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Section II: Emerging Uses of Bone Densitometry

Relationship Between Dual-Energy X-Ray Absorptiometry Volumetric Assessment and X-ray Computed Tomography−Derived Single-Slice Measurement of Visceral Fat

Yi Xia,[*,1] *David L. Ergun,*[1] *Wynn K. Wacker,*[1] *Xin Wang,*[2] *Cynthia E. Davis,*[3] *and Sanjiv Kaul*[4]

[1]*GE Healthcare Lunar, Madison, WI, USA;* [2]*Applied Statistics Laboratory, GE Global Research Center, Niskayuna, NY, USA;* [3]*Computational Biology and Biostatistics Laboratory, GE Global Research Center, Niskayuna, NY, USA; and* [4]*Cardiovascular Medicine Division, Oregon Health and Sciences University, Portland, OR, USA*

Abstract

To reduce radiation exposure and cost, visceral adipose tissue (VAT) measurement on X-ray computed tomography (CT) has been limited to a single slice. Recently, the US Food and Drug Administration has approved a dual-energy X-ray absorptiometry (DXA) application validated against CT to measure VAT volume. The purpose of this study was to develop an algorithm to compute single-slice area values on DXA at 2 common landmarks, $L_{2/3}$ and $L_{4/5}$, from an automated volumetrically derived measurement of VAT. Volumetric CT and total body DXA were measured in 55 males (age: 21−77 yr; body mass index [BMI]: 21.1−37.9) and 60 females (age: 21−85 yr; BMI: 20.0−39.7). Equations were developed by applying the relationship of CT single-slice area and volume measurements of VAT to the DXA VAT volume measure as well as validating these against the CT single-slice measurements. Correlation coefficients between DXA estimate of single-slice area and CT were 0.94 for $L_{2/3}$ and 0.96 for $L_{4/5}$. The mean difference between DXA estimate of single-slice area and CT was 5 cm^2 at $L_{2/3}$ and 3.8 cm^2 at $L_{4/5}$. Bland-Altman analysis showed a fairly constant difference across the single-slice range in this study, and the 95% limits of agreement for the 2 methods were −44.6 to +54.6 cm^2 for $L_{2/3}$ and −47.3 to +54.9 cm^2 for $L_{4/5}$. In conclusion, a volumetric measurement of VAT by DXA can be used to estimate single-slice measurements at the $L_{2/3}$ and the $L_{4/5}$ landmarks.

Key Words: dual-energy X-ray absorptiometry; visceral fat; X-ray computed tomography.

Introduction

Assessment of visceral adipose tissue (VAT) is important because of its metabolically active profile as a pathogenic fat depot *(1)*. It is strongly associated with cardiometabolic disease risks *(2,3)* and can also serve as a leading indicator for the development of metabolic syndrome and type 2 diabetes *(4−8)*. Volumetric measurement of VAT mostly relies on imaging methods, such as X-ray computed tomography (CT) and more recently magnetic resonance imaging (MRI) *(9−13)*. Many investigators use abdominal VAT volume as a measurement endpoint *(14−16)*, whereas others have opted to use single-slice area measurements because of radiation dose and cost concerns *(7,17−19)*.

The selection of the best representative single-slice location for VAT is still a subject of debate *(20−24)* and will remain so when considering the added complication of race, sex, age, and various study endpoints *(25)*. Two distinct landmarks commonly used are the $L_{4/5}$ *(7,12,18,26−28)* and $L_{2/3}$ *(17,19,24)* locations. Other locations have also been

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*Address correspondence to: Yi Xia, PhD, GE Healthcare Lunar, PO Box 7550, Madison, WI 53707. E-mail: Yi.Xia@ge.com

proposed *(21,29)*, including umbilicus *(5,30)* and 5−10 cm above $L_{4/5}$ *(20,25)*. The selection of a best representative location is not the subject of this study; instead, our focus is the dual-energy X-ray absorptiometry (DXA) measurement of single-slice VAT at the commonly used $L_{2/3}$ and $L_{4/5}$ landmarks.

Recently, the US Food and Drug Administration approved a method, CoreScan[a] (GE Healthcare, Madison, WI), for measuring volumetric VAT using DXA. The technical performance of the DXA VAT measurement has been validated using volumetric CT as the reference standard *(31)*. A single-slice area from a DXA VAT measurement can be implemented using the relationship between CT volume and single-slice VAT measures *(12,21)*. In this study, we use the relationship between single-slice and volumetric measures of VAT from CT to develop equations to compute single-slice measures of VAT from the DXA VAT volume measurements of the same subjects who were used for our VAT volume validation study. To our knowledge, this is the first attempt to develop single-slice VAT from DXA and compare it against CT.

Subjects and Methods

Patient Population and Protocol

The study comprised 124 subjects (61 females and 63 males) who underwent abdominal CT and a total body DXA scan on the same day. Subjects were recruited across 5 age categories (18−30, 31−50, 51−60, 61−80, and 81−90 yr) and 3 body mass index (BMI) categories (normal: 18.0−24.9, overweight: 25.0−29.9, and obese: 30.0−40.0 kg/m^2). Details of CT and DXA acquisition and analysis have been reported elsewhere *(31)*. Briefly, standard total body DXA images were acquired using the Lunar iDXA[a] densitometer (GE Healthcare, Madison, WI), and VAT volumes over the DXA android region were automatically generated with enCORE software version 13.6 (GE Healthcare, Madison, WI). Abdominal CT scans (120 kVp with 5-mm slice thickness) were acquired over 150 mm of the abdomen, starting at the top of the S1 landmark and extending toward the head. A subject-specific threshold in Hounsfield units was used in the CT analysis to identify VAT in the intra-abdominal cavity from the CT image data.

CT Single-Slice Analysis

CT slices at the $L_{2/3}$ and $L_{4/5}$ landmarks were identified from the reconstructed CT 3-dimensional images by counting the vertebrae. After the identification of the CT slice, the subcutaneous fat was removed using a semiautomatic method. A subject-specific threshold developed in previous report *(31)* was applied to the CT slice for the calculation of cross-sectional VAT. This analysis was performed independently by a single operator (XW) at GE Global Research Center (Niskayuna, NY), and an over-read was performed on approximately 10% of the data by a second operator (CED). Data were then transferred to GE Healthcare Lunar (Madison, WI) for equation development and validation.

Relationship Between CT Single-Slice and Volume VAT

Scatterplots between CT single-slice and volume measurements were performed for both $L_{2/3}$ and $L_{4/5}$. Regression analysis was used to examine gender differences and develop relationship between single-slice and volume measures. The linear relationship, in the form of single-slice VAT (cm^2) = a * VAT volume + b, as demonstrated by regression analysis, was applied to DXA VAT volume to derive single-slice values at $L_{2/3}$ and $L_{4/5}$.

Equation Validation

Analyses were performed using $L_{2/3}$ and $L_{4/5}$ VAT for each gender and for both genders combined. The Pearson correlation coefficients between the CT and DXA single-slice VAT were calculated in Excel[b], along with 95% confidence intervals from Fisher Z transformation. Bland-Altman analysis was also performed. Deming regressions of DXA on CT single-slice VAT were performed to detect proportional and constant bias. Analyse-it[b] Method Evaluation version 2.25 (Analyse-it Software, Ltd, Leeds, UK) was used for the Bland-Altman and Deming analysis. A significance level $\alpha = 0.05$ was used for all tests.

Results

Table 1 shows the subjects' characteristics separated by gender. Nine of the study subjects were excluded from the analysis because of defects in the CT scan (metal artifacts, no iliac crest present, and problems with image quality). The remaining 60 female and 55 male subjects were used in this study. The study subjects covered a wide range of age (21−85 yr) and BMI (20−39.7 kg/m^2). The resulting CT VAT volumes ranged from 42 to 3932 cm^3. CT single-slice VAT at $L_{2/3}$ ranged from 3.5 to 372.1 cm^2 and at $L_{4/5}$ from 12.2 to 378.1 cm^2.

Figure 1 illustrates the scatterplot between CT single-slice and volume measures. Single-slice VAT at $L_{2/3}$ (left) was highly correlated with VAT volume, and the relationship was similar for both genders. Single-slice VAT at $L_{4/5}$ (right) appeared to have more noise in the relationship, and there was an obvious gender difference.

Combined gender regression analysis (Table 2) found no gender differences in the $L_{2/3}$ slope and intercept, with the intercept not significantly different from 0 ($p = 0.5$). There was a significant gender difference in slope ($p < 0.001$), but not intercept, for the $L_{4/5}$ analysis. The $L_{4/5}$ intercept of 10.2 cm^2 was statistically significant. One female subject was excluded from the $L_{4/5}$ analysis as

[a]Trademark of General Electric Company.

[b]Excel is a trademark of Microsoft Corporation in the United States and other countries. Analyse-it is a product of Analyse-it Software, Ltd.

Table 1
Descriptive Statistics of the Study Subjects

	Female (N = 60)				Male (N = 55)			
Variable	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum
Age (yr)	48.4	14.3	21.2	85.4	49.3	14.2	21.1	77.1
Height (cm)	164.5	6.7	150.1	178.1	178.7	7.1	160.0	194.1
Weight (kg)	71.9	13.7	54.0	111.4	88.7	17.3	54.1	135.3
BMI (kg/m^2)	26.5	4.5	20.0	39.7	27.6	4.1	21.1	37.9
Waist circumference (cm)	87	14	68	129	97	12	74	127
Hip circumference (cm)	108	11	92	139	109	9	87	137
Waist/hip ratio	0.806	0.074	0.667	1.087	0.888	0.075	0.779	1.115
Total body region % fat	35.5	7.2	22.1	50.5	26.3	6.9	10.6	40.6
Android height (cm)	9.02	0.49	7.85	9.99	9.91	0.54	8.71	10.73
Android fat mass (g)	2237	1351	494	5943	2455	1306	402	6158
Android % fat	38.0	12.2	14.2	60.4	33.6	10.6	8.0	50.0
Gynoid % fat	41.2	6.3	29.4	51.6	26.5	7.0	6.7	41.7
Albumin/globulin ratio	0.911	0.228	0.414	1.515	1.276	0.312	0.603	2.653
CT VATV (cm^3)	673.5	760.8	41.7	3932.1	1341.0	947.9	169.3	3845.9
CT $L_{2/3}$ VATA (cm^2)	67.3	77.0	3.5	358.4	136.2	94.5	13.8	372.1
CT $L_{4/5}$ VATA (cm^2)	76.6	80.6	12.2	378.1	103.6	67.8	14.4	286.2

Abbr: BMI, body mass index; CT, computed tomography; SD, standard deviation; VATA, visceral adipose tissue area; VATV, visceral adipose tissue volume.

an extreme outlier (standardized residual 6.0). The strong relationship between the CT slice area and volume suggests that it can be used to develop equations to calculate single-slice VAT from DXA VAT volume. Single-slice VAT for $L_{2/3}$ can be computed from DXA VAT volume for both males and females as

$$\text{VAT } L_{2/3}\left(\text{cm}^2\right) = 0.1 * \text{DXA VAT volume}\left(\text{cm}^3\right) \quad (1)$$

Single-slice VAT for $L_{4/5}$ can be computed for females as

$$\text{VAT } L_{4/5}\left(\text{cm}^2\right) = 0.096 * \text{DXA VAT volume}\left(\text{cm}^3\right) + 10.2\ \text{cm}^2 \quad (2)$$

and for males as

$$\text{VAT } L_{4/5}\left(\text{cm}^2\right) = 0.069 * \text{DXA VAT volume}\left(\text{cm}^3\right) + 10.2\ \text{cm}^2 \quad (3)$$

Agreement between DXA-computed single-slice measurement and CT was examined by comparing the results

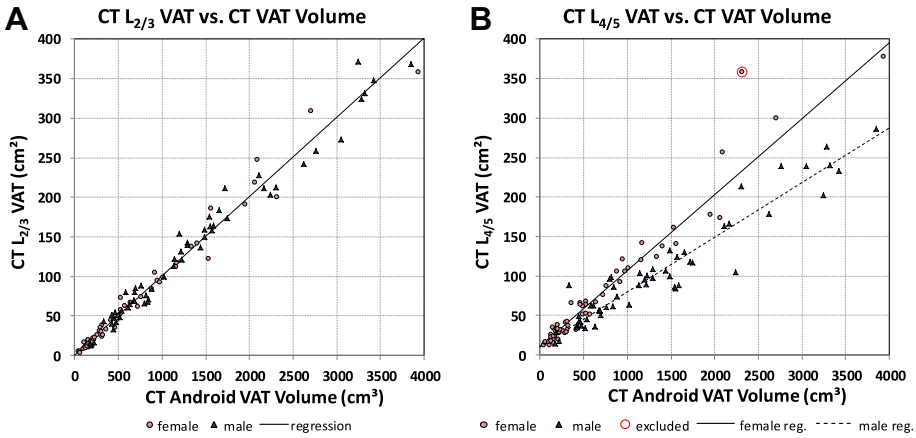

Fig. 1. Scatterplots between CT single-slice and volume measures for (**A**) $L_{2/3}$ and (**B**) $L_{4/5}$. CT, computed tomography; VAT, visceral adipose tissue.

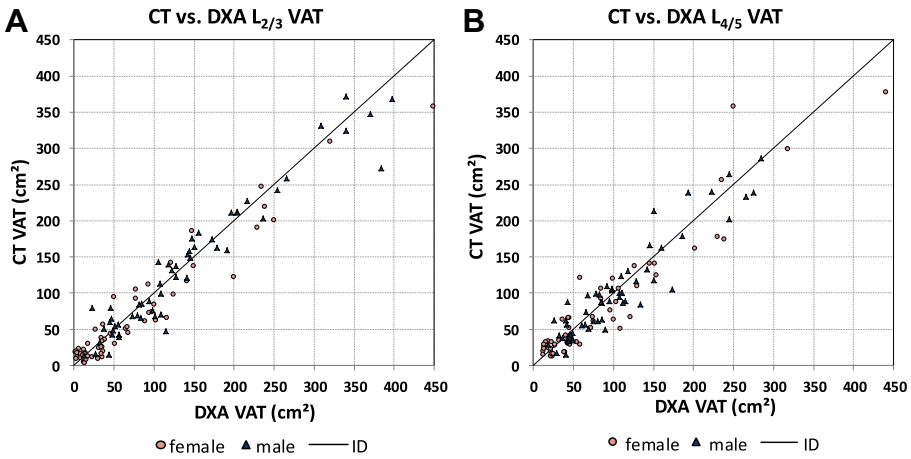

Fig. 2. Plot of DXA-computed single-slice VAT measurement against CT for (**A**) $L_{2/3}$ and (**B**) $L_{3/4}$. CT, computed tomography; DXA, dual-energy X-ray absorptiometry; VAT, visceral adipose tissue.

along the identity line in correlation analysis (Fig. 2). The Pearson correlation coefficient (r) with 95% confidence interval between CT and DXA single-slice VAT was 0.94 (0.92, 0.96) for $L_{2/3}$ and 0.96 (0.95, 0.98) for $L_{4/5}$.

Bland-Altman analyses of the agreement between the CT and DXA single-slice VAT (Fig. 3) showed a statistically significant ($p = 0.037$) +5 cm^2 bias (CT as the standard) for $L_{2/3}$ with 95% limits of agreement −44.6 to +54.6 cm^2. For $L_{4/5}$, the bias was +3.8 cm^2 and not significantly different from 0 ($p = 0.12$), with the 95% limits of agreement −47.3 to +54.9 cm^2.

Deming regressions of the CT and DXA VAT areas found slopes ($L_{2/3}$ 1.07, $L_{4/5}$ 1.03) and intercepts ($L_{2/3}$ −1.6 cm^3, $L_{4/5}$ +1.6 cm^3), which were not significantly different from the identity values of 1 and 0.

Discussion

In this study, we describe an algorithm to calculate single-slice VAT at the $L_{2/3}$ and $L_{4/5}$ levels from a DXA VAT volume measurement. It is interesting to note that the intercept for the calculation of single-slice VAT at $L_{4/5}$ does not go through 0 (Eqs. 2 and 3). There are 2 possible explanations. First, in a significant number of individuals, the location of $L_{4/5}$ was below the iliac crest and therefore outside the lower boundary of the DXA android region. Second, based on limited profile data, single-slice VAT at $L_{4/5}$ appears more variable than $L_{2/3}$ and less indicative of the VAT volume in the DXA android region. For cases where DXA VAT volume is below the detection threshold, single-slice VAT should be reported as $\leq$10.2 cm^2.

The estimated single-slice VAT area is in good agreement with CT measurements. The average difference between DXA and CT single-slice VAT was 5 cm^2 for $L_{2/3}$ slice and 3.8 cm^2 for $L_{4/5}$ slice. These differences are relatively small compared with the average CT single-slice VAT of 67 cm^2 for females and 136 cm^2 for males at $L_{2/3}$ as well as 77 cm^2 for females and 104 cm^2 for males at $L_{4/5}$. The difference for $L_{2/3}$ is statistically significant, and further analysis showed a significant difference for females (bias = +7 cm^2 with $p = 0.028$), but not for males (bias = +2.7 cm^2 with $p = 0.45$), suggesting that further adjustment may be warranted for the $L_{2/3}$ estimation for females. The difference for $L_{4/5}$ is not statistically significant, and no adjustment is currently indicated.

Bland-Altman plots (Fig. 3) suggest constant bias for estimated DXA single-slice VAT across the range of values observed in our study ($L_{2/3}$ from 3.5 to 372.1 cm^2 and $L_{4/5}$ from 12.2 to 378.1 cm^2). The fact that the Deming regression slopes are not significantly different from 1 further indicates that the bias is independent of total VAT in this range. Several studies have proposed that single-slice VAT values above thresholds of 106−110 and 160 cm^2 are associated with elevated or greater risk for metabolic syndrome and coronary heart disease *(28,32,33)*. The bias observed in this study is less than 5% of those values. In addition, a 4.8% coefficient

Table 2
Combined Gender Regression Analysis for $L_{2/3}$ and $L_{4/5}$ Regions

Slice	df	Slope (95% CI)	Intercept (95% CI)	Male slope difference (95% CI)	SEE
$L_{2/3}$	114	0.100 (0.099, 0.102)	—	—	13.4
$L_{4/5}$	111	0.096 (0.091, 0.101)	10.2 (5.7, 14.7)	−0.0269 (−0.032, −0.022)	16.3

Abbr: CI, confidence interval; df, degrees of freedom; SEE, standard error of the estimate.

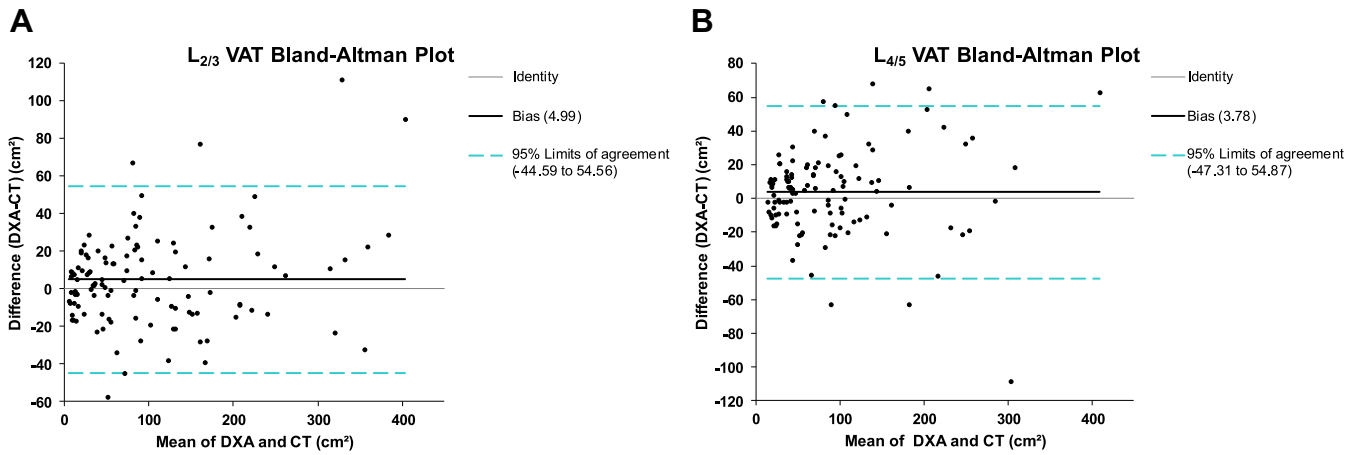

Fig. 3. Bland-Altman analyses of agreement between DXA-computed single-slice VAT measurement and CT for (**A**) $L_{2/3}$ and (**B**) $L_{3/4}$. CT, computed tomography; DXA, dual-energy X-ray absorptiometry; VAT, visceral adipose tissue.

of variation was reported for DXA VAT for an average observed VAT volume of approximately 1000 cm^3 *(34)*. The relationship between VAT volume and area indicates that there should be similar precision for DXA VAT slice areas of about 100 cm^2. The small bias and good precision suggest that DXA single-slice VAT has adequate accuracy and precision to evaluate potential disease outcomes associated with elevated VAT.

DXA offers a low cost, low dose, and automated alternative to quantify VAT as compared with CT or MRI. A typical DXA total body examination will expose a patient to 0.96 μSv radiation dose compared with a 3100 μSv abdominal CT scan. The scan takes 3−5 min to complete, and the calculation of VAT is automatic. These advantages have the potential to make DXA the method of choice for VAT measurement. For investigators and clinicians who want to use both DXA and CT, or switch from CT to DXA, a common challenge has been the comparability of data obtained from these different technologies. These results should address that problem, although a small cross-calibration study is recommended to ensure maximum correspondence between devices.

The relationships shown in Eqs. 1−3 should only be used for Lunar DXA devices, currently Prodigy and iDXA, to estimate DXA single-slice VAT. The equations were derived from volumetric VAT acquired and analyzed using CT under a specific protocol against which the Lunar DXA VAT volume was calibrated. Applying these equations to other DXA devices that may be calibrated to different CT protocols could be a problem because the quantification of volumetric VAT in CT can be affected by the selection of different regions, slice thickness, or tissue threshold, and this could result in larger bias and variation.

There are some limitations in this study. First, this is the retrospective analysis of data from a previously conducted clinical study. Sample size was thus not designed to detect a specific VAT area difference threshold. The study subjects were predominately white with BMI within 18−40 kg/m^2. However, the results did demonstrate that such an analysis is a reasonable first step to estimate CT single-slice VAT from a DXA measurement. Second, this study did not include locations other than the $L_{2/3}$ and $L_{4/5}$ landmarks. It may be useful to examine additional locations, such as the umbilicus, to expand the utility of DXA VAT area measurements.

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