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The bioelectrical impedance analysis (BIA) international database: aims, scope, and call for data

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1 The Bioelectrical Impedance Analysis (BIA) International Database: Aims, Scope,

2 and Call for data

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140 Abstract

Background: Bioelectrical impedance analysis (BIA) is a technique widely used for 141 estimating body composition and health-related parameters. The technology is relatively 142 simple, quick, and non-invasive, and is currently used globally in diverse settings, 143 including private clinicians' offices, sports and health clubs, and hospitals, and across a 144 spectrum of age, body weight, and disease states. BIA parameters can be used to estimate 145 body composition (fat, fat-free mass, total-body water and its compartments). Moreover, 146 147 raw measurements including resistance, reactance, phase angle, and impedance vector 148 length can also be used to track health-related markers, including hydration and malnutrition, and disease-prognostic, athletic and general health status. Body composition 149 shows profound variability in association with age, sex, race and ethnicity, geographic 150 ancestry, lifestyle, and health status. To advance understanding of this variability, we 151 152 propose to develop a large and diverse multi-country dataset of BIA raw measures and derived body components. The aim of this paper is to describe the 'BIA International 153 154 Database' project and encourage researchers to join the consortium.

Methods: The Exercise and Health Laboratory of the Faculty of Human Kinetics, University of Lisbon has agreed to host the database using an online portal. At present, the database contains 277,922 measures from individuals ranging from 11 months to 102 years, along with additional data on these participants.

159 Conclusion: The BIA International Database represents a key resource for research on160 body composition.

161 Keywords: Reactance, Phase angle, Vector length, Body composition, Nutrition,

162 Obesity, Consortium

163 Background

The use of bioelectrical impedance analysis (BIA) to investigate human body 164 composition began in the 1960s, when Thomasett showed that total body water (TBW) 165 could be estimated from whole-body impedance ¹. Subsequent development of this 166 approach has substantially extended its capacity to provide information about tissue 167 composition and function ²⁻⁵. The feasibility, portability, and safety of BIA makes it 168 relatively unique among body composition methods 6 . The technology is relatively 169 simple, quick, and non-invasive, and is currently used globally in diverse settings, 170 including private clinicians' offices, sports and health clubs, and hospitals, and across a 171 spectrum of age, body weight, and disease states. In turn, this has resulted in an 172 exponential increase in the availability of BIA data. As yet, however, the potential of this 173 high data volume has not been comprehensively exploited to improve our understanding 174 175 of human body composition variability, in relation to sex, age, health status, lifestyle and 176 population.

Several different approaches can be used to extract information on body composition 177 from BIA. In the single frequency approach (SF-BIA), through the application of a 50 178 kHz alternating current, BIA provides measures of impedance (Z, ohm) by conductive 179 180 tissues such as blood, muscle/organs and cerebrospinal fluid. Z comprises a purely 181 resistive component (resistance, R, ohm) that is related to water and electrolytes in fluids 182 and tissues, and a capacitive component (reactance, Xc, ohm) responsible for the delay of the current entering cells, associated with cell membrane integrity and cell interfaces 183 184 $^{7.8}$. While single-frequency 50 kHz BIA machines are popular, tetra polar multi-frequency BIA (MF-BIA) or bioelectrical impedance spectroscopy (BIS) instruments also provide 185 186 frequency-specific readings at 50 kHz.

One approach to estimating body composition from raw BIA data is to predict TBW or 187 fat-free mass (FFM) from the impedance index, calculated as the square of height (HT, 188 cm) over impedance (HT²/Z). Based on research studies, numerous such equations have 189 been published for healthy populations and with diseases ^{1, 9-33}. This approach can be 190 191 extended to the main compartments of TBW, extracellular water (ECW) and intracellular water (ICW), by exploiting the fact that whether the current passes only through ECW, 192 or through both ECW and ICW, depends on its frequency ^{34, 35}. At the cellular level, BIA-193 derived body cell mass ^{18, 36, 37}, and at the tissue level, skeletal muscle (SM) mass, can be 194

accurately predicted in healthy populations, as compared to magnetic resonance imaging 195 or computerized tomography 38 . These components have a recognized implication in 196 health and performance, specifically intracellular water ³⁹⁻⁴¹, but also in disease 197 susceptibility due to increased levels of fatness and loss of SM ⁴²⁻⁴⁵. The latter is also a 198 key characteristic of sarcopenia, a SM disease rooted in adverse muscle changes that 199 accrue across a lifetime ⁴⁶. Indeed, for sarcopenia diagnosis, BIA has been recognized as 200 a useful tool to estimate SM quantity (mass) and quality (amount of strength and/or power 201 per unit of SM mass)⁴⁶. 202

203 A second approach focuses on direct measures provided by BIA that have been widely 204 used to explore malnutrition, growth and development, athletic performance, sexual dimorphism, pregnancy, and ageing in several populations ⁴⁷⁻⁵⁵. Indeed, the raw BIA 205 parameter phase angle (PhA), representing the arc tangent of Xc/R, is a compound 206 207 indicator of the distribution between intra and extracellular fluids and of body cell mass ^{8, 53}. There has been growing interest in the use of such raw BIA parameters as proxy 208 markers of health, physical fitness and function, and disease status, avoiding the need for 209 prediction equations ⁵⁶⁻⁶⁴. However, the practical application of PhA measurements to 210 define nutrition status still requires normative values. To date, reference data for PhA are 211 available for healthy American ^{65, 66}, German ⁶⁷ and Swiss ⁶⁸ adult populations, as well as 212 athletes ⁶⁹ and UK children ⁷⁰, but given the large inter individual variability associated 213 with factors such as age, sex and ethnicity, consensus on the normal range is still lacking 214 and more comprehensive standards are required. 215

216 An interesting extension of the insights from research on PhA is represented by bioelectrical impedance vector analysis (BIVA) ⁷¹, which in turn has been developed in 217 different ways. BIVA 71, 72 analyzes R and Xc, and the derived variables PhA and vector 218 length (i.e., Z,) without relying on assumptions of a fixed FFM hydration, or on constant 219 220 body geometry and resistivity values. Particularly, PhA describes the direction of the 221 vector on the R-Xc graph and represents the distance from the vector to the X axis. Classic BIVA adjusts raw BIA parameters for HT, whereas specific BIVA standardizes on the 222 basis of estimated body volume, derived from data on both HT and cross-sectional area. 223 This means that specific (sp) BIVA parameters (Rsp, Xcsp, Zsp) are influenced by the 224 properties of the tissues rather than body size and shape. BIVA allows a better 225 226 understanding of body composition variability than does PhA alone independent of vector 227 length, or R independent of Xc. In classic BIVA, variation in vector length indicates different hydration conditions for a given PhA ⁷¹, whereas in specific BIVA it indicates different levels of FM% ⁷²⁻⁷⁴. Hence, both classic and specific BIVA can be used simultaneously ⁷⁵. Population-specific reference values for classic and specific BIVA are available for U.S. children, adolescents, and adults, Italian children and adolescents, Italian-Spain young adults and elderly Italians ^{72-74, 76-79}, but factors such as race and ethnicity, geographic ancestry, lifestyle, socio-economic status have not yet been considered in depth.

Body composition shows profound variability in association with age, sex, race and ethnicity, geographic ancestry, lifestyle and health status. In turn, this incorporates variability both in bio-conducting tissues, and also in total and regional body composition ^{52, 80-82}. To date, due in part to the difficulty of applying most methods at scale, we lack a large representative body composition database that incorporates variability in age, sex, race and ethnicity, geographic ancestry, lifestyle, environment, socio economic factors and athletic status.

Developing such a database for BIA would allow a range of potential applications.Among these we highlight:

- Developing a comprehensive integrated model of healthy body composition by
 pooling BIA data across multiple populations.
- Relating BIA data to other phenotype data on health, lifestyle and disease state.
- The capacity for BIA data to guide clinical management across a wide range of
 disease states.
- The capacity for BIA data to help assess the efficacy of large public health interventions.
- The capacity for BIA data to be routinely collected by individuals in the home,
 gyms and health clubs, in order to help them maintain healthy weight and body
 composition.
- To contribute to academic training and teaching by enabling the use of a large and unique dataset adequately managed.
 - 9

Beyond the direct implications for health, increasing the capacity to measure body composition at scale may have substantial economic benefits, through increasing the success of lifestyle interventions, optimising drug dose calculations, and improving the efficiency of healthcare.

The aim of this project is therefore to build a large and diverse dataset of BIA raw measures and derived body components by pooling data from multiple countries. These data can be shared for research investigations to enable a better understanding about body composition variability in association with age, sex, race and ethnicity, geographic ancestry, lifestyle and health status and to develop robust normative values. Here, we describe this ongoing 'BIA International Database' project and encourage researchers, especially those from low- and middle-income countries, to contribute data.

267

268 Call for data

The BIA International Database had its genesis in 2017 at a Summer School training workshop in Sardinia, Italy (<u>https://sssnsa.wordpress.com/</u>), when the idea and benefits of compiling all published BIA measurements on humans was proposed. Alone, each individual dataset is unable to tackle relevant questions in sports, nutritional, and medical sciences, whereas combining information across studies offers many new opportunities.

The application of BIA to humans vastly increased since 2000⁸³, with 19713 publications between 1960 and 2021 based on a search in the ISI Web of Science core collection using the search string ((Bioeletrical impedance analysis) OR BIA OR bioimpedance), as illustrated in **Figure 1**.

278 **INSERT FIGURE 1**

This large-scale application of BIA demonstrates the data that is potentially available for 279 pooled analysis. We therefore invite contributions from researchers worldwide. The 280 Faculty of Human Kinetics of University of Lisbon agreed to host the database, and a 281 total of 276,410 measurements (1 record = 1 measurement on 1 person) have been initially 282 of 283 uploaded to the website. The URL the website is 284 https://labes.fmh.ulisboa.pt/projetos/a-decorrer/item/101-bia-international-database.

286 Overall Approach and Procedures

This is an ongoing project, soliciting collaboration among researchers for sharing BIA datasets with particular emphasis on low-income countries to complement the extensive data from high-income countries already received and published in the literature. All participants included in the final dataset have provided their consent to participate in the study conducted by each contributor, following the approval granted by the institution's ethics committee.

293 We will address the following steps:

294 Step 1: Building a large database of BIA raw and derived parameters, with the 295 following characteristics:

- Minimal BIA and associated data: age, sex, anthropometry (body mass and height), R, Xc, Z, and PhA, population, year of data collection, device characteristic (SF-BIA, MF-BIA / BIS), and health status.
- Additional data: segmental raw BIA measures (R, Xc, PhA, Z), for specific
 BIVA, arm, waist and calf circumferences, race and ethnicity (White, Black,
 Hispanic, Asian, Other), and geographic ancestry (Africa, America, Central South
 Asia, East Asia, Europe, Middle East, Oceania).

3. Desirable additional data: to explore links between BIA raw parameters and 303 other outcomes: other body composition data (e.g., dual-energy X-ray 304 absorptiometry- DXA total and regional estimates), physiological/metabolic data 305 (e.g., glucose, lipid, and protein metabolism, hormones), and physical function 306 307 (e.g., strength and physical performance), athletic status, education, socioeconomic and lifestyle characteristics (e.g., physical activity, diet). Specific 308 guidelines for preparing the database for providing these additional variables will 309 be detailed the website https://labes.fmh.ulisboa.pt/projetos/a-310 on decorrer/item/101-bia-international-database. 311

All data are de-identified, being either the data of partners or collaborators of the consortium, or open-access public use files from international databases (e.g., <u>NHANES</u>).

285

In order to integrate disparate and heterogeneous data, we will compare and harmonise 314 different acquisition technologies and operation procedures of BIA, including the 315 316 calibration and standardization of methods (data quality assessment) while also taking into consideration the position in which the exam was performed (i.e., standing, sitting, 317 and lying). The end result of this step will comprise information on representative groups 318 of children, adults, and elderly people; it will be a large and homogeneous database of 319 BIA raw and derived parameters, demographics, anthropometrics, and when available, 320 321 metabolic variables, education, lifestyle, and socio-economic information, performance-322 related information, and data on other body components such as those derived from DXA.

323 Step 2. Data Management

The data will be deposited at the research database at Lisbon. The site is interactive and contains the number and type of measurements made in any target country.

326 Regarding data security, all included datasets will be part of projects approved by the respective ethics committee of each research group. After confirmation of inclusion by 327 the management group, each individual in each database will be given a new code (related 328 to the current project) to further guarantee confidentiality and privacy. Hence, the 329 received databases have already codified data without any personal identifier, making the 330 331 data untraceable to the corresponding individual, and complying with the General Data Protection Regulation (GDPR) key requirements. Furthermore, all received data will be 332 converted into password protected files and stored at FMH server, with access limited to 333 the chairman of the management group, Analiza M Silva, or designated members. 334

Access to the whole or part of the database will be supervised, as authors aiming to use 335 336 the database must first obtain the approval by the management group, providing their 337 intended analysis (i.e., scope and aim of the analysis, the intended variables and sample characteristics, as well a list of authors and a brief chronogram) and assuring that rules of 338 privacy and data protection will be complied with. After following these steps, and if 339 accepted by the management group, a separate password-protected file will be generated 340 including the selected columns of interest. A detailed record will be created to monitor 341 342 this data-sharing process.

343 Step 3. Data Analysis

A short description of the types of data already available in the database is displayed in
Figure 2, including the geographical distribution of where the data was collected, the sex
and age distribution of the sample.

347 **INSERT FIGURE 2**

An overall description of the types of data available in the database can be also found on the website under the "data overview tab". A more comprehensive understanding of the database contents can be obtained by downloading the excel file example including details on the variables included in the main database.

So far, the database includes 277,922 measurements of children and adult male (n=59,450) and female measurements (n=218,472) aged between 11 months up to 102 years, mainly healthy. As an indication of the size of the database and the variability in the data it contains, **Figure 3** illustrates data from heathy individuals, stratified by sex and age (<18 and \ge 18 years) for the relationship between impedance index (cm²/kHz) and FFM (assessed by DXA).

358

INSERT FIGURE 3

The plots illustrated in Figure 3 show the strong association between impedance index and FFM assessed by DXA in both sexes and age categories, particularly in children, underscoring the relevance of the impedance index as an indicator of volume, though a large inter individual variability is observed in males and females among age categories.

363 Step 4. Data access

364 If the contributors wish to perform an analysis in the database several steps are required. Briefly, contributors should: i) Examine the list of planned analyses; ii) check out sample 365 data set to determine if there are sufficient data; iii) download and fill out a template form 366 with a succinct summary, including the variables from the dataset that will be required; 367 368 iv) agree up front to the publication policy and approve the manuscript within 21 days. The management group will discuss the idea and will provide feedback within 4 weeks 369 along with a form to be signed and returned. If the analysis is not performed within 18 370 371 months of approval the application will be removed from the planned analyses.

372 Step 5. Publication policy

The new knowledge provided by the BIA International database will be disseminated through scientific publications as a key performance indicator for academic partners, remaining a priority for the project, subject to intellectual property restrictions and the publication management model.

377 Individuals submitting data will be acknowledged as authors on publications from the database that use the data they contributed, allowing up to 2 authors per contributed 378 dataset. Manuscripts using the database must adhere to a number of rules that have been 379 agreed upon by the management group, including that draft manuscripts must be 380 approved by the management group, though the authors still maintain the authority and 381 ownership of their own dataset, allowing them to use their dataset for other purposes. This 382 may generate a large author list but follows the common practice in many multi-383 laboratory collaborations. 384

385

386 Discussion

This paper describes the BIA International Database goals, scope, and issues a "call for data". Through pooling BIA raw and derived population-based data from several countries, our consortium will be able to break new ground exploring human body composition variability and its potential associations with environment, lifestyle, socioeconomic factors, disease-related malnutrition, and sports-related outcomes, while also providing normative values for diagnostic purposes.

We anticipate the impact of this project in several different contexts. First, we expect to improve understanding of the factors that drive the individual variability evident in figure 3 plots. Evidence has been accumulating underlining the influence of the life cycle, sexual dimorphism, race and ethnicity, geographic ancestry, athletic and disease status ^{47, 48, 50,} ^{51, 55, 59, 60, 84, 85} on variability in raw BIA variables among populations. A comprehensive appreciation of these factors is required for a better understanding of the wide variability in body composition, with emphasis on regional and total fatness and SM.

Second, by providing a target to achieve a "healthier" body composition, this project will
 contribute to the design of appropriate lifestyle interventions, enabling personalised
 exercise or dietary interventions and improving optimal clinical decision making. For

instance, by proposing robust normative values for BIA-derived SM, cancer treatment
doses can be optimized and the benefits of chemotherapy maximized, as SM loss is
associated with an increased toxicity of chemotherapy and thus poorer prognosis ⁸⁶. Drug
clearance rates depend on body composition and, consequently, we expect that normative
values for BIA-derived body components may advance therapeutic options.
Individualized prevention of non-communicable diseases and risk factors may also
benefit from personalized data at the population level.

410 Third, this project will contribute to stimulating research, technology development and 411 innovation. The large database will contribute to strengthening of scientific knowledge and to the academic training of young researchers. This new knowledge will benefit the 412 research community by providing a simple and practical way of using quality data. 413 Additionally, the BIA International Database findings will contribute to developing 414 415 potential technological outputs, with benefits for a wide range of stakeholders, including fitness and sports fields, the healthcare system and the general public that can benefit 416 417 from potential applications of the findings into technological products and services.

Finally, we expect environmental and social impacts from this project. The social value 418 419 of the BIA international outputs is potentially substantial. The project will include and 420 analyse data from both high- and low-income populations, helping understand the social determinants of body composition variability 87. We look forward in particular to 421 422 receiving data from vulnerable populations in countries with weaker health systems and 423 those facing existing humanitarian crises, in order to identify new opportunities whereby 424 body composition assessment can aid in describing and combating the emerging double burden of malnutrition at the individual level ⁸⁸. More generally, the project provides a 425 426 new basis for personalized medicine, addressing age, race and ethnicity, geographic ancestry, disease-related malnutrition, environment, and socio-economic factors. This is 427 challenging across worldwide populations that are facing an obesity epidemic, related 428 429 non-communicable diseases and demographic changes due to e.g., ageing and migration. This contributes to healthier communities, enables informed disease prevention, 430 ultimately reducing healthcare costs that represents an increased proportion of overall 431 state spending. Nevertheless, we anticipate some limitations in the process of building the 432 dataset, as it is likely that the repository will lack representation from ethnic minorities 433 given the principles for indigenous data sovereignty and governance (https://www.gida-434

global.org/history-of-indigenous-data-sovereignty), as there are population groups for
whom the sharing of biometric data with overseas entities is difficult.

437

438 Conclusion

The goals, scope and procedures of the 'BIA International Database' project are described and we issue a "call for data". The consortium aims to pool raw and derived populationbased BIA data from multiple countries to enable analyses that capture the heterogeneity of the global population. We expect this project to provide a comprehensive integrated model of healthy body composition, clarify its wide variability, and contribute to developing and improving diagnostic tools.

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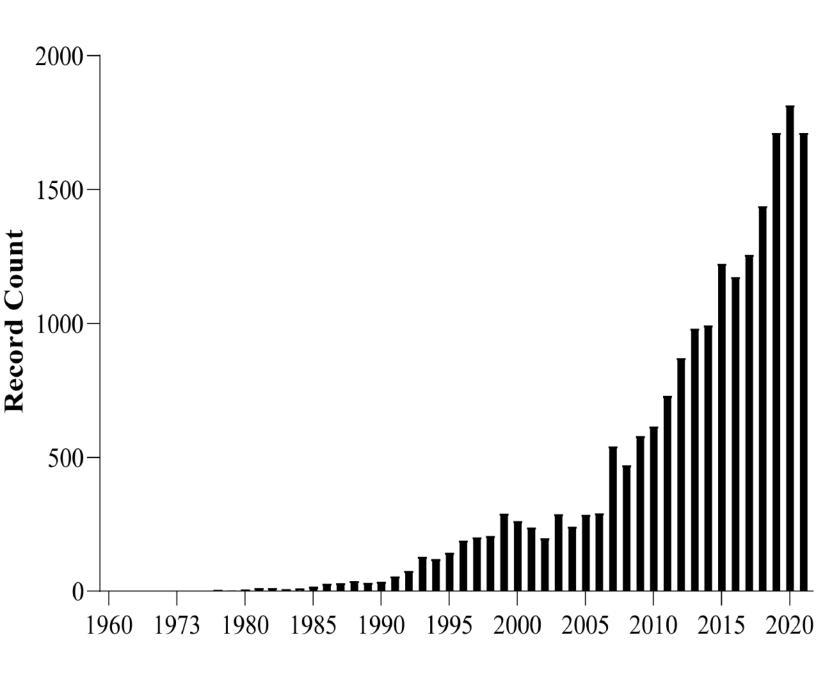
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893	Figure I agende
894	Figure Legends
895	Figure 1. ISI-indexed publications using bioelectrical impedance analysis.
896	Figure 2. Data collected by sex regarding age (A) and region (B).
897 898 899 900 901	Figure 3. Graphical representation of the relationship between impedance index (cm^2/kHz) and FFM (assessed by DXA), stratified by age and sex, in (A) female children and adolescents (<18 years, N=2190), (B) male children and adolescents (<18 years, N=3574), (C) female adults (\geq 18 years, N=4741), and (D) male adults (\geq 18 years, N=5205).

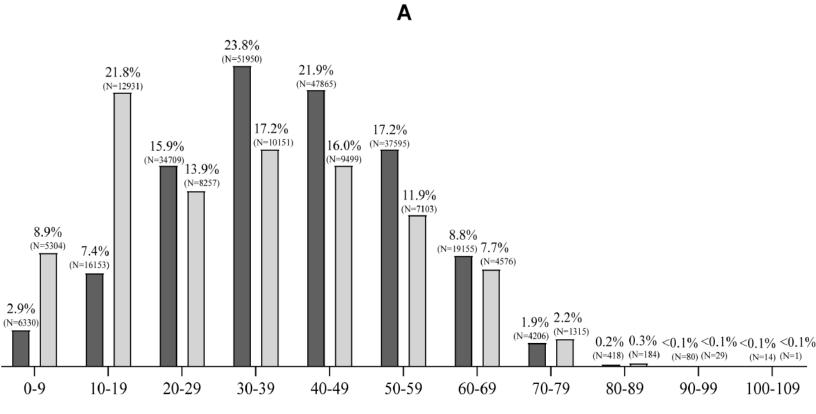
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