Original article

Validation of quantitative computed tomography-derived areal bone mineral density with dual energy X-ray absorptiometry in an elderly Chinese population

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Keywords: bone mineral density; osteoporosis; quantitative computed tomography; dual energy X-ray absorptiometry

Background The performance of computed tomography X-ray absorptiometry (CTXA) against the dual energy X-ray absorptiometry (DXA) as standard has not been studied in Chinese population. The aim of this study was to evaluate the precision of this measurement and validate the value of quantitative computed tomography (QCT) by comparing CTXA results with DXA results in an elderly Chinese population.

Methods One hundred and three females of 46 to 76 years old and 49 males of 52 to 76 years old were recruited from the Prospective Urban Rural Epidemiology study. All subjects underwent hip scans by both QCT and DXA on the same day. For precision determination, 30 subjects had duplicate DXA hip scans. The hip QCT data of a subset of 27 subjects were separately analyzed by two observers and reanalyzed by one observer at a different time. The inter- and intra-observer variations of CTXA measurement were assessed, and the difference and correlation between CTXA and DXA results were analyzed.

Results The inter- and intra-observer variations of CTXA were 0.070 and 0.024 g/cm^2 in the femoral neck (FN), and 0.030 and 0.012 g/cm^2 in the total hip (TH), which were comparable to the DXA inter-scan variations (0.013 g/cm^2 for FN and 0.014 g/cm^2 for TH). The results of CTXA bone mineral density (BMD) were highly correlated with those of DXA (R^2 = 0.810 for FN and R^2 = 0.878 for TH). The BMD values of CTXA in FN and TH were lower than those of DXA by 21.0% and 17.8% (P<0.05), respectively. However, after appropriate transformation, the difference was eliminated and a comparable T score could be obtained.

Conclusions CTXA shows good agreement with DXA for the measurement of BMD in the proximal femur, which makes QCT suitable for the quantification of bone mineral content in the hip and helpful for the diagnosis of osteoporosis.

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Hip fracture is the most severe clinical consequence of osteoporosis with high morbidity and mortality, and it causes a huge burden on public medical care.[1-3] The areal bone mineral density (aBMD) measured by dual energy X-ray absorptiometry (DXA) at the proximal femur has been widely used for the assessment of bone fragility, and the T score of this measurement is recognized as the standard for the diagnosis of osteoporosis worldwide.[4] The projection nature of this two-dimensional measurement requires appropriate positioning of the subject in order to achieve accurate results.[5] However, adequate positioning of the proximal femur in patients with newly fractured hips is impracticable due to the insufferable pain and limitation of the articular movement, which restricts the clinical application of DXA in patients with acute hip fractures. With the development of quantitative computed tomography (QCT) techniques, two-dimensional aBMD of the proximal femur can be derived from the three-dimensional computed tomography (CT) dataset with a calibration phantom being simultaneously scanned beneath the body. This makes it possible to assess the anatomical morphology and structural mechanical properties of the proximal femur in hip fracture patients with one single CT scan, without additional radiation or relocation of the patients.[6-9]

In the present study, aBMD results of the proximal femur measured by QCT were compared with DXA results. The correlation of bone mineral density (BMD) detected by DXA and QCT was evaluated in several prior studies for vertebral cancellous bone.[7,8,10,11] However, few studies were focused on the hip. A study in 91 elderly Australian women showed the aBMD results of the proximal femur measured by QCT and DXA were highly correlated, and QCT may be a helpful substitute to diagnose osteoporosis.[12] Here we make a comparison between QCT aBMD and DXA aBMD of the hip in an elderly Chinese population to evaluate the value of QCT in the quantification of bone mineral content of the hip.

METHODS

Subjects

The subjects of this study were from the participants of

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a large-scale, multi-nation, the Prospective Urban Rural Epidemiology (PURE) study in Beijing.[13] This study was registered in www.clinicaltrials.gov as China Action on Spine and Hip Status (CASH) study (NTC 01758770). Males >50 years old and females >45 years old were eligible. There were 103 females of 46 to 76 years old, and 49 males of 52 to 76 years old. All subjects of this study were living independently in communities of Beijing. The subjects had DXA and QCT scans on the same day. The study was approved by the Ethic Committee of Beijing Jishuitan Hospital and written informed consent was obtained from all participants before the measurement.

DXA measurements

The left hip DXA was performed using an iDXA scanner (GE Lunar, Madison, WI, USA) and analyzed using the manufacturer's software. The aBMD of the femoral neck (FN) and total hip (TH) region of interest (ROI) was obtained and the T scores of these two ROIs were calculated based on the Chinese reference.[14] Details of the measurement procedure were described previously.[12] The results were reported in terms of grams per square centimeter hydroxyapatite equivalent. The precision for this device was carried out by scanning 30 subjects twice with reposition. Daily quality control measurements were performed on the DXA machine to ensure scanner reliability. Height and weight of the subjects were measured.

QCT measurements

QCT was performed using a Toshiba Aquilion 16-slices CT scanner (Toshiba, Tokyo, Japan) with a solid phantom (Mindways Software Inc., Austin, TX, USA). Both hips were scanned in the supine position from the top of acetabulum to 1.0 cm below the femoral lesser trochanter. Scan parameters were 120 KV, 125 mA, 1.0 mm thickness, 50 cm field of view, standard reconstruction. Images were then transferred to QCT workstation and analyzed using the CTXA hip function version 4.2.3 of Mindways QCT pro software (Mindways Software Inc., Austin, TX, USA). After image segmentation and manipulation of the proximal femur rotation and reposition in three orthogonal planes with three-dimentional (3D) CT dataset, two-dimensional projection images were generated and QCT-derived equivalent aBMD was obtained for the FN and TH hip ROIs. The rotation function helped make bone CT data into a standard configuration to facilitate projection of the hip CT data into an image suitable for the placement of conventional hip ROIs (Figure 1). Results for QCT-derived aBMD were reported in terms of equivalent calibrated aqueous potassium phosphate density. The reproducibility of QCT measurement was evaluated with a subset of 27 subjects analyzed by two observers independently, and by one observer in duplicate, two weeks apart.

Statistical analysis

Continuous variable was described as mean ± standard deviation (SD). The unpaired *t*-test (Student's *t*-test) was used to compare means between groups. The relationship

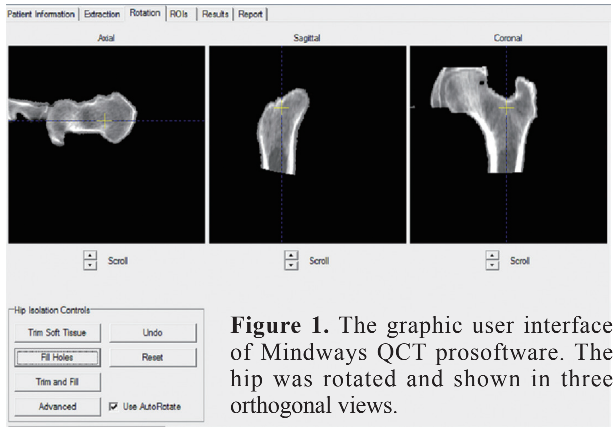

Figure 1. The graphic user interface of Mindways QCT prosoftware. The hip was rotated and shown in three orthogonal views.

between CTXA and DXA and correlation coefficients were analyzed using linear regression. Bland-Altman analyses were used to describe the consistency between aBMD from QCT and DXA. The reproducibility of QCT and DXA was measured as the root-mean-square errors (RMS errors). Since the difference between DXA and QCT aBMD may be due to the different calibrations, this difference may be reduced by fitting the data to the following equations (Mindways regression equations): FN: QCT_{DXA} aBMD=(CTXA+0.001)/0.775 and TH: QCT_{DXA} aBMD=(CTXA+0.007)/0.834. All statistical analyses were completed with SAS software 9.0.1 (SAS Institute, Cary, NC, USA). Statistical significance was accepted at $P<0.05$.

RESULTS

Characteristics of study participants

Characteristics of the subjects are shown in Table 1. Men were taller ($P<0.001$) and weighed more ($P=0.001$) than women without a significant difference in age and body mass index (BMI).

Difference in BMD measured by QCT and DXA

Results of the BMD measurements are summarized in Table 2. QCT-derived aBMD was lower than the DXA-derived aBMD at both sites by 21.0% and 17.8%. This difference was eliminated after application of the QCT-transformed aBMD (QCT_{DXA}BMD) using the Mindways regression equations.

Precision of QCT and DXA BMD measurement

Precision results of QCT and DXA are summarized in Table 3. Intra-observer precision values, ranging from 0.012 g/cm^2 (RMS errors) for the TH to 0.024 g/cm^2 (RMS errors) for the FN, were generally lower than inter-observer values. The most precise values were found for the DXA inter-scans, with RMS errors of 0.013 g/cm^2 for FN to 0.014 g/cm^2 for TH.

Table 1. Characteristics of the subjects

Variables	Male (*n*=49)	Female (*n*=103)	*P* values
Age (years)	63.8±5.6	62.0±6.8	0.106
Height (cm)	167.6±6.5	157.7±5.8	<0.001
Weight (kg)	73.1±13.2	65.9±8.9	0.001
BMI (kg/m^2)	25.9±3.6	26.5±3.6	0.300

Table 2. Results of the aBMD measurements (g/cm^2)

Variables	Total (*n*=152)		Male (*n*=49)		Female (*n*=103)	
	FN	TH	FN	TH	FN	TH
DXA aBMD	0.82±0.12	0.90±0.14	0.87±0.12	0.96±0.13	0.80±0.12	0.87±0.13
QCT aBMD	0.64±0.11	0.74±0.13	0.68±0.10	0.80±0.12	0.62±0.10	0.71±0.12
QCT_{DXA} aBMD	0.82±0.14	0.90±0.15	0.88±0.14	0.97±0.14	0.80±0.13	0.86±0.14

FN: femoral neck. TH: total hip. aBMD: areal bone mineral density. QCT_{DXA} aBMD values are QCT aBMD values transformed using Mindways regression equations.

Table 3. Precision results of QCT and DXA

Variables	QCT		DXA
	Intra-operator RMS error	Inter-operator RMS error	Inter-scans RMS error
FN (g/cm^2)	0.024	0.070	0.013
TH (g/cm^2)	0.012	0.030	0.014

RMS error: root-mean-square error.

Correlation between DXA and QCT measurements

Figure 2 presents the Bland-Altman analyses using the converted data for the two sites of the proximal femur. Bland-Altman analyses confirmed measurement similarity between instruments with a mean bias of –0.002 (SD=0.05) g/cm^2 for TH and –0.005 (SD=0.06) g/cm^2 for FN. The correlation were significant for both the TH (*P*=0.004) and FN (*P*<0.001).

Figure 3 shows the linear regression plots of QCT-transformed aBMD and the DXA-derived aBMD. R^2 values were 0.810 for FN and 0.878 for TH.

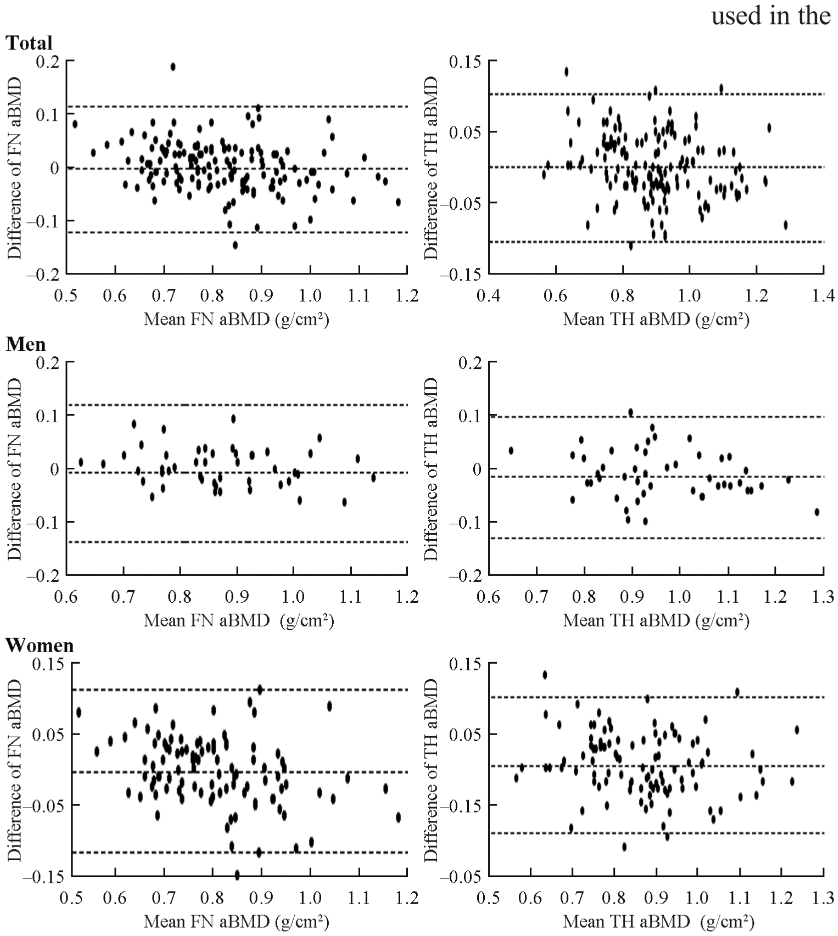

Figure 2. Bland-Altman analyses demonstrate absolute differences (DXA-derived aBMD – QCT_{DXA} aBMD) versus their mean value for TH and FN aBMD confirming instrument similarity.

DISCUSSION

Since the BMD changing over age is slow and subtle, good precision of a BMD measurement is a prerequisite for the clinical application of this technology in the management of osteoporosis. CTXA of the hip is an emerging volumetric BMD assessment technique, which is not yet sufficiently studied. Lang et al have shown that the precision of duplicate QCT scans of cadaveric femurs was excellent.[15] Previous study demonstrated that the precision of CTXA duplicate hip scans was slightly better than DXA.[12] Due to the radiation exposure, repeating the hip scan is not advisable. However, the duplicate CT scan of the hip may not be necessary because of the volumetric nature of the CT dataset. The measurement error is caused mainly by the manipulation of the image segmentation and rotation of the hip. This error can be reduced by proper training, in fact, our unpublished data show that 0.012 g/cm^2 RMS error can be achieved by skillful operators. Another advantage of CTXA is that the rotation of the proximal femur can be visualized with QCT images, while it is not in the DXA position. Our results indicate that with proper training QCT intra-observer precision error is comparable with that of GE iDXA.

Since DXA hip BMD has been well accepted and widely used in the diagnosis of osteoporosis and assessment of hip fracture risk, it is critical for a new technology of hip BMD measurement to demonstrate a DXA comparable performance. In keeping with the results from a previous study showing that hip CTXA aBMD was highly correlated with the Hologic DXA results,[10] we found that aBMD values derived from the QCT CTXA hip function had a good correlation with results obtained from a GE iDXA device.

Our study showed that QCT-derived aBMD values were lower than the corresponding DXA-derived aBMD values, with differences at the FN and TH of 0.08 and 0.16 g/cm^2, respectively. However, differences between QCT-transformed aBMD and DXA-derived aBMD were almost negligible. Shepherd et al have shown that GE-Lunar aBMD values at both FN and TH sites were consistently higher compared to Hologic values, with the differences at the FN and TH being 0.15 and 0.07 g/cm^2, respectively.[16] Khoo et al[12] have reported some causes of the differences between QCT-transformed aBMD and DXA-derived aBMD, including the different calibration phantoms used by QCT and DXA and the difference in the calculation of BMD. Though direct normal hip QCT data of Chinese was not available, the QCT-transformed aBMD was comparable with

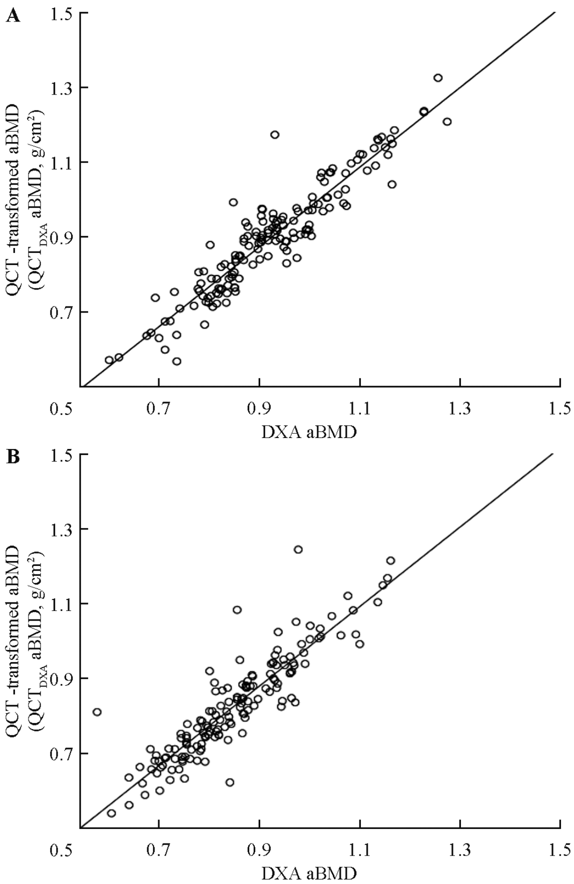

Figure 3. Plots of aBMD results measured by QCT vs. DXA in TH (**A**) and FN (**B**).

GE DXA results: a comparable T score of the hip can be obtained by comparing with GE DXA reference data. The CTXA aBMD and T score can be used in the diagnosis and management of osteoporosis as a substitute of DXA aBMD.

Evaluation of bone strength is important in the diagnosis of osteoporosis. DXA has limitations for assessment of bone strength owing to the complex 3D geometry of the hip, low spatial resolution, and its two-dimensional nature. QCT offers complete 3D information, bone geometry, and the ability of distinguishing differences between bone microstructures. QCT-based finite element models can improve the prediction of mechanical properties by combining information about BMD distribution, femoral geometry, femoral size, bone material properties and loading configuration.[17-19]

Our study has several limitations. The number of male volunteers was moderate, and larger numbers of male volunteers may be needed to improve correlations at the femur. CTXA uses higher radiation than DXA. However, CTXA has the advantage of combining data with routine hip CT scans without extra radiation and it is anticipated that CTXA can be widely used for hip fracture management.

In conclusion, hip aBMD measured by CTXA has comparable precision to DXA. There is a good correlation between QCT-transformed aBMD and GE Lunar iDXA aBMD for the TH and FN in elderly Chinese. With appropriate adjustment, CTXA can produce DXA comparable aBMD and T scores and can be widely used in the diagnosis of osteoporosis and helpful for the operation planning in elderly patients with hip fractures.

REFERENCES

1. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. Lancet 2002; 359: 1761-1767.
2. Compston J, Cooper A, Cooper C, Francis R, Kanis JA, Marsh D, et al. Guidelines for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK. Maturitas 2009; 62: 105-108.
3. Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. J Bone Miner Res 2007; 22: 465-475.
4. Genant HK, Grampp S, Gluer CC, Faulkner KG, Jergas M, Engelke K, et al. Universal standardization for dual X-ray absorptiometry: patient and phantom cross-calibration results. J Bone Miner Res 1994; 9: 1503-1514.
5. Fan B, Lu Y, Genant H, Fuerst T, Shepherd J. Does standardized BMD still remove differences between Hologic and GE-Lunar state-of-the-art DXA systems? Osteoporos Int 2010; 21: 1227-1236.
6. Cheng XG, Lowet G, Boonen S, Nicholson PH, Brys P, Nijs J, et al. Assessment of the strength of proximal femur in vitro: relationship to femoral bone mineral density and femoral geometry. Bone 1997; 20: 213-218.
7. Guglielmi G, van Kuijk C, Li J, Meta MD, Scillitani A, Lang TF. Influence of anthropometric parameters and bone size on bone mineral density using volumetric quantitative computed tomography and dual X-ray absorptiometry at the hip. Acta Radiol 2006; 47: 574-580.
8. Lang TF, Guglielmi G, van Kujik C, De Serio A, Cammisa M, Genant HK. Measurement of bone mineral density at the spine and proximal femur by volumetric quantitative computed tomography and dual energy X-ray absorptiometry in elderly women with and without vertebral fractures. Bone 2002; 30: 247-250.
9. Cheng XG, Li J, Lu Y, Keyak J, Lang T. Proximal femoral density and geometry measurements by quantitative computed tomography: Association with hip fracture. Bone 2007; 40: 169-174.
10. Ebbesen EN, Thomsen JS, Beck-Nielsen H, Nepper-Rasmussen HJ, Mosekilde L. Vertebral bone density evaluated by dual-energy X-ray absorptiometry and quantitative computed tomography *in vitro*. Bone 1998; 23: 283-290.
11. Jergas M, Breitenseher M, Glüer CC, Yu W, Genant HK. Estimates of volumetric bone density from projectional measurements improve the discriminatory capability of dual X-ray absorptiometry. J Bone Miner Res 1995; 10: 1101-1110.
12. Khoo BC, Brown K, Cann C, Zhu K, Henzell S, Low V, et al. Comparison of QCT-derived and DXA-derived areal bone mineral density and T scores. Osteoporos Int 2009; 20: 1539-1545.
13. Teo K, Chow CK, Vaz M, Rangarajan S, Yusuf S. The

Prospective Urban Rural Epidemiology (PURE) study: examining the impact of societal influences on chronic noncommunicable diseases in low-, middle-, and high-income countries. Am Heart J 2009; 158: 1-7.
14. Cheng XG, Yang DZ, Zhou Q, Zhuo TJ, Zhang HC, Xiang J, et al. Age-related bone mineral density, bone loss rate, prevalence of osteoporosis, and reference database of women at multiple centers in China. J Clin Densitom 2007; 10: 276-284.
15. Lang TF, Keyak JH, Heitz MW, Augat P, Lu Y, Mathur A, et al. Volumetric quantitative computed tomography of the proximal femur: precision and relation to bone strength. Bone 1997; 21: 101-108.
16. Shepherd JA, Fan B, Lu Y, Lewiecki EM, Miller P, Genant HK. Comparison of BMD for Prodigy and Delphi spine and femur scans. Osteoporosis Int 2006; 17: 1303-1308.
17. Dall'Ara E, Luisier B, Schmidt R, Kainberger F, Zysset P, Pahr D. A nonlinear QCT-based finite element model validation study for the human femur tested in two configurations *in vitro*. Bone 2013; 52: 27-38.
18. Genant HK, Libanati C, Engelke K, Zanchetta JR, Høiseth A, Yuen CK, et al. Improvements in hip trabecular, subcortical, and cortical density and mass in postmenopausal women with osteoporosis treated with denosumab. Bone 2013; 56: 482-488.
19. Nicks KM, Amin S, Melton LJ 3rd, Atkinson EJ, McCready LK, Riggs BL, et al. Three-dimensional structural analysis of the proximal femur in an age-stratified sample of women. Bone 2013; 55: 179-188.

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