ELSEVIER
Bone xx (2006) xxx–xxx
BONE
www.elsevier.com/locate/bone

Proximal femoral density and geometry measurements by quantitative computed tomography: Association with hip fracture

X. Cheng [a], J. Li [b], Y. Lu [b], J. Keyak [c], T. Lang [b],*

[a] Department of Radiology, Beijing Ji Shui Tan Hospital, Beijing, China
[b] Department of Radiology, University of California San Francisco, 185 Berry Street, Suite 350, San Francisco, CA 94143-0946, USA
[c] Department of Orthopaedic Surgery, University of California, Irvine, CA, USA

Received 5 April 2006; revised 8 June 2006; accepted 29 June 2006

Abstract

Introduction: Bone mineral density and geometry measurements by volumetric quantitative computed tomography (vQCT) have been utilized in clinical research studies of aging, pharmacologic intervention and mechanical unloading, but there is relatively little information about the association of these measures with hip fracture. To address this issue, we have carried out a study comparing vQCT parameters in elderly Chinese women with hip fractures with measurements in age-matched controls.
Materials and methods: Forty-five women (mean age 74.71 ± 5.94) with hip fractures were compared to 66 age-matched control subjects (mean age 70.70 ± 4.66). vQCT was employed to characterize the volumetric bone mineral density in cortical, trabecular, and integral volumes of interest in the proximal femur. In addition to the volume of interest measurements, we computed the cross-sectional areas of the femoral neck and intertrochanteric planes, the femoral neck axis length, indices of femoral neck bending and compressive strength, and measures of femoral neck cortical geometry. To determine if cortical geometry measures were associated with hip fracture independently of trabecular vBMD, we carried out multi-variate analyses including these parameters in a logistic regression model.
Results and conclusions: All vQCT measurements discriminated between fractured subjects and age-matched controls. There was no significant difference in predictive strength between volumetric and areal representations of BMD and trabecular and integral vBMD showed comparable discriminatory power, although both of these measures were more correlated to fracture status than cortical vBMD. We found that fractured subjects had larger femoral neck cross-sectional areas, consistent with adaptation to lower BMD in these osteoporotic subjects. The larger neck cross-sectional areas resulted in bending strength indices in the fractured subjects that were comparable or larger than those of the control subjects. In multi-variate analyses, reduced femoral neck cortical thickness and buckling ratio indices were associated with fracture status independently of trabecular vBMD.

Keywords: Bone QCT; Bone densitometry; Osteoporosis; Hip fracture

Introduction

Areal bone mineral density (aBMD) measured by dual X-ray absorptiometry is strongly associated with hip fracture both cross-sectionally [1] and prospectively [11,23], but is limited in the information it provides on the pathophysiology of hip fracture because it is a hybrid measure combining bone density and size [10], which may be independently related to hip fracture risk. Volumetric quantitative computed tomography (vQCT), on the other hand, provides measures of trabecular and cortical volumetric BMD (vBMD) as well as measures of bone size such as tissue volume and cross-sectional area [5,7,17,18]. vQCT has become an increasingly important clinical research tool in analyzing the effect of age [22], drug therapy [3,4], mechanical unloading [16], and other phenomena on the density and geometry of bone. The density, geometry, and strength measures derived from vQCT images have been correlated to bone strength [6,8,14,17], thereby providing a theoretical link to fracture risk. However, there is little direct information

---

* Corresponding author. Fax: +1 415 353 9423.
E-mail address: Thomas.Lang@radiology.ucsf.edu (T. Lang).

8756-3282/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.bone.2006.06.018

regarding their association with hip fracture, the key clinical endpoint in osteoporosis.

The paucity of data relating vQCT measures to hip fracture is due to the fact that hip vQCT measures have only recently been included as primary measurements in large population studies and because metallic artifacts and cohort effects complicate retrospective studies. An alternative, but logistically challenging approach is to image individuals immediately after their fracture and prior to surgery. In the only published case–control study of this type, Cody et al. compared DXA and hip vQCT measurements in elderly male and female African- and Caucasian-American subjects with femoral neck fractures to age-, gender-, and ethnicity-matched controls [7,9]. They found that in men, cervical fractures were associated with lower bone density throughout the hip, but that in women they were associated with reduced femoral neck cancellous BMD, with reduced cortical BMD in the greater trochanter and with increased femoral head width.

In order to derive more comprehensive information regarding the association of vQCT bone density and hip geometry measures with hip fracture, we have carried out a case–control study comparing elderly Chinese women imaged within 48 h of their hip fracture to age-matched controls. We utilized a vQCT image analysis program that has been widely employed in a range of clinical research studies [3,4,16,17]. In this study, we examined the associations of volumetric bone density measures, areal bone density measures, geometry measures and indices of strength, and cortical thickness with fractures of the proximal femur.

Materials and methods

Study subjects

Forty-five women with atraumatic hip fractures (34 cervical, 11 trochanteric), aged 65 or older were recruited from the emergency room, Department of Traumatology and Orthopedic Surgery, Beijing Ji Shui Tan hospital. Atraumatic fracture was defined as resulting from a low-energy fall from standing or sitting height. In order to minimize changes in BMD due to the fracture, only those subjects whose fractures had occurred within the last 48 h were accepted into the study. Potential hip fracture subjects were referred to the ER CT scanning service and to the study by their orthopedic surgeons. If the patient was female and over 65 years old, then the radiologist explained the study to the subject and asked the subject if she was willing to participate in the study. If the subject agreed to participate, she was asked to sign the consent form, fill out a questionnaire about the circumstances of the fall and other information regarding metabolic bone disease. The questionnaire permitted exclusion of those subjects with known health conditions affecting the bone mineral status of the hip, including metabolic bone disease or previous fractures of the hip. In addition to the subjects, 66 women over 65 years old in good health and with no conditions affecting bone metabolism (established from the same questionnaire) were invited from the surrounding community to participate in the study. The study was reviewed and approved by the Internal Review Boards of the Beijing Ji Shui Tan hospital and the University of California, San Francisco. Informed Consents were obtained for all study participants.

vQCT acquisitions

All QCT acquisitions utilized a GE CT Pro FII CT scanner (GE Medical Systems, Beijing China). Subjects were positioned supine on the CT table. An Image Analysis QCT calibration phantom (Image Analysis, Columbia KY, USA) was placed under the subject between the hips. The superior aspect of the helical scan was 5 mm above the acetabulum and the inferior limit 5 mm below the lesser trochanter. Scan parameters were 3 mm section thickness (pitch = 1), 120 kVp, 200 mAs, with an in-plane pixel size of 0.88 mm. The CT images were archived to DICOM CD and forwarded to University of California, San Francisco for analysis.

vQCT image analysis

Image analysis

A previously described image analysis program [16,17] was employed to analyze the QCT scans. For subjects with hip fractures, the software analyzed the contralateral proximal femur. For control subjects, the left hip was analyzed. The software defined the periosteal boundaries of the hip, and defined measurement regions encompassing the greater and lesser trochanters, the femoral neck, and the entire hip. Within each region, the program characterized the volumetric bone mineral density (vBMD), volume (VOL), and bone mineral content (BMC) of the total tissue envelope, the cortical bone, and the trabecular bone. Because DXA measurements of the hip were not available for the subjects with hip fractures, we computed areal bone mineral density (aBMD) from each of the regions by projecting each region into the anteroposterior plane and dividing the projected region area into the total BMC of that region. The program searched along the femoral neck axis between the lateral aspect of the femoral head and the lateral edge of the proximal femur and computed the cross-sectional area within the periosteal boundary as a function of position along the neck axis. The minimum of this function occurred at the femoral neck (MNCS) and the maximum is the plane between the lesser and greater trochanters (MXCS). In addition to the cross-sectional area measures, the program also calculated a femoral neck axis length as the distance between the MNCS and MXCS locations. The tissue volumes and cross sections quantified by our analysis program are displayed in Fig. 1. According to methods recently described [16], we computed a femoral neck bending/torsional strength index (NBSI), which

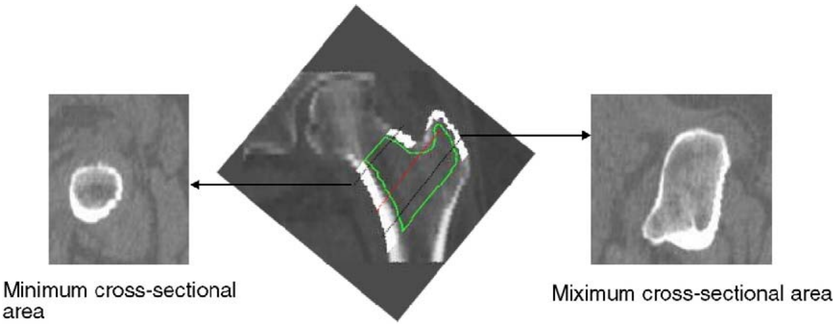

Fig. 1. Regions of interest for bone density and geometry measures. (Center) Coronal mid-section through hip. White pixels are cortical region of interest. Trabecular region of interest is within green boundary. Red line is boundary between trochanteric and femoral neck sub-regions of total femur. Black lines correspond to femoral neck minimum area cross-section (left) and intertrochanteric maximum area cross-section (right). The distance along the femoral neck axis between these two cross-sections is the femoral neck axis length. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Characteristics of patients and controls[a]

	Controls (N=66)	Fracture subjects (N=45)	p
Age (years)	70.7 (4.7)	74.7 (5.9)	0.0006[b]
Weight (kg)	62.2 (10.2)	58.7 (10.8)	NS[b]
Height (cm)	157.7 (5.2349)	159.2 (5.0541)	NS[b]
BMI	25.0 (3.7)	23.1 (3.9)	NS[b]

[a] Mean and standard deviation (in parenthesis).

[b] p values of age, weight, height, and BMI were calculated by Student's t test.

was calculated as an elastic modulus-weighted effective polar moment of inertia (I_x+I_y) of the MNCS cross section divided by the calculated bone width W.

$$\mathrm{NBSI} = \frac{I_x + I_y}{W} \quad I_x = \frac{1}{e_\mathrm{b}}\sum_i e_i{*}(x_i - \bar{x})^2{*}\mathrm{d}A$$
$$I_y = \frac{1}{e_\mathrm{b}}\sum_i e_i{*}(y_i - \bar{y})^2{*}\mathrm{d}A$$
$$W = 2{*}\sqrt{\frac{\mathrm{MNCS}}{\pi}}$$

($\bar{x}$, $\bar{y}$) are the elastic modulus weighted centroid of the cross-section. The e_i is the elastic modulae, which were determined parametrically from the BMD of each voxel in the entire MNCS cross-section using relationships developed by Keyak et al. [15] and e_b is the elastic modulus of cortical bone. Femoral neck and trochanteric compressive strength indices (NCSI and TCSI) were computed as the square of the integral vBMD (FNiBMD and TriBMD) of each region multiplied by the cross-sectional area values for those regions (MNCS for femoral neck, MXCS for trochanteric region).

$$\mathrm{NCSI} = \mathrm{FNiBMD}^2{*}\mathrm{MNCS}$$

$$\mathrm{TCSI} = \mathrm{TriBMD}^2{*}\mathrm{MXCS}$$

In addition to the femoral neck and trochanteric strength indices, we also computed indices of femoral neck cortical geometry. We calculated the ratio of cortical to total tissue volume in the femoral neck. The cortical thickness index for the femoral neck region of interest was computed as:

$$\mathrm{iCThi} = 0.5{*}\left[\sqrt{\frac{\frac{\mathrm{FNvol}}{\mathrm{FNlength}}}{\pi}} - \sqrt{\frac{\frac{(\mathrm{FNvol} - \mathrm{FNcvol})}{\mathrm{FNlength}}}{\pi}}\right]$$

FNvol is the volume of the integral femoral neck region, FNcvol is the volume of the femoral neck cortical region of interest, and FN length is the length of the femoral neck region along the femoral neck axis. The buckling ratio BR was estimated as BR=(iCThi/iBThi), where the effective bone half-width (iBthi) is taken as:

$$\mathrm{iBThi} = 0.5{*}\sqrt{\frac{\frac{\mathrm{FNvol}}{\mathrm{FNlength}}}{\pi}}$$

Statistical analysis

All statistical analyses were performed using SAS 9.0 (SAS Institute, Cary, NC). Means and standard deviations were used to describe the data. Student's t test was used to compare the characteristics between fractured and controlled subjects. The discriminant utilities of volumetric bone density and contents geometric parameters, bone volume, strength indices, cortical thickness, neck length, etc. were evaluated using a generalized linear model after adjustment of age, height, and weight of study participants. The area under receiver operating characteristics curves (AUC) was derived based on the logistic regression equations and p values of AUC of logistic regression equations were derived using the bootstrap method. Age, height, and weight-adjusted odds ratios were normalized to the standard deviations of the parameters and 95% confidence intervals were reported. To determine whether the properties of the trabecular and cortical compartments were associated with hip fracture independently, we computed p values and AUC values for cortical thickness index, cortical volume/total volume, and BR after addition of femoral neck trabecular vBMD to the multi-variate model. The level of statistical significance was 5% throughout the paper.

Results

Descriptive statistics

Controls were not significantly different than subjects in weight, and height, but were on average 4 years younger than fracture subjects ($p<0.05$) (Table 1).

BMD measurements

Results for BMD are summarized in Table 2. Subjects with fractures had 23–24% lower aBMD ($p<0.0001$) than age-matched controls in the femoral neck, trochanteric, and total femur compartments as well as lower vBMD in all compart-

Table 2
Volumetric BMD (vBMD, g/cm^3) and areal BMD (aBMD, g/cm^2) mean values and standard deviations (in parentheses) in controls and in subjects with fractures

		Controls (N=66)	Fracture subjects (N=45)	p[a]	AUC[b]	Adjusted OR (95% CI)[c]
Femoral neck	Integral aBMD[d]	0.518 (0.100)	0.400 (0.081)	<0.0001	0.84	4.08 (2.15, 8.69)
	Integral vBMD	0.248 (0.040)	0.195 (0.032)	<0.0001	0.87	5.57 (2.73, 13.51)
	Trabecular vBMD	0.057 (0.036)	0.027 (0.024)	0.0015	0.80	2.65 (1.50, 5.06)
	Cortical vBMD	0.508 (0.036	0.477 (0.037)	0.0046	0.80	2.36 (1.34, 4.44)
Trochanter	Integral aBMD[d]	0.774 (0.132)	0.585 (0.111)	<0.0001	0.86	6.91 (3.27 17.60)
	Integral vBMD	0.217 (0.038)	0.166 (0.0303)	<0.0001	0.87	5.39 (2.70, 2.65)
	Trabecular vBMD	0.083 (0.030)	0.043 (0.022	<0.0001	0.88	6.77 (3.18, 17.77)
	Cortical vBMD	0.487 (0.031	0.462 (0.031)	0.0068	0.80	2.09 (1.25, 3.67)
Total femur	Integral aBMD[d]	0.777 (0.127	0.600 (0.107	<0.0001	0.88	6.93 (3.23, 18.14)
	Integral vBMD	0.220 (0.037	0.171 (0.029	<0.0001	0.87	5.63 (2.77, 13.60)
	Trabecular vBMD	0.081 (0.029)	0.044 (0.020)	<0.0001	0.88	6.84 (3.18, 18.27)
	Cortical vBMD	0.476 (0.028)	0.450 (0.027)	0.0017	0.81	2.48 (1.44, 4.52)

[a] p value was calculated by generalized linear model after adjustment by age, height, and weight.

[b] AUC of ROC curve based on logistic regression equations.

[c] Age, height, and weight adjusted odds ratio per SD of parameters and 95% confidence interval.

[d] Calculated from QCT images.

Table 3
Geometric parameter means and standard deviations (in parentheses) in controls and in subjects with fractures

		Controls (N=66)	Fracture subjects (N=45)	p [a]	AUC [b]	Adjusted OR (95% CI) [c]
Integral tissue volume (cm^3)	Femoral neck	16.062 (2.647)	16.561 (2.835)	ns	0.76	0.90 (0.58, 1.39)
	Trochanteric	76.445 (11.135)	74.744 (14.992)	ns	0.78	1.42 (0.92, 2.28)
	Total femur	101.290 (15.492)	101.280 (19.570)	ns	0.78	1.22 (0.78, 1.92)
Cortical tissue volumes (cm^3)	Femoral neck	6.077 (0.873)	5.236 (1.103)	0.0018	0.82	2.69 (1.52, 5.33)
	Trochanteric	21.833 (3.420)	18.191 (4.732)	0.0006	0.82	2.81 (1.63, 5.34)
	Total femur	30.664 (4.686)	26.026 (6.458)	0.0011	0.81	2.62 (1.53, 4.94)
Cross-sectional areas (cm^2)	Minimum (neck)	11.762 (1.471)	12.765 (2.419)	0.0076	0.79	0.50 (0.29, 0.81)
	Maximum (troch)	31.652 (3.298)	30.877 (2.506)	ns	0.79	1.58 (0.97, 2.67)
Strength indices	NBSI (cm^3)	0.534 (0.111)	0.538 (0.214)	ns	0.76	0.86 (0.53, 1.35)
	NCSI (g^2/cm^4)	0.726 (0.202)	0.491 (0.162)	<0.0001	0.84	4.77 (2.38, 10.99)
	TCSI (g^2/cm^4)	1.515 (0.491)	0.882 (0.314)	<0.0001	0.89	8.18 (3.63, 22.62)
Neck length	Femoral neck axis length (cm)	27.944 (3.151)	27.995 (4.360)	ns	0.77	1.17 (0.76, 1.80)

[a] p value was calculated by generalized linear model after adjustment by age, height, and weight.
[b] AUC of ROC curve based on logistic regression equations.
[c] Age, height, and weight adjusted odds ratio per SD of parameters and 95% confidence interval.

ments and all regions ($0.00001 < p < 0.001$). The percentage difference between the fracture and controls was larger for trabecular vBMD at both regions (48%–50%) than for integral vBMD (10%–25%) or cortical vBMD (5–8%).

Geometric measurements

Results for geometric measurements and strength estimates are displayed in Table 3. As measured by integral tissue volumes, fracture and control subjects had roughly similar bone sizes. However, cortical tissue volumes (Table 3) values (Table 4) were 14–17% smaller in fracture subjects ($0.0006 < p < 0.001$). Femoral neck cross-sectional area was about 8% larger in subjects with hip fractures, but trochanteric cross-sectional area was similar in the two groups.

Strength estimates

Strength estimate results are also summarized in Table 3. The bending strength estimate weighted by elastic modulus (emBSI) was similar for subjects with hip fractures and controls. Axial compressive strength was 30–40% smaller in the fracture subjects, both at the femoral neck and trochanter ($p < 0.0001$).

Femoral neck cortical structure indices

Subjects with fractures had lower values of cortical thickness index, buckling ratio, and cortical/integral volume ratio (percentage difference 17–19%, $p < 0.0001$ for all comparisons). In the multi-variate models designed to test whether trabecular vBMD and cortical structure indices were independently associated with hip fracture status, we found that the cortical thickness index and Cortical Volume/Integral Volume ratio, but not the buckling ratio, continued to differ significantly between fracture subjects and controls after adjustment for trabecular vBMD ($p < 0.05$). When data were adjusted for measures of integral aBMD and vBMD, the femoral neck cortical structure indices no longer discriminated between subjects with hip fractures and controls.

Discussion

Although the prospective association of areal BMD measures with hip fractures is well-known, and the cross-sectional association of volumetric trabecular and cortical BMD measures with hip fracture was reported by Cody et al. [7], our study was novel in its comprehensive analysis of differences in proximal femoral geometry in subjects with hip fractures and

Table 4
Femoral neck cortical geometry parameter means and standard deviations (in parentheses) in controls and in subjects with fractures

	Controls (N=66)	Fracture subjects (N=45)	p [a, b]	AUC [c,b]	Adjusted OR (95% CI) [d,b]
Cortical volume/total volume	0.3826 (0.0499)	0.3175 (0.0481)	<0.0001	0.855	4.637 (2.416, 10.180)
			0.0443	*0.904*	*2.212 (1.020, 4.807)*
Cortical thickness index (iCthi) (cm)	0.5778 (0.0732)	0.4771 (0.0732)	<0.0001	0.864	5.575 (2.751, 13.095)
			0.0461	*0.906*	*2.386 (1.015, 5.617)*
Buckling ratio	0.2149 (0.0318)	0.1744 (0.0289)	<0.0001	0.856	4.706 (2.441, 10.403)
			ns	*0.901*	*1.879 (0.907, 3.891)*

[a] p value was calculated by generalized linear model after adjustment by age, height, and weight.
[b] Italicized values are p values, AUC values, and odds ratios (OR) for cortical geometry indices after adjustment for age, height, weight, and femoral neck trabecular BMD.
[c] AUC of ROC curve based on logistic regression equations.
[d] Age, height, and weight adjusted odds ratio per SD of parameters and 95% confidence interval.

controls. We observed that the cross-sectional area of the femoral neck was larger in the subjects with hip fracture than in the controls. The finding of larger cross-sectional bone dimensions is consistent with the report of Cody et al. [7], who observed that fractured subjects had a larger femoral head width. In contrast with the study by Gluer et al., who found that increased width of the trochanteric region (but not the femoral neck region) measured from pelvic radiographs was weakly associated with incident hip fracture in the prospectively designed Study of Osteoporotic Fracture [12], our QCT-based study did not observe an association of trochanteric cross-sectional area with hip fracture, although this may be due to the many differences between the studies, including the ethnicity of the subjects and the imaging modality used. The finding of larger femoral neck cross-sectional area for fracture subjects in our own study and that of Cody et al. [7] may reflect compensation for bone loss in the fracture subjects, who had much lower BMD, cortical volume, and indices of cortical thickness in all proximal femoral regions. The larger femoral neck cross-sectional area was consistent with the finding of comparable or larger bending strength indices measured between the fracture subjects and controls, despite the lower trabecular BMD and thinner femoral neck cortex in the former. These findings indicate that such indices should be interpreted with care as potential diagnostic measures.

Another novel aspect of our study was the observation of large differences in proximal femoral cortical structure indices between subjects with hip fracture and controls, indicating that the fracture subjects had a weaker and potentially less mechanically stable cortex. Potentially because the proximal femoral cortex is a large fraction of the integral bone mass of the hip, the cortical structure indices did not appear to discriminate between fracture subjects and controls after adjustment for measures of integral aBMD and vBMD. However, the apparent cortical thickness and the ratio of cortical to total volume were associated with fracture after adjustment of the data for femoral neck trabecular vBMD, supporting the idea that the density of trabecular bone and the proportion of bone volume and thickness occupied by the cortex may be independently correlated to hip fracture.

This study has several strengths. The recruitment of subjects within 48 h of their hip fracture allowed for measurements within the time frame before musculoskeletal changes associated with rehabilitation could confound the comparison. Additionally the bone analysis program used in this study employed a more comprehensive sampling strategy than that of Cody et al. [7], which examined small regions of trabecular bone in the femoral head and trochanteric regions, a core of cortical bone in the greater trochanter, and the width of the femoral head. Although it has important strengths, our study also has limitations. These include the limitation to Chinese subjects, the cross-sectional design, and the relatively small number of subjects, which prevented us from being able to separately characterize intra- and extra-capsular fractures, and limited the overall statistical significance of the analyses. An important technical limitation in our study is the effect of partial volume averaging on our cortical bone measurements [2,13]. Partial volume averaging occurs when the dimensions of the structure being imaged are smaller than the spatial resolution of the imaging system. The effect of partial volume averaging on thin cortices is to lower the apparent BMD and to increase the apparent cortical thickness. Cortical bone is thought to have a constant intrinsic BMD of 1.05 g/cm^3 [19] but because of the blurring effect of partial volume averaging, the apparent cortical volumetric BMD is a function of the cortical thickness and the cortical porosity. Thinner structures appear to have lower BMD, with larger errors in apparent thickness and volume. Our hip cortical region of interest is primarily composed of the inferomedial cortex of the proximal femur, for which thickness values exceeding 3–4 mm have been reported in humans, but also includes the thin superomedial cortex (thickness $\approx$ 0.3 mm) [21]. Evidence from a study of cadaveric proximal femoral specimens indicates that the inferior cortex changes little in thickness with age, but that there is considerable thinning of the superior cortex [20]. Thus, although our study did show that subjects with hip fracture had significantly lower apparent cortical thickness values, and lower ratio of cortical volume and thickness to total femoral neck volume and thickness, it is important to take into account the fact that our cortical parameters principally reflect the thick inferior cortex, which changes little with age.

In summary, subjects with hip fractures had much lower values of BMD and apparent cortical thickness, but larger femoral neck cross-sectional area, than control subjects who were reasonably well matched in age and body size. The fracture–control differences in bone density and size support the idea that larger bone cross-sectional areas represent an adaptation to the increased bending strains associated with the greater bone loss in the subjects with hip fracture. In the moment of inertia-based bending strength indices, the effect of increased bone size appeared to counteract the effect of reduced BMD, resulting in calculated bending strength indices that were equivalent in the subjects with fractures. This potential adaptation to bending strain did not protect the compressive strength estimates, which were substantially lower in subjects with hip fracture.

Acknowledgments

This study was funded by a grant from Eli Lilly.

References

[1] Augat P, Fan B, Lane NE, Lang TF, LeHir P, Lu Y, et al. Assessment of bone mineral at appendicular sites in females with fractures of the proximal femur. Bone 1998;22:395–402.

[2] Augat P, Gordon CL, Lang TF, Iida H, Genant HK. Accuracy of cortical and trabecular bone measurements with peripheral quantitative computed tomography (pQCT). Phys Med Biol 1998;43:2873–83.

[3] Black DM, Bilezikian JP, Ensrud KE, Greenspan SL, Palermo L, Hue T, et al. One year of alendronate after one year of parathyroid hormone (1–84) for osteoporosis. N Engl J Med 2005;353:555–65.

[4] Black DM, Greenspan SL, Ensrud KE, Palermo L, McGowan JA, Lang TF, et al. The effects of parathyroid hormone and alendronate alone or in combination in postmenopausal osteoporosis. N Engl J Med 2003; 349:1207–15.

[5] Camp JJ, Karwoski RA, Stacy MC, Atkinson EJ, Khosla S, Melton LJ, et al. A system for the analysis of whole-bone strength from helical CT images. Proc-SPIE 2004;5369:74–88.

[6] Cody D, McCubbrey D, Divine G, Gross G, Goldstein S. Predictive value of proximal femoral bone densitometry in determining local orthogonal material properties. J Biomech 1996;29:753–61.

[7] Cody DD, Divine GW, Nahigian K, Kleerekoper M. Bone density distribution and gender dominate femoral neck fracture risk predictors. Skeletal Radiol 2000;29:151–61.

[8] Cody DD, Gross GJ, Hou FJ, Spencer HJ, Goldstein SA, Fyhrie DP. Femoral strength is better predicted by finite element models than QCT and DXA. J Biomech 1999;32:1013–20.

[9] Cody DD, Hou FJ, Divine GW, Fyhrie DP. Femoral structure and stiffness in patients with femoral neck fracture. J Orthop Res 2000; 18:443–8.

[10] Cummings S, Marcus R, Palermo L, Ensrud K, Genant H. Does estimating volumetric bone density of the femoral neck improve the prediction of hip fracture? J Bone Miner Res 1994;9:1429–32.

[11] Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, et al. Bone density at various sites for prediction of hip fractures: the study of osteoporotic fractures. Lancet 1993;341:72–5.

[12] Glüer CC, Cummings SR, Pressman A, Li J, Glüer K, Faulkner KG, et al. Prediction of hip fractures from pelvic radiographs: the study of osteoporotic fractures. J Bone Miner Res 1994;9:671–7.

[13] Hangartner T, Gilsanz V. Evaluation of width and density of cortical bone by computed tomography. J Bone Miner Res 1995;10:S472.

[14] Keyak JH, Kaneko TS, Tehranzadeh J, Skinner HB. Predicting proximal femoral strength using structural engineering models. Clin Orthop Relat Res 2005:219–28.

[15] Keyak JH, Lee IY, Skinner HB. Correlations between orthogonal mechanical properties and density of trabecular bone: use of different densitometric measures. J Biomed Mater Res 1994;28:1329–36.

[16] Lang T, LeBlanc A, Evans H, Lu Y, Genant H, Yu A. Cortical and trabecular bone mineral loss from the spine and hip in long-duration spaceflight. J Bone Miner Res 2004;19:1006–12.

[17] 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;21:101–8.

[18] Lang TF, Li J, Harris ST, Genant HK. Assessment of vertebral bone mineral density using volumetric quantitative CT. J Comput Assist Tomogr 1999;23:130–7.

[19] Martin RB, Burr DB. Non-invasive measurements of long bone cross-sectional moment of intertia by photon absorptiometry. J Biomechanics 1984;17:195–201.

[20] Mayhew PM, Thomas CD, Clement JG, Loveridge N, Beck TJ, Bonfield W, et al. Relation between age, femoral neck cortical stability, and hip fracture risk. Lancet 2005;366:129–35.

[21] Prevrhal S, Fox JC, Shepherd JA, Genant HK. Accuracy of CT-based thickness measurement of thin structures: modeling of limited spatial resolution in all three dimensions. Med Phys 2003;30:1–8.

[22] Riggs BL, Melton Iii III LJ, Robb RA, Camp JJ, Atkinson EJ, Peterson JM, et al. Population-based study of age and sex differences in bone volumetric density, size, geometry, and structure at different skeletal sites. J Bone Miner Res 2004;19:1945–54.

[23] Schott AM, Cormier C, Hans D, Favier F, Hausherr E, Dargent-Molina P, et al. How hip and whole-body bone mineral density predict hip fracture in elderly women: the EPIDOS Prospective Study. Osteoporos Int 1998; 8:247–54.