ORIGINAL ARTICLE

Comparison of high-resolution peripheral quantitative computerized tomography with dual-energy X-ray absorptiometry for measuring bone mineral density

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BACKGROUND/OBJECTIVES: The objective of this study was to compare the measurement of areal bone mineral density (aBMD) by dual-energy X-ray absorptiometry (DXA) with the measurement of volumetric bone mineral density (vBMD) by high-resolution peripheral computerized tomography (HR-pQCT) in subjects with a wide range of body mass indices (BMI).
SUBJECTS/METHODS: We scanned the arms and legs of 49 premenopausal women, aged 21–45 years, with BMI from 18.5 to 46.5, by HR-pQCT and found that there was a nonsignificant change in vBMD associated with increased BMI, whereas aBMD (DXA) was associated with a positive significant increase. HR-pQCT scans a slice at the extremity of the tibia and radius, whereas DXA scans the entire leg and arm.
RESULTS: The correlation coefficients (r) of BMD (DXA) of the legs with BMI were 0.552, $P < 0.001$, with %fat it was 0.378, $P < 0.01$ and with W it was 0.633, $P < 0.001$. The r of BMD (DXA) of the arms with BMI was 0.804, $P < 0.001$, with %fat it was 0.599, $P < 0.001$ and with W it was 0.831, $P < 0.001$, whereas the r of the average bone density (D100) of legs and arms measured by HR-pQCT with BMI, W and %fat were not significant.
CONCLUSIONS: Although HR-pQCT and DXA scan different parts of the bone, the high r of BMD with BMI and low r of bone density measured by HR-pQCT with BMI suggest that BMD measured by DXA is artifactually increased in the presence of obesity.

European Journal of Clinical Nutrition (2017) **71,** 778–781; doi:10.1038/ejcn.2016.178; published online 19 October 2016

INTRODUCTION

Dual-energy photon absorptiometry (DXA) has long been the standard for monitoring areal bone mineral density (aBMD). However, the accuracy of DXA in obesity has been challenged.[1] We have compared volumetric bone mineral density (vBMD) measured by high-resolution peripheral computerized tomography (HR-pQCT) with the results obtained by DXA (aBMD) in a group of 49 healthy premenopausal, normally menstruating women, aged 21–45 years, spanning a range of BMI (18.1–46.5). They were exercising < 4 h per week, and did not have conditions or medications known to affect bone; we wanted to see whether the results of scanning with HR-pQCT paralleled those of DXA in subjects with a wide range of BMI. The subjects gave informed consent, and the study was approved by our institutional review board.

Table 1 shows the demographics of the study population.

STATISTICS AND GENERAL METHODS

Using data from 187 female individuals between 18 and 45 years of age, the mean and s.d. for the total body bone density by DXA are 1.2044 and 0.1107, respectively. Using these results and assuming a correlation between the two measurements of BMD equal to 0.7 gives a s.d. for the difference between two measurements equal to 0.0857. This calculation assumes that the s.d.'s of BMD are equal for the two instruments. A sample of size 45 has a power of 80% for detecting a difference between mean BMD of the two instruments equal to 0.0386. This corresponds to detecting a difference equal to 3.2% of the mean.

DXA

Areal BMD of all bones in all areas was measured by DXA (GE Lunar iDXA, Madison, WI, USA) in whole-body mode. Participants were measured on the same densitometer with the same software, scan speed and technologist. The long-term stability was assessed by daily measurements of the Lunar spine phantom. The long-term precision was 0.35%, and the least significant change for BMD measurements was 1.00%. The software provides values for the masses of muscle, fat and bone for the whole-body and specific regions.

HR-pQCT imaging

Structural bone parameters of the nondominant distal radius and left distal tibia were assessed by HR-pQCT (XtremeCT Scanco Medical AG, Brutisellen, Switzerland). A stack of 110 slices with a nominal voxel size of 82 μm was obtained, with the most distal computerized tomographic (CT) slice placed 9.5 mm from the endplate of the radius or 22.5 mm from the endplate of the tibia. The coefficient of variation of a phantom containing hydroxyl-apatite (HA) rods embedded in resin (QEM, Moehrendorf, Germany) was 0.7% to 1.5%. The volume of interest was automatically separated into a cortical area (Ct Ar) and trabecular area (Tb Ar). D100 is the average vBMD in a scanned region. One scan of the distal radius was excluded because the subject was unable to control the shaking of her hand.

RESULTS

Table 1 shows that the average and compact bone density (HR-pQCT) are both higher in the radius than in the tibia, whereas DXA shows a higher bone density for the legs (weight-bearing bone) compared with the arms. Slice area (which reflects cross-sectional

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Table 1. Demographic and scanner parameters of the study population

Variable	Units	Mean	s.d.	Min	Max
Age	Years	32.4	6.4	21	44.7
Weight (*W*)	kg	73	21.3	46.7	131.5
Height (*H*)	m	1.63	0.05	1.48	1.77
BMI	kg/m^2	27.3	6.7	18.1	46.5
Tibia HR-pQCT					
Slice area	mm^2	679	109.6	483.2	948.4
Perimeter	mm	101.9	8.5	85.5	120.6
Cortical thickness	mm	1.2	0.22	0.75	1.8
Cortical area	mm^2	122.3	22.1	78.75	193.5
Average bone density	mg HA/cm^3	309.7	47.1	226.4	454
Compact bone density	mg HA/cm^3	910.3	38.1	827	1018
Trabecular bone density	mg HA/cm^3	170.5	36.5	87	263
Radius HR-pQCT					
Slice area	mm^2	240.7	42	149.6	337.1
Perimeter	mm	65.3	6.2	50.6	78.6
Cortical thickness	mm	0.84	0.15	0.48	1.24
Cortical area	mm^2	54.7	7.88	35.5	71.6
Average bone density	mg HA/cm^3	345.5	57.35	231.9	482.4
Compact bone density	mg HA/cm^3	918.4	41.61	793.5	1010.1
Trabecular bone density	mg HA/cm^3	160	35.97	83.8	256
BMD DXA					
Legs	g/cm^2	1.2276	0.1119	1.021	1.674
Arms	g/cm^2	0.7665	0.1159	0.586	1.167

Abbreviations: BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; HA, hydroxyl apatite; HR-pQCT, high-resolution peripheral computerized tomography.
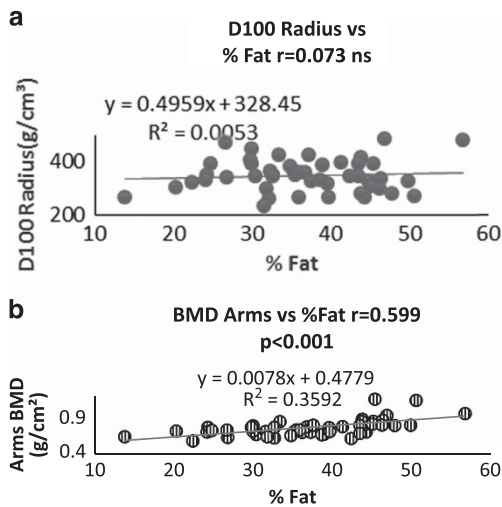

Figure 1. (**a**) D100 Radius and (**b**) BMD Arms vs %Fat.

area) and Cortical thickness are greater in the tibia than in the radius, and this difference in geometry makes it difficult to interpret the difference in volumetric bone density (HR-pQCT); bone strength is dependent inter alia on cross-sectional area and cortical thickness.[2]

Figure 1 shows that BMD arms is significantly correlated with % fat, whereas D100 (average vBMD by HR-pQCT) is nonsignificantly correlated with %fat. Table 2 shows that there is significant *r* between BMD (DXA) of legs and arms with BMI, as well as *W* and %fat, whereas there is no significant *r* between D100 (HR-pQCT) and these variables. There is no significant *r* between age and

BMD or between age and D100 radius, but there is a significant *r* between age and D100 tibia

Table 3 shows that SI area (cross-sectional area) Tibia is correlated with *W*, BMI, %fat and Age. SI area radius is correlated with *W*, BMI and age. Adult bones expand in diameter throughout adult life, apparently in adaptation to changing mechanical demands[3]—seen by HR-pQCT, but not by DXA. The increased bone cross-sectional area should decrease BMD (DXA) with increased BMI, instead of the increase that we found.

Figure 2 shows the *r* between D100 radius vs %fat and BMD arms vs %fat. The residuals of D100 (HR-pQCT)/BMD (DXA) plotted against % fat have no significant *r* with the radius/arms ($r = -0.186$ ns), but for the tibia/legs $r = -0.378$, $P < 0.01$ are shown in Figure 3.

DISCUSSION
Bolotin *et al.* showed that all soft tissue (fat and muscle) inhomogeneities could cause inaccuracies as large as 20–50% in BMD measured by DXA.[1] They reported that the ratio of fat to lean and the ratio of yellow to red bone marrow in the region of interest have a major effect on the measured BMD. We have shown *in vitro* that surrounding fat markedly alters the result of BMD measured by DXA.[4] We have shown that this happens to a lesser extent with HR-pQCT.[5]

Bosy–Westphal *et al.* have shown that the configuration of fat and muscle around the bone and fat within the bone can markedly alter the measured BMD result. This is probably because DXA can distinguish only two components in one pixel using the attenuation ratio of two different X-ray energies, whereas the output actually consists of three components—bone, fat and muscle. In pixels containing bone, the composition of the soft tissue cannot be measured, and thus in those pixels soft tissue has to be extrapolated from adjacent areas. This assumption is invalid if the composition of the soft tissue in front of, or behind the bone

Table 2. Correlations of BMD and D100 of arms and legs

Item #	r
1 Legs BMD vs W	0.639
2 Legs BMD vs BMI	0.552
3 Legs BMD vs % Fat	0.378
4 Legs BMD vs Age	0.114
5 Arms BMD vs W	0.831
6 Arms BMD vs BMI	0.804
7 Arms BMD vs % Fat	0.599
8 Arms BMD vs Age	0.105
9 Tibia D100 vs W	0.089
10 Tibia D 100 vs BMI	0
11 Tibia D100 vs % Fat	0.121
12 Tibia D100 vs Age	0.305
13 Rad D100 vs W	0.014
14 Rad D100 vs BMI	0
15 Rad D100 vs % Fat	0.073
16 Rad D100 vs Age	0.189
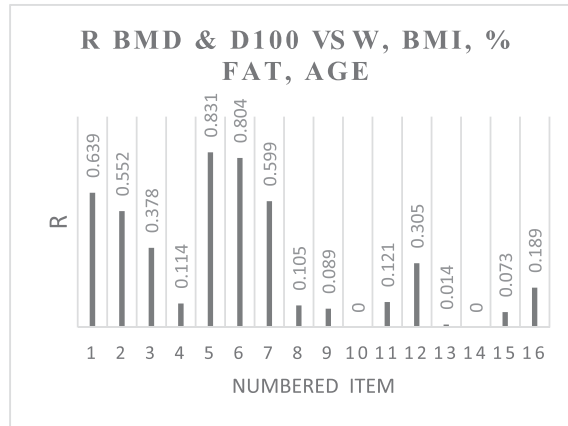
R BMD & D100 VS W, BMI, % FAT, AGE

| NS	<0.279
p<0.01	0.279-0.361
p<0.001	>0.451

Abbreviations: BMD, bone mineral density; NS, not significant.

Table 3. Correlations of Slice Area of arms and legs with various parameters

Item #	r
1 Sl Area Tibia vs W	0.564
2 Sl Area Tibia vs BMI	0.466
3 Sl Area Tibia vs % Fat	0.226
4 Sl Area Tibia vs Age	0.394
5 Sl Area Radius vs W	0.496
6 Sl Area Radius vs B BMI	0.444
7 Sl Area Radius vs % Fat	0.193
8 Sl Area Radius vs A Age	0.404
9 Sl Area Tibia vs BMD Legs	0.462
10 Sl Area Radius vs BMD Arms	0.377
11 Sl Area Tibia vs D100 Tibia	-0.495
12 Sl Area Radius vs D100 radius	-0.59

R SL AREA WITH VS, BMI, % FAT, AGE & BMD

NS	<0.279
p<0.01	0.279-0.361
p<0.001	>0.451
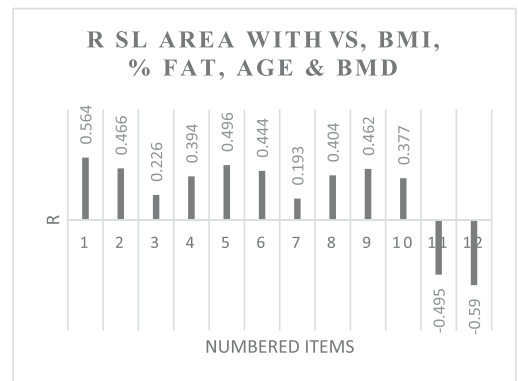
Abbreviations: BMD, bone mineral density; NS, not significant.

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or the bone marrow fat differs in composition from soft tissue next to the bone. An undetected loss of fat either in front of, behind or within the bone leads to an increase in pixel density that may lead to an overestimation of BMD.[6]

The difference in *r* between BMI and the bone parameters measured by HR-pQCT and those measured by DXA may possibly be explained by a difference in the effect of fat on the absorption of X-rays causing an artifactual increase in BMD measured by DXA.

The measurement of BMD by HR-pQCT did not parallel that of DXA in subjects with increasing BMI. Our results by HR-pQCT were obtained with Scanco I, which has a voxel size of 82 μm³. The results of Scanco I partially depend on identification of bone obtained by the absorption of X-rays in the region of interest. This study should be repeated with Scanco II, which is a second-generation HR-pQCT scanner with a voxel size of 61 μm³.[7] This will provide a geometric measurement of the amount of bone, the result of which does not depend on the absorption of X-rays. We have shown by radiogrammetry that geometric measurements of bone thickness are not altered by surrounding fat.[8] The decreased dependence (with Scanco II) on absorption of X-rays may permit a
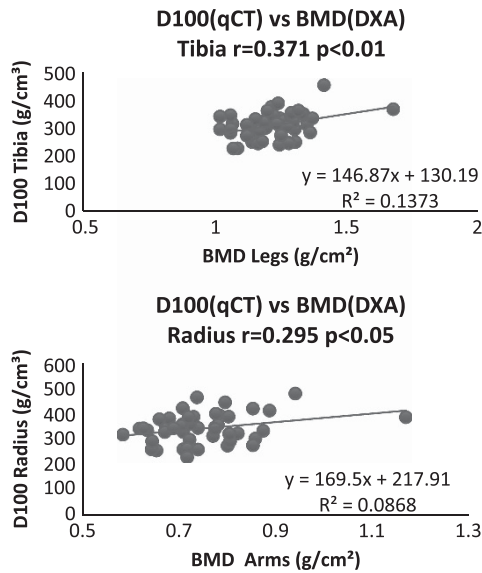
D100(qCT) vs BMD(DXA)
Tibia r=0.371 p<0.01

$$y = 146.87x + 130.19$$
$$R^2 = 0.1373$$

D100(qCT) vs BMD(DXA)
Radius r=0.295 p<0.05

$$y = 169.5x + 217.91$$
$$R^2 = 0.0868$$

Figure 2. D100(qCT) vs BMD(DXA).

Residuals qCT Tibia\BMD Legs v % Fat r=-0.378 p<0.01

$$y = -3.2869x + 121.05$$
$$R^2 = 0.1427$$

Residuals qCT Radius\BMD Arms v % Fat r=-0.186 ns
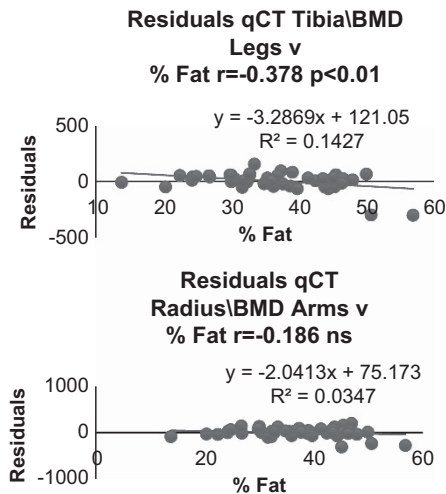

$$y = -2.0413x + 75.173$$
$$R^2 = 0.0347$$

Figure 3. Residuals of qCT/BMD vs %Fat.

more accurate assessment of the ability of HR-pQCT to measure BMD independently of the amount of surrounding fat.

DXA and HR-pQCT scan different parts of long bones. HR-pQCT shows that increasing BMI is associated with increased bone cross-section. This would tend to decrease measured BMD (DXA) as opposed to the increase that we observed with increasing BMI.

CONCLUSIONS

Our study suggests that the increased BMD (DXA) found with increased BMI may partly be an artifact caused by absorption of X-rays by fat and muscle. It is important to validate the measurement of BMD by DXA in the context of obesity because of the large number of studies that depend on it.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

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