# Age-related changes in bone density, geometry and biomechanical properties of the proximal femur: CT-based 3D hip structure analysis in normal postmenopausal women

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## Abstract

The geometry as well as bone mineral density (BMD) of the proximal femur contributes to fracture risk. How and the extent to which they change due to natural aging is not fully understood.

We assessed BMD and geometry in the femoral neck and shaft separately, in 59 normal Japanese postmenopausal women aged 54 to 84 years, using clinical computed tomography (CT) and commercially available software, at baseline and 2 year follow up. This system detected significant reductions over the 2-year interval in total BMD (%change/year=-0.900±0.257, $p<0.0005$), cortical cross-sectional area (CSA) (-0.800±0.423 %/year, $p<0.05$) and cortical thickness (-1.120± 0.453 %/year, $p<0.01$) in the femoral neck. In the femoral shaft, cortical BMD decreased significantly (-0.642± 0.188 %/year, $p<0.005$). Regarding biomechanical parameters in the femoral neck, the cross-sectional moment of inertia (CSMI) and section modulus (SM) decreased (-1.38± 3.65 %/year, $p<0.01$ and -1.37± 2.96 %/year, $p<0.005$) and the buckling ratio (BR) increased significantly (1.48± 4.81 %/year, $p<0.05$), whereas no changes were found in the femoral shaft.

The distinct patterns of age-related changes in the geometry and biomechanical properties in the femoral neck and shaft suggest that improved geometric measures are possible with the current

non-invasive method using clinical CT.



CT-based Hip Structure Analysis

cross-section of femoral neck

cross-section of femoral shaft

baseline — after 2 year

CSMI
SM
BR

baseline — after 2 year

CSMI
SM
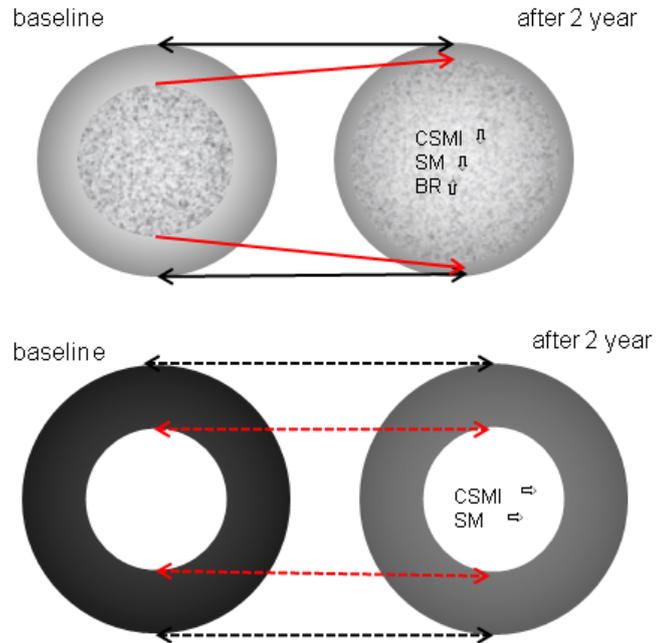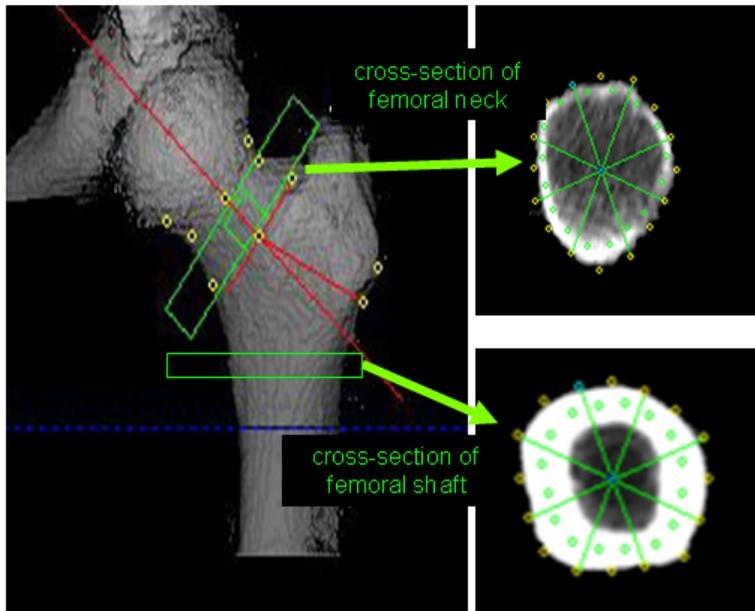
**Keywords:** Hip geometry, bone mineral density (BMD), computed tomography (CT), osteoporosis

## Introduction

The incidence of vertebral fracture increases linearly with aging and correlates closely with a decline in spinal bone mineral density (BMD). The incidence of hip fracture, on the other hand, increases exponentially with advancing age, although hip BMD decreases linearly, suggesting that age-related factors other than BMD contribute substantially to the fragility of the proximal femur. Declining BMD and geometry of the proximal femur, as well as an increase in the incidence of fall are believed to underlie the increased risk of hip fracture in the elderly [1-3]. Non-invasive techniques can provide bone structural information, beyond simple bone densitometry, to help assess fracture risk.

The aging skeleton is characterized by a deterioration of the trabecular microstructure, increased endocortical bone resorption, decreased cortical bone density or increased cortical porosity, and increased periosteal bone formation [4]. In postmenopausal women, the rate of periosteal bone formation declines to a greater extent, while endosteal bone resorption is more elevated, compared with age-matched men. However, the natural course of these cortical changes with aging has not been well elucidated, and how faithfully non-invasive methods can detect these changes over time is also unknown.

Age-related changes in the cortical bone of the femoral neck as well as the shaft have been investigated by means of histology or computed tomography (CT) images. Although cross-sectional analyses of age-related changes in hip geometry have been reported using clinical CT [5-6] or dual X-ray absortiometry (DXA) [7], there have been no reports of age-related changes in geometry along with BMD in the femoral neck and shaft simultaneously, and which also followed the changes longitudinally in the same subjects.

Here we report the results of longitudinal as well as cross-sectional analyses of clinical CT on age-related changes in BMD, geometry and biomechanical properties of the proximal femur, neck and shaft separately, in the same cohort of healthy postmenopausal Japanese women. The information provided in this study may form the basis for future investigation into how osteoporosis intervention impacts the biomechanical properties along with the structure of the femoral neck and shaft.

## Subjects and Methods

### Subjects

   The subjects were 59 postmenopausal women who had volunteered to have spinal BMD measurements taken annually by DXA[8] and agreed to participate in the current prospective CT study. They were aged 54 to 84 (67.0±7.4) years of age and had no physical problems in daily life. Their BMD values in the lumbar spine and the proximal femur were above 70% of the Japanese young adult mean[9]. None of the participants had any prevalent radiological vertebral fracture based on the semi-quantitative method of Genant[10], or any history of fragility fractures of hip, radius and humerus.   They were enrolled in hip CT studies in August 2006 or December 2006 at the baseline, and in August 2008 or December 2008 for the follow-up study.   Table 1 summarizes their demographic features.

   The study was reviewed and approved by the appropriate Internal Review Boards at Nagasaki University Hospital.   Written informed consent to participate was obtained from all subjects.


### CT data acquisition

   A multi-detector-row CT (MDCT) scanner (Aquilion16, Toshiba Medical Systems Corporation, Tokyo, Japan) at Nagasaki University

Hospital was used, and the same X-ray scan conditions, including kVp, mAs and beam pitch, were employed for the baseline and follow-up studies. The average number of slices was 690 ±33.3. CT scanning of the proximal femur was performed twice during a 2-year period (1.99 ± 0.01 years). The reference phantom, which was scanned simultaneously, was a B-MAS200 (Fujirebio Inc, Japan) containing hydroxyapatite at 0, 50, 100, 150 and 200 mg/cm$^3$. The scanning conditions were adjusted to 120kV, 250mA and a reconstruction thickness of 0.5 mm, and the spatial resolution was 0.625x0.625 mm. The radiation dose was 19.7mGy at maximum, as shown by the CTDIvol [3].

The subjects were scanned in the supine position, with the reference phantom placed under them so as to cover a region from the top of the acetabulum to 5 cm below the bottom of the lesser trochanter in both hip joints. A bolus bag was placed between the subject and the CT calibration phantom. The CT scanner table height was set to the center of the greater trochanter.

**Analysis of BMD and geometry data obtained by CT**

The BMD and geometry data of the proximal femur were analyzed by a radiologist (M.I.), using commercial software (QCT PRO; Mindways, Austin, USA). The exact 3-D rotation of the femur and

the threshold setting for defining the bone contours appeared to be the two most critical steps to ensure the accuracy and reproducibility of the automated procedure.   The femoral neck axis was identified visually and automatically with the "Optimize FN Axis" algorithm. The CT values were converted to BMD scale using a solid reference phantom. QCT BIT processing was then performed with a fixed bone threshold for inner cortical separation, which was set to 350 mg/cc for all of the CT images.

The BMD and the areas (CSA) of total and cortical regions of the cross-sectional femoral neck, as well as cortical thickness and the cortical perimeter, were calculated using QCT PRO software. Trabecular BMD and CSA were calculated on the basis of the total and cortical BMD and CSA. Cortical thickness was measured as the average of the whole cortex [11].   In the cross-sectional femoral shaft, the cortical BMD, CSA and perimeter were determined.   As biomechanical parameters, the cross-sectional moment of inertia (CSMI), section modulus (SM) and buckling ratio (BR) were obtained for the femoral neck, and CSMI and SM for the femoral shaft.   SM is a parameter calculated as the CSMI divided by the distance to the center of mass (CM) ($d_{max}$). BR was calculated as the $d_{max}$ divided by the average cortical thickness in this study.   They are derived in a manner intended to be consistent with the

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DXA-based HSA method implemented by Tom Beck [12].

The reproducibility (% coefficient of variation) of the analysis by the QCT PRO program was calculated using five repeated analyses with visual matching each time from seven healthy subject CT data sets from this study without visible artifact; coefficient of variation (%) as the root mean square standard deviation divided by the mean, for the total BMD was 1.49%, cortical BMD 2.63%, total mass 1.12%, total area 1.71%, cortical area 2.11%, cortical perimeter 2.11%, and cortical thickness 3.58% for FN.  In the femoral shaft, the CV% was 0.52% for cortical BMD, 0.77% for cortical CSA, 1.10% for perimeter, 2.19% for CSMI and 1.00% for SM.

The high correlation (r=0.84 to 0.98; p<0.0001 in all) between the baseline and follow-up measurements (shown in Table 3) indicates the high reproducibility of the measurements using clinical CT and of the analysis performed by this application.

**Statistical analysis**

In the cross-sectional study, we calculated a linear regression as a function of age, and the correlation coefficients (r).  In the longitudinal study, the follow-up data was compared with the baseline data using t-test, and also for each case, the average

percent (%) changes of the follow-up data from the baseline were calculated, and the data obtained in the femoral neck and the femoral shaft were compared using t-test. These are expressed as average values (mean) and standard deviations (SD), assuming a two-sided level of significance of 5% ($p < 0.05$). These analyses were performed using SPSS version 11.

**Results**

*Correlation between age and BMD/geometry/biomechanical properties at the baseline*

Table 1 summarizes the demographic features of the 59 participants.　They were healthy postmenopausal Japanese women who volunteered this study, and their ages ranged over 30 years, from 54 to 84 (67.0±7.4) years.　They did not have any fractures or a diagnosis of osteoporosis according to the BMD criteria of Japanese Society for Bone and Mineral Research (JSBMR)[9].　As a first step to obtaining information on the natural course of structural changes with advancing age, we examined if there were any correlations between the ages of the subjects and BMD/geometry/biomechanical properties of the proximal femur at baseline.

As shown in Table 2, at the femoral neck, the total BMD (-3.07 g/cm$^3$/year; r=0.39, p<0.005) and total bone mass (-0.019 g/year; r=0.47, p<0.0005) negatively correlated with age, while total CSA exhibited no correlation (0.008 cm$^2$/year; r=0.08, ns).　Cortical CSA (-0.028 cm$^2$/year; r=0.51, p<0.0001), cortical bone mass (-0.019 g/year; r=0.46, p<0.0005) and cortical thickness (-0.025 mm/year; r=0.46, p<0.0005) also negatively correlated with age, while cortical BMD exhibited no correlation (-0.997 mg/cm$^3$/year;

r=0.15, ns).   The bone perimeter exhibited a positive correlation with age (0.014 mm/year; r=0.23, p<0.05).

At the femoral shaft, cortical BMD (-1.965 mg/cm$^3$/year; r=0.29, p<0.001) and cortical CSA (-0.011 cm$^2$/year; r=0.26, p<0.05) negatively correlated with age, while the bone perimeter did not exhibit any correlation.

Regarding the biomechanical properties shown in Table 2, CSMI (-0.008 cm$^4$/year; r=0.37, p<0.005) and SM (-0.006 cm$^3$/year; r=0.41, p<0.005) at the femoral neck exhibited a significant negative correlation with age. These changes were smaller at the femoral shaft (-0.005 cm$^4$/year; r=0.17, ns for CSMI, -0.005 cm$^3$/year; r=0.28, p<0.05 for SM).   BR at the femoral neck displayed a positive correlation with age (0.104/year; r=0.51, p<0.0001) (Table 2).

**Longitudinal changes at 2-year follow-up**

Next, we re-examined all of the participants after 2 years to address whether the current CT-based HSA detected parameter changes over the 2-year interval.   Table 3 summarizes the average values at baseline and the 2-year follow-up for the densitometric and geometrical measurements as well as the biomechanical properties.   In each case, the correlations of the changes from the

baseline were high, ranging from r=0.84 to 0.98 (all; p<0.0001).

Importantly, the current CT system detected significant decreases from baseline in total BMD (-0.900± 0.257 %/year; p<0.0005), cortical CSA (-0.800± 0.423 %/year; p<0.05) and cortical thickness (-1.120± 0.453 %/year; p<0.01) at the femoral neck, and also a decrease in the cortical BMD of the femoral shaft (-0.642± 0.188 %/year; p<0.005) (Table 3).   These changes in the longitudinal analysis were consistent with the results of the cross-sectional analysis presented above (Table 2).

Our system did not detect any significant changes in the biomechanical properties of the femoral shaft (Table 3).   However, a worsening of all the biomechanical properties of the femoral neck the 2-year period was observed; CSMI (-1.38± 3.65 %/year; p<0.01) and SM (-1.37± 2.96 %/year; p<0.005) decreased, and BR increased from the baseline (1.48± 4.81 %/year; p<0.05) (Table 3).

Table 3 also summarizes the results of the longitudinal analysis by comparing the average % changes at the femoral neck versus the shaft.   The average % change in cortical BMD was significantly higher in the femoral shaft than in the neck (0.081± 0.274 %/year, ns in FN, and -0.642± 0.188 %/year, p<0.005 in FS).   The average % decreases in the CSMI and SM were significantly greater

in the femoral neck (-1.38±3.65 %/year, p<0.01 for CSMI and

-1.37±2.96 %/year, p<0.05 for SM) than in the shaft (-0.16±

2.30 %/year, ns for CSMI and -0.32± 2.43 %/year, ns for SM) (Table

3).

**Discussion**

It is widely recognized that aging has a substantial impact on the geometry of the proximal femur [4], and data on age-related changes in the hip geometry not only provides crucial insight into the pathogenesis of hip fracture, but also should help form the basis for evaluating and understanding the efficacy of intervention. Important questions that remain unanswered include the extent to which age-related geometry changes actually occur, skeletal sites and time scale of these changes, whether they can be detected by non-invasive techniques, and how long an interval is required to demonstrate the clinical efficacy of a certain intervention to prevent or reverse such changes. Practically, since most clinical trials are terminated within 3 years, it is critically important to know whether the effects of any intervention on age-related changes in geometry can be detected non-invasively within the time scale of 2-3 years.

There has been no report to our knowledge on the demonstration of age-related and/or skeletal site-specific changes in the 3D geometry of the proximal femur. The results of our cross-sectional analysis by CT are qualitatively similar to those obtained in a previous DXA-based HSA in a similar population of postmenopausal Japanese women [13]. However, the % changes with aging in the biomechanical parameters such as SM and BR are larger in the

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current CT-based analysis than in the previous DXA-based study. In this respect, the 3D $d_{max}$ calculation may have contributed to the increased sensitivity to the age-related changes in SM and BR in the current study.

According to the previous DXA-based HSA studies that analyzed the effects of anti-osteoporosis drugs on the geometry[14-16], distinct effects on the femoral neck and shaft were observed.   In the current study using non-invasive CT scanning of the proximal femur, all of the biomechanical parameters, CSMI, SM and BR, worsened significantly with advancing age in the femoral neck, while those in the femoral shaft did not change.

The current study using a CT-based system demonstrated that cortical BMD was maintained at a higher level in the femoral shaft than in the femoral neck from the period of early post-menopause through advanced age, and that the decline in cortical BMD was much greater in the femoral shaft than the femoral neck (Table 3). It is counterintuitive that the femoral shaft would maintain a higher BMD throughout this period but nevertheless exhibit a larger bone loss than the femoral neck, since in comparison with the cortex of the femoral shaft[17], the femoral neck is thought to suffer from high cortical porosity.   This may reflect a partial volume effect in measuring cortical BMD and thickness by CT, and higher resolution

CT or more detailed histological analysis of the cortical bone in femoral neck and shaft may be required to validate the current findings.

The current system did not detect any significant change in the cortical BMD of the femoral neck, but detected changes in cortical thinning at the same site (Table 3).   The border between the cortical and cancellous compartments becomes less obvious with aging, and the progression of cortical porosity in the endocortical region makes it difficult to distinguish it from the thinning of the cortex.   Due to this limitation inherent in clinical CT, an alteration in cortical thickness, and not cortical bone density, may have been detected as an age-related change.   Further efforts to improve the methodology of delineating the border between cortical and trabecular components accurately are thus required.

The findings that the bone perimeter and total CSA in the femoral neck did not change over a 2 year follow-up, while cortical CSA and thickness at the same site decreased significantly, imply that the current CT-based HSA was capable of detecting the progression of endocortical resorption, while the alteration in periosteal apposition rate, at least during this 2 year period, was too small to be detected. Taken together with the results of the cross-sectional analysis at baseline that both the bone perimeter and total CSA in the femoral

neck correlated positively with age, a longer follow-up period would allow a determination of whether the periosteal bone formation continues at a slow pace.

In conclusion, the data presented in this study on age-related alterations in the geometry and biomechanical properties at distinct sites of the proximal femur should provide a basis for an improved understanding the pathogenesis of fracture, and also serve as a foundation for the design of new anti-fracture remedies in postmenopausal women.

**References**

1. F. Rivadeneira, M.C. Zillikens, C.E.D.H. De Laet, A. Hofman, A.G. Uitterlinden, T.J. Beck, et al., Femoral neck BMD is a strong predictor of hip fracture susceptibility in elderly men and women because it detects cortical bone instability: The Rotterdam Stud, J. Bone Miner. Res. 22 (2007) 1781–1790.

2. S. Kaptoge, T.J. Beck, J. Reeve, K.L. Stone, T.A. Hillier, J.A. Cauley, et al., Prediction of incident hip fracture risk by femur geometry variables measured by hip structural analysis in the study of osteoporotic fractures, J. Bone Mier. Res. 23 (2008) 1892-1904.

3. M. Ito, N. Wakao, T. Hida, Y. Matsui, Y. Abe, K. Aoyagi, et al., Analysis of hip geometry by clinical CT for the assessment of hip fracture risk in elderly Japanese women, Bone 46 (2010) 453-457.

4. E. Seeman, P.D. Delmas, Bone quality-the material and structural basis of bone strength and fragility, N. Engl. J. Med. 354 (2006) 2250-2261.

5. G. Sigurdsson, T. Aspelund, M. Chang, B. Jonsdottir, S. Sigurdsson, G. Eiriksdottir, et al, Increasing sex difference in bone strength in old age: The age, gene/environment susceptibility-reykjavik study (AGES-REYKJAVIK), Bone 39 (2006) 644-651.

6. B.L. Riggs, L.J. Melton, R.A. Robb, J.J. Camp, E.J. Atkinson, J.M. Peterson, 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. 19 (2004) 1945-1954.

7. J. Takada, T.J. Beck, K. Iba, T. Yamashita, Structural trends in the aging proximal femur in Japanese postmenopausal women, Bone

41 (2007) 97-102.

8. M. Ito, A. Nishida, J. Kono, M. Kono, M. Uetani, K. Hayashi, Which bone densitometry and which skeletal site are clinically useful for monitoring bone mass? Osteoporos. Int. 14 (2003) 959-964.

9. H. Orimo, Y. Hayashi, M. Fukunaga, T. Sone, S. Fujiwara, M. Shiraki, et al., Osteoporosis Diagnostic Criteria Review Committee: Japanese Society for Bone and Mineral Research. Diagnostic criteria for primary osteoporosis: year 2000 revision, J. Bone Miner. Metab. 19 (2001) 331-337.

10. H.K. Genent, C.Y. Wu, C. van Kuijk, M.C. Nevitt, Vertebral fracture assessment using a semiquantitative technique, J. Bone Miner. Res. 8 (1993) 1137-1148.

11. J. Power, N. Loveridge, A. Lyon, N. Rushton, M. Parker, J. Reeve, Bone remodeling at the endocortical surface of the human femoral neck: a mechanism for regional cortical thinning in cases of hip fracture, J. Bone Miner. Res. 18 (2003) 1775-1780.

12. Kaptoge S, Beck TJ, Reeve J, Stone KL, Hiller TA, Cauley JA, et al., Prediction of incident hip fracture risk by femur geometry variables measured by hip structural analysis in the study of osteoporotic fractures, J. Bone Miner. Res. 23(2008) 1892-1904.

13. J. Takada, T.J. Beck, K. Iba, T. Yamashita, Structural trends in the aging proximal femur in Japanese postmenopausal women, Bone 41 (2007) 97-102.

14. K. Uusi-Rasi, L.M. Semanick, J.R. Zanchetta, C.E. Bogado, E.F. Eriksen, M. Sato, et al., Effects of teriparatide [rhPTH (1-34)] treatment on structural geometry of the proximal femur in elderly osteoporotic women, Bone 36 (2005) 948-958.

15. S.L. Bonnick, T.J. Beck, F. Cosman, M.C. Hochberg, H. Wang, A.E. de Papp, DXA-based hip structural analysis of once-weekly bisphosphonate-treated postmenopausal women with low bone

mass, Osteoporos. Int. 20 (2009) 911-921.

16. M. Ito, T. Sone, M. Fukunaga, Effect of minodronic acid hydrate on hip geometry in Japanese women postmenopausal osteoporosis, J. Bone Miner. Metab. 28 (2010) 334-341.

17. V. Bousson, A. Meunier, C. Bergot, E. Vicaut, M.A. Rocha, M.H. Morais, et al., Distribution of intracortical porosity in human midfemoral cortex by age and gender, J. Bone Miner. Res. 16 (2001) 1308-1317.

Table 1 Demographics of participants

|  |  | mean | SD |
|---|---|---|---|
| age | years | 67.0 | 7.4 |
| body weigt | kg | 54.7 | 14.2 |
| body height | cm | 150.2 | 14.3 |
| age at menopause | years | 50.4 | 4.1 |
| femoral neck BMD | g/cm$^2$ | 0.752 | 0.095 |
| T-score | 1 | -1.2 | 0.8 |
| Z-score | 1 | 0.8 | 0.7 |

BMD; bone mineral density measured by DXA

Table 2 Correlations between age and BMD, geometry and biomechanical properties at the baseline

| | measurement | change/year | unit | r | p |
|---|---|---|---|---|---|
| FN BMD/geometry | | | | | |
| | total BMD | -3.065 | mg/cm$^3$/year | 0.39 | <0.005 |
| | total CSA | 0.008 | cm$^2$/year | 0.08 | ns |
| | total bone mass | -0.019 | g/year | 0.47 | <0.0005 |
| | cortical BMD | -0.997 | mg/cm$^3$/year | 0.15 | ns |
| | cortical CSA | -0.028 | cm$^2$/year | 0.51 | <0.0001 |
| | cortical bone mass | -0.019 | g/year | 0.46 | <0.0005 |
| | cortical thickness | -0.025 | mm/year | 0.46 | <0.0005 |
| | perimeter | 0.014 | mm/year | 0.23 | <0.05 |
| FS BMD/geometry | | | | | |
| | cortical BMD | -1.965 | mg/cm$^3$/year | 0.29 | <0.01 |
| | cortical bone area | -0.011 | cm$^2$/year | 0.26 | <0.05 |
| | perimeter | 0.007 | mm/year | 0.10 | ns |
| biomechanical property | | | | | |
| FN | CSMI | -0.008 | cm$^4$/year | 0.37 | <0.005 |
| | SM | -0.006 | cm$^3$/year | 0.41 | <0.005 |
| | BR | 0.104 | 1/year | 0.51 | <0.0001 |
| FS | CSMI | -0.005 | cm$^4$/year | 0.17 | ns |
| | SM | -0.005 | cm$^3$/year | 0.28 | <0.05 |

FN; femoral neck, FS; femoral shaft
BMD; bone mineral density, CSA; cross-sectional area
CSMI; cross-sectional moment of inertia, SM; section modulus, BR; buckling ratio

Table 3  Longitudinal changes in BMD, geometry and biomechanical properties during the two-year follow up

| measurement | unit | baseline | follow-up | %change/year | p | p (vs FS) | correlations (baseline and follow-up) | p* |
|---|---|---|---|---|---|---|---|---|
| **FN BMD/geometry** | | | | | | | | |
| total BMD | $mg/cm^3$ | 335.7 ± 58.7 | 329.8 ± 58.5 | -0.900 ± 0.257 | <0.0005 | - | 0.98 | <0.0001 |
| total CSA | $cm^2$ | 5.75 ± 0.74 | 5.78 ± 0.84 | 0.417 ± 0.424 | ns | - | 0.90 | <0.0001 |
| total bone mass | g | 1.89 ± 0.30 | 1.86 ± 0.28 | -0.613 ± 0.390 | ns | - | 0.92 | <0.0001 |
| cortical BMD | $mg/cm^3$ | 687.9 ± 48.4 | 688.6 ±47.7 | -0.081 ± 0.274 | ns | <0.05 | 0.84 | <0.0001 |
| cortical CSA | $cm^2$ | 1.96 ± 0.41 | 1.92 ± 0.37 | -0.800 ± 0.423 | <0.05 | ns | 0.94 | <0.0001 |
| cortical bone mass | g | 1.34 ± 0.31 | 1.32 ± 0.29 | -0.776 ± 0.529 | ns | - | 0.94 | <0.0001 |
| cortical thickness | mm | 1.83 ± 0.40 | 1.78 ± 0.36 | -1.120 ± 0.453 | <0.01 | - | 0.94 | <0.0001 |
| perimeter | mm | 5.78 ± 0.50 | 5.78 ± 0.56 | 0.024 ± 0.316 | ns | ns | 0.88 | <0.0001 |
| **FS BMD/geometry** | | | | | | | | |
| cortical BMD | $mg/cm^3$ | 1022.6 ± 52.5 | 1011.5 ± 49.9 | -0.642 ± 0.188 | <0.005 | - | 0.86 | <0.0001 |
| cortical CSA | $cm^2$ | 3.58 ± 0.31 | 3.56 ± 0.32 | -0.752 ± 0.499 | ns | - | 0.97 | <0.0001 |
| perimeter | mm | 8.78 ± 0.48 | 8.80 ± 0.51 | 0.114 ± 0.413 | ns | - | 0.88 | <0.0001 |
| **biomechanical property** | | | | | | | | |
| FN  CSMI | $cm^4$ | 0.613 ± 0.156 | 0.597 ± 0.159 | -1.38 ± 3.65 | <0.01 | <0.01 | 0.96 | <0.0001 |
| SM | $cm^3$ | 0.448 ±0.105 | 0.437 ± 0.108 | -1.37 ± 2.96 | <0.005 | <0.05 | 0.97 | <0.0001 |
| BR | 1 | 7.06 ± 1.67 | 7.20 ± 1.61 | 1.48 ± 4.81 | <0.05 | - | 0.94 | <0.0001 |
| FS  CSMI | $cm^4$ | 1.304 ± 0.236 | 1.298 ± 0.231 | -0.16 ± 2.30 | ns | - | 0.96 | <0.0001 |
| SM | $cm^3$ | 1.082 ±0.142 | 1.075 ± 0.139 | -0.32 ± 2.43 | ns | - | 0.93 | <0.0001 |

data are shown as mean ±SD

FN; femoral neck, FS; femoral shaft
BMD; bone mineral density, CSA; cross-sectional area
CSMI; cross-sectional moment of inertia, SM; section modulus, BR; buckling ratio
p value; significance in %change /year of parameters
p (vs FS); significance in % change/year in FN against % change/year in FS
p* value; significance in correlation between baseline and follow-up measurements