Peripheral Quantitative Computed Tomography of the Femoral Neck in 60 Japanese Women

T. Horikoshi, N. Endo, T. Uchiyama, T. Tanizawa, H. E. Takahashi*

Department of Orthopedic Surgery, Niigata University School of Medicine, 1-757 Asahimachi-dori, Niigata City 951-8510, Japan

Received: 23 June 1998 / Accepted: 1 July 1999

Abstract. Peripheral quantitative computed tomography (pQCT) is able to evaluate trabecular and cortical bone separately, and to determine geometric properties from cross-sectional images for noninvasive assessments of mechanical strength. In order to assess the diagnostic value of pQCT of the femoral neck, 60 healthy women were examined with a new pQCT machine, XCT-3000 (Norland-Stratec, Germany), which is suitable for direct measurement of the hip. The region of interest chosen was the center of the femoral neck. pQCT of the distal radius and dual energy X-ray absorptiometry (DXA) of the lumbar spine and femoral neck were also performed.

The study demonstrated that total bone mineral density (BMD) (femoral MD) and trabecular BMD (femoral-TBD) decreased with advancing age. Percent cortical area showed a small but significant decrease with advancing age and % trabecular area increased slightly. Both the endosteal perimeter and the periosteal perimeter were relatively constant with aging. Bone strength index (BSI) and stress-strain index (SSI), which reflect the mechanical strength of bone, declined with advancing age, especially after menopause. Femoral TBD correlated strongly with femoral neck BMD by DXA and L2-L4 BMD by DXA but femoral-CBD did not correlate with femoral neck BMD by DXA. Volumetric BMD of the femoral neck and distal radius were closely correlated. It is concluded that (1) cortical thinning occurs with aging by endocortical resorption and loss of femoral-TBD; (2) loss of femoral-CBD occurred at a slower rate than radial CBD, perhaps due to the weight-bearing effect; (3) biomechanical parameters such as the BSI and SSI may reflect increasing fragility of the femoral neck in pre- and postmenopausal women; (4) pQCT of the femoral neck had diagnostic value at least equivalent to that of DXA or pQCT of the distal radius.

Key words: Peripheral quantitative computed tomography — Femoral neck-bone mineral density — Geometry — Osteoporotic fracture.

Increasing longevity has made osteoporosis and osteoporotic fractures major health care and economic problems. Femoral neck fracture is one of the most serious complications of osteoporosis. It is sometimes life threatening for the aged, and requires surgical treatment and hospitalization in most cases [1, 2]. The incidence of femoral neck fracture has increased in recent years [3–6], therefore, it is important to predict osteoporotic fracture risk as an aid in taking preventive measures. Fragility of the skeleton is mainly dependent on bone mineral density (BMD), but structural properties of both the cortical shell and the trabecular pattern independent of BMD also greatly affect strength of the bone [7–9].

Peripheral quantitative computed tomography (pQCT) has the advantage of measuring the volumetric, not areal, BMD. pQCT is also able to evaluate trabecular bone separately from cortical bone, so when compared with other densitometries it is more sensitive to changes in bone mineral content (BMC) and BMD in the course of bone metabolic disease or during the administration of drugs [10, 11]. Moreover, cross-sectional images can give a great deal of information about geometrical parameters of bone for noninvasive assessments of mechanical strength.

Use of pQCT measurements at the distal radius have been shown to be useful for the diagnosis of osteoporosis and for predicting the risk of spinal and hip fractures [9, 12]. However, in DXA studies, BMD measurements of the femoral neck were better predictors of the risk of hip fractures than measurements of the distal radius, spine, and calcaneus [13]. Therefore, direct pQCT measurement of the femoral neck might help to evaluate the risk of fractures there.

This study evaluated pQCT of the femoral neck as a noninvasive method for assessing the risk of osteoporotic hip fractures.

Materials and Methods

Subjects

A total of 60 healthy female volunteers, aged 23–81 years, were studied: 27 were premenopausal and 33 were postmenopausal, and the mean age at menopause was 50.9 ± 2.7 years (Table 1). The study protocol was approved by the hospital ethics committee. Written informed consent was obtained prior to examination.

Methods

pQCT of the Femoral Neck. The XCT-3000 machine (Norland-Stratec, Pforzheim, Germany) is a pQCT that is a micocomputercontrolled translation-rotated tomographic scanner with an X-ray souce and 12 semiconductor detectors and enables direct measurements of the human hip region. CT scan was carried out with a

Correspondence to: N. Endo

^{}Present address:* Niigata Bone Science Institute, 1-17-8 Nagata, Niigata City 950-0932, Japan

Table 1. Characteristics of the study population

single slice of 700 μ m in voxel size. It has a narrow 30 cm-wide gantry, which facilitates positioning of the femoral neck. The examinee was placed in the sitting position on a chair in front of the gantry with his/her thigh (femoral shaft) abducted and internally rotated to keep the long axis of the femoral neck perpendicular to the gantry during the examination. The chair in front of the gantry can be translated into a range of 100 cm in a horizontal direction. We used the manufacturer's provided leg holder to keep the hip at an angle of 45° of abduction and 15° of internal rotation to exclude anterversion of the femoral neck. After obtaining a scout scan from the intertrochanteric region to the subcapital region, the CT scan was carried out at the site of the center of the left femoral neck in all cases (Figs. 1, 2). Each CT scan was made perpendicular to the long axis of the femoral neck. The entire scanning time was approximately 8 minutes.

Volumetric BMDs of the femoral neck, total BMD (femoral-BD), trabecular BMD (femoral-TBD), and cortical BMD (femoral-CBD) were determined separately. These parameters were derived using the manufacturer's supplied analysis package.

Geometrical parameters such as the cross-sectional area, % trabecular area, % cortical area, average cortical thickness, periosteal perimeter, and the endosteal perimeter were obtained automatically by cross-sectional image analysis.

The BSI and SSI were also calculated as noninvasive indicators of the mechanical strength of bone. Both BSI and SSI have been proven to be directly proportional to the breaking force of long bones in cadaveric or animal studies. BSI is regarded as an indicator of bending strength and SSI as an indicator of torsional strength [14–16].

The *in vitro* precision of XCT-3000 was found by measuring a manufacturer's supplied QA phantom with four different densities five times. The *in vivo* precision was found by measuring volumetric BMD of the femoral neck three times in each of three women after repositioning. Precisions were expressed as coefficient of variation (% CV).

pQCT of the Distal Radius. Two scans of different sites were made at the distal radius by a XCT-960 machine (Norland-Stratec, Pforzheim, Germany) on the left forearm (nondominant) in 55 of the 60 women. Scanning sites were located at the distal 4% and 20% of the length of the ulna from its distal end. Total and trabecular BMDs (radial-BD, radial-TBD, respectively) were obtained at the distal 4% site where the trabecular bone content is high and the cortex is thin. The scanning site of cortical bone density of the distal radius (radial-CBD) was determined at the distal 20% site where the cortical content is high, because the cortical BMD is affected by the partial volume effect at the distal site [17].

Dual Energy X-ray Absorptiometry. Areal BMD of the left femoral neck and lumbar spine (L2-L4) was determined by DXA (QDR-2000: Hologic, Waltham, MA, USA). Relationships between these

Fig. 1. The long axis of the examinee's femoral neck was kept perpendicular to the gantry, with a leg holding device that keeps the hip at an angle of 45° of abduction and 15° of internal rotation.

BMD and pQCT values of the femoral neck were analyzed. These three different densitometries were performed on the same day.

Results

Precision of the XCT-3000

The % CV referred to the phantom of the XCT-3000 was less than 1.0% (0.02–0.36%, average 0.23%) *in vitro.* The *in vivo* study with three examinees, % CV of femoral-BD, femoral-TBD, and femoral-CBD were 1.40%, 2.45%, 1.43%, respectively.

Fig. 2. CT scan was made at the center of the neck. Scanning plane is illustrated. After obtaining a scout scan from the intertrochanteric region to the subcapital region, the level of the CT scan was adjusted to the center of the left femoral neck.

pQCT of the Femoral Neck

Volumetric bone mineral measurements were performed for total, trabecular, and cortical bone. The mean values of femoral-BD, femoral-TBD, and femoral-CBD were $365.0 \pm$ 77.3, 212.5 ± 50.4 , 875.1 ± 41.1 mg/cm³, respectively. Femoral-BD and femoral-TBD decreased significantly with age (Fig. 3). Though neither body weight nor the body mass index (BMI) predicted these BMDs, body height correlated moderately with volumetric BMD (Table 2).

Percent cortical area at the femoral neck decreased significantly with age whereas % trabecular area increased (Fig. 4). Both periosteal and endosteal perimeter of the cortex showed no significant change with advancing age (Fig. 5).

BSI showed a linear age-related decline. SSI curved downward at the perimenopausal age (Fig. 6 a,b).

pQCT of the Distal Radius

50

60

age (years)

The mean values of radial-BD, radial-TBD, and radial-CBD were 353.2 mg/cm³, 158.1 mg/cm³, 1130.2 mg/cm³, respectively. This volumetric BMD correlated well with those of the femoral neck, except for CBD (Table 3).

b

80

70

90

Femoral-CBD (dotted line) = $908.548 - .657$ * age; R^2 = .073 Radial-CBD (solid line) = $1288.055 - 3.238$ * age; R^2 = .387

r-values are shown

 $\binom{a}{P}$ = 0.0001; $\binom{b}{P}$ = 0.05

Dual Energy X-ray Absorptiometry

Femoral-BD and femoral-TBD correlated strongly with femoral neck BMD by DXA $(r = 0.877, 0.812,$ respectively) and moderately with lumbar spine BMD by DXA (r $= 0.610, 0.569,$ respectively). However, femoral-CBD showed only a weak correlation with BMD by DXA, whereas radial-CBD correlated significantly (Table 3).

Discussion

It is important to evaluate the bone fragility of the femoral neck, such as bone mass and the geometry and property of bone, to predict the risk of hip fracture [18–22]. The diagnostic reliability of various noninvasive measurements, such as X-ray absorptiometry (SXA, DXA), quantitative ultrasound (QUS), quantitative computed tomography (QCT), have been reported [23–26]. Cross-sectional images by QCT give much information about the geometry of trabecular structure and the cortical shell. Trabecular bone, which is much more sensitive to changes in bone metabolism than cortical bone, can be analyzed separately, which is advantageous for the early detection of quantitative and qualitative changes. The validity of volumetric bone mineral measurement of the distal radius for the evaluation of age-related bone loss and for the diagnosis of osteoporosis has been proven [27]. Animal studies suggest that analysis of trabecular bone by pQCT may be a reasonable noninvasive surrogate for measurements by histomorphometry [28]. Many cadaveric or animal pQCT analyses combined with mechanical testing reveal that geometrical parameters of the cortical shell such as cortical thickness, cortical area, and cross-sectional second moment of inertia have close relationships with the bending or torsional strength of intact bones [9, 14–16].

The XCT-3000, which is a recently introduced pQCT machine, has a large gantry opening of 300 mm, which enables measurement of BMD and geometrical parameters in subjects with larger thighs (up to 300 mm in width); the machine also measures the hip, knee, and dental region. The *in vitro* and *in vivo* precision studies show that reproducibility of the measured BMDs by XCT-3000 is good enough for clinical use in analyses of the femoral neck compared with the reported value [29].

In the present study, femoral-BD and femoral-TBD decreased significantly with aging, but femoral-CBD showed no change. The findings in the femoral neck and distal radius disagree on this point because age-related loss of radial-CBD is as fast as radial-BD and radial-TBD. Is the femoral neck cortex less subject to an age-related increase in intracortical porosity than the distal radius? Could weight-bearing on the femoral neck, to some degree, pre-

% cross-sectional area

% trabecular area(solid line) = $49.146 + .276$ *age; R \land 2 = .212 % cortical area(dotted line) = $24.108 - .208$ *age; R^2 = .274

Fig. 4. Age-related changes in % trabecular (\bigcirc) and % cortical (\triangle) area in cross-sectional image.

Fig. 5. Age-related changes in the periosteal (\bigcirc) and endosteal (\triangle) perimeter. The endosteal perimeter increases with age whereas the periosteal perimeter was relatively constant.

vent or minimize such an age-related increase in intracortical porosity?

Cross-sectional image analyses revealed an age-related increase in the % trabecular area and a decrease in the % cortical area without much change in total bone area. This suggests that trabecularization of the inner cortex compensates in part for the loss of the trabecular bone. This idea is consistent with findings by histomorphometric analyses of the femoral neck and ilium [30].

Though not significantly, the endosteal perimeter increased with age whereas the periosteal perimeter was relatively constant. These result support the idea that endocortical trabecularization by increased resorption caused some of the thinning of the cortex in postmenopausal elderly women [31, 32].

Some long bones such as the radius, ulna, and femur show an increase in their diaphyseal cross-sectional size and cross-sectional moment of inertia in the elderly by periosteal deposition. This increase has been proposed as a mechanism to maintain the mechanical strength of bones [33, 34]. But in the femoral neck, neither total bone area nor periosteal perimeter increased with age. Still, in our study, the older women were shorter, and the shorter women had the

Fig. 6. Age-related changes in Bone-Strength Index **(a)** and Stress-Strain Index **(b).** Dotted line indicates average age at menopause in postmenopausal women. BSI = 9693661.9–112812.1*age, r = 0.695, *P* < 0.0001; SSI = 1384.7–12.7*age, r = −0.683 *P* < 0.0001.

narrower femoral necks. Therefore, this cross-sectional study could not reveal if this compensatory mechanism did or did not occur in the femoral neck.

Mechanically, the bending strength of a tubular structure is proportional to the product of its cross-sectional moment of inertia (CSMI) multiplied by its elastic modulus (E). In long bones, cortical BMD is directly proportional to E, so it could be substituted for E. Therefore, the strength of long bones such as the femoral neck, femoral shaft, and radius can be expressed as an index, consisting of the product $CSMI \times CBD = Bone$ Strength Index (BSI), which provides an index of bending strength. Feretti et al. [14] found that BSI of rat femora linearly correlated highly with the measured breaking force in the 3-point bending test.

The SSI is also based on the theory of the stability of mechanical structures in bending or torsion. It is calculated as a function of the polar moment of resistance of the cortical area, taking into account the maximum strain and cortical BMD. SSI of the human radius did not vary with age in healthy men but decreased in healthy women older than 52 years [14–16].

In our study these biomechanical parameters of the femoral neck showed an age-related decline (Fig. 6). The SSI especially declined after 50 years of age when most women experience natural menopause. These results were similar to a previous report about an age-related change in the SSI of the distal radius. An increased fracture incidence in postmenopausal women may be explained in part by a decrease in BSI or SSI in addition to the loss of BMD. However, in order to validate the BSI or the SSI as indicators of the risk of fractures, a long-term cohort study would be needed.

A close relationship was found between femoral neck BMD by pQCT and BMD by DXA. Femoral-BD and femo-

Table 3. Correlation among L2-4 BMD, femoral neck BMD, radial-BD, radial-TBD, radial-CBD, and femoral-BD, femoral-TBD, and femoral-CBD by pQCT

	Femoral-BD	Femoral-TBD	Femoral-CBD
L ₂ -4 BMD by DXA	$0.610^{\rm a}$	$0.569^{\rm a}$	$0.268^{\rm b}$
Femoral neck BMD by DXA	$0.877^{\rm a}$	0.812^a	0.170
Radial-BD	0.639^{a}		
Radial-TBD		$0.517^{\rm a}$	
Radial-CBD			0.351 ^b

Radial-BD, -TBD, and -CBD were measured by a XCT-960. Femoral-BD, -TBD and -CBD were measured by XCT-3000

 $\binom{a}{P}$ = 0.0001; $\binom{b}{P}$ = 0.05

ral-TBD correlate strongly with femoral neck BMD by DXA, but moderately with lumbar spine BMD by DXA. Femoral-CBD showed only a weak correlation with BMD by DXA. From these results it is speculated that age-related bone loss in the femoral neck depends on the loss of femoral-TBD and cortical thickness, and not on the loss of femoral-CBD. When compared with pQCT values of the distal radius, the coefficients of correlation of femoral-BD and femoral-TBD with lumbar spine BMD by DXA were equivalent, and higher with femoral neck BMD by DXA. However, unlike femoral-CBD, radial-CBD correlated significantly with BMD by DXA. A possible reason for this difference lies in the structure of the cortex. Compared with the distal 20% of radius, the femoral neck cortex is less parallel, and therefore is more susceptible to the partial volume effect which might lead to incorrect estimation of its cortical BMD.

This is the first clinical pQCT study of the femoral neck. Total, trabecular, and cortical volumetric BMD were obtained with high precision, and close relationships to pQCT of the distal radius and DXA of the femoral neck and lumbar spine were confirmed. Volumetric BMD and geometric parameters of the trabecular structure and the cortex obtained from cross-sectional image analyses have the potential to provide a noninvasive surrogate for conventional bone histomorphometry. Moreover, age-related and transmenopausal changes of BMD and geometric parameters of the femoral neck may partly account for the increased incidence of femoral neck fractures in elderly women. We conclude that pQCT of the femoral neck will help in assessing the risk of osteoporotic fractures.

Acknowledgments. We would like to thank Mr. Yoshiaki Tanaka for his help in the study. We also acknowledge Ms. Akemi Ito and Ms. Hiroe K. Ishigaki for their technical support and preparation of the manuscript.

References

- 1. Wolinsky FD, Fitzgerald JP, Stump TE (1997) The effect of hip fracture on mortality, hospitalization, and functional status: a prospective study. Am J Public Health 87:398–403
- 2. Baudoin C, Fardellone P, Bean K, Ostertag-Ezembe A, Hervy F (1996) Clinical outcomes and mortality after hip fracture: a 2-year follow-up study. Bone 18 (suppl):149–157
- 3. Kannus P, Parkkari J, Sievanen H, Heinonen A, Vuori I, Jarvinen M (1996) Epidemiology of hip fractures. Bone 18 (suppl):57S–63S
- 4. Lau EM (1996) The epidemiology of hip fracture in Asia: an update. Osteoporosis Int 6 (suppl 3):19–23
- 5. Kawashima T (1989) Epidemiology of the femoral neck fracture in 1985, Niigata Prefecture, Japan. J Bone Miner Metab 7:46–54
- 6. Dohmae Y, Takahashi HE, Kawashima T, Tanizawa T, Nishida S (1991) Epidemiology of femoral neck fractures in 1989, Niigata prefecture, Japan. J Bone Miner Metab 9 (suppl):20–24
- 7. Cheng XG, Lowet G, Boonen S, Nicholson PH, Brys P, Nijs J, Dequaker J (1997) Assessment of the strength of proximal femur in vitro: relationship to femoral bone mineral density and femoral geometry. Bone 20:213–218
- 8. Nakabayashi Y, Wevers HW, Cooke TD, Griffin M (1994) Bone strength and histomorphometry of the distal femur. J Arthroplasty 9:307–315
- 9. Augut P, Reeb H, Claes LE (1996) Prediction of fracture load at different skeletal sites by geometric properties of the cortical shell. J Bone Miner Res 11:1356–1363
- 10. Gasser JA (1995) Assessing bone quantity by pQCT. Bone 17 (suppl):145–154
- 11. Ferretti JL (1995) Perspectives of pQCT technology associated with biomechanical studies skeletal research employing rat models. Bone 17:353–364
- 12. Schneider P, Börner W (1990) Ability of peripheral QCT at the radius in comparison to DEXA of the spine to diagnose vertebral fractures in postmenopausal women. Osteoporosis 59:921–924
- 13. 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
- 14. Ferretti JL, Gaffuri O, Capozza R, Cointry G, Bozzini C, Olivera M, Zanchetta JR, Bozzini CE (1995) Dexamethasone effects on structural, geometric and material properties of rat femur diaphyses as described by peripheral quantitative computed tomography (pQCT) and bending tests. Bone 16:119– 124
- 15. Ferretti JL, Capozza RF, Tysarczyk-Niemeyer G, Schiessl H, Steffens M (1995) Tomographic determination of stability parameters allows estimation of bending or torsion strength of human radius. Proc Perth Int Bone Meeting. Fremantle (Australia):48
- 16. Ferretti JL, Capozza RF, Zanchetta JR (1996) Mechanical validation of a tomographic (pQCT) index for noninvasive estimation of rat femur bending strength. Bone 18:97–102
- 17. Louis O, Van den Winkel P, Covens P, Schoutens A, Osteaux M (1993) Size of cortical bone and relationship to bone mineral density assessed by quantitative computed tomography image segmentation. Invest Radiol 28:802–805
- 18. Schurch MA, Rizzoli R, Mermillod B, Vasey H, Michel JP, Bonjour JP (1996) A prospective study on socioeconomic as-

r-values are shown

pects of fracture of the proximal femur. J Bone Miner Res 11:1935–1942

- 19. Ray NF, Chan JK, Thamer M, Melton LJ III (1997) Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: report from the National Osteoporosis Foundation. J Bone Miner Res 12:24–35
- 20. Mosekilde L, Mosekilde L (1988) Iliac crest trabecular bone volume as predictor for vertebral compressive strength, ash density and trabecular bone volume in normal individuals. Bone 9:195–199
- 21. Edmondston SJ, Singer KP, Day RI, Price RI, Breidahl PD (1997) Ex vivo estimation of thoracolumbar vertebral body compressive strength: the relative contributions of bone densitometry and vertebral morphometry. Osteoporosis Int 7: 142–148
- 22. Chen XG, Lowet G, Boonen S, Nicholson PH, Brys P, Nijs J, Dequeker J (1997) Assessment of the strength of proximal femur in vitro: relationship to femoral bone mineral density and femoral geometry. Bone 20:213–218
- 23. Funck C, Wüster C, Alenfeld FE, Pereira-Lima JFS, Fritz T, Meeder PJ, Götz M, Ziegler R (1996) Ultrasound velocity of the tibia in normal German hip fracture patients. Calcif Tissue Int 58:390–394
- 24. Mautalen C, Vega E, González D, Carrilero P, Otaño A, Silberman F (1995) Ultrasound and dual X-ray absorptiometry densitometry in women with hip fracture. Calcif Tissue Int 57:165–168
- 25. Karlsson MK, Johnell O, Nilsson BE, Sernbo I, Obrant KJ (1993) Bone mineral mass in hip fracture patients. Bone 14: 161–165
- 26. Hwang SN, Wehrli FW, Williams JL (1997) Probability-based structural parameters from three-dimensional nuclear mag-

netic resonance images as predictors of trabecular bone strength. Med Phys 24:1255-1261

- 27. Hasegawa Y, Kushida K, Yamazaki K, Inoue T (1997) Volumetric bone mineral density using peripheral quantitative computed tomography in Japanese women. Osteoporosis Int 7:195–199
- 28. Rosen HN, Tollin S, Balena R, Middlebrooks VL, Beamer WG, Donohue LR, Rosen C, Turner A, Holick M, Greenspan SL (1995) Differentiating between orchiectomized rats and controls using measurements of trabecular bone density: a comparison among DXA, histomorphometry, and peripheral quantitative computerized tomography. Calcif Tissue Int 57: 35–39
- 29. Genant HK, Engelike K, Fuerst T, Gluer CC, Grampp S, Harris ST, Jergas M, Lang T, Lu Y, Majumdar S, Mathur A, Takada M (1996) Noninvasive assessment of bone mineral and structure: state of the art. J Bone Miner Res 11:707–730
- 30. Nishihara A (1995) Femoral neck and iliac bone histomorphometry in femoral neck fracture. J Jpn Orthop Assoc 69: 156–167
- 31. Han ZH, Palnitkar S, Rao DS, Nelson D, Parfitt AM (1996) Effect of ethnicity and age or menopause on the structure and geometry of iliac bone. J Bone Miner Res 11:1967–1975
- 32. Aguado F, Revilla M, Villa LF, Rico H (1997) Cortical bone resorption in osteoporosis. Calcif Tissue Int 60:323–326
- 33. Bouxsein ML, Myburgh KH, van der Meulen MC, Lindenberger E, Marcus R (1994) Age-related differences in crosssectional geometry of the forearm bones in healthy women. Calcif Tissue Int 54:113–118
- 34. Bohr HH, Schaadt OP (1990) Structural changes of the femoral shaft with age measured by dual photon absorptiometry. J Bone Miner 11:357–362