Comparison of dual-energy X-ray absorptiometry and magnetic resonance imaging–measured adipose tissue depots in HIV-infected and control subjects1–4

Rebecca Scherzer, Wei Shen, Peter Bacchetti, Donald Kotler, Cora E Lewis, Michael G Shlipak, Mark Punyanitya, Steven B Heymsfield, and Carl Grunfeld for the Study of Fat Redistribution Metabolic Change in HIV Infection

ABSTRACT
Background: Studies in persons without HIV infection have compared adipose tissue measured by dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI), but no such study has been conducted in HIV-infected (HIV +) subjects, who have a high prevalence of regional fat loss.

Objective: We compared DXA- with MRI-measured trunk, leg, arm, and total fat in HIV + and control subjects.

Design: A cross-sectional analysis was conducted in 877 HIV + subjects and 260 control subjects in FRAM (Study of Fat Redistribution and Metabolic Change in HIV Infection), stratified by sex and HIV status.

Results: Univariate associations of DXA with MRI were strongest for total and trunk fat \( (r \geq 0.92) \) and slightly weaker for leg \( (r \geq 0.87) \) and arm \( (r \geq 0.71) \) fat. The average estimated limb fat was substantially greater for DXA than for MRI for HIV + and control men and women (all \( P < 0.0001) \). Less of a difference was observed in trunk fat measured by DXA and MRI, but the difference was still statistically significant \( (P < 0.0001) \). Bland-Altman plots showed increasing differences and variability. Greater average limb fat in control and HIV + subjects (both \( P < 0.0001) \) was associated with greater differences between DXA and MRI measurements. Because the control subjects had more limb fat than did the HIV + subjects, greater amounts of fat were measured by DXA than by MRI when control subjects were compared with HIV + subjects. More HIV + subjects had leg fat in the bottom decile of the control subjects by DXA than by MRI \( (P < 0.0001) \).

Conclusions: Although DXA- and MRI-measured adipose tissue depots correlate strongly in HIV + and control subjects, differences increase as average fat increases, particularly for limb fat. DXA may estimate a higher prevalence of peripheral lipatrophy than does MRI in HIV + subjects. Am J Clin Nutr 2008;88:1088–96.

INTRODUCTION

Both dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI) have been used in previous studies to measure regional and total adiposity, but each method relies on assumptions that are not always recognized or appropriate. Only MRI and computed tomography (CT) can directly measure adipose tissue (1) and measure visceral and subcutaneous adipose tissue (SAT) separately. The major limitations include the cost and limited availability of MRI and the radiation exposure associated with CT. Most studies use DXA because of its availability and relatively low cost. DXA uses proprietary equations to estimate the amount of fat based on relative density. DXA quantifies fat, rather than adipose tissue. According to the 5-level body-composition classification system (2), fat is a molecular-level component and adipose tissue is a tissue-level component. Eighty percent of adipose tissue is composed of fat (3, 4). On the other hand, fat can be distributed in tissue other than adipose tissue, such as liver and muscle (3). There is a high correlation between DXA-measured fat and MRI- or CT-measured adipose tissue. Compared with MRI and CT, DXA cannot separate visceral fat from subcutaneous trunk fat and cannot discern organ fatty infiltration.

In the setting of HIV infection, the introduction of combination antiretroviral therapy was followed by the observation of changes in fat distribution and metabolic abnormalities (5). In the era of antiretroviral therapy, HIV infection has been associated with a syndrome of lipatrophy, which is characterized by a loss of SAT, particularly in the limbs and lower trunk, without loss of visceral adipose tissue (VAT) (6, 7). It is therefore of interest whether measurements of fat by DXA and MRI are comparable in patients with HIV infection and whether earlier conclusions

1 From the University of California, San Francisco, CA (RS and PB); the Obesity Research Center, St Luke’s–Roosevelt Hospital and Institute of Human Nutrition, Columbia University College of Physicians and Surgeons, New York, NY (WS); St Luke’s–Roosevelt Hospital, Columbia University, New York, NY (DK); the Division of Preventive Medicine, University of Alabama, Birmingham, AL (CEL); the University of California and the Veterans Affairs Medical Center, San Francisco, CA (MGS and CG); St Luke’s–Roosevelt Hospital, Columbia University, New York, NY (MP); and Merck & Co, Rahway, NJ (SBH).

2 The funding agency played no role in the conduct of the study, collection of the data, management of the study, analysis of the data, interpretation of the data, or preparation of the manuscript. A representative of the funding agency participated in planning the protocol. As part of the standard operating procedures of CARDIA, the manuscript was reviewed at the NHLBI, but no revisions were requested.

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4 Reprints not available. Address correspondence to C Grunfeld, University of California, Veterans Affairs Medical Center, Metabolism Section 111F, 4150 Clement Street, San Francisco, CA 94121. E-mail: carl.grunfeld@ucsf.edu.

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DXA COMPARED WITH MRI IN HIV+ AND CONTROL SUBJECTS

SUBJECTS AND METHODS

Protocol and subjects

FRAM enrolled 1175 HIV+ and 297 control men and women between 2000 and 2002. FRAM was designed to evaluate the prevalence and correlates of changes in fat distribution, insulin resistance, and dyslipidemia in a representative sample of HIV+ and control subjects in the United States. The methods were described in detail previously (12). HIV+ subjects were recruited from 16 HIV or infectious disease clinics or cohorts in 1999. Control subjects were recruited from 2 centers of the Coronary Artery Risk Development in Young Adults (CARDIA) study (13). CARDIA subjects were originally recruited as a sample of healthy white and African American men and women aged 18–30 y from 4 cities in 1985–1986 for a longitudinal study of cardiovascular disease risk factors. Subjects were recruited from the general population in 3 of the cities and from the membership of a prepaid health care program in the fourth city. CARDIA subjects from the year 15 exam were recruited for the FRAM cohort. The protocol was approved by institutional review boards at all sites.

MRI and DXA measurements were available in 78% of FRAM participants. Most of the subjects underwent DXA and MRI on the same day (76%), within the same week (9%) or the same month (9%). Only 6% of the subjects received DXA and MRI more than 1 month apart. Subjects were asked to fast before MRI and DXA scan acquisition protocol was standardized across sites, and the IRC performed site visits to ensure protocol adherence. Imaging techniques and anatomical sites (based on bone landmarks) were identical between HIV+ and control subjects. Tissue areas (cm²) were calculated by summing specific tissue pixels and then multiplying by individual pixel surface area. The volume per slice (cm³) of each tissue was calculated by multiplying area by thickness. The volume of each tissue for the space between 2 consecutive slices was calculated via a mathematical algorithm (15). When a single limb was outside the field of view, volume in the measured limb was doubled to obtain total limb volume. For comparison with DXA, adipose tissue volumes from MRI were multiplied by 0.9 kg/L to convert to kg fat mass, because adipose tissue has a density of 0.9 g/cm³ (16). Anatomic sites considered in this analysis were as follows: trunk (defined as upper trunk plus lower trunk plus VAT), arm, leg, and total adipose tissue.

Body composition

Anthropometric measurements

All staff were centrally trained and certified to make anthropometric measurements. The subjects wore light clothing or a hospital gown and no shoes. Height was measured to the nearest 0.1 inch or 1 cm and weight was measured to the nearest 0.1 lb or 1 kg by using calibrated stadiometers and scales, respectively. Body mass index (BMI) was calculated as weight (kg)/height squared (m).

Magnetic resonance imaging

Whole-body MRI was performed to quantify regional and total adipose tissue (14). Body composition was measured by MRI with subjects in the supine position, arms extended over head, and analyzed as described in detail elsewhere (6, 7, 12, 14). In brief, using the intervertebral space between the fourth and fifth lumbar vertebrae as origin, transverse images (10-mm slice thickness) were obtained every 40 mm from hand to foot. MRI scans were segmented with the use of image analysis software (Tomovision Inc, Montreal, Canada). All scans were read at a single image reading center (IRC) at the Obesity Research Center, St Luke’s–Roosevelt Hospital, New York, NY. The MRI scan acquisition protocol was standardized across sites, and the IRC performed site visits to ensure protocol adherence. Imaging techniques and anatomical sites (based on bone landmarks) were identical between HIV+ and control subjects. Tissue areas (cm²) were calculated by summing specific tissue pixels and then multiplying by individual pixel surface area. The volume per slice (cm³) of each tissue was calculated by multiplying area by thickness. The volume of each tissue for the space between 2 consecutive slices was calculated via a mathematical algorithm (15). When a single limb was outside the field of view, volume in the measured limb was doubled to obtain total limb volume. For comparison with DXA, adipose tissue volumes from MRI were multiplied by 0.9 kg/L to convert to kg fat mass, because adipose tissue has a density of 0.9 g/cm³ (16). Anatomic sites considered in this analysis were as follows: trunk (defined as upper trunk plus lower trunk plus VAT), arm, leg, and total adipose tissue.

Statistical methods

Spearman correlation coefficients were calculated to examine the relation of each DXA-measured adipose region with the corresponding MRI-measured region (trunk, leg, arm, and total), because many measures were found to be nonnormally distributed. For each region, differences between DXA and MRI were compared by using Wilcoxon’s signed-rank test. The percentage difference between DXA and MRI was calculated as follows:

\[
\text{Percentage Difference} = \frac{\text{DXA} - \text{MRI}}{\text{DXA}} \times 100\%
\]
TABLE 1
Characteristics of the HIV-infected (HIV+) and control men and women

<table>
<thead>
<tr>
<th></th>
<th>HIV men (n = 625)</th>
<th>Control men (n = 135)</th>
<th>HIV women (n = 252)</th>
<th>Control women (n = 125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>43.0 (37.0–48.0)²</td>
<td>40.0 (38.0–43.0)²</td>
<td>41.0 (36.0–47.0)</td>
<td>42.0 (38.0–44.0)</td>
</tr>
<tr>
<td>Race (n [%])</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>354 (57)</td>
<td>78 (58)¹</td>
<td>91 (36)</td>
<td>63 (50)¹</td>
</tr>
<tr>
<td>African American</td>
<td>190 (30)</td>
<td>57 (42)</td>
<td>129 (51)</td>
<td>62 (50)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>64 (10)</td>
<td></td>
<td>24 (10)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>17 (3)</td>
<td></td>
<td>8 (3)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175.3 (170.8–180.3)</td>
<td>178.5 (175.0–182.5)²</td>
<td>162.5 (157.6–166.5)</td>
<td>164.5 (161.0–170.5)²</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.2 (67.3–82.5)</td>
<td>84.0 (76.6–95.8)</td>
<td>68.1 (58.7–80.5)</td>
<td>75.1 (62.1–88.6)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.2 (22.1–26.4)</td>
<td>26.7 (24.5–30.1)</td>
<td>25.8 (22.0–30.5)</td>
<td>27.6 (23.0–33.1)</td>
</tr>
<tr>
<td>HIV-related factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current CD4 (cells/μL)</td>
<td>344.5 (213.5–525.5)</td>
<td>195</td>
<td>374.0 (196.0–561.0)</td>
<td>—</td>
</tr>
<tr>
<td>HIV RNA (1000/mL)</td>
<td>0.4 (0.4–10.0)</td>
<td></td>
<td>0.4 (0.4–14.2)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Subjects with missing measurements of adipose tissue by magnetic resonance imaging or dual-energy X-ray absorptiometry were excluded from the data.
² Median; interquartile range in parentheses (all such values).  
³ Significantly different from the respective control group (Wilcoxon’s rank-sum test for continuous variables and Fisher’s exact test for categorical variables): *P ≤ 0.0001, †P = 0.001.

(DXA – MRI)/MRI × 100. Separate analyses were conducted for HIV+ men, HIV+ women, control men, and control women. Analyses were also stratified by ethnicity and by DXA machine type.

The Bland-Altman (18) method was used to assess the agreement between DXA and MRI. For each subject, we calculated the mean of the fat estimates from the 2 methods and then calculated their difference. A graph of the difference between methods against the mean was plotted. The limits of agreement for the 2 methods, essentially the 95% CI for the prediction of the difference between DXA and MRI, were calculated, as was the precision of those limits. In addition, the correlation (ρ) between the average difference and the SEE were calculated. This latter value represents the average expected error, as opposed to the maximum error, represented by the limits of agreement.

For the purposes of comparing DXA with MRI, we defined lipoatrophy as leg SAT below the 10th percentile of the control subjects, with men and women done separately, as in previous analyses (19). Leg SAT distributions were displayed as histograms overlaid with smoothed curves from kernel density estimates, and the prevalence of lipoatrophy by DXA and MRI was compared by using McNemar’s test.

Multivariable regression equations were calculated with the difference between DXA- and MRI-measured trunk, leg, arm, or total fat as the dependent variable. Models were constructed for each outcome by using HIV status, demographics (sex, age, and race), and DXA machine type (Hologic compared with GE Lunar) as predictor variables. Interactions between HIV status, sex, ethnicity, and age were also assessed and included if they were statistically significant. The linearity assumption was tested for

TABLE 2
Comparison of adipose tissue mass measured by dual-energy X-ray absorptiometry (DXA) or magnetic resonance imaging (MRI) in HIV-infected (HIV+) and control subjects by sex

<table>
<thead>
<tr>
<th>Sex and region</th>
<th>DXA kg</th>
<th>MRI kg</th>
<th>Spearman’s ρ</th>
<th>DXA kg</th>
<th>MRI kg</th>
<th>Spearman’s ρ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>625</td>
<td>625</td>
<td></td>
<td>135</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>Trunk fat</td>
<td>7.5 (4.9–10.9)²</td>
<td>7.0 (4.7–10.7)²</td>
<td>0.92</td>
<td>10.7 (7.5–14.1)</td>
<td>10.0 (7.1–13.3)</td>
<td>0.94</td>
</tr>
<tr>
<td>Leg fat</td>
<td>3.2 (2.1–5.1)</td>
<td>2.6 (1.8–3.6)³</td>
<td>0.87</td>
<td>7.2 (5.8–9.4)</td>
<td>4.2 (3.4–5.5)</td>
<td>0.91</td>
</tr>
<tr>
<td>Arm fat</td>
<td>1.2 (0.8–1.8)</td>
<td>0.9 (0.7–1.2)³</td>
<td>0.71</td>
<td>2.3 (1.8–2.9)</td>
<td>1.0 (0.8–1.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Total fat</td>
<td>12.9 (9.1–18.7)</td>
<td>10.7 (7.9–15.5)³</td>
<td>0.92</td>
<td>21.3 (16.8–27.3)</td>
<td>15.4 (11.8–20.4)</td>
<td>0.95</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>252</td>
<td>252</td>
<td></td>
<td>125</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>Trunk fat</td>
<td>12.1 (7.6–16.2)</td>
<td>13.2 (8.2–18.8)³</td>
<td>0.96</td>
<td>13.6 (7.3–19.5)</td>
<td>14.2 (8.2–20.5)</td>
<td>0.96</td>
</tr>
<tr>
<td>Leg fat</td>
<td>7.8 (5.4–11.1)</td>
<td>6.0 (4.1–8.9)³</td>
<td>0.95</td>
<td>12.5 (9.6–15.8)</td>
<td>8.3 (6.1–10.7)</td>
<td>0.93</td>
</tr>
<tr>
<td>Arm fat</td>
<td>2.5 (1.6–3.6)</td>
<td>1.4 (0.9–2.1)³</td>
<td>0.85</td>
<td>3.6 (2.5–4.9)</td>
<td>1.8 (1.2–2.3)</td>
<td>0.88</td>
</tr>
<tr>
<td>Total fat</td>
<td>23.6 (15.9–32.5)</td>
<td>20.9 (13.5–29.6)³</td>
<td>0.96</td>
<td>31.6 (20.9–40.1)</td>
<td>25.3 (16.0–32.9)</td>
<td>0.96</td>
</tr>
</tbody>
</table>

¹ Subjects with missing measurements of adipose tissue by MRI or DXA were excluded from the data. MRI volumes were multiplied by 0.9 kg/L to convert them to kg.
² Median; interquartile range in parentheses (all such values).
³ Significantly different from DXA, *P < 0.0001 (Wilcoxon’s signed-rank test).
continuous measures by adding quadratic terms to the models and by examining generalized additive models (20). To account for possible differences between study sites, likelihood ratio testing was used to determine whether a random site effect should be added to the model. CIs were determined by using the bias-corrected accelerated bootstrap method (21), with $P$ values defined as the one minus the highest confidence level that still excluded zero; this was necessary because the error residuals appeared to be non-Gaussian. All analyses were conducted by using the SAS system, version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Subjects

Body composition measurements by MRI and DXA were available for 1137 subjects whose characteristics are presented in Table 1. Compared with HIV+ subjects, control subjects were slightly taller and weighed more ($P \leq 0.001$) and had greater amounts of fat and adipose tissue as measured by DXA and MRI (Table 2).

Univariate comparisons between DXA and MRI

DXA-estimated fat was consistently larger than MRI-estimated adipose tissue ($P < 0.0001$) in every depot and subgroup, with the exception of trunk in women, for which the MRI-measured value was larger than the DXA-measured value (Table 2). Despite these large differences, all DXA-measured fat depots were strongly correlated with their corresponding MRI measures ($r = 0.71$ to 0.96; all $P < 0.0001$), but correlations tended to be slightly weaker for arm than for leg, trunk, and total fat (Table 2).

The percentage difference between DXA and MRI was greater for leg and arm and less for trunk (Figure 1). In control subjects, the median percentage difference in DXA-estimated fat compared with MRI-estimated adipose tissue was up to 69% higher for leg and up to 120% higher for arm. In HIV+ subjects, the median percentage difference in DXA-estimated fat compared with MRI was up to 30% higher for leg and up to 75% higher for arm. The difference was much less for trunk fat; the median DXA measure was 5% higher in men and 9% lower in women than was the MRI measure, for both control and HIV+ subjects. Similarly, the median percentage differences were larger for total fat in

![Figure 1](https://academic.oup.com/ajcn/article-abstract/88/4/1088/4650019)

FIGURE 1. Percentage differences in adipose tissue estimated by dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI) in men (A) and women (B). Results are medians ± 95% CIs in HIV-infected (HIV+) and control subjects. $P$ values represent differences between the 2 groups by Wilcoxon’s rank-sum test.
control subjects than in HIV+ subjects (up to 20% higher in HIV+ subjects and up to 35% higher in control subjects; \( P < 0.001 \)).

Bland-Altman analysis was used to assess the agreement between DXA and MRI by plotting the difference (DXA – MRI) against the amount of fat by using the average of the 2 methods. The largest relative differences between DXA and MRI were found for limb fat, whereas trunk fat showed the least difference (Figure 2). More bias was seen for the control subjects than for the HIV+ subjects for leg, arm, and total fat (all \( P < 0.01 \) for HIV+ compared with control subjects; test of difference in \( \rho \)). As measured by SEE, precision appeared similar in HIV+ and control subjects.

The amount of bias increased and the precision decreased as the average amount of limb fat increased. For example, at 5 kg of average leg fat, the estimated bias (mean \( \pm \) SD) was 1.3 \( \pm \) 1.7 in HIV+ subjects and 1.6 \( \pm \) 1.3 in control subjects. By contrast, at 15 kg of leg fat, estimated bias was 3.9 \( \pm \) 5.2 in HIV+ subjects and 4.8 \( \pm \) 3.9 in control subjects.

Bias in trunk fat was weaker and showed sex differences. A weak positive bias was seen in men, which indicated that DXA tended to estimate higher amounts of trunk fat than did MRI as average trunk fat increased, whereas a negative bias was seen in women. In men, more trunk fat bias was seen in control subjects than in HIV+ subjects (\( P = 0.0003 \)); in women, more bias was seen in the HIV+ subjects (\( P < 0.0001 \)).

An examination of ethnic differences found that correlations between DXA and MRI measurements tended to be slightly stronger in African Americans than in whites, regardless of HIV status (differences in \( r = 0.04 \) to 0.11, \( P < 0.003 \)). Bland-Altman analysis showed similar bias in African Americans and whites; an exception was seen for trunk fat, ie, trunk fat showed a slight positive bias (in contrast with the negative bias seen for other women) for white control women but no bias for African American HIV+ men (in contrast with the positive bias seen for other men).

**Prevalence of lipoatrophy by DXA and MRI**

Because leg SAT is the depot most affected by HIV lipoatrophy, we compared the distributions of leg fat by DXA and of adipose tissue mass by MRI (Figure 3). HIV+ subjects had a dramatically lower distribution of fat than did control subjects as measured by both DXA and MRI (\( P < 0.0001 \) in both men and women). However, a more pronounced upward shift in the distribution of DXA-estimated leg fat than in MRI-estimated leg fat was observed in control subjects. The prevalence of lipoatrophy

![FIGURE 2. Bland-Altman plots of comparisons in leg fat (A), arm fat (B), total fat (C), trunk fat in men (D), and trunk fat in women (E) in HIV-infected (HIV+, C) and control (C) subjects estimated by dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI). Note that the y axes are different in panels B and C.](https://academic.oup.com/ajcn/article-abstract/88/4/1088/4650019)
in HIV+ subjects, on the basis of leg fat (defined as being in the lowest decile of control subjects by DXA and MRI), was higher with DXA than with MRI in both men (69% of HIV+ men by DXA compared with 50% of HIV+ men by MRI; \(P < 0.0001\)) and women (47% of HIV+ women compared with 33% of HIV+ women; \(P < 0.0001\)).

**Multivariable associations with difference between DXA and MRI**

To further explore the findings of differences in measurement of leg and trunk fat, we conducted multivariable analyses to examine the associations of HIV status, demographics, and DXA machine with DXA-MRI differences (Table 3). Trunk fat estimates showed differences between DXA and MRI for women compared with men (1.24 kg; \(P < 0.0001\)), for African Americans compared with whites (−0.76 kg; \(P < 0.0001\)), for the DXA Hologic machine compared with the Lunar machine (−1.13 kg; \(P = 0.003\)), and with increasing age (0.15-kg increase per decade; \(P = 0.039\)), but little difference in trunk fat was seen between HIV+ subjects and control subjects (−0.96 kg; \(P = 0.084\)) after adjustment.

Unlike the findings with trunk fat, the largest difference in leg fat by DXA compared with MRI was in HIV status, ie, the difference was larger in control subjects than in HIV+ subjects (2.2 kg; \(P < 0.0001\)). The difference in DXA compared with MRI was larger in women than in men (0.94 kg; \(P < 0.0001\)) and in African Americans than in whites (0.46 kg; \(P < 0.0001\)).

**DISCUSSION**

Although DXA-measured fat is strongly correlated with MRI-measured adipose tissue, our main finding was that associations were biased in both HIV+ and control populations. As the average amount of fat increases, the difference between DXA and MRI tends to increase, with DXA giving larger estimates of fat, particularly for limb fat. Because control subjects have more limb fat than do HIV+ subjects and because control subjects showed a greater upward shift in DXA-measured fat, DXA estimated a higher prevalence of peripheral lipoatrophy than did MRI in HIV+ subjects. Although there is no accepted cutoff that defines HIV-associated lipoatrophy, we compared the prevalence of subjects with leg SAT below the 10th percentile with that of the control subjects and found a higher prevalence of this definition of lipoatrophy by DXA than by MRI. In contrast, differences in DXA and MRI trunk fat estimates were much

![FIGURE 3. Density plots of comparisons of leg fat in HIV-infected (HIV+) and control (C) men (A and B) and women (C and D) by dual-energy X-ray absorptiometry (DXA) (A and C) and magnetic resonance imaging (MRI) (B and D). Distribution of height-normalized leg fat is shown by histogram; the decile reference line was defined by using cutoffs from the control men or women.](https://academic.oup.com/ajcn/article-abstract/88/4/1088/4650019)

Note: 69 percent of HIV and 10 percent of Controls have Leg < 10th percentile of Control Men (\(p<0.0001\)).

Note: 50 percent of HIV and 10 percent of Controls have Leg < 10th percentile of Control Men (\(p<0.0001\)).

* lipoatrophy is defined as having leg fat below the 10th percentile cutpoint of Control men.
smaller in all subgroups, and there were sex- and race-related differences.

DXA and MRI measure distinct but overlapping compartments. DXA estimates fat content by tissue density, whereas MRI measures adipose tissue volume. In addition to cellular lipids, adipose tissue contains extracellular water (≈12% of total volume in analyses of excised specimens; 22), a small amount of intracellular water, other types of cells besides adipocytes, and extracellular solids. Although these relations may be affected by fat depletion and composition changes related to lipodystrophy, these factors do not fully explain the findings because bias was also seen in control subjects. Furthermore, if the inclusion of the nonlipid component obtained in the MRI analysis was the cause of the difference, one would expect MRI to give higher results than DXA; however, the opposite was true.

Our finding that DXA and MRI are highly correlated but have important biases is supported by previous work in smaller studies of HIV-uninfected subjects. A positive bias was found in a comparison of DXA- with MRI-measured limb fat in a small study of 16 healthy men and women (11). A study of 13 healthy premenopausal women found a high correlation but poor agreement between DXA, MRI, and underwater-measured adiposity, with differences between DXA and MRI attributed to fat calibration errors (9). Investigators concluded that no method can yet be regarded as a satisfactory reference technique.

Our finding that bias is proportional to the average amount of fat is similar to findings in the general population of more errors by DXA in healthy men with higher adiposity and body thickness (23). Park et al believe that the precision and accuracy of DXA-measured trunk fat may be diminished by several factors, such as observer error in delineating specific regions because of the inability of X-rays to detect the small amount of soft tissue mass.

For the trunk, we found positive bias in men, but negative bias in women. This may have been due to the fact that DXA estimates do not differentiate between intraabdominal and subcutaneous fat, and the women in our study had less VAT but more upper and lower trunk SAT than did the men in both the HIV+ and control groups (6, 7). A small 12–16-wk study of HIV+ subjects (8) found that DXA and MRI estimates of changes in SAT and VAT were strongly associated ($R^2 = 0.70, P < 0.001$), although DXA estimated larger changes in total body fat than did MRI.

A possible contributor to these differences is that DXA-measured fat also includes fat that MRI cannot detect in adipose tissue. For example, in the trunk region, fat in the liver, intestine, and all other viscera are not included in MRI-measured adipose tissue. Likewise, intramuscular fat cannot be detected by MRI. In addition, small adipose tissue depots below the resolution of MRI are not included in MRI estimates. These small adipose tissue depots include some of the VAT and intermuscular adipose tissue depots in both the trunk and limb regions. These differences may partially explain why DXA-measured fat is higher than MRI-measured adipose tissue. Additionally, in our MRI and DXA protocol, the cutoff between limbs and trunk in MRI and DXA were not identical. DXA-measured limb fat may include more hip fat than MRI-measured limb adipose tissue. The bias identified in the Bland-Altman analysis may also be due to more fat in the hip region in heavier subjects, and women have more fat in the hip region than do men. However, these latter issues do not apply to arm fat, which shows similar trends.

What is the significance of these differences between DXA and MRI? Both DXA and MRI have been used in previous studies to estimate regional and total adiposity in HIV infection, but results from studies using DXA may not be directly extrapolated to studies in which MRI or other methods are used. Consequently, comparisons of HIV+ and control subjects and the prevalence or amount of lipodystrophy will differ depending on which method is used to quantify regional adipose tissue and on how lipodystrophy is defined. However, when certain guidelines are followed (24), DXA has been found to have adequate internal validity for measuring body-composition changes.

One limitation of our study was the lack of an absolute reference standard for estimating regional fat quantities. Another limitation was that several different DXA machine models were used in this study. A previous study found that, although fan- and pencil-beam models are highly correlated, small but significant differences exist between the instruments (25). However, sensitivity analysis including only Hologic machines, admittedly including both fan- and pencil-beam models, did not change our
key finding that DXA is more likely than MRI to detect lipatrophy in HIV+ subjects. DXA and MRI estimates of regional fat also differ because the cuts are slightly different: DXA cuts are at an angle perpendicular to the femoral neck, whereas MRI cuts are perpendicular to the longitudinal axis of the body. Although the vast majority of subjects had DXA and MRI scans performed on the same day, we also examined the association of time between scans on differences between DXA- and MRI-measured fat but found little association ($\rho \approx -0.02$ or less, $P > 0.70$). Finally, direct comparison is limited by the fact that DXA measures fat by attenuation of X-ray, whereas MRI directly measures AT volume (3).

Additional studies in other populations are required to characterize the differences between DXA and MRI measurements of adipose tissue, including a study of the effect of testing differences on the clinical outcomes of the 2 techniques. Comparison of DXA and MRI with other methods, such as CT, should also be made among HIV+ subjects, because small studies of HIV-infected subjects have found important differences in variability and accuracy between these 2 methods (26, 27). For example, the slice traditionally used in CT studies of VAT is not as good a marker of visceral adiposity as is that used in MRI measures (28). In the current study, we found that although DXA-measured adipose tissue correlated strongly with MRI-measures in both HIV+ and control subjects, the differences between MRI and DXA increased as the average amount of fat increased, particularly for limb fat. DXA may therefore estimate a higher prevalence of peripheral lipatrophy in HIV+ subjects. Both leg and arm fat were higher when measured by DXA, but the DXA-MRI differences varied among important subgroups, such as leg fat between HIV+ and control subjects and trunk fat between men and women. Therefore, caution is advised when making comparisons of fat measured with different techniques.

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APPENDIX A

Sites and investigators

University Hospitals of Cleveland (Barbara Gripshover); Tufts University (Abby Shevitz and Christine Wanke); Stanford University (Andrew Zolopa and Lisa Gooze); University of Alabama at Birmingham (Michael Saag and Barbara Smith); John Hopkins University (Joseph Cofrancesco and Adrian Dobs); University of Colorado Heath Sciences Center (Constance Benson and Lisa Kosmiski); University of North Carolina at Chapel Hill (Charles van der Horst); University of California at San Diego (W Christopher Mathews and Daniel Lee); Washington University (William Powderly and Kevin Yarasheski); VA Medical Center, Atlanta (David Rimland); University of California at Los Angeles (Judith Currier and Matthew Leibowitz); VA Medical Center, NY (Michael Simberkoff and Juan Bandres); VA Medical Center, WA DC (Cynthia Gibert and Fred Gordin); St Luke’s–Roosevelt Hospital Center (Donald Kotler and Ellen Engelson); University of California at San Francisco (Morris Schambelan and Kathleen Mulligan); Indiana University (Michael Dube); Kaiser Permanente, Oakland (Stephen Sidney); University of Alabama at Birmingham (Cora E Lewis).

Data Coordinating Center

University of Alabama, Birmingham (O Dale Williams, Heather Mcreath, Charles Katholi, George Howard, Tekeda Ferguson, and Anthony Goudie).

Image Reading Center

St Luke’s–Roosevelt Hospital Center (Steven Heymsfield, Jack Wang, and Mark Punyanitya).

Office of the Principal Investigator

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