, 23].

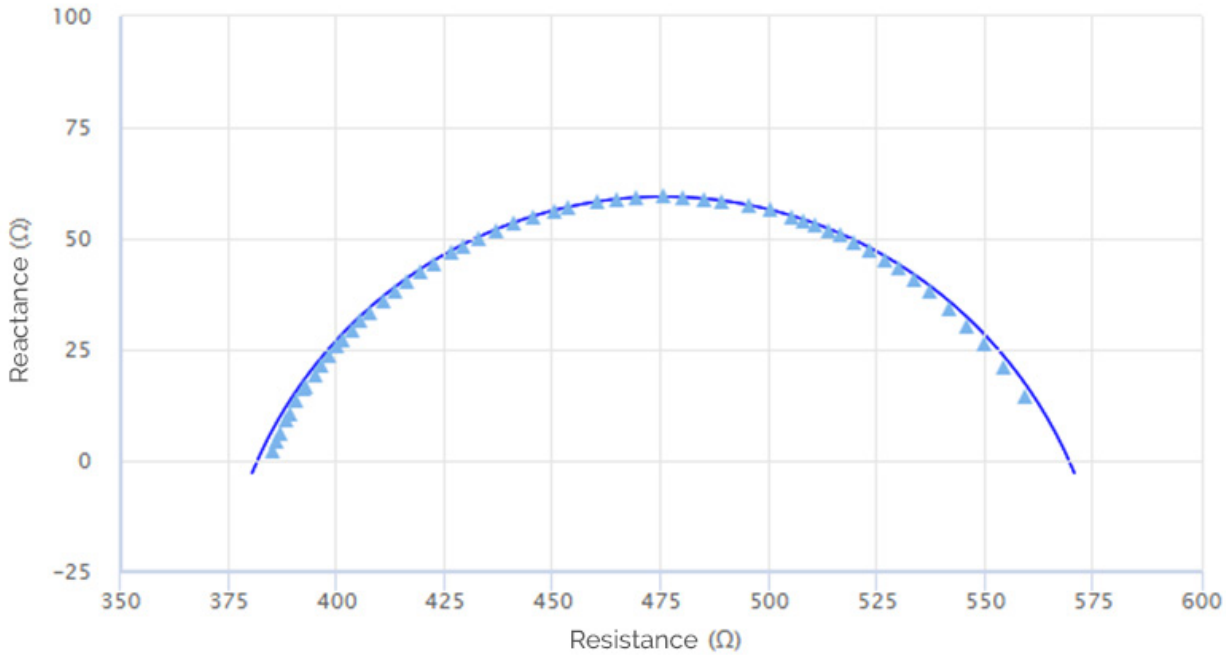


Figure: Graphical representation of Cole-Cole modeling. Each triangle represents a BIA data measurement at a precise frequency, over a range of 1 to 1000 kHz. The solid line represents the obtained Cole-Cole modeling. The position of the triangles relative to the Cole-Cole modeling allows for controlling the quality of the measurement.

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