

## Original

# Comparison of bioelectrical impedance with skinfold thickness and x-ray absorptiometry to measure body composition in HIV-infected with lipodystrophy

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### Abstract

**Introduction:** Human immunodeficiency virus (HIV)-associated lipodystrophy syndrome (LS) includes body composition and metabolic alterations. Lack of validated criteria and tools make difficult to evaluate body composition in this group.

**Objective:** The aim of the study was to compare different methods to evaluate body composition between Brazilians HIV subjects with (HIV+LIPO+) or without LS (HIV+LIPO-) and healthy subjects (Control).

**Methods:** in a cross-sectional analyses, body composition was measured by bioelectrical impedance analysis (BIA), skinfold thickness (SF) and dual-energy x-ray absorptiometry (DXA) in 10 subjects from HIV+LIPO+ group; 22 subjects from HIV+LIPO- group and 12 from Control group.

**Results:** There were no differences in age and body mass index (BMI) between groups. The fat mass (FM) (%) estimated by SF did not correlate with DXA in HIV+LIPO+ group ( $r = 0,46 / p > 0,05$ ) and had fair agreement in both HIV groups (HIV+LIPO+ = 0,35/ HIV+LIPO- = 0,40). BIA had significant correlation in all groups ( $p < 0,05$ ) and strong agreement, meanly in HIV groups, for FM (HIV+LIPO+ = 0,79/ HIV+LIPO- = 0,85 / Control = 0,60) and for fat free mass (FFM) (HIV+LIPO+ = 0,93 / HIV+LIPO- = 0,92 / Control = 0,73).

**Discussion:** Total fat mass can be measured by BIA with good precision, but not by SF in HIV-infected patients with LS. Segmental BIA, tripartal SF, circumferences of arms, waist and legs maybe alternatives that need more studies.

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Key words: *Electric impedance. Body composition. HIV-associated lipodystrophy syndrome. Photon absorptiometry.*

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### COMPARACIÓN DE IMPENDANCIA BIOELÉCTRICA CON GROSOR DE PLIEGUES CUTÁNEOS Y ABSORCIOMETRÍA DE RAYOS X PARA MENSURAR LA COMPOSICIÓN CORPORAL DE PERSONAS CON VIH CON LIPODISTROFIA

### Resumen

**Introducción:** El síndrome de lipodistrofia (SL) asociado al virus de inmunodeficiencia humana (HIV) incluye alteraciones en la composición corporal y metabólica. La falta de herramientas adecuadas y criterios válidos dificultan la evaluación de la composición corporal en este grupo.

**Objetivo:** El objetivo del estudio fue comparar distintos métodos para evaluar la composición corporal entre individuos brasileños con HIV que tenían (HIV+LIPO+) o no LS (HIV+LIPO-) e individuos sanos (control).

**Métodos:** Estudio transversal en el que fue evaluada la composición corporal por análisis de impedancia bioeléctrica (BIA), pliegues cutáneos (SF) y absorciometría de rayos X de doble energía (DXA) en un grupo de 10 individuos con HIV+LIPO+, 22 individuos del grupo HIV+LIPO- y 12 individuos del grupo control.

**Resultados:** No hubo diferencias en la edad e índice de masa corporal (IMC) entre grupos. La masa grasa (MG) (%) estimada por SF no se correlacionó con DXA en pacientes del grupo HIV+LIPO+ ( $r = 0,46 / p > 0,05$ ) y había leve concordancia en ambos grupos con HIV (HIV+LIPO+ = 0,35/ HIV+LIPO- = 0,40). BIA tuvo una correlación significativa en todos los grupos ( $p < 0,05$ ) y fuerte acuerdo, principalmente en grupos HIV para MG (HIV+LIPO+ = 0,79 / HIV+LIPO- = 0,85 / Control = 0,60) y para la masa libre de grasa (HIV+LIPO+ = 0,93/ HIV+LIPO- = 0,92 / Control = 0,73).

**Discusión:** La masa grasa total puede ser medida por BIA con precisión, pero no por SF en los individuos con HIV y LS. BIA segmentaria, SF del tríceps, circunferencia de brazos, cintura y piernas, pueden ser alternativas que necesiten más estudios.

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Palabras clave: *Bioimpedancia eléctrica. Composición corporal. VIH. Lipodistrofia. Absorciometría de rayos X de energía dual.*

## Abbreviations

HIV-1: Human immunodeficiency virus 1.

LS: Lipodystrophy syndrome.

BIA: Bioelectrical impedance.

SF: Skinfold thickness.

DXA: Dual-energy x-ray absorptiometry.

BMI: Body mass index.

FM: Fat mass.

FFM: Fat free mass.

HAART: Highly active antiretroviral therapy.

WC: Waist circumference.

MAC: Mid-arm muscle circumference.

## Introduction

Aids had killed million of people since its discovery in 1981. The global percentage of people living with HIV-1 have been stabilizing.<sup>1</sup> Brazil doesn't differ from this scenario, with a prevalence of 0,6%, in 2007 and showing stabilization in various states such as São Paulo.<sup>2</sup>

The dramatic improvement on life expectancy was, in great part, due to highly active antiretroviral therapy (HAART), however side effects were soon recognized, including changes in body fat distribution and metabolic disturbances.<sup>3</sup> Together, these abnormalities comprise LS.<sup>4,5</sup>

The body composition of HIV-infected patients had changed along the history, in the past it was common to observe cachectic individuals, preferentially, with lost of lean mass instead of FM and now we verify lost of fat mass with similar more than lean mass.<sup>6</sup> The LS is characterized by combinations of lipoatrophy (subcutaneous fat depletion in the face, arms, legs and buttocks) and/or lipohypertrophy (accumulation of fat in the abdomen, cervical and dorsocervical area, visceral and the breast).<sup>7</sup>

Until this moment, there is a lack of validated diagnostic criteria and tools are unsatisfactory for clinical care and for research in LS. The body fat redistribution is typically identified by physical examination and self report. A variety of techniques have been used to assess body composition such as anthropometry, BIA, DXA, computed tomography, magnetic resonance imaging and ultrasonography.<sup>8</sup>

DXA, computed tomography and magnetic resonance imaging are considered accurate methods for estimating body FM in HIV-infected patients but cannot be used routinely, because of expenses and need for experienced technicians.<sup>9</sup> BIA and anthropometry are two inexpensive bedside techniques that are widely used in clinical practice and could be an alternative<sup>10</sup>. The aim of this study was to compare estimates of body FM and FFM by BIA and SF measurements with values obtained from DXA.

## Methods

### *Study population*

A cross-sectional study to compare body composition and metabolic abnormalities was conducted in Medical School Hospital at University of São Paulo, Brazil between august 2007 and march 2008. This study was approved by the Ethical Committee and all volunteers gave their written informed consent.

The subjects were divided into three groups: HIV-infected men undergoing HAART with LS (HIV+LIPO+); HIV-infected men undergoing HAART without LS (HIV+LIPO-) and healthy men (Control).

Patients were included if they were male, had more than 18 years of age, with stable weight (10% of variation in the last 6 months), body mass index between 18.5 kg/m<sup>2</sup> and 30 kg/m<sup>2</sup>. Patients were excluded if they were in use of glucocorticoids in the last year and if they had serious alteration in cardiac, lung, liver, kidney or thyroid function.

Control group was recruited from Hospital employees. All HIV-infected patients were recruited from the infection disease ambulatory. They were included if they were receiving HAART for at least 6 months, free of acute AIDS-related events and with a CD4 count more than 200 copies/mm<sup>3</sup>.

### *Criteria for the lipodystrophy syndrome*

HIV-infected men were included in the group with lipodystrophy (HIV+LIPO+) if the lost of subcutaneous fat was detected (arms, legs or face) by the same investigator and self reported by the patient. The subjective definition includes only lipoatrophy and the patients could have or not lipohypertrophy together.<sup>11</sup>

### *Biochemical parameters*

CD4 count was done by flow cytometry (FacsCalibur®) and viral load determination assay with detection of 50 copies/ml plasma by branched DNA test, using Quantiplex bDNA® of Siemens.

### *Anthropometry*

Anthropometric measurements were performed in all patients by the same trained dietitian. BMI was calculated from the height and weight values. Body circumferences and SF at biceps, triceps, subscapular and suprailiac were measured to the nearest 0.2 mm in standing position using a Lang SF caliper® (Cambridge Scientific Industries, Cambridge, MA) according to the standard techniques.<sup>12</sup> Measurements were obtained by the mean of 3 determinations taken on right side of the body.

Waist circumference (WC) was measured by placing a measuring tape horizontally around the part of the trunk located midway between the lower costal margin (bottom of lower rib) and the iliac crest (top of pelvic bone) with the person standing.<sup>13</sup> Mid-arm circumference was assessed at the measured midpoint of upper right arm to the nearest 0.1 cm. Mid-arm muscle circumference (MAC) was determined using the standard equation of Frisancho, data.<sup>14</sup>

#### Body composition

The logarithm of the sum of the SF thicknesses was obtained, from which the density of the FFM was calculated according to Durnin and Womersley data, adapted for age and sex.<sup>15</sup> Percentage of body FM was then calculated using Siri's equation.<sup>16</sup>

BIA included measurements of resistance and reactance by a 4-terminal impedance analyzer (model BIA-103; RJL-system®, Detroit, MI) using a single-frequency with current at 50 kHz while the subjects were supine with arms and legs extended. Electrodes were attached at standardized positions on the right side of the body. FFM was estimated using the prediction equation developed by Kotler et al. (1996).<sup>17</sup> Body FM was then calculated by subtracting the FFM from the total weight.

$$\text{FFM} = 0.50 \left[ \frac{\text{HT}^{1.48}}{Z^{0.55}} \times \frac{1.0}{1.21} \right] + 0.42 \text{Wt} + 0.49$$

Ht = height, Wt = weight, and Z (impedance)  $Z^2 = R^2 + Xc^2$  where R = resistance Xc = reactance

The segmental BIA considered the whole body as three cylinders: arm, trunk and leg. The positions of electrodes are described elsewhere.<sup>18,19</sup> The results are shown as resistance values and the leg index of the conductive volume, by using the formula  $\text{leg length}^2 / \text{resistance}$ .<sup>19</sup>

Whole-body DXA scans (Hologic QDR 4500A scanner®, Hologic Inc, Waltham, MA) were performed and analyzed by an independent observer. The measurements provided FM and FFM of regional and total body.

#### Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS), version 15. After testing normality (Komogorov-Smirnov), one-way analysis of variance (ANOVA) was used to compare groups. All continuous variable were expressed as means  $\pm$  standard deviation (SD) and differences were admitted as statistically significant when  $p$  value  $< 0.05$ . Tukey test was used for post hoc analysis.

Categorical variables were compared using chi square test and giving frequencies of each variable in

each group. Correlations were calculated using Pearson correlation coefficient.

To detect agreement between the methods we considered DXA as reference method (gold standard) and applied St Laurent coefficient test. A value above 0.81 was considered almost perfect and beyond 0.40 as a fair strength of agreement.

## Results

#### Clinical and demographic characteristics

Forty seven patients were enrolled at this study. Of these, three were excluded because of hypothyroidism, weight gain higher than 10% in a short period of time and undernutrition. All patients who all who fulfilled the inclusion criteria, accept to participate of the study.

All the subjects were male and with similar age ( $p = 0.25$ ). HIV+LIPO+ were represented by 10 patients ( $46 \pm 5$  yrs); HIV+LIPO- by 22 patients ( $43 \pm 6$  yrs), and control group by 12 subjects ( $45 \pm 5$  yrs).

The groups were comparable regarding the CD4 count (HIV+LIPO+ =  $551 \pm 300$  cells/mm<sup>3</sup>; HIV+LIPO- =  $454 \pm 186$  cells/mm<sup>3</sup>, NS) and only 5 patients had viral load more than 50 copies/mm<sup>3</sup>.

The mean time since the diagnosis of HIV was similar between groups (HIV+LIPO+ =  $114 \pm 27$  months and HIV+LIPO- =  $96 \pm 64$  months;  $p > 0.05$ ). The duration of HAART was also similar between groups (HIV+LIPO+ =  $110 \pm 23$  months; HIV+LIPO- =  $78 \pm 52$  months;  $p$  value  $> 0.05$ ).

The combination of different antiretroviral classes was similar between HIV-infected groups. The most common therapy prescribed were 2 nucleoside-reverse transcriptase inhibitor (NRTI) + 1 non- nucleoside-reverse transcriptase inhibitor (NNRTI) (30%), 1 NRTI + 1 NNRTI + 1 protease inhibitor (PI) (30%) and 2 NRTI + 1 PI (20%) in HIV+LIPO+ group. In HIV+LIPO- group, the results were 54%, 14% and 27%, respectively.

#### Body composition assessment

BMI was similar between groups. There was no significant difference between the 3 groups regarding DXA-values for lean mass (table I). Leg and total body FM values, however, were significantly lower in HIV+LIPO+.

Table II documents anthropometric variables. Arm circumference and triceps SF were lower, indicating fewer subcutaneous fat in HIV+LIPO+ when compared to others groups. It was found an excellent correlation between MAC and lean mass determined by DXA ( $r = 0.718$   $p < 0.05$ ). SF values were significantly correlated with DXA only in Control group ( $r = 0.704$ ) and waist circumference values were significantly correlated in all groups.

	HIV+LIPO+	HIV+LIPO-	Control	p value
<i>Total Body</i>				
Fat mass, kg	12 (5) <sup>a</sup>	14 (6)	19 (4)	0.02
Lean mass, kg	54 (7)	54 (7)	56 (6)	0.76
Fat mass, %	17 (5) <sup>a</sup>	20 (6)	24 (4)	0.02
<i>Arms</i>				
Fat mass, kg	0.482 (0.32)	0.682 (0.33)	0.675 (0.17)	0.21
Lean mass, kg	3.430 (0.74)	3.550 (0.65)	3.740 (0.44)	0.51
Fat mass, %	15 (6)	15 (3)	15 (5)	0.22
<i>Legs</i>				
Fat mass, kg	1 (0.6) <sup>ab</sup>	2 (0.8) <sup>a</sup>	3 (1.2)	< 0.01
Lean mass, kg	9 (1.3)	10 (1.2)	10 (1.5)	0.12
Fat mass, %	11 (5) <sup>ab</sup>	17 (7)	22 (7)	< 0.01
<i>Trunk</i>				
Fat mass, kg	7 (3)	8 (4)	10 (2)	0.37
Lean mass, kg	28 (3)	27 (4)	27 (2)	0.86
Fat mass, %	21 (6)	22 (7)	26 (3)	0.13

*Abbreviations:* HIV+LIPO+ = HIV-infected man with lipodystrophy syndrome; HIV+LIPO- = HIV-infected man without lipodystrophy syndrome; Control = Healthy subjects.

Results are expressed as mean value and standard deviation.

ANOVA test was used. Level of significance  $p < 0.05$  (a  $\neq$  control; b  $\neq$  HIV+LIPO-).

	HIV+LIPO+	HIV+LIPO-	Control	p value
Body weight, kg	69 (11)	73 (12)	78 (9)	0.13
Height, cm	171 (6)	172 (5)	172 (6)	0.82
Body mass index, kg/m <sup>2</sup>	24 (3)	24 (3)	26 (3)	0.11
Waist circumference, cm	89 (7)	90 (10)	92 (6)	0.71
Arm circumference, cm	29 (4) <sup>a</sup>	30 (3)	32 (2)	0.04
<i>Skinfold thickness (mm):</i>				
Triceps	7 (2) <sup>a</sup>	8 (2) <sup>a</sup>	12 (3)	< 0.01
Biceps	6 (2)	5 (2)	5 (2)	0.08
Subscapular	19 (6)	16 (6)	20 (5)	0.12
Suprailiac	11 (5)	12 (8)	16 (5)	0.16
Sum of skinfolds, mm	43 (12)	42 (16)	53 (14)	0.06
Mid-arm muscle circumference, cm	26 (4)	28 (3)	28 (1)	0.36

*Abbreviations:* HIV+LIPO+ = HIV-infected man with lipodystrophy syndrome; HIV+LIPO- = HIV-infected man without lipodystrophy syndrome; Control = Healthy subjects.

Results are expressed as mean value and standard deviation.

ANOVA test was used. Level of significance  $p < 0.05$  (a  $\neq$  control; b  $\neq$  HIV+LIPO-).

Only Control group had significant correlation and good agreement between FM estimated by SF with FM measured by DXA. Although, the agreement were fair strength in both HIV groups (table III). In relation to BIA, the correlation and the agreement analysis were reported in table IV. BIA was correlated positively and significantly with DXA in all groups and with substantial agreement.

No differences were observed by resistance value or the leg index of the conductive volume.

## Discussion

We used methods to assess body composition in HIV-infected man with LS and compare to HIV-infected man without LS and to controls. DXA was used as gold standard, and fewer prior studies have specifically examined agreement between methods to assess LS in HIV-infected patients.

All groups were homogenous for age and BMI, time of undergoing HAART and type of HAART. DXA

**Table III**  
Percentage of fat mass by SF and its correlation and agreement with DXA in each groups: HIV patients with LS (HIV+LIPO+) and without (HIV+LIPO-) and healthy (Control) groups

	HIV+LIPO+	HIV+LIPO-	Control
Fat mass, %	22 (4)	20 (4) <sup>a</sup>	25 (4)
Correlation	0,46	0,79**	0,83**
Agreement	0,35 (0,19; 0,60)	0,40 (0,13; 0,78)	0,74 (0,50; 0,89)

Abbreviations: HIV+LIPO+ = HIV-infected man with lipodystrophy syndrome; HIV+LIPO- = HIV-infected man without lipodystrophy syndrome; Control = Healthy subjects.

The correlation test used was Pearson and \* =  $p < 0,05$  \*\* =  $p < 0,01$ .

The agreement test used was St Laurent. Values above 0.81 was considered almost perfect and beyond 0.40 as a fair strength of agreement.

**Table IV**  
Body composition by BIA and its correlation and agreement with DXA in each groups: HIV patients with LS (HIV+LIPO+) and without (HIV+LIPO-) and healthy (Control) groups

	HIV+LIPO+	HIV+LIPO-	Control
Fat mass, %	18 (4) <sup>a</sup>	19 (4)	22 (2)
Correlation	0,66*	0,74**	0,71**
Agreement	0,65 (0,38; 0,86)	0,69 (0,60; 0,86)	0,58 (0,45; 0,73)
Fat mass, kg	13 (5)	14 (5)	17 (3)
Correlation	0,87 **	0,90**	0,61*
Agreement	0,79 (0,40; 0,96)	0,85 (0,74; 0,93)	0,60 (0,41; 0,87)
Fat free mass, kg	56 (7)	58 (7)	61 (6)
Correlation	0,93 **	0,92 **	0,73 **
Agreement	0,89 (0,79; 0,96)	0,85 (0,73; 0,93)	0,61 (0,32; 0,91)

Abbreviations: HIV+LIPO+ = HIV-infected man with lipodystrophy syndrome; HIV+LIPO- = HIV-infected man without lipodystrophy syndrome; Control = Healthy subjects.

The correlation test used was Pearson and \* =  $p < 0,05$  \*\* =  $p < 0,01$ .

The agreement test used was St Laurent. Values above 0.81 was considered almost perfect and beyond 0.40 as a fair strength of agreement.

results demonstrated statistically reduced leg fat in HIV+LIPO+ when compared to HIV+LIPO- and control groups, confirming the peripheral lipoatrophy. Leg fat was the depot most affected in HIV-infection and was in agreement with others studies.<sup>20-23</sup> Lean mass did not differ between groups which could, at least in part, explain the relative preservation of lean mass in aids patients under antiretroviral drug.<sup>8</sup>

Anthropometric measurements were important to detect loss of regional FM and total lean mass. Arm circumference was significantly lower in HIV+LIPO+ when compared to control group, suggesting that bone, muscle or fat tissue could be altered. It was found an excellent correlation between MAC and LM determined by DXA which suggests an adequate applicability of MAC in clinical practice in aids patients with LS. Also waist circumference was correlated with trunk fat mass from DXA, suggesting being another practical important instrument. Our mean triceps SF values were similar to other study that used triceps SF as definition to lipoatrophy.<sup>24</sup> However, our results were not correlated with arm fat mass determined by DXA.

Our results demonstrated that the estimation of FM by SF were neither correlated nor in agreement with DXA in HIV+LIPO+ group. Durnin and Womersley

equation to predict FM was designed from healthy population and may not be useful for disease related groups.<sup>10,25</sup> Batterham, Garcia and Greenop (1999) compared 6 equations to estimate FM by SF in aids patients and none had agreement with DXA.<sup>26</sup>

The mean result from this study was that BIA could accurate predict FFM and FM in HIV-infected man with SL, when using Kotler's equation. This equation was validated in a study involving HIV-infected patients.<sup>17</sup> Forrester, Sheehan and Joffe (2008) also found good correlation between BIA and DXA in HIV-infected men ( $r = 0.89$  for LM, and  $r = 0.88$  for FM,  $p < 0.05$ ).<sup>27</sup> Aghdassi et al. (2007) also found good agreement between BIA and DXA in a group of 47 HIV-infected male subjects receiving HAART. Their results suggest that BIA (using the prediction equation in the manufactures' software of RJL system, model BIA-103) could be used for routine assessment of total body FM in male subjects with HIV-infection.<sup>9</sup>

Segmental BIA could be an alternative method to detect changes in fat mass. Until now, there were no suitable equations validated to estimate FFM and FM in HIV-infected patients with lipodystrophy. Only one study was found comparing segmental fat mass by BIA

**Table V**  
Legs indices and resistance values in segment of arms, trunk and leg in each groups: HIV patients with LS (HIV+LIPO+) and without (HIV+LIPO-) and healthy (Control) groups

	HIV+LIPO+	HIV+LIPO-	Control
Leg length <sup>2</sup> / resistance at 50 KHz resistance	43 (5)	44 (7)	46 (7)
Arm	225 (45)	215 (30)	207 (25)
Trunk	71 (21)	75 (20)	62 (6)
Leg	206 (20)	206 (34)	184 (24)

*Abbreviations:* HIV+LIPO+ = HIV-infected man with lipodystrophy syndrome; HIV+LIPO- = HIV-infected man without lipodystrophy syndrome; Control = Healthy subjects.

Results are expressed as mean value and standard deviation.

ANOVA test was used. Level of significance  $p < 0.05$  (a  $\neq$  control; b  $\neq$  HIV+LIPO-).

in HIV- infected individuals with or without lipodystrophy.<sup>10</sup> The study did not have a reference method to compare and observe that the group with lipodystrophy had higher leg resistance index than the group without lipodystrophy, but the discriminative power of BIA between patients with or without lipodystrophy was not improved by the use of leg segmental BIA. New formulas or methods are necessary.

Our main result indicates BIA as clinical effective and practical method to access total body composition in HIV-infected man with lipodystrophy syndrome. More studies are needed to establish more non-invasive clinical methods to access fat mass in these subjects, including segmental BIA and anthropometry.

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