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## Hip Structural Geometry in Old and Old-Old Age: Similarities and Differences between Men and Women

Laurel B. Yates<sup>1,2</sup>, David Karasik<sup>2,3</sup>, Thomas J. Beck<sup>4</sup>, L. Adrienne Cupples<sup>5</sup>, and Douglas P. Kiel<sup>2,3</sup>

<sup>1</sup>Division of Aging, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA

<sup>2</sup>Harvard Medical School, Boston, MA, USA

<sup>3</sup>Institute for Aging Research, Hebrew SeniorLife, Boston, MA, USA

<sup>4</sup>Department of Radiology, The Johns Hopkins University, Baltimore, MD, USA

<sup>5</sup>Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA

### Abstract

**Introduction**—Changes in hip structure and geometry during aging contribute to decreased bone strength. Little is known, however, about these characteristics at advanced age, when fragility fractures are common. We examined hip structural geometry in men and women of old (72–84 years) and old-old (85–96 years) age to determine (1) gender differences; (2) whether or not these differences are consistent with the increased occurrence of hip fracture in elderly women, compared to men; and (3) whether or not gender-specific changes are consistent with the increased occurrence of fragility fractures after age 80 in both men and women.

**Methods**—We used Hip Structure Analysis (HSA) software to analyze bone densitometry scans from 916 community-dwelling men and women aged 72–96 years. We examined gender differences in hip geometry by age group (72–74, 75–79, 80–84, and  $\geq 85$  years) and between gender-specific age groups using multivariable linear regression.

**Results**—At the femoral narrow neck, there was no gender difference at age 72–74 in bone mineral density (BMD), cortical thickness (CT), and buckling ratio (BR). In contrast, at age 85 or older women had 13% less BMD and CT than men and 8% higher BR. At the intertrochanteric region, women  $\geq 85$  years had 25–31% less BMD, cross-sectional bone area (CSA), and CT than men of comparable age, and 38% higher BR. These gender differences were approximately 10–20% greater than those between men and women in their 70s. In gender-specific comparisons, women showed increasing change in structural geometry with increasing age. At both narrow neck and trochanteric regions, women  $\geq 85$  years had nearly 35% higher BR, 15% less BMD and CT, and 10% less CSA than women aged 72–74 years. At the narrow neck they also had 6% greater outer diameter than the youngest women and 8% lower section modulus (Z), an index of bending strength. In contrast, men showed significant age differences only at the narrow neck region, and only at 85 years or older, including 22% higher BR, 10% less BMD and CT, and 5% greater outer diameter, compared to men in their early 70s. Unlike women, men showed no age-associated decline in section modulus.

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**Corresponding author:** Laurel B. Yates, M.D., M.P.H., Division of Aging, Brigham and Women's Hospital, 1620 Tremont Street, Boston, MA 02120. Telephone: (617) 525-7812; FAX: (617) 525-7739. Email: lbyates@partners.org.

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**Conflicts of Interest:** Dr. Beck's institution (The Johns Hopkins University) has licensed the Hip Structure Analysis software to Hologic Inc. The other authors have no conflicts of interest.

**Conclusions**—Gender differences in hip geometry consistent with increased fragility and fracture risk in elderly women, compared to men, continue into old-old age. Both men and women 85 or older show the most unfavorable features, suggesting a structural basis for the increased occurrence of hip fracture in both sexes at advanced age.

### Keywords

Hip structure analysis; bone geometry; aging; gender differences; osteoporosis

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### Introduction

The greater prevalence of bone fragility [1,2] and increased rates of fragility fractures [3] with advancing age in women, compared to men, are explained in part by the larger skeletal size and bone mass of men, even after adjustment for body size [4,5]. In addition, although women and men both lose bone mineral during aging because of endocrine [6–8], paracrine [9,10], and cellular factors [11,12], the effect is more profound in women, beginning even before menopause [13,14], but notably accelerating afterward with rapid decline in estrogen [15,16]. Bone strength, however, is determined not only by the amount of bone mineral, but also by its spatial distribution with respect to the loading forces that may be encountered [17]. Studies using principles from engineering analysis and biomechanics to explore skeletal structural parameters of bone strength [18–20] have been extended by recent investigations [21–29], and a more complete understanding of factors that may contribute to gender differences in bone fragility and fracture risk in old age is emerging.

In tubular bones such as the femur, sex differences in size and strength result from greater periosteal apposition in males and greater endocortical apposition in females in the peripubertal period [30]. Although this leads to a wider periosteal diameter in males, cortical thickness and volumetric density are no different by sex. Nevertheless, cortical bone mass is greater in males, and placement of the cortex further from the neutral axis of the bone confers greater biomechanical advantage and strength to withstand bending [30]. During aging, periosteal bone formation is slowed, but the process continues in both sexes, together with endocortical resorption, resulting in widening of both periosteal and endocortical diameters. Although cross-sectional studies of aging individuals suggest that periosteal apposition is greater in men than in women [23,27], data from one longitudinal study suggest that the rate may be faster in women [31]. In both sexes, however, periosteal widening occurs more slowly than endocortical widening, leading to increased cortical thinning and susceptibility to local buckling [23]. This structural instability may occur at an earlier point in the life of a woman than of a man because of the sexual dimorphism in bone geometry [23,32].

In spite of increased understanding of structural characteristics and changes that can confer bone fragility during aging, there is a lack of information about these characteristics and gender differences at very advanced ages, when the effects of progressive alterations might be expected to put men and women at greatest fracture risk. Few investigations have included participants older than age 80, and individuals older than 85 years are especially underrepresented, even though they constitute the most rapidly growing population group [33] and are 10–15 times more likely to experience fragility fractures than persons aged 60–65 [3,34]. Furthermore, men 80 years or older are even less well-studied than women of similar age, in spite of recent attention to male osteoporosis [35–37].

Therefore, the purpose of this study was to describe characteristics of hip structural geometry in community-dwelling men and women of old age (72–84 years) and old-old age (85–96 years) to address two incompletely understood questions relative to increased bone fragility in older individuals. First, what are the gender differences in hip structural geometry at advanced ages,

and are these differences consistent with the greater rates of hip fracture in elderly women compared to elderly men? Second, do characteristics of hip structural geometry in old-old age differ from those at younger old age, and, if so, are the differences consistent with the accelerated rate of fragility hip fractures that occur after age 80 in both men and women?

## Materials and methods

### Study population

These analyses used data from participants in the Framingham Study, a population-based longitudinal study of risk factors for heart disease. An original cohort of 2875 Caucasian women and 2334 Caucasian men, aged 28–62 years, was assembled in 1948 from a two-thirds sampling of households in Framingham, MA [38]. Surviving participants have provided extensive health-related information by questionnaire and have undergone physical examination and other testing biennially since baseline. Cohort members who had bone densitometry assessment at examination 22 (1992–1993) in the ancillary Framingham Osteoporosis Study [39] are included in the present analyses. Valid bone mineral density measurements of the hip were obtained in 916 participants (343 men, 573 women), representing 67% of the surviving cohort. The study was approved by the appropriate institutional review boards and written informed consent was obtained from all subjects.

### Bone densitometry

Proximal femur (neck and trochanter) bone mineral density (BMD) was measured ( $\text{g}/\text{cm}^2$ ) using dual x-ray absorptiometry (Lunar DPX-L; Lunar Corporation, Madison, WI). Region area also was measured ( $\text{cm}^2$ ) and bone mineral content (BMC; g) derived in conventional manner using the Lunar software. The right hip was scanned ( $n = 883$ ) unless there was history of fracture or hip joint replacement, in which case the left hip was scanned ( $n = 33$ ). Standard positioning and quality control procedures were used as previously described [40].

### Hip structural analysis

The proximal femur densitometry scans were analyzed for geometric properties of bone structure using the Hip Structure Analysis (HSA) software program developed by Beck and colleagues [18]. The HSA technique extends principles first described by Martin and Burr [41] and calculates dimensions of bone cross-sections at specific locations across the proximal femur using bone mass images generated by absorptiometry scanners. The analysis has been described in detail and illustrated in previous publications [21,23,42]. In brief, the HSA program measures bone mineral density and geometry of cross-sections using distributions of mineral mass traversing the bone axis, averaged for precision over five parallel lines ( $\sim 5$  mm) across the bone axis. Two femur regions were analyzed and used in this study: 1) the femoral neck at its narrowest point (“narrow neck”; NN); and 2) the intertrochanteric (IT) region, along the bisector of the shaft and femoral neck axes. Areal BMD ( $\text{g}/\text{cm}^2$ ), bone cross-sectional area (CSA;  $\text{cm}^2$ ), subperiosteal outer diameter (cm), and section modulus ( $Z$ ;  $\text{cm}^3$ ) were determined directly from the bone profile at each region, using algorithms described previously [21]. CSA is equivalent to the amount of bone surface area in the cross-section after excluding soft tissue space and is proportional to conventional bone mineral content in the corresponding cross-section. In mechanical terms CSA is an indicator of resistance to loads directed along the bone axis. Section modulus ( $Z$ ) is an indicator of strength of the bone to resist bending and torsion. Femoral neck length (cm) also was measured [42].

Estimates of average cortical thickness (CT; cm) were calculated by modeling cortices of the NN and IT cross-sections as concentric circles and assuming that 60% of the measured mass is cortical and 40% is trabecular in the NN region, and that 70% is cortical in the IT region [21]. Buckling ratio (BR), a mechanical index of wall stability in thin-walled tubes, was

calculated as the distance from the center of mass to the medial or lateral cortex (whichever distance was larger) divided by the estimated average cortical thickness. High values of BR can approximate conditions in osteoporotic bone in which the cortex has become structurally unstable.

Repeated bone densitometry scans that could permit an assessment of HSA precision were not collected in this study, but precision error (CV%) for HSA variables at the NN and IT regions by scanner manufacturer and model have been published [42].

### Other measurements

Age at time of scan was determined by records of birth date. Height (without shoes) was measured to the nearest one-fourth inch using a stadiometer. Weight was measured using a standardized balance beam scale. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ).

### Statistical analyses

Anthropometric and bone geometric measures were checked for missing data, outliers, and normality. Scans with structural features greater or less than 3 standard deviations (SD) from mean values were examined for sources of error, such as excessive hip anteversion, incomplete (cut-off) image, or scan quality issues. Such scans were reanalyzed by HSA if appropriate, and valid re-analyzed values were used in subsequent statistical analyses. Unadjusted comparisons between genders for age, height, weight, body mass index, and each geometric measure were performed using Student's t-test. Because bone dimensions and cross-sectional properties are at least partly dependent on body size and are affected by age [5,23,31], differences between genders and among gender-specific age groups then were assessed using general linear models (GLM) adjusting for age, height, and weight. However, because buckling ratio is a ratio of two dimensions, it was not corrected for body size (see discussion). Nevertheless, it is age-dependent, and gender comparisons were therefore age-adjusted. To compare the magnitude of gender differences in geometric parameters, which have different units of measure, normalized values (percent differences) were generated by expressing the gender difference in adjusted least squares (LS) mean value for each parameter as a percentage of the corresponding LS mean value for men (referent). To compare age differences in geometric parameters, we defined four age groups: 72–74, 75–79, 80–84, and  $\geq 85$  years. For age comparisons according to gender, normalized values (percent differences) were generated using the youngest gender-specific age group (72–74 years) as the referent. Subsequent to analysis of variance, statistical significance of age group comparisons was assessed using Dunnett's test for multiple comparisons.

Pearson correlation coefficients were calculated to explore relationships between conventional and geometric DXA parameters. We investigated whether changes seen in geometric parameters differed from those apparent in BMD alone by comparing models with and without BMD as a covariate. Model 1 included adjustment for age and body size, as previously described. Model 2 included additional adjustment for conventional femoral neck BMD, measured by the Lunar densitometer. Model 3 included the adjustments of Model 1, as well as adjustment for BMD measured by the HSA software in the region used to derive geometry. Differences between Models 1 and 2 demonstrate the effect of correcting for conventional BMD, although the mineral mass used in estimates of geometric parameters is not the same as that used by the densitometer to estimate conventional BMD. Differences between Models 1 and 3, however, should better explain why bones with equivalent BMD might differ geometrically at the same location.

All analyses were conducted using SAS statistical software (version 9.1; SAS Institute Inc., Cary, NC), and results were considered statistically significant at the 0.05 level.

## Results

Bone densitometry scans from 916 men and women were submitted for hip structure analysis. The percent of geometric features that could not be measured was 0.8% in the narrow neck region and 1.1% for most intertrochanteric features, typically because of hip positioning or obscured femoral neck margins. Truncated images of the femur shaft resulted in a failure rate of 9.9% for estimated IT cortical thickness and buckling ratio, parameters which use shaft outer diameter in the estimate. A scan was not excluded entirely from the study for loss of only isolated measurements at one bone region. The total number of scans providing valid structural measurements for analyses was 914.

### Correlations between conventional and geometric DXA parameters

Using gender-pooled data, BMD measured by HSA at the narrow neck was highly correlated with femoral neck BMD measured by the Lunar software ( $r = 0.85$ ,  $p < 0.0001$ ). Narrow neck CSA was highly correlated with the Lunar-measured bone mineral content ( $r = 0.89$ ,  $p < 0.0001$ ), as expected, because the geometric parameter and the conventional parameter both quantify the amount of bone in the femur neck. Conventional femoral neck area is a crude measure of the average outer diameter of the neck because the length of the region along the neck is generally a default value. In our data, correlation of conventional femoral neck area with HSA narrow neck outer diameter was 0.68. Cortical thickness and section modulus of the narrow neck were significantly ( $p < 0.0001$ ) correlated with conventional neck BMD (CT,  $r = 0.84$ ; Z,  $r = 0.72$ ). Buckling ratio has a non-linear and negative relationship with BMD (i.e., varies as  $1/BR$ ), and the correlation between BR and conventional BMD was  $-0.63$ . In our gender-specific data, the correlations between conventional and geometric DXA parameters were somewhat higher overall in men than in women, likely because the 1.5 cm conventional femoral neck region is more like a narrow cross-section in the larger bones of men, while it encompasses a greater and more dimensionally variable proportion of the whole femoral neck in women.

### Gender differences

Characteristics and descriptive statistics of the study population are reported in Table 1. The average age of the sample was 79 years (range 72–96 years), similar for men and women. There were 584 participants in their seventies (233 men, 351 women) and 330 in their eighties or nineties (109 men, 221 women), of whom 109 were age 85 or older (37 men, 72 women). As expected, men on average were taller and heavier than women, but no different from women in body mass index.

Table 2 displays gender differences in geometric measures before and after adjustment for age and body size (height and weight). Buckling ratio was adjusted for age but not body size (see discussion). Group mean values are also given for conventional BMD, BMC, and region area of the femoral neck as measured by the Lunar software. In unadjusted analyses men and women were significantly different in all measures ( $p < 0.001$ ). Consistent with their larger bones, men had higher values than women except in buckling ratio (BR), for which women had higher values. After adjustment, the magnitude of gender differences was reduced, but remained statistically significant ( $p < 0.001$ ). The greatest differences between men and women after adjustment were in section moduli (Z), 22% to 27% lower in women ( $p < 0.0001$ ), cross-sectional areas (CSA), 15–20% less in women ( $p < 0.0001$ ), and estimated cortical thickness (CT), 7–19% thinner in women ( $p < 0.001$ ). In contrast, BR was 7% higher in women compared



to men at the femoral narrow neck ( $p < 0.001$ ) and 28% higher at the intertrochanteric region ( $p < 0.0001$ ).

Table 3 illustrates the percent differences between women and men in hip geometry after adjusting for age and body size (Model 1), and after including additional adjustment for conventional femoral neck BMD (Model 2) or BMD of the corresponding region by HSA (Model 3). Adjustment for BMD had little effect on outer diameters (as expected), but interesting effects on other geometric differences. For equivalent BMD, women still demonstrated significantly lower bending resistance (section modulus) at both narrow neck and intertrochanteric regions, although the differences were smaller. Bone cross-sectional area, as an index of resistance to axial loads, also remained smaller in women with BMD equivalent to men. However, the gender difference in buckling ratio reversed after adjustment for BMD, suggesting that men have larger values than women for equivalent levels of BMD (not significant at IT region with Model 2).

### Gender differences in BMD and hip structural geometry at different ages

Figure 1 illustrates differences in size-adjusted BMD and hip geometry between men and women within the same age group. At the femoral narrow neck, gender differences at age 72–74 years were negligible ( $< 2\%$ ) in BMD, CT, and BR. In contrast, in the oldest age group ( $\geq 85$  y), women had significantly lower BMD and CT than men ( $-13\%$  for each measure;  $p \leq 0.03$ ) and greater BR (8%, but not statistically significant). The oldest group also showed substantial gender difference in narrow neck CSA (21%,  $p < 0.001$ ), notably greater than the difference in CSA between men and women in the youngest group.

At the intertrochanteric region, older age also was associated with greater gender differences in BMD and hip geometry measures. This was particularly evident for men and women 85 years or older in BMD (25% less in women;  $p < 0.0001$ ), CSA (29% less in women;  $p < 0.0001$ ), and CT (31% less in women;  $p < 0.0001$ ). Most dramatically, women 85 or older had IT buckling ratios 38% higher than comparably aged men ( $p = 0.001$ ), a difference almost 20% greater than gender differences in BR for men and women in their early 70s.

Although women in all age groups differed significantly ( $< 0.0001$ ) from men in outer diameter and section modulus at both narrow neck and IT regions, the differences were approximately the same across age groups (7–11% smaller diameter and 21–26% lower Z at the neck, compared to men in the same age group; 4–7% smaller diameter and 22–34% lower Z at the IT region).

The effects of BMD on gender differences in hip geometry are shown in Table 4. Outer diameters were 8–11% smaller in women across age groups whether or not they were corrected for BMD (Model 1 compared to Models 2 and 3). Cross-sectional area and section modulus also remained significantly smaller in women across age groups even after adjustment for BMD (Models 2 and 3), with only two exceptions. Without BMD adjustment (Model 1), femoral narrow neck buckling ratios differed significantly only in the 75–79 y age group, although gender differences in BR in all age groups were highly significant at the IT region. Adjustment for conventional femoral neck BMD (Model 2) eliminated the gender difference in BR at the IT region but not at the femoral neck. Adjustment for BMD measured by HSA (Model 3) led to significant gender differences in buckling ratios in all age groups (lower values in women) at both narrow neck and IT regions.

### Gender-specific differences in BMD and hip structural geometry with increasing age

Figure 2 illustrates age trends in size-adjusted BMD and hip geometry assessed by HSA at the narrow neck and IT regions in women and men separately. The three older age groups are

compared (percent difference) to the 72–74 y group. Table 5 summarizes the differences between the oldest ( $\geq 85$  y) and youngest groups and shows the effects of adjustment for BMD within each gender.

Among women, consistent trends in geometric parameters occurred with increasing age ( $p_{\text{trend}} 0.03$  for NN section modulus,  $p_{\text{trend}} \leq 0.006$  all other measures except IT outer diameter and section modulus [no significant trend]). Women 85 or older exhibited the greatest differences, with BR 25% (IT region) to 34% (neck region) higher than values for women aged 72–74 years. Compared to the youngest women, the oldest also had approximately 10–15% less BMD and CT, 7–10% less CSA, and 6% greater neck outer diameter. Furthermore, compared even to women in their younger 80s, women 85 or older showed significant ( $p < 0.05$ ) structural differences at the femoral neck, including 6% less BMD, 3% increased outer diameter, and 10% higher BR. Thus the oldest women had wider femurs (n.s. at IT) containing less bone tissue (CSA), thinner cortices, less bending resistance (n.s. at IT), and significantly greater buckling ratios. After adjustment for BMD (Table 5), CSA and BR differences became non-significant, although section moduli were significantly higher in the oldest group at both regions for equivalent BMD measured by HSA (Model 3).

Among men (Figure 2 and Table 5), significant age differences in structural parameters were apparent only at the femoral narrow neck, and only in men 85 or older. Compared to men in their early 70s, the oldest men demonstrated patterns and magnitudes of differences in hip structural geometry that were similar to differences seen in comparisons of women 85 or older to younger women, including lower BMD (10%;  $p = 0.04$ ), smaller CSA (5%, but not statistically significant), increased outer diameter (5%;  $p = 0.005$ ), thinner cortex (10%;  $p = 0.04$ ), and higher BR (22%;  $p < 0.0001$ ). Men age 85 or older also showed structural differences at the femoral neck compared even to men in their younger 80s, including higher BR (14%,  $p = 0.008$ ) and increased outer diameter (4%,  $p = 0.007$ ). Men in their early 80s exhibited patterns of structural change at the femoral neck similar to the oldest men, but they were not statistically different from men in their early 70s. Men showed no age-associated difference in femoral neck section modulus, unlike women.

At the intertrochanteric region, men displayed a trend ( $p = 0.03$ ) toward increased bone outer diameter with increasing age, but no other significant age-related differences in hip geometry. Similar to women, section modulus was significantly higher in the oldest group of men compared to the youngest after adjustment for BMD estimated by HSA.

As one would expect in adult bones, femoral neck length showed no age-associated change in either women or men (data not shown).

## Discussion

The community-dwelling elderly men and women in this study exhibited significant gender differences in hip structural geometry. Furthermore, the differences increased with age. These results support the hypothesis that elderly women, compared to men of similar age, have increased hip fracture risk because of greater cortical instability (thinner cortex and higher buckling ratio) and reduced structural capacity to resist compressive or bending forces (smaller bone cross-sectional area and diminished section modulus). The gender differences in features of structural fragility were greatest between men and women in the oldest-old age group (85–96 years). This finding supports the observation that elderly women have greater hip fracture risk than elderly men, but it also suggests that the gender difference in fracture risk increases even more at advanced age. In this study women had diminished bone mineral density compared to men, but the difference generally was less than that for geometric measures of bone structure, even after adjustment for body size, especially in women in their seventies.

The gender differences in BMD and inferences that might be drawn are worthy of specific comment. In the femoral neck region these differences were influenced by the opposing effects of the amount of bone in the region (CSA and BMC, determined by HSA and conventional methods, respectively) and the external dimensions of the bone (as apparent in outer diameter and region area, respectively). For example, compared to the women, the femoral necks of the men contained 15% more bone surface (CSA). However, because their femoral necks were 8% wider in diameter, the adjusted BMD of the men was only 7% greater than that of the women. This means that in absolute terms the strength difference between genders is underestimated by the BMD difference. The size-adjusted BMD data would suggest that the femoral necks of the women were 7% (measured at the HSA site) and 11% (measured at the conventional site) weaker than those of the men. However, the resistance to axial loads (CSA) was 15% lower in the women compared to the men. Furthermore, because of the non-linear effect of outer diameter, the gender difference in bending resistance (section modulus) was even greater, with the women having 22% lower value in Z than the men. The gender difference in load resistance was even larger at the intertrochanteric region. When we examined gender differences in geometry adjusted for BMD, we found that women with the same BMD as men, independent of body size, had 7–10% lower resistance to axial loads and 16–18% lower bending resistance. While women had higher buckling ratios in absolute terms, for an equivalent BMD their BR were actually lower than the BR in men. This would suggest that compared to the femurs of women, the femurs of men would have a greater susceptibility to buckling at a similar BMD level.

Among women, comparisons across age groups revealed a consistent and progressively worsening pattern of hip structural geometry with increasing age. Women age 85 years or older had the most unfavorable features, but the changes that were obvious at advanced age also were apparent at age 75. Among men, however, age group differences in structural features were significant only at the femoral neck and only among men age 85 or older, although men in their earlier 80s showed similar patterns. Except for section modulus, the features of increased fragility at the femoral neck seen in the oldest men were similar to those seen in the oldest women. Our finding that these men did not have decreased section modulus, in contrast to the decrease seen at the femoral neck with increasing age in the women, is particularly noteworthy, because it may explain the higher resilience of the male femur to bending forces generated by falls. When geometric features were adjusted for BMD assessed by HSA, we found that in both men and women the bending resistance was actually larger in the oldest group for an equivalent BMD. This is consistent with the observation that expansion of outer diameter can preserve this parameter with a smaller amount of bone tissue. Age effects on buckling ratio became non-significant in both men and women after adjusting for BMD. This suggests that buckling ratio and BMD capture similar geometric information.

Our data confirm findings reported by other population-based cohorts of community dwelling, predominantly white elders with regard to gender differences in hip structural characteristics and trends with aging toward increased fragility [5,21,28,31,43], while substantially extending the age range of these types of data to 96 years. The gender differences we found are similar to those reported by Kaptoge et al. [31] and are consistent with NHANES III data on analyses at the femoral neck [5]. However, the magnitudes of differences between men and women in our study differ modestly from these previous studies, most probably because their populations were younger (59–69 years [5] and 67–79 years [31]) and because one study [31] adjusted for body size using average, mixed gender population data rather than individual data. Nevertheless, both of these other studies as well as ours found bone cross-sectional area and section modulus to be the greatest discriminators between genders in hip structural characteristics. In our study intertrochanteric buckling ratio and cortical thickness also differed significantly between men and women, which may partially explain the pronounced gender difference in hip fracture incidence at older age. Buckling ratio estimates have been noted to



be significantly higher in hip fracture cases compared to sex- and age-matched controls [23, 24,44]. Similarly, cortical thinning has been observed in femoral fracture cases, including disproportional thinning in cortical regions likely to be loaded maximally on impact from a fall [45–47].

In comparing buckling ratio between genders, we adjusted for age but not body size. In precise terms, buckling ratio is not a strength measurement, but rather a dimensionless geometric configuration that describes threshold behavior beyond which strength may be compromised under compressive loads because of local buckling of thin regions. Unlike section modulus or CSA, one would not adjust buckling ratio for body size to correct for the fact that larger bones must be stronger in bigger subjects.

In both men and women, there were no strong age trends in section moduli at either the femoral neck or the intertrochanteric region, consistent with the observation that expansion of bone outer diameter tends to preserve resistance to pure bending [47,48]. However, expansion of outer diameter combined with cortical thinning means that the compensatory changes are accomplished with progressively less bone, i.e., a wider bone requires less bone tissue for the same section modulus. The potential compromise from this effect is an increase in susceptibility to local cortical buckling. The significant upward trends in buckling ratio with increasing age (higher BR values increase susceptibility) suggest a structural basis for the gender difference in hip fracture type in old age. Among women, femoral neck fractures from low trauma occur more frequently than trochanteric fractures before age 60, but increasing numbers of trochanteric fractures occur in older age [49]. The elderly women in our study showed significant age-associated increases in buckling ratio at both the femoral neck and the intertrochanteric region, suggesting that strength is compromised at both sites. The elderly men, however, showed a significant age-associated increase in buckling ratio only at the femoral neck. This suggests that with aging, the femoral neck in men is less able to withstand bending forces without buckling and thus is less resistant to fracture. Indeed, among men, cervical fractures occur much more frequently than trochanteric fractures in older age [49].

With regard to hip structure in aging, our data extend previous studies by demonstrating that changes in geometric features consistent with increased fragility and fracture risk continue into old-old age, beyond 85 years, an age range that has been excluded from or minimally represented in other investigations. Furthermore, these changes occur in very elderly men as well as in women. One of the most significant findings that emerged by including older participants was the observation that men and women age 85 or older showed the most unfavorable hip geometry. In many measures these differences were significantly greater than among men and women even in their early 80s, and dramatically worse than among those in their 70s. These differences parallel the markedly increased hip fracture rates among both men and women age 80 or older, compared to persons in their seventies, both in the United States and many other countries [3,50–52].

A major strength of this study is the use of a large, population-based cohort of older men and women, including substantial numbers of both men and women over age 80, with many older than 85 years. The participants were generally healthy, ambulatory, community-dwelling elders carrying out routine levels of activities.

Several potential limitations must be acknowledged. Although our data are population-based, they are drawn from a mostly non-Hispanic white cohort and may not be generalizable to other ethnic populations. In addition, the bone densitometry scans used in the hip structure analyses were obtained in 1992–1993, and secular trends as well as period-cohort effects may limit extrapolating our findings to different generations. However, if such a trend did exist in our study sample, it should have been demonstrated by a longer and wider femoral neck in the

younger subjects (age in lower 70s), compared to the older (age in higher 80s). As discussed and shown in Table 5, this was not the case.

This was a cross-sectional study and we can only infer that geometric features seen among groups of individuals of different ages reflect the natural history of aging bone. Nevertheless, the pattern of our results is in agreement with the few studies [22,31,53] that have obtained longitudinal data to describe the evolution of hip structural parameters with age, although those data are available only over relatively short times (mean 2.7–3.5 years).

We did not have measures of skeletal muscle or lean body mass to directly assess the contribution of skeletal loading, which affects mechanical properties of bones and perhaps accounts for decline in strength of aged bones [54]. As other studies have done [5,28,31,53], we adjusted for body mass and size using weight and standing height, although variations in height because of vertebral collapse in the very old can be confounding. A related issue is that CSA and section modulus tend to scale better with lean body mass [22,55] than with total weight, and men are proportionately leaner than women [56]. This may mean that some of the residual gender differences in geometry after correction for height and weight may be due in part to the smaller lean mass fraction in women. On the other hand, the forces generated in falls are a function of total body mass, not lean mass, inferring that relative strength to resist trauma still would be lower in women than in men.

Our study of bone geometric features is restricted by the inherent limitations of DXA technology. Current scanners cannot reliably measure small changes in dimensions in an individual that are structurally important. Thus large populations, such as included in this study, are required to provide statistical power in analyses of structure. Furthermore, subperiosteal bone margins may not be detected accurately in osteoporotic bone, thereby underestimating bone outer diameter, especially in old persons with very low bone mineral density and cortical porosity. Finally, estimates of average cortical thickness and buckling ratio in the HSA method include several assumptions about shape of tubular bones and the assigned fractions of cortical and trabecular bone. Nevertheless, until new methods of quantifying bone structural morphology are available and practical for application in population-based studies, the analysis of hip structural geometry with bone absorptiometry provides at least an insight into geometric changes that may have clinical importance.

In conclusion, in this study of elderly men and women of old age (72–84 years) and old-old age (85–96 years), significant gender differences in hip structural geometry were clearly apparent. These differences suggest that elderly women may have greater risk of hip fracture than elderly men because of inherent structural features of the proximal femur that lead to increased bone fragility. Furthermore, both men and women of oldest-old age have indices of bone strength that are notably worse than those of men and women in their seventies and early eighties. Thus the accelerated rates of hip fracture after age 80 both in men and in women may be explained at least in part by unfavorable distribution of bone tissue with ensuing increased bone fragility. Because these structural changes are consistent with imbalances in processes of bone modeling and remodeling, including periosteal apposition and endocortical resorption, continued focus is warranted on developing therapeutic agents to regulate cellular aspects of bone formation and destruction and thereby maintain or restore bone strength.

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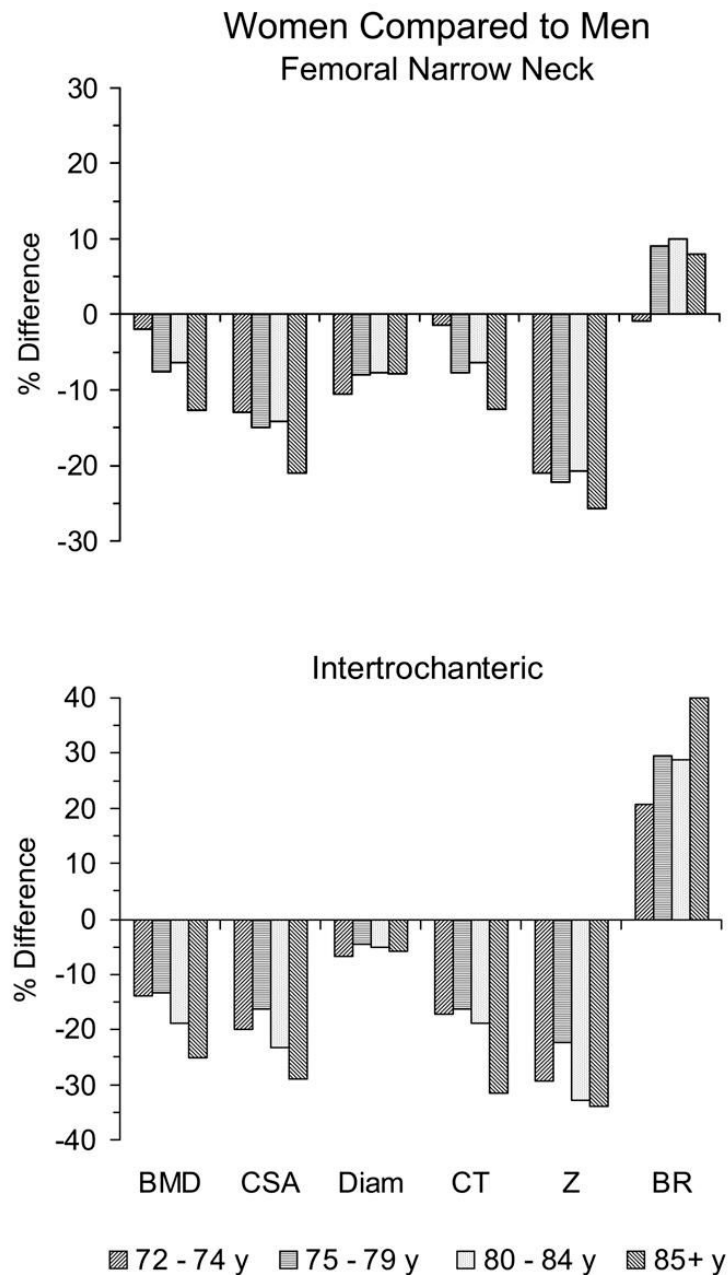
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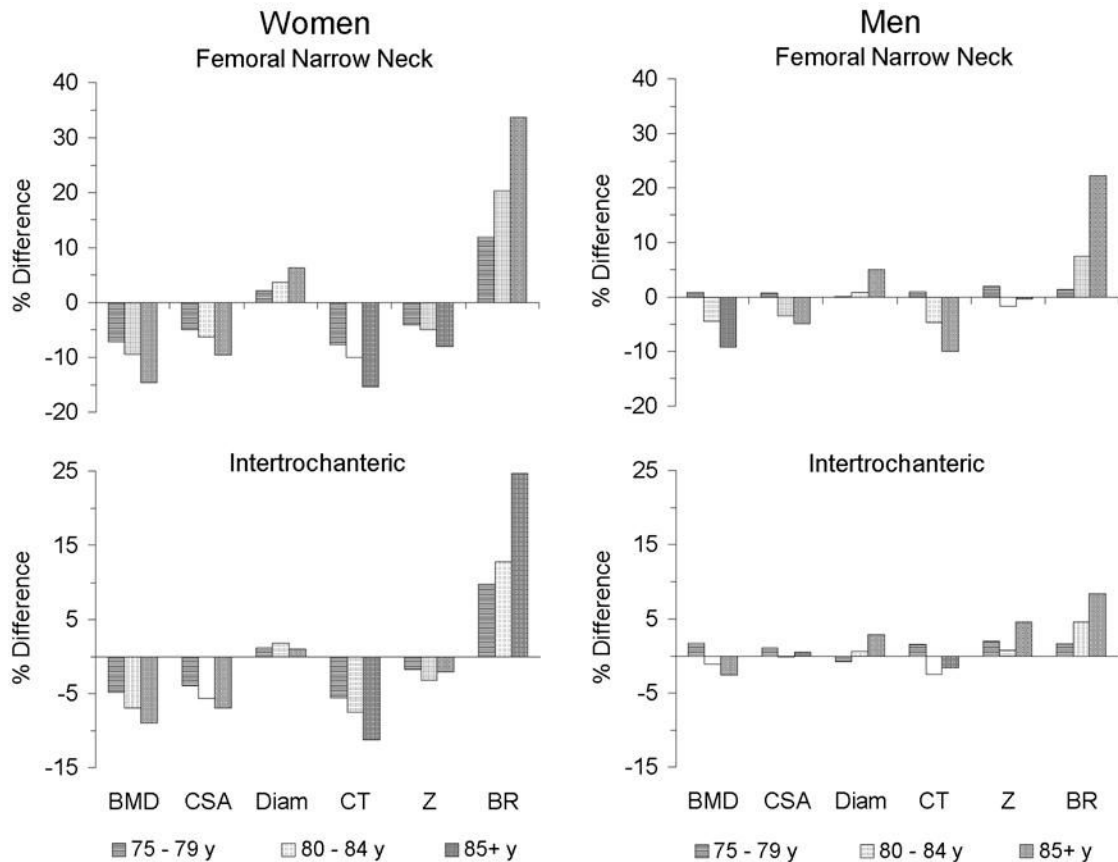
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**Figure 1.**

Effects of age on gender differences in hip structural geometry at the femoral narrow neck and intertrochanteric regions. Women are compared to men in four age groups (72–74, 75–79, 80–84, and 85 years or older). For each age group the percent difference between genders, referent to men, is shown for HSA-measured bone mineral density (BMD), cross-sectional area (CSA), outer diameter (Diam), average cortical thickness (CT), and section modulus (Z) after adjustment for age, height, and weight. Buckling ratio (BR) was not adjusted for height and weight. All gender differences were statistically significant ( $p < 0.05$ ) at the femoral neck except BMD and CT in groups 72–74 and 80–84 years and BR in all groups except 75–79 years. At the IT region all gender differences were statistically significant.



**Figure 2.** Gender-specific effects of age on hip structural geometry at the femoral narrow neck and intertrochanteric regions. The three older groups (75–79, 80–84, and 85 years or older) are compared to the youngest (72–74 y) for women (left panels) and men (right panels) in HSA-measured bone mineral density (BMD), cross-sectional area (CSA), outer diameter (Diam), average cortical thickness (CT), and section modulus (Z) after adjustment for age, height, and weight. Buckling ratio (BR) was not adjusted for height and weight. Percent differences in measures within each gender-specific age group are referent to the youngest group (72–74 y). Among women, all measures showed statistically significant age-associated differences except intertrochanteric outer diameter and Z. Among men, significant age differences were seen only for men 85 or older, and only at the femoral neck, in BMD, outer diameter, CT, and BR.

**Table 1**

Characteristics of participants. Values for age groups are numbers of participants within each group (% of gender-specific population). Values for other characteristics are group mean values ( $\pm$  standard deviation, SD).

	<b>Women</b> <b>(n = 572)</b>	<b>Men</b> <b>(n = 342)</b>
Age (y)	78.8 (4.7)	78.3 (4.4)
Age Groups (n, %)		
72–74 y (175)	110 (19.2)	65 (19.0)
75–79 y (409)	241 (42.1)	168 (49.1)
80–84 y (221)	149 (26.1)	72 (21.1)
> 85 y (109)	72 (12.6)	37 (10.8)
Height (cm)	155.2 (6.5)	169.8 (7.0)
Weight (kg)	64.4 (12.7)	78.2 (13.2)
Body Mass Index (kg/m <sup>2</sup> )	26.7 (5.0)	27.0 (4.0)

**Table 2**

BMD and hip structural geometry in women and men. Measures are from Hip Structure Analysis (HSA) except for BMD, BMC, and Area at the Lunar femoral neck, which are from the Lunar densitometer. Unadjusted data are mean values ( $\pm$  standard deviation, SD). Adjusted data are group least squares mean values ( $\pm$  standard error of the mean, SEM) after adjustment for each individual's age, height, and weight. BR, dimensionless, was not adjusted for height and weight.

	Unadjusted		Adjusted	
	Women	Men	Women	Men
<b>Narrow Neck</b>				
Neck Length (cm)	4.58 (0.67)	5.39 (0.81) ****	4.68 (0.04)	5.23 (0.05) ****
BMD (g/cm <sup>2</sup> )	0.63 (0.14)	0.75 (0.15) ****	0.66 (0.01)	0.71 (0.01) ****
Cross Sectional Area (cm <sup>2</sup> )	1.76 (0.36)	2.42 (0.47) ****	1.88 (0.02)	2.22 (0.03) ****
Outer Diameter (cm)	2.94 (0.28)	3.38 (0.27) ****	3.00 (0.01)	3.27 (0.02) ****
Cortical Thickness (mm)	1.22 (0.03)	1.44 (0.03) ****	1.26 (0.01)	1.35 (0.02) ****
Section Modulus (cm <sup>3</sup> )	0.92 (0.24)	1.43 (0.32) ****	1.00 (0.01)	1.29 (0.02) ****
Buckling Ratio	14.40 (5.28)	13.32 (3.55) ***	14.35 (0.19)	13.40 (0.25) ***
<b>Lunar Femoral Neck</b>				
BMD (g/cm <sup>2</sup> )	0.70 (0.12)	0.86 (0.14) ***	0.73 (0.01)	0.82 (0.01) ****
BMC (g)	4.79 (0.55)	5.61 (0.45) ****	3.61 (0.03)	4.44 (0.05) ****
Area (cm <sup>2</sup> )	3.37 (0.72)	4.84 (0.94) ****	4.92 (0.02)	5.39 (0.03) ****
<b>Intertrochanteric</b>				
BMD (g/cm <sup>2</sup> )	0.61 (0.15)	0.81 (0.16) ****	0.64 (0.01)	0.76 (0.01) ****
Cross Sectional Area (cm <sup>2</sup> )	3.04 (0.72)	4.53 (0.93) ****	3.28 (0.03)	4.12 (0.05) ****
Outer Diameter (cm)	5.22 (0.39)	5.92 (0.46) ****	5.37 (0.02)	5.67 (0.03) ****
Cortical Thickness (mm)	2.24 (0.06)	3.32 (0.07) ****	2.53 (0.03)	3.14 (0.06) ****
Section Modulus (cm <sup>3</sup> )	2.69 (0.78)	4.68 (1.10) ****	3.02 (0.04)	4.13 (0.05) ****
Buckling Ratio	13.49 (5.49)	10.43 (3.26) ****	13.46 (0.21)	10.50 (0.28) ****

\*\*\* P < 0.001

\*\*\*\* P < 0.0001

**Table 3**

Differences (%) between women and men in hip structural geometry, referent to men. Model 1 adjusted for age, height, and weight. Model 2 included adjustments of Model 1, as well as adjustment for femoral neck BMD measured by the Lunar densitometer. Model 3 included adjustments of Model 1, as well as adjustment for BMD measured by HSA at the corresponding region. In all models, the dimensionless Buckling Ratio was not adjusted for height and weight.

	Difference between Women and Men (%)		
	Model 1	Model 2	Model 3
<b>Narrow Neck</b>			
Cross Sectional Area	-15.2 <sup>****</sup>	-6.2 <sup>****</sup>	-10.3 <sup>****</sup>
Outer Diameter	-8.4 <sup>****</sup>	-9.8 <sup>****</sup>	-9.6 <sup>****</sup>
Cortical Thickness	-6.7 <sup>***</sup>	+5.6 <sup>***</sup>	+0.6 <sup>****</sup>
Section Modulus	-22.2 <sup>****</sup>	-15.5 <sup>****</sup>	-17.5 <sup>****</sup>
Buckling Ratio	+7.1 <sup>***</sup>	-17.6 <sup>****</sup>	-14.4 <sup>****</sup>
<b>Intertrochanteric</b>			
Cross Sectional Area	-20.5 <sup>****</sup>	-12.0 <sup>***</sup>	-7.2 <sup>****</sup>
Outer Diameter	-5.2 <sup>****</sup>	-6.1 <sup>****</sup>	-7.2 <sup>****</sup>
Cortical Thickness	-19.3 <sup>****</sup>	-9.6 <sup>****</sup>	-3.7 <sup>****</sup>
Section Modulus	-26.82 <sup>****</sup>	-20.4 <sup>****</sup>	-15.9 <sup>****</sup>
Buckling Ratio	+28.2 <sup>****</sup>	-3.00	-13.4 <sup>****</sup>

\*\*\*  
P < 0.001

\*\*\*\*  
P < 0.0001



**Table 4**

Gender differences in hip structural geometry at older ages. Differences (%) in each age group were calculated referent to the men. In Model 1 data were adjusted for age, height, and weight. Model 2 included adjustments of Model 1, as well as adjustment for femoral neck BMD measured by the Lunar densitometer. Model 3 included adjustments of Model 1, as well as adjustment for BMD measured by HSA at the corresponding region. In all models, dimensionless Buckling Ratio was not adjusted for height and weight.

	Difference (%) between Women and Men			
	72-74 y	75-79 y	80-84 y	≥ 85 y
<b>Narrow Neck</b>				
<b>Cross Sectional Area</b>				
Model 1	-13.0***	-15.0****	-14.1****	-21.0****
Model 2	-7.4**	-7.0****	-2.3	-8.6**
Model 3	-11.6****	-9.2****	-9.6****	-13.0****
<b>Outer Diameter</b>				
Model 1	-10.6****	-8.0****	-7.7****	-7.9****
Model 2	-11.2****	-9.2****	-9.5****	-12.4****
Model 3	-10.9****	-9.2****	-8.9****	-10.4****
<b>Cortical Thickness</b>				
Model 1	-1.4	-7.7*	-6.3	-12.5*
Model 2	+6.1*	+2.6	+9.1**	+9.9*
Model 2	+0.8***	+0.4***	+0.5**	+1.1****
<b>Section Modulus</b>				
Model 1	-21.1****	-22.2****	-20.7****	-25.7****
Model 2	-16.7****	-16.2****	-11.6**	-18.6****
Model 3	-19.7****	-16.7****	-16.3****	-19.5****
<b>Buckling Ratio</b>				
Model 1	-0.9	+9.1*	+10.0	+8.0
Model 2	-18.5****	-17.9****	-16.7***	-19.7****
Model 3	-14.7****	-16.1****	-12.8****	-13.0****
<b>Intertrochanteric</b>				
<b>Cross Sectional Area</b>				
Model 1	-20.1****	-16.4****	-23.4****	-29.1****
Model 2	-15.2****	-8.7****	-13.6****	-16.3****
Model 3	-9.0****	-5.2****	-8.3****	-11.7****
<b>Outer Diameter</b>				
Model 1	-7.7****	-4.5****	-5.1****	-6.0**
Model 2	-7.1****	-5.3****	-6.3****	-8.8**
Model 3	-8.3****	-6.1****	-7.4****	-10.2****
<b>Cortical Thickness</b>				
Model 1	-17.3****	-16.3****	-18.7****	-31.4****
Model 2	-11.0**	-7.0**	-8.6*	-17.7**
Model 2	-3.4	-3.1*	-2.2	-9.3**
<b>Section Modulus</b>				
Model 1	-29.2****	-22.4****	-28.3****	-33.9****
Model 2	-25.4****	-16.6****	-21.0****	-23.6****
Model 3	-20.4	-13.4****	-15.1****	-18.6****
<b>Buckling Ratio</b>				
Model 1	+20.6****	+29.6****	+28.8****	+38.2****
Model 2	-1.7	-5.4	-0.8	-1.6
Model 3	-11.6****	-15.5****	-11.5****	-10.6*

\* P < 0.05

\*\* P < 0.01

\*\*\* P < 0.001

\*\*\*\* P < 0.0001

Table 5

Gender-specific differences in hip structural geometry with age. For simplicity, data are shown only for differences (%) between the oldest ( $\geq 85$  y) and youngest (72–74 y) age groups, referent to the youngest. In Model 1 data were adjusted for age, height, and weight. Model 2 included adjustments of Model 1, as well as adjustment for femoral neck BMD measured by the Lunar densitometer. Model 3 included adjustments of Model 1, as well as adjustment for BMD measured by HSA at the corresponding region. In all models, dimensionless Buckling Ratio was not adjusted for height and weight.

	Women			Men		
	$\geq 85$ y vs. 72–74 y (% difference)			$\geq 85$ y vs. 72–74 y (% difference)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
<b>Narrow Neck</b>						
Cross Sectional Area	-9.6 <sup>***</sup>	-1.7	+2.5	-4.9	+0.4	+3.2 <sup>*</sup>
Outer Diameter	+6.3 <sup>****</sup>	+4.6 <sup>***</sup>	+3.1 <sup>*</sup>	+5.00 <sup>***</sup>	+4.4 <sup>**</sup>	+3.7 <sup>***</sup>
Cortical Thickness	-15.4 <sup>****</sup>	-6.5 <sup>***</sup>	+0.0	-9.9 <sup>*</sup>	-4.0	-0.1
Section Modulus	-8.0 <sup>*</sup>	-1.8	+5.9 <sup>*</sup>	-0.4	+4.3	+7.5 <sup>**</sup>
Buckling Ratio	+33.7 <sup>****</sup>	+9.9 <sup>*</sup>	+0.8	+22.3 <sup>****</sup>	+8.0 <sup>*</sup>	+2.6
<b>Intertrochanteric</b>						
Cross Sectional Area	-7.0 <sup>*</sup>	+1.4	+0.6	+0.5	+5.0 <sup>*</sup>	+2.8
Outer Diameter	+1.1	+0.9	+0.9	+2.9	+2.6	+2.7
Cortical Thickness	-11.2 <sup>*</sup>	-2.4	-2.8 <sup>*</sup>	-1.6	+4.7	+1.4
Section Modulus	-2.1	+5.1	+5.0 <sup>*</sup>	+4.6	+8.3 <sup>*</sup>	+6.6 <sup>*</sup>
Buckling Ratio	+24.8 <sup>****</sup>	+3.3	+3.5	+8.3	-6.8	-6.1

\* P < 0.05  
 \*\* P < 0.01  
 \*\*\* P < 0.001  
 \*\*\*\* P < 0.0001