

Association between bone indices assessed by DXA, HR-pQCT and QCT scans in post-menopausal women

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Abstract Quantitative computed tomography (QCT), high-resolution peripheral QCT (HR-pQCT) and dual X-ray absorptiometry (DXA) scans are commonly used when assessing bone mass and structure in patients with osteoporosis. Depending on the imaging technique and measuring site, different information on bone quality is obtained. How well these techniques correlate when assessing central as well as distal skeletal sites has not been carefully assessed to date. One hundred and twenty-five post-menopausal women aged 56–82 (mean 63) years were studied using DXA scans (spine, hip, whole body and forearm), including trabecular bone score (TBS), QCT scans (spine and hip) and HR-pQCT scans (distal radius and tibia). Central site measurements of areal bone mineral density (aBMD) by DXA and volumetric BMD (vBMD) by QCT correlated significantly at the hip ($r = 0.74$, $p < 0.01$). Distal site measurements of density at the radius as assessed by DXA and HR-pQCT were also associated ($r = 0.74$, $p < 0.01$). Correlations between distal and central site measurements of the hip and of the tibia and radius showed weak to moderate correlation between vBMD by HR-pQCT and QCT ($r = -0.27$ to 0.54). TBS correlated with QCT at the lumbar spine ($r = 0.35$) and to trabecular indices of HR-pQCT at the radius and tibia ($r = -0.16$ to 0.31 , $p < 0.01$). There was moderate to strong agreement between measuring techniques when assessing the same skeletal site. However, when assessing correlations between central and distal sites, the associations were only

weak to moderate. Our data suggest that the various techniques measure different characteristics of the bone, and may therefore be used in addition to rather than as a replacement for imaging in clinical practice.

Keywords aBMD · vBMD · QCT · DXA · HR-pQCT

Introduction

Osteoporosis is a metabolic disorder resulting from changes in bone mineral density, bone geometry and microstructure that leads to an increased susceptibility to fractures. Currently, diagnosis of osteoporosis is based on areal bone mineral density (aBMD; g/cm^2) values gained from 2D techniques (dual X-ray absorptiometry or DXA scans). However, aBMD has been shown to be only a partial predictor of fracture risk [1, 2]. This may in part be due to the fact that 2D measures do not fully reflect the distribution of bone mass, including the relative contribution from cortical and trabecular bone or the microarchitecture of the bone matrix. For these aspects, imaging techniques such as quantitative computed tomography (QCT) and high-resolution pQCT (HR-pQCT) may present much better alternatives. QCT techniques enable measurements at central sites such as lumbar spine and hip [3] and are considered to measure true volumetric BMD (vBMD; mg/cm^3). HR-pQCT, an improved detector technique combined with beam acquisition originally designed for micro-computed tomography, permits in vivo assessment of trabecular and cortical architecture and vBMD at distal sites such as the tibia and radius [4]. In addition, these images can be used for microstructural finite element analysis (FEA) that integrates BMD with bone geometry and structure to estimate bone strength under various loading conditions [4].

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For the above-mentioned reasons, 3D images have become important clinical research tools when investigating, e.g., hip and femoral bone structure [5, 6], the effects of therapeutic agents [7, 8] and age- and sex-related changes [9, 10]. Furthermore, the trabecular bone score (TBS) derived from textural images (by DXA) of the spine is related to microarchitecture and fracture risk [11]. Whether these different measuring techniques can supplement each other or can fully replace DXA scanning by improving prediction of fracture risk and treatment outcomes is, however, still speculative.

The fact that DXA scans are still the first choice when evaluating bones may relate to the lower relative cost compared to the other techniques. DXA scans are easy to perform and the daily operation costs are low. QCT scans are more cost-effective than DXA scans, and the dose of radiation is much higher. A HR-pQCT scanner, on the other hand, is quick to use, but relatively expensive to purchase and still a rather exclusive measurement not available at all treatment centres.

Only very few studies have so far investigated the associations between indices of DXA, HR-pQCT and QCT scans and TBS. In previous studies including only premenopausal women, central site correlations were reported between aBMD and vBMD varying from $r = 0.77$ to 0.79 , while distal and central associations of vBMD varied from $r = 0.36$ to 0.78 [12]. In a group of pre- and post-menopausal mixed-race women, authors reported TBS correlations between $r = 0.20$ and 0.52 at peripheral sites by HR-pQCT and at central sites by QCT from $r = 0.35$ to 0.66 [13].

To the best of our knowledge, no study has yet investigated the relationship between all the above-mentioned scanning techniques in only post-menopausal women. Therefore, the aim of this study is to assess the correlations between central and distal measurements of aBMD, and TBS as assessed by DXA, and vBMD, geometry, microstructure and strength as measured by 3D scanning techniques in terms of QCT- and/or HR-pQCT scans, at central and peripheral sites within a relatively large group of post-menopausal Caucasian women.

Materials and methods

Study population

A total of 125 women aged 63 years (range 56–82) participated in the study. The major inclusion criterion was post-menopausal status. Eighty-one of the women were diagnosed with osteopenia as they had been screened by DXA (T -score: -1 to -2.5) in order to be included in an ongoing randomized clinical trial (NCT01690000). Data on the women are derived from baseline before any study-related action was taken. Forty-four of the subjects included in this

analysis had been recruited as healthy controls for participation in two cross-sectional studies and did not have DXA scans performed prior to their inclusion; i.e., they were not selected/included due to a known low bone mass [14, 15]. The exclusion criteria for the study were as follows: impaired renal function (plasma creatinine >120 $\mu\text{mol/l}$), diagnosed with malignant disease within 2 years, intestinal malabsorption, abuse of alcohol, medical condition known to affect bone including drugs with effects on calcium homeostasis and bone metabolism. None of the study subjects were on treatment with experimental drugs at the time of investigations.

All subjects studied were recruited to the respective studies by a mailed letter sent to a random sample of the general background population inviting them to participate in the studies.

All subjects provided informed consent prior to participation in the studies. All studies were approved by the regional ethics committee (#M-2010-0296; #M2012-252-12; #M2011-0260).

The following measurements were conducted as a part of an integrated study program for the subjects; i.e. all scans were performed within 2 weeks of each other.

Osteodensitometry by DXA

We measured areal bone mineral density (aBMD; g/cm^2) on the right forearm, lumbar spine (L1–L4), the left hip region, and whole body (sub-total) using a Hologic Discovery scanner (Hologic, Inc., Waltham, MA, USA). The forearm included radius + ulnar (total, ultra-distal, one-third and mid). For each scan, the system automatically calculates the region of interest (ROI). When evaluating the forearm, the ROI is based on the length of the forearm divided by three, plus 10 mm to allow for the ultra-distal region.

According to the product information, the total radiation dose was a maximum of 0.95 mSV, equal to approx. 120 days of normal background radiation in Denmark [16].

HR-pQCT

At the distal tibia and distal radius, we measured volumetric bone mineral density (vBMD; mg/cm^3), geometry, microarchitecture, and strength on the right side using a high-resolution pQCT scanner (Xtreme CT scanner, Scanco Medical AG, Brüttisellen, Switzerland). Each scan comprised 110 slices corresponding to a 9.02-mm axial 3D representation with an isotropic voxel size of 82 μm . The tibia and radius were immobilized in a carbon fibre cast during the measurements. A scout view was used to define the measurement region, using an offset from the endplate of the radius and tibia by 9.5 and 22.5 mm, respectively. Daily and weekly phantom scans were performed.

According to the manufacturer's default methods (by Xtreme CT scanner, Scanco Medical AG), trabecular bone density (D_{trab}) was calculated as an average mineral density within the trabecular region assuming a density of fully mineralized bone of 1.2 mg hydroxyapatite (HA)/cm³, thereby calculating trabecular bone volume per tissue volume (BT/BV) [17].

Trabecular architecture was assessed as trabecular number (Tb.N), which was obtained using a model-independent distance transformation method; trabecular thickness (Tb.Th) and trabecular spacing (Tb.Sp) were then derived from BV/TV and Tb.N [Tb.Th = (BV/TV)/Tb.N; Tb.Sp = (1 – BV/TV)/Tb.N]. Cortical thickness (Ct.Th) was measured according to the manufacturer's standard patient protocol.

In addition, HR-pQCT images were used for FEA [18]. Model solving was performed by Scanco FEA software v1.13. The evaluation is described in detail by Hansen et al. [19]. In short, bone voxels are converted into equally-sized square elements resulting in approx. two and five billion element models for radius and tibia, respectively. According to the product information from the manufacturer, the radiation dose of each scan was <0.0030 mSV, which is approximately equal to half a day of background radiation [16]. The parameter of interest was failure load.

Quantitative computed tomography (QCT)

We measured vBMD (mg/cm³) at the lumbar spine (L1–L2) and proximal femur by QCT using a Philips Brilliance 40-slice multidetector helical CT scanner (Phillips, Eindhoven, The Netherlands). We scanned with a dose modulation tool (Z-DOM, Phillips) at a voltage of 120 kV. Slice thickness and slice spacing were 3 mm. The field of view was 360 mm and collimation was 40 × 0.625 mm. According to the manufacturer, the total radiation dose was a maximum of 2.75 mSV, equal to less than 1 year of background radiation [16]. The vBMD was determined using QCTPro (version 4.2.3, Mindways Software, Inc., Austin, TX, USA) in conjunction with a solid-state CT calibration phantom (Model 3, Mindways Software), which was scanned simultaneously with the patients. We performed analysis of the proximal femur by automatic bone segmentation including the total hip and femoral neck [20]. The separation algorithm for cortical bone was pre-set at 350 mg/cm³.

The reproducibility [coefficient of variation (CV%)] of the analyses by QCTPro was calculated by repeating evaluation analyses of ten subjects' data, showing a CV from vBMD of 0.8 % at the total hip and 1.1 % at L1 + L2.

Trabecular bone score (TBS)

Lumbar spine TBS was extracted from DXA images using iNsign software (Medimaps, France). The score was

evaluated by determination of the grey-level variations of the anterior–posterior DXA image of the lumbar spine [21]. A higher score indicates a better microstructure (high trabecular number and connectivity and low trabecular separation). The mean value of each vertebra (L1–L4) was collected into a single score.

Statistical analysis

We report results as mean ± standard deviation (SD) or median with interquartile range (IQR 25–75 %) unless otherwise stated. Associations between variables were assessed by linear regression analyses calculating Pearson's correlation coefficient (*r*) and the regression coefficient (*β*) with 95 % confidence interval (95 % CI). *p* < 0.05 was considered statistically significant. We used IBM SPSS Statistics version 21 (IBM, New York, USA) for the statistical analyses.

Results

Descriptive data are shown in Table 1. The mean age of the participants was 63 years (range 56–82).

DXA, TBS and HR-pQCT

Correlations between TBS, aBMD values at different skeletal sites, and indices of HR-pQCT at distal radius and tibia are shown in Table 2. Significant correlations were observed, and at distal sites, in particular at the distal radius, moderate to strong (*r* = 0.48–0.75) associations were seen in relation to aBMD at the ultra-distal forearm. Furthermore, moderate correlations were observed between geometric indices of cortical area by tibia (*r* = 0.55) and radius (*r* = 0.63), and aBMD at distal forearm (data not shown).

Failure load of radius and tibia correlated significantly with all skeletal sites (*p* < 0.01), and a strong correlation (*r* = 0.80) was present between aBMD at the distal forearm and failure load of distal radius by HR-pQCT. Overall, TBS showed only weak correlation to trabecular indices of the radius and tibia (*r* = –0.16 to 0.31, *p* < 0.01).

Adjusting the correlations for age did not change the results (data not shown).

HR-pQCT and QCT

Table 3 shows correlations between peripheral HR-pQCT measurements of radius and tibia and central vBMD measurements by QCT at the lumbar spine and total hip. At the radius and tibia, vBMD total bone density by HR-pQCT correlated moderately with integral total hip vBMD

Table 1 Descriptive data

	Median (IQR)
Age (years), mean (range)	63 (56–82)
Height (cm)	165.0 (161.0–169.6)
Weight (kg)	67.1 (60.5–76.0)
BMI (kg/m ²)	24.8 (22.2–27.5)
Smokers, <i>n</i> (%)	6 (5 %)
DXA BMD (<i>n</i> = 125)	
Lumbar spine (g/cm ²)	0.857 (0.808–0.952)
Hip, total (g/cm ²)	0.795 (0.740–0.848)
Hip, neck (g/cm ²)	0.654 (0.620–0.707)
Forearm, ultradistal (g/cm ²)	0.319 (0.295–0.351)
Whole body, subtotal (g/cm ²)	0.851 (0.810–0.907)
QCT (<i>n</i> = 98)	
Spine, trabecular vBMD (mg/cm ³)	98 (81–114)
Total hip, integral vBMD (mg/cm ³)	253 (234–282)
Total hip, cortical vBMD (mg/cm ³)	909 (878–938)
Total hip, trabecular vBMD (mg/cm ³)	132 (120–142)
HR-pQCT	
Distal radius (<i>n</i> = 118)	
Total bone density (mg HA/cm ³)	264 (220–302)
Cortical bone density (mg HA/cm ³)	839 (782–881)
Trabecular bone density (mgHA/cm ³)	125 (98–149)
Ct.Th (mm)	0.64 (0.49–0.74)
Tb.Th (mm)	0.06 (0.05–0.06)
Tb.N (mm ⁻¹)	1.80 (1.50–2.03)
Tb.Sp (mm)	0.50 (0.43–0.61)
TrBV/TV (mm)	0.10 (0.08–0.12)
Tb.N.SD (mm)	0.24 (0.18–0.34)
Failure load (N)	3038 (2708–3417)
Distal tibia (<i>n</i> = 123)	
Total bone density (mg HA/cm ³)	249 (216–278)
Cortical bone density (mg HA/cm ³)	819 (784–851)
Trabecular bone density (mg HA/cm ³)	149 (123–168)
Ct.Th (mm)	0.91 (0.75–1.06)
Tb.Th (mm)	0.07 (0.06–0.08)
Tb.N (mm ⁻¹)	1.69 (1.48–1.91)
Tb.Sp (mm)	0.52 (0.46–0.59)
TrBV/TV (mm)	0.12 (0.10–0.14)
Tb.N.SD (mm)	0.24 (0.20–0.31)
Failure load (N)	8579 (7891–9690)

Median with 25–75 % interquartile range

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($r = 0.54$, $r = 0.50$, respectively). Cortical vBMD by HR-pQCT and QCT showed correlation coefficients of $r = -0.39$ at radius and $r = -0.27$ at tibia, while indices of trabecular vBMD correlated by $r = 0.37$ at radius and $r = 0.44$ at tibia. Adjusting for age did not change the results (data not shown).

Geometric indices of tibia and radius correlated weakly to moderately with QCT sites ($r = 0.19$ – 0.48 , data not shown). The correlations with microstructural architecture showed significance, although weak, at several measurement sites.

Failure load at both tibia and radius showed weak or no correlations with QCT vBMD.

DXA, TBS, and QCT

Table 4 shows correlations between aBMD at different skeletal sites and central sites of vBMD by QCT. At most sites, significant correlations were present. A moderate to strong correlation was seen between vBMD integral total hip and aBMD total hip ($r = 0.74$). Integral vBMD at femoral neck correlated significantly with aBMD at femoral neck ($r = 0.64$). TBS showed weak correlation with vBMD, with the highest value measured at the lumbar spine ($r = 0.35$, $p < 0.01$).

Discussion

In the present study we compared TBS, aBMD, vBMD, geometry, microstructure and strength as measured by DXA, QCT and HR-pQCT at central sites (hip and lumbar spine) and peripheral sites (tibia and radius) on the same subjects.

Significant correlations were found at multiple skeletal sites between aBMD and vBMD as measured by DXA and HR-pQCT. In particular, distal site associations showed agreement between aBMD at the ultra-distal forearm and distal radius vBMD and failure load. Central site measurements of the hip and femoral neck between integral vBMD by QCT and aBMD by DXA reflected each other with moderate to strong correlations. Peripheral and central site measurements of vBMD by QCT and HR-pQCT corresponded weakly to moderately in terms of total bone density. TBS showed weak correlation with trabecular indices of peripheral as well as central sites by HR-pQCT and QCT.

In accordance with our study, Liu et al. [12] investigated the association between DXA, HR-pQCT and QCT in premenopausal women ($N = 69$, mean age 37.5 years). The authors showed central site associations of the hip in agreement with our results, although we demonstrated a stronger association at distal sites compared to the study by Liu et al. ($r = 0.63$ – 0.74 vs. $r = 0.33$ – 0.45). Compared to our results, the authors reported stronger correlations between central and distal sites measurements along with a stronger association at the lumbar spine between aBMD and vBMD.

These differences may be due to the age differences and menopausal status, as the mean age in the present study is 63 years. By age, osteoarthritis is known to affect DXA

Table 2 Correlation between indices assessed by DXA and HR-pQCT scans. Pearson's correlation coefficient (*r*)

DXA					
HR-pQCT	TBS (L1–L4)	Lumbar spine, aBMD	Total hip, aBMD	Ultra-distal forearm, aBMD	Whole-body, aBMD
Radius					
vBMD					
Total bone density (mg HA/cm ³)	0.19*	0.17*	0.44**	0.74**	0.33**
Cortical bone density (mg HA/cm ³)	0.07	0.08	0.37**	0.48**	0.19*
Trabecular bone density (mg HA/cm ³)	0.31**	0.31**	0.31**	0.75**	0.35**
Microarchitecture					
Ct.Th (mm)	0.08	0.12	0.39**	0.57**	0.24**
Tb.Th (mm)	0.17*	0.09	0.20*	0.46**	0.15*
Tb.N (mm ⁻¹)	0.25**	0.27**	0.16*	0.54**	0.24**
Tb.Sp (mm)	-0.24**	-0.23**	-0.11	-0.43**	-0.18*
TrBV/TV (mm)	0.31**	0.30**	0.28**	0.73**	0.30**
Tb.N.SD (mm)	-0.21*	-0.18*	-0.09	-0.33**	-0.11
Strength					
Failure load (N)	0.29**	0.43**	0.47**	0.80**	0.40**
Tibia					
vBMD					
Total bone density (mg HA/cm ³)	0.10	0.14	0.43**	0.63**	0.28**
Cortical bone density (mg HA/cm ³)	0.10	0.17*	0.29**	0.44**	0.17*
Trabecular bone density (mg HA/cm ³)	0.12	0.11	0.36**	0.62**	0.31**
Microarchitecture					
Ct.Th (mm)	0.06	0.12	0.35**	0.46**	0.26**
Tb.Th (mm)	0.06	-0.09	0.05	0.36**	0.08
Tb.N (mm ⁻¹)	0.09	0.24**	0.40**	0.46**	0.30**
Tb.Sp (mm)	-0.09	-0.17*	-0.35**	-0.46**	-0.26**
TrBV/TV (mm)	0.13	0.11	0.36**	0.62**	0.31**
Tb.N.SD (mm)	-0.16*	-0.13	-0.30**	-0.33**	-0.18*
Strength					
Failure load (N)	0.20*	0.38**	0.45**	0.66**	0.46**

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* $p < 0.05$; ** $p < 0.01$

measurements [22] especially in the spine, which may explain our weak correlation. Furthermore, although our results did not differ after adjusting for age, the correlations may still be affected by age, as multiple factors such as hormonal changes and bone loss rates change following menopause [23].

The present study showed agreement between distal site measuring techniques in terms of aBMD by DXA and vBMD by HR-pQCT. This is most likely explained by the

area of interest being closely situated in the two techniques, and our findings are in accordance with other studies [24–26]. Furthermore, in both scanning techniques, the right forearm was the primary arm chosen for the scans, making the correlation more precise, as small differences between right and left may exist [27].

In general, central site measurements corresponded weakly to moderately to distal sites, which indicates that peripheral measures do not completely reflect the bone composition of

Table 3 Correlations between indices assessed by HR-pQCT and QCT scans. Pearson’s correlation coefficient (*r*)

QCT, vBMD				
HR-pQCT	Lumbar spine	Total hip		
	Trabecular	Integral	Cortical	Trabecular
Radius				
vBMD				
Total bone density (mg HA/cm ³)	0.32**	0.54**	-0.37**	0.44**
Cortical bone density (mg HA/cm ³)	0.29**	0.49**	-0.39**	0.33**
Trabecular bone density (mg HA/cm ³)	0.18*	0.29**	-0.19*	0.37**
Microarchitecture				
Ct.Th (mm)	0.32**	0.48**	-0.37**	0.34**
Tb.Th (mm)	0.18*	0.30**	-0.07	0.20*
Tb.N (mm ⁻¹)	0.11	0.11	-0.12	0.27**
Tb.Sp (mm)	-0.01	-0.05	0.13	-0.18*
TrBV/TV (mm)	0.18*	0.29**	-0.19*	-0.37**
Tb.N.SD (mm)	-0.00	-0.07	0.14	-0.14
Strength				
Failure load (N)	0.25**	0.28**	-0.26**	0.27**
Tibia (mg HA/cm³)				
vBMD				
Total bone density	0.30**	0.50**	-0.32**	0.51**
Cortical bone density (mg HA/cm ³)	0.25**	0.39**	-0.27**	0.28**
Trabecular bone density (mg HA/cm ³)	0.24**	0.32**	-0.17*	0.44**
Microarchitecture				
Ct.Th (mm)	0.25**	0.44**	-0.37**	0.36**
Tb.Th (mm)	0.15	0.21*	-0.08	0.23*
Tb.N (mm ⁻¹)	0.15	0.18*	-0.14	0.31**
Tb.Sp (mm)	-0.17*	-0.18*	0.10	-0.30**
TrBV/TV (mm)	0.24**	0.32**	-0.17*	0.44**
Tb.N.SD (mm)	-0.18*	-0.24**	0.14	-0.30**
Strength				
Failure load (N)	0.18	0.17	-0.18*	0.26**

HA hydroxyapatite

* *p* < 0.05; ** *p* < 0.01

the central sites. This is further supported by Tsurusaki et al. [25], suggesting that correlation values are influenced by the measurement area as different bone loss patterns are seen in trabecular and cortical compartments, and between weight-bearing and non-weight-bearing portions. In addition, despite demonstrating similar aBMD at the spine, Kazakia et al. [24] showed a large heterogeneity in peripheral site measurements in 52 post-menopausal women. HR-pQCT measurements of tibia and radius showed completely different bone structures,

and in particular values of microarchitecture differed by 50–100 % between the subjects [24].

In line with other studies, we found moderate to strong correlations between central site measurements of the total hip and femoral neck [12, 28]. Our results indicated that DXA aBMD of the hip may only to some extent provide an indication of bone health and fracture risk, and the addition of 3D images with their information on bone distribution is still needed.

On the basis of our data, we suggest that further studies on the ability of the scanning modalities are still needed to predict the fracture risk and treatment response in osteoporotic patients. Owing to its cost, effectiveness and accessibility, DXA is still the first choice when evaluating bones. As HR-pQCT scanners are easy to use and radiation dose is low, this is an attractive additional measuring technique that will most likely become more widespread. Despite the additional information gained from central site QCT scans, the radiation dose is high compared to the other techniques.

When used in clinical practice it must be emphasized that despite the various techniques available, the imaging techniques may be used in addition to rather than in replacement of each other.

The relationship between TBS and QCT, and HR-pQCT has only been sparsely investigated. A study by Silva et al. [13] investigated these correlations in 115 pre- and post-menopausal women, and in partial accordance with our results the authors demonstrated weak to moderate associations with TBS. The results were further supported by Popp et al. [29] in 72 healthy pre-menopausal women, showing similar correlations. As TBS reflects the heterogeneity of trabecular structures of lumbar vertebrae, it is taken into account in the descriptions of its correlations that it should correlate more strongly with trabecular indices than with cortical parameters. The relatively weak correlations, however, may suggest that TBS reflects other properties of bone than traditional density measurements. This is further supported by Silva et al. [13], explaining the findings due to differences in trabecular microstructure between central and peripheral sites.

There are several strengths to the study. This is, to our knowledge, the first study of its kind among post-menopausal women to demonstrate the correlations between aBMD, vBMD, microstructure and strength at central and peripheral sites using DXA, QCT and HR-pQCT. The fact that our study group consisted of post-menopausal women heightens its importance, as the major bone changes appear around menopause.

There are, however, limitations to our study. Our population was heterogenic and consisted of normal, osteopenic and osteoporotic women, resulting in a very wide spectrum of BMDs.

Table 4 Correlation between indices assessed by DXA and QCT scans. Pearson's correlation coefficient (*r*)

DXA	QCT, vBMD						
	Lumbar spine	Total hip			Femoral neck		
		Trabecular	Integral	Cortical	Trabecular	Integral	Cortical
TBS lumbar spine	0.35**	0.27**	−0.10	0.26**	0.30**	−0.19*	0.16
Lumbar spine, aBMD	0.35**	0.20*	−0.19*	0.14	0.17*	−0.8	−0.04
Total hip, aBMD	0.28**	0.74**	−0.57**	0.63**	0.64**	−0.51**	0.46**
Femoral neck, aBMD	0.31**	0.62**	−0.38**	0.56**	0.69**	−0.49**	0.56**
Ultra-distal forearm, aBMD	0.33**	0.37**	−0.32**	0.36**	0.28**	−0.23*	0.26**
Whole-body, aBMD	0.25**	0.29**	−0.19*	0.17*	0.23*	−0.32**	0.06

* $p < 0.05$; ** $p < 0.01$

In conclusion, there was moderate to strong agreement between measuring techniques in terms of DXA, HR-pQCT and QCT when assessing the same area in postmenopausal women. However, when assessing correlations between central and distal sites, the associations were only weak to moderate. Our data suggest that the various techniques measure different characteristics of bone, and in clinical practice they can only supplement rather than replace each other. In addition, the study calls for further research on the ability of the different scanning modalities, alone or in combination, to predict risk of fractures and responses to treatment of patients with osteoporosis.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interests regarding the publication of this paper.

References

- Schott AM, Cormier C, Hans D, Favier F, Hausherr E, Dargent-Molina P, Delmas PD, Ribot C, Sebert JL, Breart G, Meunier PJ (1998) How hip and whole-body bone mineral density predict hip fracture in elderly women: the EPIDOS prospective study. *Osteoporos Int* 8:247–254
- Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM (1993) Bone density at various sites for prediction of hip fractures. The study of osteoporotic fractures research group. *Lancet* 341:72–75
- Gupta R, Cheung AC, Bartling SH, Lissauskas J, Grasruck M, Leidecker C, Schmidt B, Flohr T, Brady TJ (2008) Flat-panel volume CT: fundamental principles, technology, and applications. *Radiographics* 28:2009–2022
- Boutroy S, Bouxsein ML, Munoz F, Delmas PD (2005) In vivo assessment of trabecular bone microarchitecture by high-resolution peripheral quantitative computed tomography. *J Clin Endocrinol Metab* 90:6508–6515
- Lang T, Koyama A, Li C, Li J, Lu Y, Saeed I, Gazze E, Keyak J, Harris T, Cheng X (2008) Pelvic body composition measurements by quantitative computed tomography: association with recent hip fracture. *Bone* 42:798–805
- Hansen S, Hauge EM, Rasmussen L, Jensen JE, Brixen K (2012) Parathyroidectomy improves bone geometry and microarchitecture in female patients with primary hyperparathyroidism: a one-year prospective controlled study using high-resolution peripheral quantitative computed tomography. *J Bone Miner Res* 27:1150–1158
- Cheung AM, Majumdar S, Brixen K, Chapurlat R, Fuerst T, Engelke K, Dardzinski B, Cabal A, Verbruggen N, Ather S, Rosenberg E, de Papp AE (2014) Effects of odanacatib on the radius and tibia of postmenopausal women: improvements in bone geometry, microarchitecture, and estimated bone strength. *J Bone Miner Res* 29:1786–1794
- Engelke K, Nagase S, Fuerst T, Small M, Kuwayama T, Deacon S, Eastell R, Genant HK (2014) The effect of the cathepsin K inhibitor ONO-5334 on trabecular and cortical bone in postmenopausal osteoporosis: the OCEAN study. *J Bone Miner Res* 29:629–638
- Nicks KM, Amin S, Melton LJ III, Atkinson EJ, McCready LK, Riggs BL, Engelke K, Khosla S (2013) Three-dimensional structural analysis of the proximal femur in an age-stratified sample of women. *Bone* 55:179–188
- Johannesdottir F, Aspelund T, Reeve J, Poole KE, Sigurdsson S, Harris TB, Gudnason VG, Sigurdsson G (2013) Similarities and differences between sexes in regional loss of cortical and trabecular bone in the mid-femoral neck: the AGES-Reykjavik longitudinal study. *J Bone Miner Res* 28:2165–2176
- Leslie WD, Johansson H, Kanis JA, Lamy O, Oden A, McCloskey EV, Hans D (2014) Lumbar spine texture enhances 10-year fracture probability assessment. *Osteoporos Int* 25:2271–2277
- Liu XS, Cohen A, Shane E, Yin PT, Stein EM, Rogers H, Kokolus SL, McMahon DJ, Lappe JM, Recker RR, Lang T, Guo XE (2010) Bone density, geometry, microstructure, and stiffness: relationships between peripheral and central skeletal sites assessed by DXA, HR-pQCT, and cQCT in premenopausal women. *J Bone Miner Res* 25:2229–2238
- Silva BC, Walker MD, Abraham A, Boutroy S, Zhang C, McMahon DJ, Liu G, Hans D, Bilezikian JP (2013) Trabecular bone score is associated with volumetric bone density and microarchitecture as assessed by central QCT and HRpQCT in Chinese American and white women. *J Clin Densitom* 16:554–561

14. Jakobsen NF, Rolighed L, Moser E, Nissen PH, Mosekilde L, Rejnmark L (2014) Increased trabecular volumetric bone mass density in familial hypocalciuric hypercalcemia (FHH) type 1: a cross-sectional study. *Calcif Tissue Int* 95:141–152
15. Jakobsen NF, Rolighed L, Nissen PH, Mosekilde L, Rejnmark L (2013) Muscle function and quality of life are not impaired in familial hypocalciuric hypercalcemia: a cross-sectional study on physiological effects of inactivating variants in the calcium-sensing receptor gene (CASR). *Eur J Endocrinol* 169:349–357
16. The Danish National Board of Health (2005) Guidelines on radiation protection when working with open radioactive sources. National Board of Health, Copenhagen, p 11
17. Laib A, Hauselmann HJ, Rueggsegger P (1998) In vivo high resolution 3D-QCT of the human forearm. *Technol Health Care* 6:329–337
18. Pistoia W, van RB, Lochmuller EM, Lill CA, Eckstein F, Rueggsegger P (2002) Estimation of distal radius failure load with micro-finite element analysis models based on three-dimensional peripheral quantitative computed tomography images. *Bone* 30:842–848
19. Hansen S, Brixen K, Gravholt CH (2012) Compromised trabecular microarchitecture and lower finite element estimates of radius and tibia bone strength in adults with turner syndrome: a cross-sectional study using high-resolution-pQCT. *J Bone Miner Res* 27:1794–1803
20. Khoo BC, Brown K, Cann C, Zhu K, Henzell S, Low V, Gustafsson S, Price RI, Prince RL (2009) Comparison of QCT-derived and DXA-derived areal bone mineral density and T scores. *Osteoporos Int* 20:1539–1545
21. Pothuaud L, Carceller P, Hans D (2008) Correlations between grey-level variations in 2D projection images (TBS) and 3D microarchitecture: applications in the study of human trabecular bone microarchitecture. *Bone* 42:775–787
22. Okano K, Ito M, Aoyagi K, Osaki M, Enomoto H, Yamaguchi K (2013) Discrepancy in bone mineral densities at different skeletal sites in hip osteoarthritis patients. *Mod Rheumatol* 24:340–342
23. Riggs BL, Melton LJ, Robb RA, Camp JJ, Atkinson EJ, McDaniel L, Amin S, Rouleau PA, Khosla S (2008) A population-based assessment of rates of bone loss at multiple skeletal sites: evidence for substantial trabecular bone loss in young adult women and men. *J Bone Miner Res* 23:205–214
24. Kazakia GJ, Hyun B, Burghardt AJ, Krug R, Newitt DC, de Papp AE, Link TM, Majumdar S (2008) In vivo determination of bone structure in postmenopausal women: a comparison of HR-pQCT and high-field MR imaging. *J Bone Miner Res* 23:463–474
25. Tsurusaki K, Ito M, Hayashi K (2000) Differential effects of menopause and metabolic disease on trabecular and cortical bone assessed by peripheral quantitative computed tomography (pQCT). *Br J Radiol* 73:14–22
26. Sornay-Rendu E, Boutroy S, Munoz F, Delmas PD (2007) Alterations of cortical and trabecular architecture are associated with fractures in postmenopausal women, partially independent of decreased BMD measured by DXA: the OFELY study. *J Bone Miner Res* 22:425–433
27. Walters J, Koo WW, Bush A, Hammami M (1998) Effect of hand dominance on bone mass measurement in sedentary individuals. *J Clin Densitom* 1:359–367
28. Cohen A, Lang TF, McMahon DJ, Liu XS, Guo XE, Zhang C, Stein EM, Dempster DW, Young P, Saeed I, Lappe JM, Recker RR, Shane E (2012) Central QCT reveals lower volumetric BMD and stiffness in premenopausal women with idiopathic osteoporosis, regardless of fracture history. *J Clin Endocrinol Metab* 97:4244–4252
29. Popp AW, Buffat H, Eberli U, Lippuner K, Ernst M, Richards RG, Stadelmann VA, Windolf M (2014) Microstructural parameters of bone evaluated using HR-pQCT correlate with the DXA-derived cortical index and the trabecular bone score in a cohort of randomly selected premenopausal women. *PLoS One* 9:e88946