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Original Article

Forearm BMD as Measured by Peripheral Quantitative Computed Tomography (pQCT) in a German Reference Population

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Abstract. Low bone mass as estimated by decreased bone mineral density (BMD) is an established predictor of osteoporotic fractures. One of the latest developments in bone densitometry is peripheral quantitative computed tomography (pQCT) of the forearm. In Germany, the CT bone scanner XCT 900 has already been widely used; however, interpretation of measurements with respect to osteoporosis risk assessment can be improved by better defined and validated reference data. In the present study, this device was used to measure BMD at the distal radius in a well-defined healthy population of 179 German adults (91 men, 88 women) aged 20–79 years. In vivo precision was 1.67% for trabecular and 0.81% for total BMD measurements. Peak values of trabecular and total BMD were observed at the ages 40–50 years in women and 30–40 years in men. Beyond these ages, both trabecular and total BMD showed a linear decline with age, decreasing by 0.85% and 1.08% per year in women and by 0.59% and 0.54% in men, respectively. Measures of BMD were not influenced by weight, height or body mass index (BMI). In both sexes, trabecular and total radial BMD showed a positive and significant correlation with femoral BMD measures obtained by dual X-ray absorptiometry (DXA). Weaker correlations were observed with DXA measures of the lumbar spine. Compared with the 95% reference range provided by the manufacturer, the distribution of age- and sex-specific values of trabecular BMD of the distal radius was shifted to lower values by up to 1 standard deviation. Thus, 17% (30 of 179) of our apparently healthy population had BMD values falling short of the suggested lower reference limit. On the other hand, the distribution of total BMD values was shifted to higher values by up to 2 standard deviations in the younger age groups. We conclude that pQCT of the radius is a precise method for measuring BMD, but that its use for osteoporosis risk assessment crucially depends on both well-defined reference data and the results of prospective studies.

Keywords: Bone densitometry; Dual X-ray absorptiometry; Osteoporosis; Peripheral quantitative computed tomography; Reference values

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Introduction

Bone densitometry has become a major tool for osteoporosis risk assessment. Different methods have been developed, while the optimal method and site of measurement are still a matter of debate [1,2].

One of the latest developments in peripheral quantitative computed tomography (pQCT), a method which allows the separate determination of trabecular bone mineral density (BMD) and cortical BMD in the peripheral skeleton (radius, tibia). One device of this type is the CT bone scanner XCT 900 (Stratec, Birkenfeld, Germany) which has been developed at the University of Würzburg [3] and has already been widely used across Germany.

There have been increasing doubts concerning the selection of reference data provided by the manufacturer, based on the considerable discrepancy between low measures of trabecular BMD at the distal radius and

normal lumbar dual X-ray absorptiometry (DXA) values among patients who did not show any clinical signs of osteoporosis. In addition, concurrent measures of total BMD were often found to be above the mean reference values. There are four possible explanations for these discrepancies: firstly, due to regional differences reference values may not be applicable to patients from other areas of Germany; secondly, the selected reference range contains only the upper range of trabecular BMD values; thirdly, the reference site of radial BMD measurement may have varied considerably by not measuring exactly at the 5% site (see Methods); and, fourthly, the selection criteria of normals were defined differently. The difficulty of choosing a definitive reference group has also been shown by others in previous studies [4].

Against this background, we decided to collect our own reference data. The distribution of BMD in this population was compared with the reference range provided by the manufacturer. In addition, BMD as measured by pQCT was correlated to BMD measures by DXA and ultrasound at different skeletal sites.

Subjects and Methods

Population

The study population comprised 88 female and 91 male Caucasians aged 20–79 years. The majority of subjects over the age of 50 years were members of a random population sample recruited for a regional population survey of vertebral osteoporosis in the framework of the European study of vertebral osteoporosis (EVOS). The remainder of the participants were volunteers (clinical staff, students and outpatients).

Exclusion Criteria

A detailed questionnaire was used to exclude patients with diseases or medications (past or present) which might have affected bone metabolism. Exclusion criteria were as follows: history of osteoporotic fractures in first degree family members, fractures after minimal trauma, milk intolerance, malabsorption syndromes, alcohol abuse, hypo- or hyperthyroidism, hypo- or hyperparathyroidism, renal and liver disease, menstrual irregularities or hypogonadism, precocious menopause (<46 years), immobilization for more than 3 weeks, use of corticosteroids, thyroid hormones, diuretics, sex hormones or sex hormone antagonists, and chemotherapy. Women using oral contraceptives were not excluded. In order to exclude vertebral fractures, a spinal radiograph was taken of persons over 45 years of age. In some clinically unsuspicious cases only a lumbar DXA measurement was taken which suggested no spinal disease.

Bone Densitometry

Peripheral QCT measurements were performed at the distal radius using the CT bone scanner XCT 900 (Stratec, Germany), version 3.3 (8/91). The source of radiation was an X-ray tube (38 keV). Measurements were taken on the non-dominant forearm at the so-called '5% site' (4% of ulna length proximal to the proximal part of the radial facies articularis carpi). In a subset (mainly participants older than 50 years) additional DXA measurements of the lumbar spine (L2–4) and the femur (neck, trochanteric region and Ward's triangle) as well as ultrasound measurements of the os calcis were performed. We used a Hologic QDR 1000 (Hologic, Waltham, MA) for the DXA measurements and a Lunar Achilles (Lunar, Madison, WI) for the ultrasound measurements.

In vitro precision of the pQCT method was assessed by daily measurements of a standard phantom with a defined content of hydroxyapatite which was provided by the manufacturer. For assessment of in vivo precision, 6 healthy persons were measured a second time after an interval of 2–10 weeks. The 'threshold' parameter (threshold means a defined value of linear attenuation of radiation at which the computer recognizes the transition from soft tissue to bone tissue) was selected according to the cortical BMD as suggested by the manufacturer (linear coefficient of attenuation 0.40–0.67 1/cm = 112–377 mg/cm^3) [3]. The trabecular BMD corresponds to the mean density of the inner bone area (45% of the total bone area) which is obtained after concentrically peeling off the outer cortical bone containing area (program 'CalcBD') [5].

Data Analysis

The resulting data on trabecular BMD and total BMD were stratified according to sex and age decades. Age- and sex-specific mean values and standard deviations were compared with the manufacturer's reference ranges. The current reference data as implemented in the database of the CT bone scanner contain reference points (mean ± SD) for the ages 20, 45, 65 and 100 years only. Values for ages in between had to be calculated in the standard way by linear connection of these fixed points. The values for 1 SD are the same for every age (Table 1).

The statistical results have been calculated using the StatWorks program (Apple Macintosh).

Results

In vitro precision of the pQCT method (daily phantom measurements) was high, with a coefficient of variation (CV) of 0.27% (n = 100, mean linear attenuation =

Table 1. Mean values of BMD (mg/cm³) in women and men for trabecular and total BMD at the distal radius as measured by pQCT in comparison with the manufacturer's reference data

	Age (yr)	Manufacturer's ref. data		Study results			Difference given in		
		Mean	SD	*n*	Mean	SD	mg/cm³	SD(m)	%
Women									
Trabecular bone density	20–29	170.94	35.5	23	162.88	31.70	− 8.08	−0.23	− 4.72
	30–39	174.14	35.5	15	146.23	41.95	−27.91	−0.79	−16.03
	40–49	176.05	35.5	15	165.23	43.28	−10.82	−0.30	− 6.15
	50–59	168.24	35.5	14	143.49	53.64	−24.75	−0.70	−14.71
	60–69	159.28	35.5	13	125.58	42.05	−33.70	−0.95	−21.16
	70–79	156.32	35.5	8	125.89	51.85	−30.43	−0.86	−19.47
Total bone density	20–29	266.99	40.0	23	347.33	38.32	+80.34	+2.01	+30.09
	30–39	269.19	40.0	15	347.84	72.60	+78.34	+1.97	+29.22
	40–49	270.80	40.0	15	368.03	66.50	+97.23	+2.43	+35.90
	50–59	268.04	40.0	14	321.44	54.28	+53.40	+1.34	+19.92
	60–69	264.27	40.0	13	272.29	85.98	+ 8.02	+0.20	+ 3.03
	70–79	259.64	40.0	8	254.29	63.61	− 5.35	−0.13	− 2.06
Men									
Trabecular bone density	20–29	218.98	32.8	20	189.16	45.70	−29.82	−0.91	−13.62
	30–39	215.81	32.8	13	200.08	43.06	−15.73	−0.48	− 7.29
	40–49	212.47	32.8	8	198.74	29.27	−13.73	−0.42	− 6.46
	50–59	207.85	32.8	17	192.21	53.58	−15.64	−0.48	− 7.52
	60–69	203.14	32.8	19	162.33	47.06	−40.81	−1.24	−20.09
	70–79	199.94	32.8	14	157.12	41.97	−42.82	−1.31	−21.42
Total bone density	20–29	336.95	47.0	20	395.39	53.20	+58.44	+1.24	+17.34
	30–39	330.38	47.0	13	413.48	58.08	+83.10	+1.77	+25.15
	40–49	322.72	47.0	8	399.91	57.85	+77.19	+1.64	+23.92
	50–59	306.65	47.0	17	386.54	51.24	+79.89	+1.70	+26.05
	60–69	289.67	47.0	19	349.66	56.56	+59.99	+1.28	+20.71
	70–79	278.41	47.0	14	322.67	68.88	+44.26	+0.94	+15.90

The manufacturer's data for each decade are calculated as shown in Methods.
SD(m), standard deviation given by the manufacturer; *n*, number of measurements.

0.5124 1/cm). When assessing the precision of radial pQCT in vivo, we found a mean CV of 1.67% (0.41–2.97) for trabecular BMD, 0.81% (0.13–2.06) for total BMD and 0.92% (0.26–1.93) for cortical BMD. We found a mean CV of 1.08% (0–2.12) for the measured area (in pixels), which indicates a good reproducibility of the measuring site.

Sex-specific mean radial pQCT values for the studied population are shown by decade on Table 1. In every decade men showed higher trabecular and total BMD values than women of the same age. Peak values were found in the age group of 40–50 years in women and 30–40 years in men.

Beyond these ages, both trabecular and total BMD declined significantly with age in both sexes (Table 2; Fig. 1a–d). The age-related decline in trabecular and total BMD was more pronounced in women than in men: trabecular BMD loss was 1.41 mg/cm³ per year (0.85%/year) in women ($p=0.023$) versus 1.18 mg/cm³ per year (0.59%/year) in men ($p=0.004$). Total BMD loss was 3.98 mg/cm³ per year (1.08%/year) in women ($p<0.001$) versus 2.25 mg/cm³ per year (0.54%/year) in men ($p<0.001$).

Table 2 shows the influence of different anthropometric parameters on radial BMD. Height was significantly associated with BMD in simple linear regression analysis. However, there was a significant decline in height with older age ($r=0.57$, $p<0.001$ in women; $r=-0.63$, $p<0.001$ in men). Multiple regression analysis controlling for age showed that body height had no age-independent influence on BMD.

Trabecular BMD was found to be 4.7%–21% lower than suggested by the manufacturer (Table 1), varying by decade. A total of 14% (12 of 88) of women and 20% (18 of 91) of men showed results below the −2 SD limit. Particularly in the older age groups (>50 years) mean values of trabecular BMD were about 1 SD lower than expected. Mean values of total BMD, however, were considerably higher than anticipated. This discrepancy was especially noticeable when measuring younger women, whereas measurements of older women showed little deviation.

A significant correlation was observed between BMD of the femoral neck (DXA) and the radius (pQCT) (Table 2; Figs 2, 3). The correlation of the BMD values of the lumbar spine (DXA) with those of the radius (pQCT), however, was lower. With respect to ultrasound measurements of the os calcis a significant correlation between pQCT values and SOS (speed of sound in m/s) was present only in men. There was no correlation with BUA (broadband ultrasound attenuation in dB/MHz) and radial pQCT measurements.

Table 2. Correlation of trabecular and total radial BMD (pQCT) with age, height, weight, BMI, BMD values of lumbar spine and femoral neck (Hologic QDR 1000), and ultrasound measurements of os calcis (Lunar Achilles)

	Trabecular BMD		Total BMD	
	Women	Men	Women	Men
Age (yr)	$r=-0.29$ $p=0.007$ $n=88$	$r=-0.27$ $p=0.009$ $n=91$	$r=-0.44$ $p=<0.001$ $n=88$	$r=-0.41$ $p=<0.001$ $n=91$
Height (cm)	NS	$r=0.26$ $p=0.014$ $n=88$	$r=0.26$ $p=0.015$ $n=87$	$r=0.29$ $p=0.006$ $n=88$
Weight (kg)	NS	NS	NS	NS
BMI (kg/m^2)	NS	NS	NS	NS
Spine L2–4 BMD (g/cm^2)	$r=0.37$ $p=0.036$ $n=32$	NS	$r=0.37$ $p=0.038$ $n=32$	$r=0.29$ $p=0.047$ $n=49$
Neck BMD (g/cm^2)	$r=0.54$ $p=0.003$ $n=28$	$r=0.65$ $p<0.001$ $n=43$	$r=0.51$ $p=0.006$ $n=28$	$r=0.66$ $p<0.001$ $n=43$
Trochanteric BMD (g/cm^2)	$r=0.42$ $p=0.028$ $n=28$	$r=0.53$ $p<0.001$ $n=43$	NS	$r=0.55$ $p<0.001$ $n=43$
Ward's triangle BMD (g/cm^2)	$r=0.71$ $p<0.001$ $n=28$	$r=0.55$ $p<0.001$ $n=43$	$r=0.56$ $p<0.002$ $n=28$	$r=0.53$ $p<0.001$ $n=43$
SOS (m/s)	NS	$r=0.48$ $p=0.001$ $n=44$	NS	$r=0.42$ $p=0.004$ $n=44$
BUA (dB/MHz)	NS	NS	NS	NS
Stiffness (%)	NS	$r=0.42$ $p=0.004$ $n=45$	NS	$r=0.40$ $p=0.007$ $n=45$

NS, not significant; BMI, body mass index = weight (kg)/[height (m)]^2; BMD, bone mineral density; SOS, speed of sound; BUA, broadband ultrasound attenuation; stiffness, combination parameter between SOS and BUA.

Discussion

Clearly defined selection criteria for an approval of BMD reference data should be required in Germany. The new pQCT device (XCT 900) was put on the market with reference data adjusted and not fully validated from its technical precursor (SCT 900) that uses an ^{125}I source [3]. Soon after the introduction of the new X-ray-based device into clinical practice, suspicion arose that pQCT measures of trabecular radial BMD were falsely low according to the reference range provided by the manufacturer. In order to investigate this problem we selected a new reference population. Reference data should be representative of the distribution of values in the general population unless pathological measures are so prevalent that it affects the distribution of values in the population. Forty per cent of our reference group were part of a population-based random sample recruited for the EC concerted epidemiological study on the prevalence of osteoporotic fractures (EVOS). Because of a different age distribution we did not compare this group with the group of mostly younger volunteers. Strict exclusion criteria were applied to all persons included into the study, which differ from those used in the XCT 900 [3], so that we can call it a super-normal reference population.

Mean values of trabecular BMD were found to be up to 1 SD lower than suggested by the manufacturer. Thus 14% of women and 20% of men showed results below the −2 SD limit. Similar results have meanwhile been reported by other investigators [6,7].

The SD values of the different age groups (as a percentage of the mean values) seem to be higher than reported for other techniques [8,9]. This might be due to different reading ranges. In addition, there may be great inter-individual differences of trabecular radial BMD and cortical wall thickness at the 5% site. It is remarkable that trabecular BMD loss after menopause is less than total BMD loss. This can be explained by an increase in bone diameter (remodelling) and a decrease in cortical wall thickness [5].

In vivo precision for trabecular radial BMD found in this investigation was lower than radius measurements by DXA [10,11] when comparing only the CVs. However, for better comparison of the CVs, the different reading ranges of these methods should be taken into account. In order to achieve precise follow-up measurements it is necessary to ensure that the second

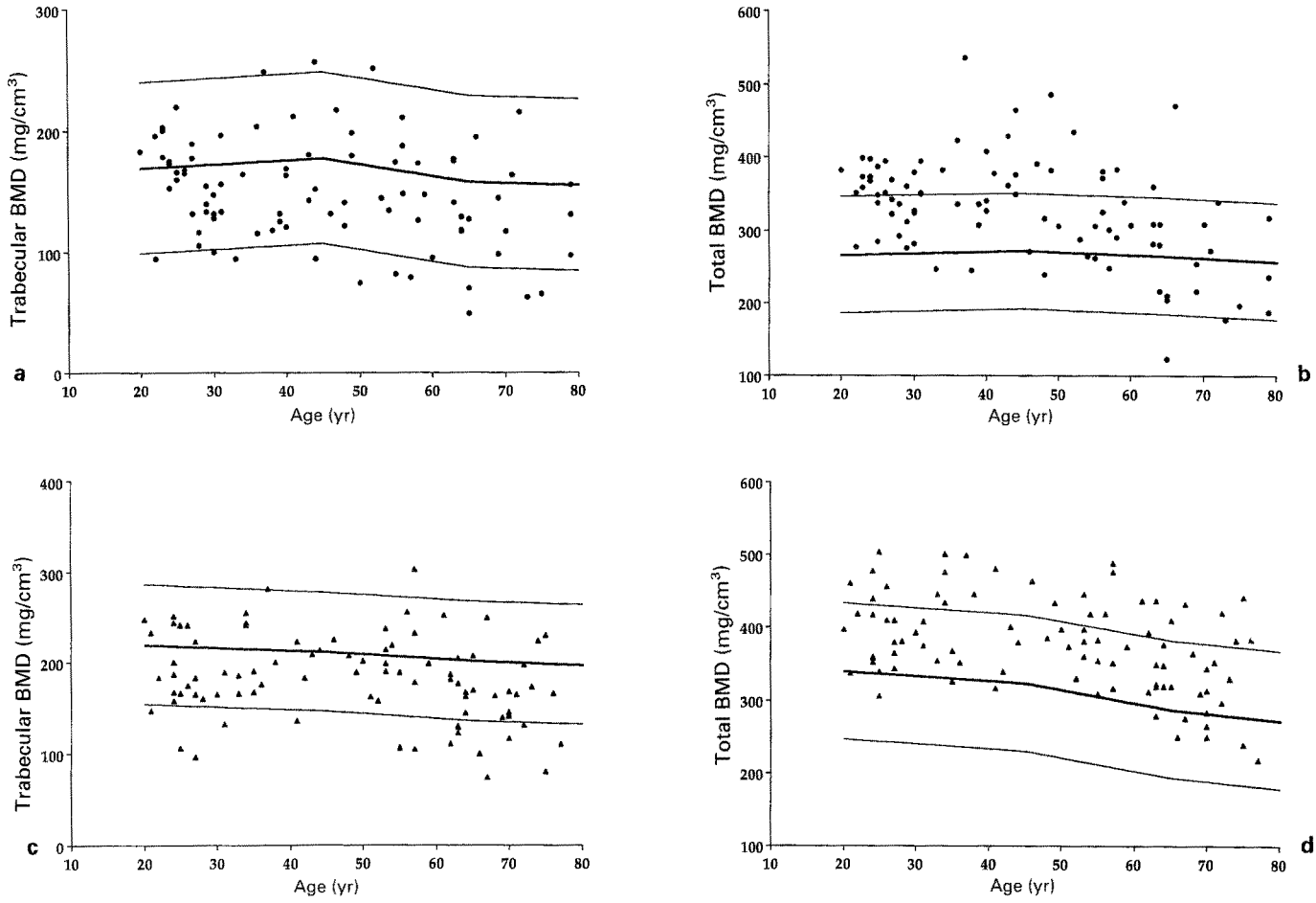

Fig. 1a–d. Age-dependent distribution of trabecular and total radial BMD (pQCT, XCT 900) with age (in years) in a female (**a**,**b**) and male (**c**,**d**) German reference population. The *lines* indicate the mean ± 2 SD of the reference data given by the manufacturer as derived from the ^{125}I-driven device (SCT 900).

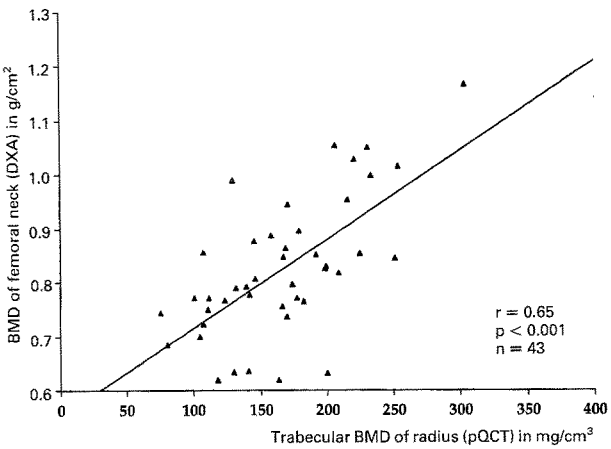

Fig. 2. Correlation between trabecular radial BMD (pQCT) in mg/cm^3 and BMD of femoral neck (Hologic QDR 1000) in g/cm^2 in 43 men.

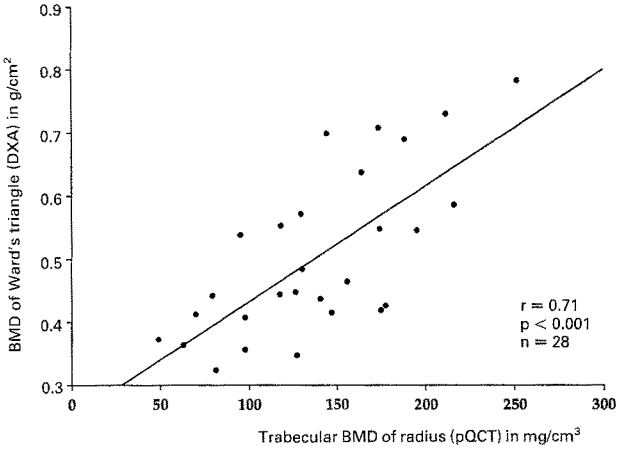

Fig. 3. Correlation between trabecular radial BMD (pQCT) in mg/cm^3 and BMD of Ward's triangle (Hologic QDR 1000) in g/cm^2 in 28 women.

measurement is taken from exactly the same site – a condition which cannot be guaranteed by fixing the measuring height manually.

We have earlier shown that BMD measurements of the radius (SPA) and of lumbar spine and femoral neck (DPA, DXA) [8,9,12], are influenced by anthropometric parameters. We therefore investigated the effects of these on BMD parameters as measured by

pQCT. However, in this study there was no significant correlation of BMD values with weight, height or BMI. In this context it should be mentioned that the pQCT system measures the true volumetric density in mg/cm^3, whereas other methods provide values in g (BMC = bone mineral content), g/cm or g/cm^2 (common definition of BMD) which are dependent on the bone mass. A different terminology such as TBD for trabecular bone density and BD for (total) bone density might be considered for the pQCT systems.

As described before [9,13,14] the correlation of BMD at peripheral sites with that at the lumbar spine is low. The coefficients of correlation are about 0.4–0.5 [9]. Measurements at a single skeletal site can not be extrapolated to indicate skeletal status at other sites [9]. Nevertheless peripheral BMD as measured by SPA [15] or DXA [16] can predict the risk of vertebral fractures.

Prospective data of radial BMD as measured by pQCT do not yet exist. The good correlation with hip BMD suggests the radial BMD may be more valuable for prediction of hip fractures than vertebral fractures, and better prediction might be achieved by differentiating between trabecular and cortical bone at the radius in prospective studies.

Theoretically, the study population from Heidelberg, could differ from the manufacturer's population generated in the area of Würzburg due to geographical differences. However, since other investigators achieved similar results [6,7], different selection criteria for the normal population by the manufacturer are to be presumed. This is in accordance with studies showing similar effects for other BMD scanners [4].

We conclude from these data that clearly defined selection and validation criteria are essential for reference data of new devices. Prospective studies are needed to clarify the role of the pQCT method, e.g. the possibility of separating trabecular and cortical BMD in the prediction of osteoporotic fractures.

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