# How to estimate body composition in Huntington's disease. A cross-sectional, observational study using multiple frequencies bioimpedance

Jéssica Rivadeneyra-Posadas, Lucía Simón-Vicente, Daniel Castillo-Alvira, Javier Raya-González, María Soto-Celix, Alejandro Rodríguez-Fernández, Álvaro García-Bustillo, Miriam Saiz-Rodríguez, Fernando Vázquez-Sánchez, Laura Aguado-García, Gonzalo Gámez Leyva-Hernández, Esther Cubo, on behalf of the Domino-HD consortium

**Introduction.** Huntington´s disease (HD) is a rare neurodegenerative disorder. Reliable information about nutritional status, especially body composition from individuals with HD is critical for clinical care and research. The ease of application and portability of multiple frequencies bioelectrical impedance analysis (mfBIA) make it an attractive tool for measuring body composition, but its accuracy in HD is unknown.

**Aim.** To evaluate the accuracy of mfBIA vs. Dual X-ray absorptiometry (DEXA) in HD.

**Patients and methods.** Cross-sectional, observational, and single-center study. HD severity was measured using motor subscale of the unified Huntington´s disease rating scale (m-UHDRS) and the total functional capacity (TFC). Body composition was measured in terms of fat-free mass (FFM), fat mass (FM), fat-free mass index (FFMI), and fat mass index (FMI). Using Bland-Altman plots, we analyzed reliability between DEXA and mfBIA using the Intraclass Correlation Coefficient with 95% confidence intervals (CI) and bias estimates for all.

**Results.** We included 16 patients with HD, 7 men, and 9 women, median age of 58.5 (32;68) years, TFC: 10 (3;13), and m-UHDRS: 31 (7;85). The reliability between mfBIA and DEXA were high for FFMI in men: 0.88 (95% CI 0.17-0.98), and women: 0.90 (95% CI 0.61- 0.98); for FMI, men: 0.97 (95% CI 0.83-0.99), and women: 0.91 (95% CI 0.68-0.98). Compared to DEXA, mfBIA slightly overestimated FFM, FM, FMI and FFMI in men and underestimated FFMI in women.

**Conclusions.** mfBIA is an easy-to-use, safe, non-invasive, accurate method for measuring body composition and nutritional status in patients with mild-moderate HD.

**Key words.** Bioimpedance. Body composition. Dual X-ray absorptiometry. Fat free mass. Huntington´s disease. Total functional capacity.

## Introduction

Huntington's disease (HD) is an inherited neurodegenerative disorder characterized by choreiform movements, psychiatric problems, and dementia [1]. HD is caused by a cytosine-adenine-guanine (CAG) trinucleotide repeat expansion in the Huntingtin (*HTT*) gene on chromosome 4 with an autosomal dominant pattern [1]. The prevalence of HD has been estimated as 10,6 and 13,7/100,000 in Western populations [2], with an average age of onset commonly in mid-life.

HD is a complex disease with a broad impact on the lives of patients, families, and caregivers. Management of HD should be provided by a multidisciplinary approach, including pharmacological and non-pharmacological interventions. As the disease progresses, other symptoms, such as weight loss, skeletal muscle wasting, and cachexia, become relevant with a decline in quality of life, increased comorbidity, and risk for mortality [1]. On the contrary, maintaining weight seems beneficial to slow HD progression [3].

The cause of weight loss in HD is unknown, but the most likely contributing factors are sympathetic hyperactivity and the signaling provided by insulin, chorea, decreased food intake due to dysphagia, and intrinsic hypermetabolic state [4]. However, body weight or Body Mass Index does not capture the relative contributions of different tissues to weight loss in HD. In this regard, body composition defined as the percentage of muscle, fat and bone is considered the most reliable anthropometric measure [5]. In HD, body composition is characterized

Research Unit. Fundación Burgos por la Investigación de la Salud (J. Rivadeneyra-Posadas, L. Simón-Vicente, A. García-Bustillo, M. Sainz-Rodríguez). Servicio de Neurofisiología Clínica (F. Vázquez-Sánchez). Neurology Department. Hospital Universitario de Burgos (L. Aguado-García, G. Gámez Leyva-Hernández, E. Cubo). Health Sciences Department (L. Simón-Vicente, A. García-Bustillo, M. Sainz-Rodríguez, E. Cubo). Education Department. Universidad de Burgos (A. García-Bustillo). Health Sciences Department. Universidad Isabel I. Burgos (M. Soto-Celix). Sports performance assessment, physical activity and health and sports injuries. Universidad de Valladolid. Soria (D. Castillo-Alvira). Sport Science Department. Universidad de Extremadura. Cáceres (J. Raya-González). Internal Medicine Department. Hospital Reina Sofia. Tudela (M. Soto-Celix). VALFIS Investigation Group. Institute of Biomedicine. Department of Physical Activity and Sport Sciences. Universidad de León. León, Spain (A. Rodríguez-Fernández).

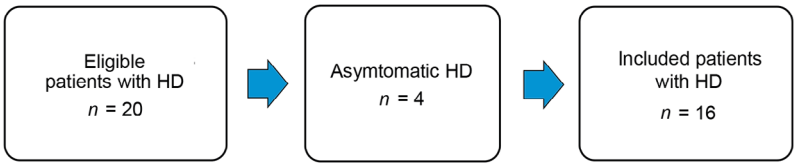
Correspondence:
Dr. Jéssica Rivadeneyra-Posadas.
Unidad de Investigación. Hospital Universitario de Burgos,
Avenida Islas Baleares, 3.
E-09006, Burgos.

E-mail:
jessicajrp@hubu.es

ORCID:
orcid.org/ 0000-0002-1725-5304 (J. R.P)

→

**Figure 1.** Analytical sample flow chart.




Acknowledgements:
We thank all the participants, their caregivers, and families who took part in 'Multi-Domain lifestyle targets for Improving Prognosis in Huntington's Disease (DOMINO-HD) Study Management Group', ENROLL study for providing the scientific platform, and all healthcare team of the Hospital Universitario de Burgos.

Accepted:
24.11.23.

Conflict of interest:
Los autores declaran no presentar conflictos de intereses.

How to cite this article:
Rivadeneyra-Posadas J, Simón-Vicente L, Castillo-Alvira D, Raya-González J, Soto-Celix M, Rodríguez-Fernández A, et al. How to estimate body composition in Huntington's disease. A cross-sectional, observational study using multiple frequencies bioimpedance. Rev Neurol 2024; 78: 17-25. doi: 10.33588/rn.7801.2023224.

*Versión española disponible en www.neurologia.com*



by reduced bone mineral density, fat mass, and lean tissue mass [6].

Different methods have been developed to determine body composition, including computed tomography, magnetic resonance, and spectroscopic imaging, classically considered the gold standard [7]. However, these can be expensive, require highly qualified personnel, and are not always available for routine clinical examination. Dual X-ray absorptiometry (DEXA) is a reliable alternative method for measuring body composition [8]. DEXA is a three-compartment model for body composition, including fat mass (FM), lean tissue mass, and bone mineral content measurement, using the transmission of high and low-energy X-rays through the body [5]. Overall, this equipment uses the X-ray beam energies which are attenuated during their passage through tissues. This attenuation is influenced by the intensity of energy and the density and thickness of human tissues. Low-density materials (i.e., soft tissues) allow more photons to pass through; thus, they attenuate the X-ray beam less than high-density materials such as bone [9]. However, although DEXA is a method that can be used in research, providing accurate estimates with a relatively low threshold of error measurement of 2-6% and low radiation exposure requires high technical skill and availability in healthcare settings.

An alternative procedure is the Bioimpedance (BIA). BIA measures the electrical properties of body tissue and uses a bi-compartment model, which partitions the body into FM and fat free mass (FFM) [10]. BIA is based on resistance caused by total water across the body to a small alternating current [11]. FM is considered a non-conductor of electric charge and is equal to the difference between body weight and FFM. FFM is considered the conducting volume that helps pass electric current due to the conductivity of electrolytes dissolved in body water. BIA uses three methods: single frequency, multiple frequencies (mfBIA), and bioimpedance spectroscopy (see supplementary file for more detailed information). Overall, mfBIA is considered more accessible for measuring body composition in research and daily clinical practice; it is easy to use, safe, non-invasive, relatively inexpensive, and portable [12].

Given the importance of measuring the nutritional status, especially body composition, this exploratory pilot study aimed to evaluate the accuracy of an eight electrode mfBIA vs. DEXA as the gold standard to measure body composition in symptomatic patients with HD.

## Material and methods

### Design

Cross-sectional, observational, and single-center design. We included a cohort of patients with HD from ENROLL, a prospective, multicenter, observational Registry Study in a Global HD Cohort [13] (Fig. 1). We carried out the study at the Hospital Universitario de Burgos and the Universidad Isabel I (ClinicalTrials.gov Identifier NCT05250323).

### Participants

We included a sample of symptomatic and ambulatory patients with a confirmed genetic mutation for HD with ≥36 CAG repeats in the *HTT* gene, who were able to walk with minimal support and had a total score on the motor subscale of the Unified Huntington Disease Rating Scale ≥4. All participants provided written informed consent. We excluded patients with diabetes mellitus on pharmacological treatment, thyroid disease, other neurodegenerative diseases, heart disease, pulmonary or skeletomuscular diseases, active cancer, and those who were pregnant or breastfeeding or on medication known to affect metabolism/endocrine function, and patients with pacemaker, electrical implants, metallic implants (except tooth implants), active prostheses or portable medical devices.

### Ethical considerations

This study was conducted according to the standards for Good Clinical Practice, the fundamental ethical principles established in the Declaration of Helsinki and the Oviedo Convention, and the requirements established in Spanish legislation in the research field. This project was approved by the ethics committee of the University Complex of Burgos y Soria (Certificate number: CEIM-2429, January 26th, 2021).

## Clinical and diet assessments

We collected sociodemographic information (gender and age), and disease severity using standardized HD assessment tools: m-UHDRS where low motor score denotes better performance; and Total Functional Capacity (TFC) [14]. TFC is derived from patients with HD and companion reports and quantifies a patient's ability to perform basic and instrumental activities (occupation, finances, housework, activities of daily living, and care level) ranging from 0 to 13, with higher scores indicating more intact functioning [14]. The severity of psychiatric symptoms was assessed using the Problems Behavior Assessment, in which higher scores indicates greater severity [15], and quality of life using the Short-Form Health Survey (SF-12), with higher scores indicating higher quality of life [16].

Dietary intake, including oral nutritional supplements or vitamin and mineral supplements, was collected by a trained nutritionist using a Spanish-validated food questionnaire of 'Seguimiento University of Navarra' (SUN) cohort study [17,18]. Food groups, macro-and micronutrients, and traditional Mediterranean diet (MeDi) adherence [19] were generated for each participant and processed by SUN team [20]. The MeDi adherence was obtained by adding the scores in the food categories (ranging 0-9) [19]; values 0-3 were considered low adherence, and values 4-9 were considered moderate/high adherence [21,22].

## Body composition and anthropometric measures

Body composition by DEXA was assessed using a Lunar Prodigy Primo model (General Electric Medical Systems Ultrasound & Primary Care Diagnostics, LLC, Madison, WI, USA). mfBIA was assessed using the Body Composition Analyzer Seca mBCA 525 (Hamburg, Germany), which uses eight electrodes. Impedance was measured with a current of 100 μA at frequencies of 1, 2, 5, 10, 20, 50, 100, 200, and 500 kHz and an impedance measuring range of 10 Ω to 1000 Ω. The following body composition measures were obtained: FM, FM Index (FMI) defined as FM/height$^2$ (kg/m$^2$), FFM was defined as lean mass plus the bone mineral content [23], and FFM Index (FFMI) defined as FFM/height$^2$ (kg/m$^2$).

We also collected other anthropometrics measurements, including weight, and height using brand electronic scale with height rod, nearest 0,01 kg and 0,1 cm, respectively (SECA, model 220, Hamburg, Germany); and waist circumference using a measuring tape, nearest 1 mm (SECA, model 201, Hamburg, Germany). Grip strength was assessed using a hand dynamometer, nearest 0,1 kg (JAMAR® PLUS+, WI, USA); and subscapular skin fold thickness using a caliper, nearest 0,2 mm (HOLTAIN, Crymych, UK). For BMI, we used the International WHO (World Health Organization) standards: <18,5 kg/m$^2$ underweight; 18,5-24,9 kg/m$^2$ normal; 25,0-29,9 kg/m$^2$ pre-obesity; 30,0-34,9 kg/m$^2$ obesity class I; 35,0-39,9 kg/m$^2$ obesity class II [24].

## Procedure

Participants were instructed not to intense exercise or drink alcohol within 12 and 24 hours respectively prior to the study visit, fast for 6-8 hours, to have an empty bladder and not to wear metal ornaments. Prior to the assessment participants rested for at least 10 minutes in the supine decubitus position. DEXA and mfBIA were performed on the same day. For DEXA assessment, participants were scanned in the decubitus supine position centered on the exam table (table pad), with their arms and legs placed along the sides of the body. The duration of measurement was 10 minutes. For mfBIA assessment, the position of the participants was also decubitus supine position (in the middle of the stretcher) with arms and legs placed at the sides of the body. The electrodes were placed on the hands (between the heads of the ulna and radius; in the middle of the joints, between the knuckle of the middle finger and the index finger), and the feet (between the heads of the tibia and fibula; and in the middle of the second and third finger joints). The average duration of the mfBIA assessment was 30 seconds.

## Statistical analysis

The Kolmogorov-Smirnov test was used to establish the normal distribution of the variables. Baseline characteristics were summarized using means and standard deviation or medians and interquartile ranges for continuous variables based on the normal distribution of the variables, and qualitative variables with percentages (%). All descriptive analyses were stratified by sex. The relationship between two quantitative variables of interest was examined using Spearman correlations ($r_s$), establishing high correlations ($r_s \geq 0,7$), moderate (0,4-0,69), and low (<0,4). To deal with missing values, we adopted case-wise deletions.

**Table I.** Baseline characteristics of the study population.

| | | Median (IQR) or *n* (%) | |
|---|---|---|---|
| | | Men (*n* = 7) | Women (*n* = 9) |
| Age (years) | | 63 (57-68) | 55 (32-61) |
| Age groups (years): | 29-40 | | 3 (33%) |
| | 41-50 | | 1 (11%) |
| | 51-60 | 2 (29%) | 4 (45%) |
| | 61-70 | 5 (71%) | 1 (11%) |
| BMI (kg/m$^2$)[a] | | 25.15 (20.83-27.95) | 23,39 (17.8-38.85) |
| BMI (groups) | Underweight (<18.5) | – | 1 (11%) |
| | Normal (18.5-24.9) | 3 (43%) | 5 (56%) |
| | Pre-obesity (25.0-29.9) | 4 (57%) | 2 (22%) |
| | Obesity class II (35.0-39.9) | | 1 (11%) |
| Calf circumferences (cm)[a] | | 32.40 (30.25-36.9) | 33.90 (28.15-40.3) |
| Waist circumferences (cm) | | 93.10 (80.5-105.2) | 73.63 (60.10-112.5) |
| Waist-to-hip ratio | | 0.97 (0.9-1.1) | 0.79 (0.7-0.9) |
| Grip strength (kg) | | 21.53 (18.3-35.8) | 12.7 (6.6-27) |
| Subscapular Skin fold thickness (mm)[a] | | 13.22 (10.9-19.9) | 14.07 (8.3-27.5) |
| Energy (kcal)[c] | | 4240.5 (2261.1-4828.4) | 3260.5 (2149.7-4241.6) |
| Protein (g)[a,c] | | 168.1 (87.5-194.3) | 128.91 (84.3-165.3) |
| Mediterranen Diet groups[d] [19,21,22]: | Low, *n* (%) | 1 (14) | 3 (34) |
| | Moderate-high, *n* (%) | 6 (86) | 5 (56) |
| Smoker, yes (%) | | 1 (14) | 2 (22) |
| Lipid lowering drugs intake, yes (%) | | 5 (71) | 3 (33) |
| Hypertension treatment, yes (%) | | 1 (14) | 2 (22) |
| Diabetes mellitus II, yes (%) | | 2 (29) | 0 |
| Comorbidity score[a] | | 2 (0-7) | 1 (0-4) |
| Intake of antichoreic drugs, yes (%)[a] | | 1 (14) | 0 (0) |
| Intake of anxiolytics/antidepressants drugs, yes (%)[a] | | 0 (0) | 0 (0) |
| UHDRS total motor score[a,b] | | 39.5 (26-44) | 23 (7-85) |
| Total functional capacity score[a] | | 9.5 (6-13) | 12 (3-13) |
| Problem behaviours assessment score[a] | | 1.5 (0-22) | 2 (0-44) |
| Short-Form Health Survey physical score[a] | | 49.15 (41.88-53.83) | 50.48 (0-55.47) |
| Short-Form Health Survey mental score[a] | | 60.55 (46.57-63.19) | 52.48 (23.5-65) |

[a] $p > 0,05$ Mann-Whitney Test: there are no significant differences in the distribution of the data; [b] Motor subscale of the unified Huntington´s disease ranting scale; [c] Base don the food intake queationnaire of the University of Navarra Follow-up study; [d] Women *n* = 8.

We analyzed the reliability between DEXA and mfBIA using the Intraclass Correlation Coefficient (ICC) estimates and their 95% confidence intervals based on absolute agreement and the two-way random-effects model. ICC values below 0,5 indicate poor reliability, between 0,5 and 0,75 moderate reliability, 0,75 and 0,9 good reliability, and excellent reliability with values >0,9 [25]. We performed Bland-Altman plots for bias assessment of FFM, FM, FFMI, and FMI.

All statistical analyses were conducted using IBM SPSS statistics for Windows, version 21.0, released 2012 (Armonk, NY: IBM Corp.) and Stata statistical software, version 15 (StataCorp. 2017, College Station, TX: StataCorp LLC.). A $p$-value < 0,05 (two-sided) was considered statistically significant.

## Results

### Sample characteristics

We included 16 Caucasian patients with HD, 7 men (44%), and 9 women (56%), with a median age of 58,5 (32-68) years, TFC: 10 (3-13), m-UHDRS: 31 (7-85), SF-12, physical subdomain: 50.21 (0-55.5), and SF-12 mental subdomain: 55,44 (23,49-65,0). According to the BMI, 56% of women had normal BMI, and 57% of men were in the pre-obesity stages. Compared to men, women were younger and had lower adherence to MeDi (Table I). As expected, compared to men, women had decreased waist circumference, waist-to-hip ratio, grip strength, and energy intake (Table I).

### Body composition parameters

When DEXA was compared to mfBIA, similar data distribution assessments were obtained for weight, FFM, FM, FFMI, and FMI between men and women (Fig. 2).

On the other hand, there were strong correlations between the lean mass (of the legs right and left and torso) compared with skeletal muscle mass in women and males (DEXA *vs* mfBIA respectively), and moderate to excellent agreement between mfBIA and DEXA for weight, FFM, FM, FFMI, and FMI, between men and women (Table II). However, mfBIA slightly overestimated FFM, FM, FMI, and FFMI in men but underestimated FFMI in women compared to DEXA (Fig. 3).

When the data was distributed in terms of BMI groups (Table III), mfBIA overestimated FFM in

men and women, with a difference of 1,17 ± 1,12kg (normal BMI group), 0,72 ± 0,65kg (pre-obesity BMI group) in men; and with a difference of 0,47 ± 0,78kg (normal BMI group), and –2,89 ± 2,47kg (pre-obesity BMI group) in women. Likewise, mfBIA underestimated FM with a difference of –0,73 ± 1,53kg (normal BMI group), overestimated FM with a difference of 0,81 ± 1,26kg (pre-obesity BMI group) in men, and overestimated FM with a difference of 0,32 ± 0,71kg (normal BMI group), and 8,09 ± 8,86kg (pre-obesity BMI group) in women.

## Discussion

There is a high demand for multidisciplinary care for patients with HD, representing a patient-centered approach to optimize the management and quality of life. Body composition is part of the nutritional assessment and monitoring of a range of medical conditions and physiological processes [8,26]. New scientific and clinical insights emphasize the importance of determining body composition as a prime indicator of nutritional and sarcopenia status to prevent physical performance deterioration and frailty [27]. According to literature review, this is the first study comparing two commonly used body composition methods, DEXA and mfBIA in patients with HD.

Our results showed that mfBIA provided accurate information compared to DEXA with good to excellent reliability. In other studies, male participants have more FFM and FFMI than females by mfBIA [28], especially in the older participants. In contrast, compared to DEXA, in healthy subjects, age, and sex seem not to contribute to the variance of FFM and lean tissue mass using mfBIA [29]. However, mfBIA overestimated FFM, FM, and FMI and slightly underestimated FFMI compared to DEXA, similar to bioimpedance spectroscopy in neuromuscular diseases [30].

In non-dialysis patients with chronic kidney disease, compared to DEXA, spectroscopy bioimpedance overestimated FFM, but underestimated FM [31], in contrast to the results obtained in an elderly cohort of Caucasian participants, where mfBIA underestimated lean body mass and overestimated FM [32]. In order to explain these contradictory results, we hypothesize different possibilities, including the BIA equipment differences (single frequency, most widely used vs. multiple frequencies), different manufacturer equations; electrode placement [33], ethnicity, body weight [34], and the in-

**Figure 2.** Data distribution of fat free mass (a), fat mass (b), fat free mass index (c), and fat mass index (D) between men and women according to DEXA and mfBIA.

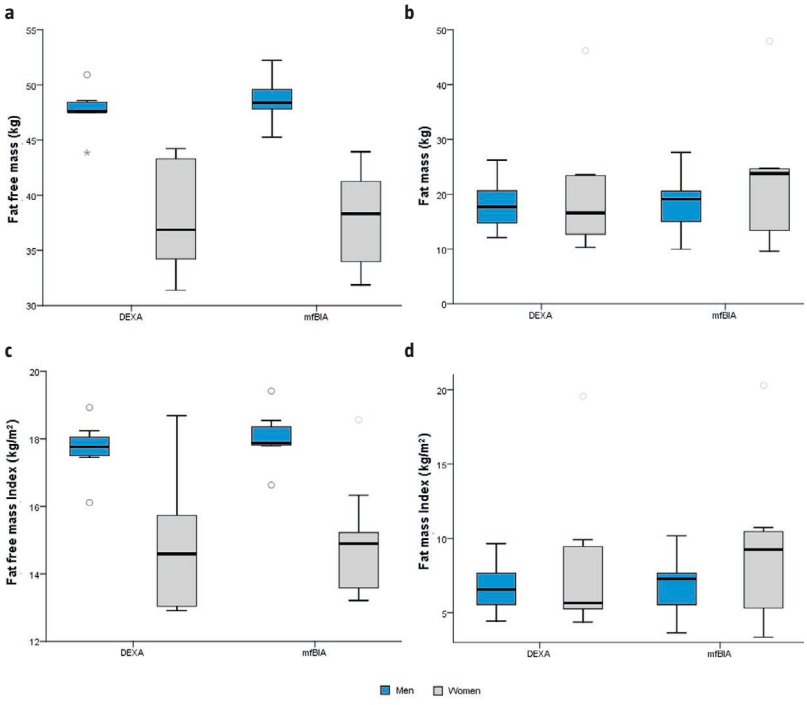
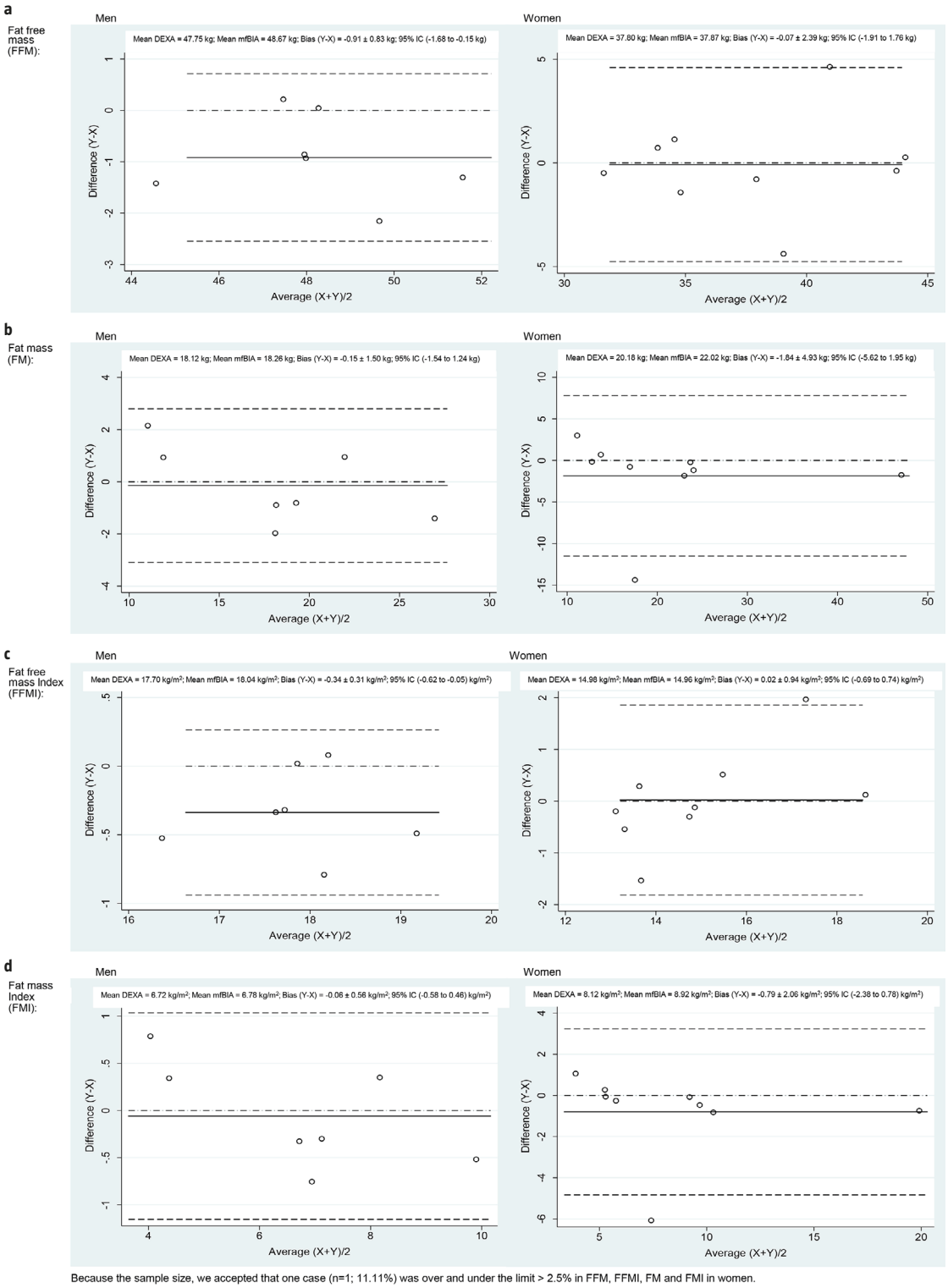



**Table II.** Body composition parameters (median, IQR) [a] by DEXA and mfBIA.

| | Men (*n* = 7) | | | Women (*n* = 9) | | |
|---|---|---|---|---|---|---|
| | DEXA | mfBIA | ICC[b] with 95% CI | DEXA | mfBIA | ICC[b] with 95% CI |
| Weight (kg) | 67.5 (57.6-75.5) | 66.8 (56.7-76.1) | 0.99 (0.95-0.99) | 58.1 (45-91.2) | 58.1 (44.7-91.9) | 0.98 (0.91-0.99) |
| Fat free mass (kg) | 47.6 (43.9-50.9) | 48.4 (45.3-52.2) | 0.86 (0.14-0.97) | 36.9 (31.4-44.2) | 38.3 (31.9-43.9) | 0.88 (0.55-0.97) |
| Fat mass (kg) | 17.7 (12.1-26.2) | 19.1 (9.9-27.6) | 0.97 (0.83-0.99) | 16.6 (10.3-46.2) | 23.8 (9.6-47.9) | 0.9 (0.65-0.98) |
| Fat free mass index (kg/m²) | 17.8 (16.1-18.9) | 17.9 (16.6-19.4) | 0.88 (0.17-0.98) | 14.6 (12.9-18.7) | 14.9 (12.9-18.7) | 0.9 (0.61-0.98) |
| Fat mass index (kg/m²) | 6.6 (4.4-9.6) | 7.3 (3.6-10.2) | 0.97 (0.83-0.99) | 5.6 (4.4-19.5) | 9.2 (3.4-20.3) | 0.91 (0.68-0.98) |

[a] $p > 0,05$ Mann-Whitney Test: there are no significant differences in the data distribution. [b] Intraclass correlation coefficient (ICC) values were calculated using a two-way random-effects model with absolute agreement and 95% Confidence Intervals (CI). All $p$ values were < 0.0001.

**Figure 3.** Bland-Alman Agreement of fat free mass (a), fat mass (b), fat free mass index (c), and fat mass index (d) between men and women according to DEXA and mfBIA.




Because the sample size, we accepted that one case (n=1; 11.11%) was over and under the limit > 2.5% in FFM, FFMI, FM and FMI in women.

**Table III.** Fat free mass and fat mass from mfBIA and DEXA by gender and BMI (all values as mean ± SD).

| | Fat free mass (kg) | | | Fat mass (kg) | | |
|---|---|---|---|---|---|---|
| | mfBIA | DEXA | Difference[a] | mfBIA | DEXA | Difference[a] |
| **Men (*n* = 7)** | 48.67 ± 2.25 | 47.75 ± 2.09 | 0.91 ± 0.83 | 18.27 ± 6.01 | 18.12 ± 5.09 | 1.15 ± 1.5 |
| Normal BMI (*n* = 3) | 48.09 ± 2.74 | 46.91 ± 2.66 | 1.17 ± 1.12 | 13.33 ± 4.62 | 14.06 ± 3.16 | –0.73 ± 1.53 |
| Pre-obesity BMI (*n* = 4) | 49.1 ± 2.14 | 48.38 ± 1.69 | 0.72 ± 0.65 | 21.97 ± 3.92 | 21.17 ± 4.05 | 0.81 ± 1.26 |
| **Women (*n* = 9)** | 37.88 ± 4.49 | 37.8 ± 4.74 | 0.07 ± 2.39 | 22.02 ± 11.34 | 20.18 ± 10.97 | 1.84 ± 4.93 |
| Underweight (*n* = 1) | 41.24 | 36.86 | 4.38 | 9.61 | 12.62 | –3.01 |
| Normal BMI (*n* = 5) | 36.61 ± 4.73 | 36.15 ± 4.66 | 0.47 ± 0.78 | 18.39 ± 5.58 | 18.07 ± 5.15 | 0.32 ± 0.71 |
| Pre-obesity BMI (*n* = 2) | 36.31 ± 3.3 | 39.2 ± 5.77 | –2.89 ± 2.47 | 24.31 ± 0.56 | 16.22 ± 8.31 | 8.09 ± 8.86 |
| Obesity class II BMI (*n* = 1) | 43.94 | 44.22 | –0.28 | 47.96 | 46.21 | 1.75 |

BMI: < 18.5, underweight; 18,5-24,9, normal; 25,0-29,9, pre-obesity; 30,0-34,9, obesity class I; 35,0-39,9, obesity class II. BMI: body mass index; mfBIA: multiple-frequency biolectrical impedance analysis; DEXA: dual x-ray absorptiometry; SD: standard deviation. [a] Difference = mfBIA minus DEXA measurements.

fluence of other factors such as limbs length, intrinsic blood chemistry, and women ovulation [5,35].

This study used DEXA as a reliable, commonly used alternative method for measuring body composition [8]. Supporting the use of DEXA as the gold standard, previous studies have shown a very high agreement of FM between DEXA and computed tomography [36], and an excellent repeatability range 1-2% for FM and 0,5-2% for lean mass [37]. We are aware that our findings should be interpreted with caution. We have collected cross-sectional data, including a small sample of HD patients with a wide range of BMI. However, the strength of this study is its uniqueness and applicability for multidisciplinary care in HD. This is the first study, establishing the reliability of mfBIA in HD, including high-quality data obtained by nutritionists with high experience in HD and mfBIA, and HD-certified neurologists.

## Future directions and conclusions

Obtaining reliable longitudinal information about nutritional status specially body composition from individuals with HD is critical for high-quality clinical care and research. Our study showed preliminary findings of good-excellent reliability between DEXA and mfBIA, suggesting that these two measurements for measuring body composition are interchangeable in patients with mild-moderate HD. Follow-up studies should be conducted to accurately evaluate disease progression and body composition.

Whit the preliminary results of this study, we hope to provide the rationality for quantifying body composition as a biomarker for disease progression with the subsequent development of nutritional strategies and interventions, to prevent disability and comorbidities in HD. We expect the results of this study will facilitate the generation of new hypotheses, but further longitudinal studies conducted in larger samples are required to confirm these preliminary findings.

### References

1. Ghosh R, Tabrizi SJ. Clinical features of Huntington's disease. Adv Exp Med Biol 2018; 1049: 1-28.
2. McColgan P, Tabrizi SJ. Huntington's disease: a clinical review. Eur J Neurol 2018; 25: 24-34.
3. Myers RH, Sax DS, Kiely DK, Mastromauro C, Cupples LA, Kiely DK, et al. Factors associated with slow progression in Huntington's disease. Arch Neurol 1991; 48: 800-4.

4. Cubo E, Rivadeneyra J, Mariscal N, Martinez A, Armesto D, Camara RJ. Factors associated with low body mass index in Huntington's disease: a Spanish multicenter study of the european huntington's disease registry. Mov Disord Clin Pract 2016; 3: 452-9.
5. Kuriyan R. Body composition techniques. Indian J Med Res 2018; 148: 648-58.
6. Costa de Miranda R, di Lorenzo N, Andreoli A, Romano L, De Santis GL, Gualtieri P, et al. Body composition and bone mineral density in Huntington's disease. Nutrition 2019; 59: 145-9.
7. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019; 48: 16-31.
8. Lorente-Ramos RM, Azpeitia-Armán J, Arévalo-Galeano N, Muñoz-Hernández A, García-Gómez JM, Gredilla-Molinero J. Dual energy X-ray absorptimetry: fundamentals, methodology, and clinical applications. Radiologia 2012; 54: 410-23.
9. Bazzocchi A, Ponti F, Albisinni U, Battista G, Guglielmi G. DEXA: technical aspects and application. Eur J Radiol 2016; 85: 1481-92.
10. Fosbøl MO, Zerahn B. Contemporary methods of body composition measurement. Clin Physiol Funct Imaging 2015; 35: 81-97.
11. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. Sensors (Basel) 2014; 14: 10895-928.
12. Kyle UG, Bosaeus I, de Lorenzo AD, Deurenberg P, Elia M, Manuel Gómez J, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. Clin Nutr 2004; 23: 1430-53.
13. Landwehrmeyer GB, Fitzer-Attas CJ, Giuliano JD, Gonçalves N, Anderson KE, Cardoso F, et al. Data analytics from Enroll-HD, a global clinical research platform for Huntington's disease. Mov Disord Clin Pract 2016; 4: 212-24.
14. Kieburtz K. Unified Huntington's Disease Rating Scale: reliability and consistency. Huntington Study Group. Mov Disord 1996; 11: 136-42.
15. Kingma EM, van Duijn E, Timman R, van der Mast RC, Roos RAC. Behavioural problems in Huntington's disease using the Problem Behaviours Assessment. Gen Hosp Psychiatry 2008; 30: 155-61.
16. Ware JE, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34: 220-33.
17. Martin-Moreno JM, Boyle P, Gorgojo L, Maisonneuve P, Fernandez-Rodriguez JC, Salvini S, et al. Development and validation of a food frequency questionnaire in Spain. Int J Epidemiol 1993; 22: 512-9.
18. Martínez-González A. The SUN cohort study (Seguimiento University of Navarra). Public Health Nutr 2006; 9: 127-31.
19. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med 2003; 348: 2599-608.
20. Carlos S, de La Fuente-Arrillaga C, Bes-Rastrollo M, Razquin C, Rico-Campà A, Martínez-González MA, et al. Mediterranean diet and health outcomes in the SUN cohort. Nutrients 2018; 10: 439.
21. De La Fuente-Arrillaga C, Vazquez Ruiz Z, Bes-Rastrollo M, Sampson L, Martinez-González MA. Reproducibility of an FFQ validated in Spain. Public Health Nutr 2010; 13: 1364-72.
22. Rivadeneyra J, Cubo E, Gil C, Calvo S, Mariscal N, Martínez A. Factors associated with Mediterranean diet adherence in Huntington's disease. Clin Nutr ESPEN 2016; 12: e7-13.
23. Pietrobelli A, Formica C, Wang Z, Heymsfield SB. Dual-energy X-ray absorptiometry body composition model: review of physical concepts. Am J Physiol 1996; 271: e941-51.
24. World Health Organization (WHO). A healthy lifestyle - WHO recommendations. URL: https: //www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recomendations. Fecha última consulta: 15.06.2022.
25. Cicchetti DV. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. Psychol Assess 1994; 6: 284-90.
26. Mazzoccoli G. Body composition: where and when. Eur J Radiol 2016; 85: 1456-60.
27. Tagliafico AS, Bignotti B, Torri L, Rossi F. Sarcopenia: how to measure, when and why. Radiologia Medica 2022; 127: 228-37.
28. Kirchengast S. Gender differences in body composition from childhood to old age: an evolutionary point of view. Kamla Raj Enterprises 2017; 2: 1-10.
29. Malavolti M, Mussi C, Poli M, Fantuzzi AL, Salvioli G, Battistini N, et al. Cross-calibration of eight-polar bioelectrical impedance analysis versus dual-energy X-ray absorptiometry for the assessment of total and appendicular body composition in healthy subjects aged 21-82 years. Ann Hum Biol 2003; 30: 380-91.
30. Ellegård L, Aldenbratt A, Svensson MK, Lindberg C. Body composition in patients with primary neuromuscular disease assessed by dual energy X-ray absorptiometry (DEXA) and three different bioimpedance devices. Clin Nutr ESPEN 2019; 29: 142-8.
31. Zhou Y, Höglund P, Clyne N. Comparison of DEXA and bioimpedance for body composition measurements in nondialysis patients with CKD. J Ren Nutr 2019; 29: 33-8.
32. Ling CHY, de Craen AJM, Slagboom PE, Gunn DA, Stokkel MP, Westendorp RG, et al. Accuracy of direct segmental multi-frequency bioimpedance analysis in the assessment of total body and segmental body composition in middle-aged adult population. Clin Nutr 2011; 30: 610-5.
33. Bioelectrical impedance analysis in body composition measurement: National Institutes of Health Technology Assessment Conference Statement (1996). Am J Clin Nutr 64 (3 Suppl): S524-32.
34. Achamrah N, Colange G, Delay J, Rimbert A, Folope V, Petit A, et al. Comparison of body composition assessment by DEXA and BIA according to the body mass index: a retrospective study on 3655 measures. PLoS One 2018; 13: e200465.
35. Stahn A, Terblanche E, Gunga HC. Use of biolectrical impedance: general principles and overview. In Predy VR, ed. Handbook of anthropometry: physical measures of human form in health and disease. New York: Springer; 2012. p. 49-90.
36. Kullberg J, Brandberg J, Angelhed JE, Frimmel H, Bergelin E, Strid L, et al. Whole-body adipose tissue analysis: comparison of MRI, CT and dual energy X-ray absorptiometry. Br J Radiol 2009; 82: 123-30.
37. Borga M, West J, Bell JD, Harvey NC, Romu T, Heymsfield SB, et al. Advanced body composition assessment: from body mass index to body composition profiling. J Investig Med 2018; 66: 887-95.

**Annex.** Methods of bioimpedance.

BIA uses three methods:

1.- Single frequency: Use a frequency of 50 kHz electric current, as if the human body is a single cylinder with constant resistivity [1], and is based on the inverse proportion between assessed impedance and total body water. It estimates total body water but shows limitations in assessing intracellular fluid [2].

2.- Multiple frequencies (mfBIA): Use more than two frequencies, recognizing that the human body has five heterogenous cylinders (two arms, trunk, and two legs) with different resistivities [3,4]. MfBIA is based on the finding that the extracellular fluid and total body water can be assessed by exposing it to low and high frequency electric currents [5] in a range between 1-1000 kHz and has a high precision of posture and contact to electrodes [4].

3.- Bioimpedance spectroscopy: Uses a broad band of frequencies and is based on the determination of resistance at zero frequency and resistance at infinity frequency to predict extracellular fluid and total body water, respectively [2,6].

### References


1. Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 1985; 41: 810-7.
2. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. Sensors (Basel) 2014; 14: 10895-928.
3. Organ LW, Bradham GB, Gore DT, Lozier SL. Segmental bioelectrical impedance analysis: theory and application of a new technique. J Appl Physiol (1985) 1994; 77: 98-112.
4. Bosy-Westphal A, Schautz B, Later W, Kehayias JJ, Gallagher D, Müller MJ. What makes a BIA equation unique? Validity of eight-electrode multifrequency BIA to estimate body composition in a healthy adult population. Eur J Clin Nutr 2013; 67 (Suppl 1): S14-21.
5. Jaffrin MY, Morel H. Body fluid volumes measurements by impedance: a review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. Med Eng Phys 2008; 30: 1257-69.
6. Smith S, Madden AM. Body composition and functional assessment of nutritional status in adults: a narrative review of imaging, impedance, strength and functional techniques. J Hum Nutr Diet 2016; 29: 714-32.


## Cómo estimar la composición corporal en la enfermedad de Huntington. Estudio transversal y observacional con bioimpedancia de múltiples frecuencias


**Introducción.** La enfermedad de Huntington (EH) es un trastorno raro neurodegenerativo. La información fiable del estado nutricional, especialmente de la composición corporal, es crítica en clínica y en investigación. La facilidad de aplicación y portabilidad del análisis de la bioimpedancia de múltiples frecuencias (mfBIA) la convierten en una herramienta atractiva para medirla, pero se desconoce su precisión en la EH.

**Objetivo.** Evaluar la precisión del mfBIA frente a la absorciometría dual de rayos X (DEXA) en la EH.

**Pacientes y métodos.** Estudio transversal, observacional y unicéntrico. La EH se midió con la subescala motora de la escala unificada de valoración de la EH y con la capacidad funcional total. La composición corporal se valoró según la masa libre de grasa (MLG), la masa grasa (MG), el índice de masa libre de grasa (IMLG) y el índice de masa grasa (IMG). Se utilizó el coeficiente de correlación intraclase con intervalos de confianza al 95% y estimaciones de sesgo mediante gráficos de Bland-Altman.

**Resultados.** Se incluyó a 16 pacientes, siete hombres y nueve mujeres, con edad media de 58,5 (32-68) años, capacidad funcional total de 10 (3-13) y escala unificada de valoración de la EH de 31 (7-85). La fiabilidad era alta entre el mfBIA y la DEXA para el IMLG en hombres, 0,88 (intervalo de confianza al 95%: 0,17-0,98), y mujeres, 0,9 (intervalo de confianza al 95%: 0,61-0,98); y para el IMG en hombres, 0,97 (intervalo de confianza al 95%: 0,83-0,99), y mujeres, 0,91 (intervalo de confianza al 95%: 0,68-0,98). El mfBIA sobreestimó ligeramente la MLG, la MG, el IMG y el IMLG en los hombres, pero subestimó el IMLG en las mujeres.

**Conclusiones.** El mfBIA es un método fácil de usar, seguro, no invasivo y preciso para medir la composición corporal y el estado nutricional en pacientes con EH leve-moderada.



**Palabras clave.** Absorciometría dual de rayos X. Bioimpedancia. Capacidad funcional total. Composición corporal. Enfermedad de Huntington. Masa libre de grasa.