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Mechanical Contributions of the Cortical and Trabecular Compartments Contribute to Differences in Age-Related Changes in Vertebral Body Strength in Men and Women Assessed by QCT-Based Finite Element Analysis

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ABSTRACT
The biomechanical mechanisms underlying sex-specific differences in age-related vertebral fracture rates are ill defined. To gain insight into this issue, we used finite element analysis of clinical computed tomography (CT) scans of the vertebral bodies of L3 and T10 of young and old men and women to assess age- and sex-related differences in the strength of the whole vertebra, the trabecular compartment, and the peripheral compartment (the outer 2 mm of vertebral bone, including the thin cortical shell). We sought to determine whether structural and geometric changes with age differ in men and women, making women more susceptible to vertebral fractures. As expected, we found that vertebral strength decreased with age 2-fold more in women than in men. The strength of the trabecular compartment declined significantly with age for both sexes, whereas the strength of the peripheral compartment decreased with age in women but was largely maintained in men. The proportion of mechanical strength attributable to the peripheral compartment increased with age in both sexes and at both vertebral levels. Taken together, these results indicate that men and women lose vertebral bone differently with age, particularly in the peripheral (cortical) compartment. This differential bone loss explains, in part, a greater decline in bone strength in women and may contribute to the higher incidence of vertebral fractures among women than men. © 2011 American Society for Bone and Mineral Research.

KEY WORDS: VERTEBRAL FRACTURE; FINITE ELEMENT ANALYSIS; QUANTITATIVE COMPUTED TOMOGRAPHY; BONE LOSS; VERTEBRAL STRENGTH; BONE STRENGTH; BIOMECHANICS

Introduction
Women have a higher incidence of osteoporotic fractures than men, over 25% of which are vertebral fractures.(1) Despite the high rate of occurrence and the significant personal and societal costs, the biomechanical mechanisms underlying vertebral fractures remain largely unknown.(2,3) It is possible that in addition to a decline in bone density, there are structural and/or geometric changes to the cortical and trabecular compartments with age that differentially affect men and women, making women more susceptible to vertebral fractures.

With age, vertebral trabecular bone begins to deteriorate, starting in the center of the vertebral body and progressing superiorly and inferiorly, with thinning of the endplates and cortical shell due to endosteal bone resorption.(4) Meanwhile, the cross-sectional area of the vertebral body increases with age in both men and women because of periosteal bone formation.(5,6) It is likely that these age-related changes in bone structure alter the mechanical contributions of the cortical and trabecular compartments of vertebral bodies, with the cortical compartment assuming a proportionally higher contribution in older subjects than in young subjects.(7,8) To date, several studies have used quantitative computed tomography (QCT)–based finite
element analysis (FEA) to determine the contributions of cortical and trabecular bone to the strength of the distal radius, proximal femur, and vertebral body. However, no studies have investigated the mechanical contributions of the bone compartments in subjects taken from a community-based study or have investigated how age and sex influence the mechanical role of trabecular and cortical bone in the thoracic and lumbar spine. Improved understanding of cortical and trabecular bone contributions to vertebral strength may guide efforts at diagnosing vertebral fragility and may enhance our understanding of therapies with differential effects on cortical vs. trabecular bone.

Conventional assessment of BMD in the spine typically analyzes only vertebrae of the lumbar region (typically L2–L4 or L1–L4), yet many fractures occur in the thoracic spine. How vertebrae from different regions of the spine lose bone with age is not well defined. Heterogeneity of age-related bone loss along the spine may contribute to higher incidence of vertebral fracture at some vertebral levels; therefore, it is possible that clinical fracture risk assessment can be improved by assessing vertebral levels in both the thoracic and lumbar spine.

In this study we used QCT-based FEA of lumbar (L3) and thoracic (T10) vertebrae of young men and women and old men and women to estimate vertebral body strength and its determinants (ie, bone density and morphology). We quantified age-related differences in the mechanical strength, bone strength, and bone density of cortical and trabecular bone compartments and determined whether these age-related differences are similar in vertebrae from the thoracic and lumbar spine and for men and women.

Methods

Subjects and Scan Parameters

Subjects were chosen from participants in the community-based Framingham Heart Study Offspring and Third Generation Multidetector CT Study. The sample consisted of 30 men aged 35 to 42 years, 30 women aged 36 to 41 years, 30 men aged 73 to 82 years, and 30 women aged 74 to 83 years (Table 1). The study protocol was approved by the Boston University School of Medicine and Hebrew Senior Life, and all subjects gave written informed consent. The study is overseen by an independent data safety and monitoring board. For each subject, finite element models were created for the vertebral bodies of the T10 and L3 vertebrae, excluding the transverse and posterior elements. If the T10 or L3 vertebral body was fractured or missing from the QCT scan volume, an adjacent vertebral body was analyzed instead (Table 1).

Scans were acquired during a 33-month period using the same eight-detector helical QCT scanner (Lightspeed Plus, General Electric, Milwaukee, WI, USA) at 120 kVp, 100–360 mAs. A chest scan imaged the area from the tracheal bifurcation to the base of the heart (approximately vertebral levels T7–T11), while an abdominal scan imaged a 150-mm-long volume superior to the upper endplate of S1 (approximately vertebral levels L2–L5). Scans had a nominal in-plane voxel size of 0.68 mm and a slice thickness of 2.5 mm. A multichambered hydroxyapatite phantom (Image Analysis, Columbia, KY, USA) was included in each scan to allow conversion of Hounsfield units to bone density (mg-HA/cm³).

Finite Element Models

QCT-based finite element models of T10 and L3 vertebrae were generated for each patient using previously published methods. Briefly, each vertebra (excluding posterior elements) was segmented from the image, rotated into a standard coordinate system, and resampled into 1-mm cube-shaped voxels. The finite element mesh was created by converting each voxel into an 8-noded brick element (Fig. 1). Elastically anisotropic and elastic-perfectly plastic material properties were assigned to each element using the QCT mineral density of the voxel along with the empirical correlations between mechanical properties and calibrated BMD for human vertebral trabecular bone. Material failure of the bone was modeled by

![Fig. 1. QCT-based finite element models of L3 vertebral bodies from a 38-year-old man (top left), 75-year-old man (top right), 40-year-old woman (bottom left), and 79-year-old woman (bottom right). Each vertebra (excluding posterior elements) was segmented from the QCT image, rotated into a standard coordinate system, and resampled into 1-mm cube-shaped voxels. The finite element mesh was created by converting each voxel into an 8-noded brick element. Elastically perfectly plastic material properties were assigned to each element using the mineral density derived from the brightness of the voxel along with the empirical correlations between mechanical properties and calibrated BMD for human vertebral trabecular bone. Images are representative of the means for peripheral bone mass.](image-url)
Second, the peripheral 2 mm of bone was removed, the
strength. The term peripheral strength is used rather than “cortical strength” because the outer 2 mm of bone contains both the real cortical shell (about 0.4 mm thick) and the adjacent trabeculae that would be unloaded upon removal of the cortical shell. We also computed the ratio of trabecular strength to total vertebral body strength. In addition to these compressive strength measures, we computed the mechanical response to anterior bending by applying a pure bending rotation to the superior endplate and computed the bending stiffness and the ratio of axial to bending stiffness. To gain an understanding of overall failure stress, we measured the average cross-sectional area (CSA) for the entire vertebral body and computed an average failure stress as the ratio of failure strength to CSA.

Statistical analysis
Two-factor ANOVA with repeated measures for T10 and L3 was used to determine age-, sex-, and vertebral level–related differences in vertebral body strength and other related outcomes. In addition, where significant interactions between factors were identified, we used unpaired t-tests to compare men and women, young and old groups, and thoracic and lumbar regions. Differences were considered significant for $p < .0125$ due to Bonferroni correction for three independent hypotheses. Correlation through thoracic and lumbar strength values was performed using paired data for all subjects. $R^2$ values were calculated for all subjects and for each sex and age group.

Results
Differential age-related declines in vertebral body mass and density for men and women
Bone mass and density declined with age in both the peripheral (cortical) and trabecular compartments of T10 and L3, with women exhibiting significantly greater losses than men (Table 3, Fig. 3). For example, total vertebral body density declined 2- to 3-fold more with age in women ($-32\%$ at T10, $-38\%$ at L3) than men ($-11\%$ at T10, $-18\%$ at L3). This decrease in total density was associated with declines in both trabecular ($-38\%$ at T10, $-43\%$ at L3) and peripheral ($-23\%$ at T10, $-30\%$ at L3) bone density for women, while men had smaller declines in trabecular bone density ($-17\%$ at T10, $-23\%$ at L3) and either no decline (T10) or only a small decline ($-11\%$ at L3) in peripheral density. Thus, total vertebral body mass was largely maintained with advancing age in men, because of small decreases in trabecular mass ($-4\%$ at T10; $-15\%$ at L3, $p = .01$), and either no change (L3) or increases in peripheral mass ($+14\%$ at T10, $p = .03$).

Differential age-related declines in vertebral strength for men and women
Vertebral strength outcomes declined with age for both men and women, with women exhibiting significantly greater losses of strength than men (Table 3, Fig. 4). For example, vertebral

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**Fig. 2.** Finite element models of vertebral bodies loaded in axial compression to 2% strain (applied displacement over total height). A thin layer of polymethyl methacrylate (PMMA) was virtually applied to the endplates to simulate conditions of experimental testing. Material failure of the bone was modeled by a von Mises failure criterion. Because failure strain is relatively independent of bone density, contour plots of strain indicate predicted regions of failure.
compressive strength decreased 2-fold more with age in women (−44% at T10, −52% at L3) than in men (−19% at T10, −27% at L3; \(p = .0008\)). Trabecular strength declined significantly and similarly for both sexes (−52% at T10, −64% at L3 for women; −29% at T10, −40% at L3 for men), whereas peripheral strength declined 4- to 10-fold more with age in women (−33% at T10, −37% at L3) than in men (−3% at T10, −9% at L3; \(p < .0001\)). As a result, the proportion of vertebral strength attributable to the peripheral compartment increased significantly with age, from 43% at T10 and 43% at L3 in women and from 42% to 53% for L3 and 39% to 47% for T10 in men (Fig. 5; no significant difference between men and women). Geometric strength increased 11 to 15% with age at both T10 and L3 for both women and men because of increased vertebral body size. Axial stiffness declined with age in both sexes but decreased more in women (−36% at T10, −44% at L3) than in men (−17% at T10, −22% at L3; \(p = .0007\)). In contrast, bending stiffness declined significantly with age in women (−23% at T10, −34% at L3) but did not change in men (−3% at T10, −6% at L3).

Correlation between strength measurements of lumbar and thoracic vertebrae

There was a moderately strong correlation between compressive strength values for L3 and T10 when all subjects were considered together (\(r^2 = 0.77\), Fig. 6). When each age-sex group was plotted independently, the correlations between vertebral body strength for L3 and T10 were lower than when all subjects were considered together, and they were higher for men than for women and higher for young subjects than old subjects, such that in older women, only 50% of the variability in T10 strength was explained by L3 strength (\(r^2 = 0.69\) for young men, \(r^2 = 0.59\) for old men).
Table 3. Results of Finite Element Analysis (mean ± standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>L3</th>
<th>T10</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Young men (n = 30)</td>
<td>Old men (n = 30)</td>
</tr>
<tr>
<td>Strength variables</td>
<td></td>
<td></td>
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<tr>
<td>Vertebral body strength (N)</td>
<td>9647 ± 2205</td>
<td>7010 ± 2735</td>
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<tr>
<td>Geometric strength (N)</td>
<td>3504 ± 547</td>
<td>3902 ± 589</td>
</tr>
<tr>
<td>Trabecular strength (N)</td>
<td>5651 ± 1537</td>
<td>3375 ± 1697</td>
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<tr>
<td>Periosteal strength (N)</td>
<td>3996 ± 726</td>
<td>3635 ± 1237</td>
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<tr>
<td>Bending stiffness (kN/m)</td>
<td>3.61 ± 1.19</td>
<td>3.40 ± 1.44</td>
</tr>
<tr>
<td>Geometric strength (N)</td>
<td>37.8 ± 7.7</td>
<td>29.4 ± 9.6</td>
</tr>
<tr>
<td>Density and mass variables</td>
<td></td>
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<tr>
<td>Vertebral body density (mg/cm³)</td>
<td>241 ± 29</td>
<td>197 ± 45</td>
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<tr>
<td>Vertebral body mass (g)</td>
<td>10.89 ± 1.98</td>
<td>9.80 ± 2.68</td>
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<tr>
<td>Trabecular mass (g/cm³)</td>
<td>217 ± 30</td>
<td>168 ± 44</td>
</tr>
<tr>
<td>Vertebral body density (mg/cm³)</td>
<td>6.94 ± 1.42</td>
<td>5.87 ± 1.76</td>
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<tr>
<td>Trabecular mass (g)</td>
<td>301 ± 27</td>
<td>266 ± 47</td>
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<tr>
<td>Peripheral density (mg/cm³)</td>
<td>3.95 ± 0.57</td>
<td>3.92 ± 0.96</td>
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<tr>
<td>Average CSA (cm²)</td>
<td>11.81 ± 1.29</td>
<td>12.60 ± 1.48</td>
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<tr>
<td>Ratios</td>
<td>Vertebral body strength/vertebral body density (N/cm²/mg)</td>
<td>39.8 ± 6.3</td>
</tr>
<tr>
<td></td>
<td>Vertebral body strength/vertebral body strength (N/cm²/mg)</td>
<td>0.58 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>Bending stiffness/axial stiffness (mm²/rad)</td>
<td>94.0 ± 15.8</td>
</tr>
<tr>
<td></td>
<td>Vertebral body strength/Ave. CSA (MPa)</td>
<td>8.16 ± 1.43</td>
</tr>
</tbody>
</table>

Main effect: a: sex-related difference; b: age-related difference; c: vertebral level-related difference (p < .0125).
Interactions: d: sex-age interaction; e: age-vertebral level interaction (p < .0125).
Post-hoc analysis: †significant difference between old and young (same sex and vertebral level, p < .0125); ‡significant difference between women and men (same age and vertebral level, p < .0125).
Discussion

In this study we used QCT-based FEA of lumbar and thoracic vertebrae of young and old men and women to determine age-related changes in mechanical strength, bone mass, and bone density of cortical and trabecular bone compartments. As expected, vertebral strength decreased with age for both men and women, but it decreased more dramatically in women than in men because of a greater decline in bone mass in both trabecular and peripheral bone compartments. Notably, in men there was little age-related decline in peripheral bone strength. These results provide evidence of a different compartment-specific pattern of age-related decline in vertebral bone mass and strength in women vs. men that may contribute to the higher incidence of vertebral fractures among women.

As expected, compressive strength predicted by finite element analysis was higher in men than women, and higher in L3 than T10, both of which can largely be explained by differences in bone size. It has previously been shown that vertebral compressive failure loads are lower in women, but estimated failure stresses are similar in both sexes, suggesting that vertebral size explains much of the difference in compressive failure loads between men and women. Our data support this, as both compressive strength and average vertebral cross-sectional area are larger in men than women, but no sex-related difference in estimated failure stress (vertebral body strength/average CSA) was observed. Similarly, previous studies have reported variation in compressive strength of human cadaveric vertebrae along the thoracic and lumbar spine, with an increase in vertebral compressive failure load and a decrease in estimated failure stress (failure load / average vertebral cross-sectional area) from the thoracic to lumbar spine. We observed a similar pattern, because T10 failure stress was higher than L3 failure stress for all groups. For these calculations we used the average CSA of the vertebral bodies. It is possible that minimum CSA instead of average CSA would yield different results for estimates of failure stress. Unfortunately, we are unable to calculate minimum CSA using our current software. However, we predict that differences observed between young and old and between thoracic and lumbar vertebrae will be maintained whether we normalize by average CSA or minimum CSA. In the absence of minimum CSA measures, geometric strength can

Fig. 3. Results for density and mass variables. Bone mass and density declined with age in both the peripheral (cortical) and trabecular compartments of T10 and L3, with women exhibiting significantly greater losses than men. Total vertebral body density declined significantly more with age in women than in men, with declines in both trabecular and peripheral bone density for women, while men had smaller declines in trabecular bone density and either no decline or only a small decline in peripheral density.

for old men, $r^2 = 0.55$ for young women, $r^2 = 0.50$ for old women).
provide similar information, because it is a strength measure that is wholly dependent on geometry (and presumably minimum CSA).

In contrast to sex-specific differences, age-related differences in compressive strength cannot be explained by changes in bone size but rather are due primarily to changes in bone mass and density. Geometric strength, a measure of the isolated contribution of bone geometry to compressive strength, was higher in old subjects than in young subjects, indicating that considering only bone size/geometry, older subjects have stronger

Fig. 5. The proportion of vertebral strength attributable to the peripheral compartment increased with age from 43% to 57% for L3 and 43% to 51% for T10 in women and from 42% to 53% for L3 and 39% to 47% for T10 in men (no significant difference between men and women).

Fig. 4. Results for strength variables. Vertebral body strength declined with age for both men and women, with women exhibiting significantly greater losses of strength than men. Trabecular strength declined significantly for both sexes, while peripheral strength declined 4- to 10-fold more with age in women than in men. Similarly, bending stiffness declined significantly with age in women but did not change in men.

Fig. 6. There was a moderately strong correlation between compressive strength values for L3 and T10 when all subjects were considered together ($r^2 = 0.77$). When each age-sex group was plotted independently, the correlation between vertebral body strength for L3 and T10 was higher for men than for women and higher for young subjects than for old subjects ($r^2 = 0.69$ for young men, 0.59 for old men, 0.55 for young women, 0.50 for old women).
vertebrae than young subjects, but this age-related increase in geometric strength was generally small and did not offset age-related declines in overall vertebral strength. This finding is supported by previous studies that have shown an increase in cross-sectional area of vertebral bodies with age.\(^5\)\(^,\)\(^6\) However, it is well established that volumetric bone density (vBMD) declines in both men and women with age, resulting in an overall loss of vertebral body strength. Previous studies have shown that vBMD is similar in young men and women,\(^5\)\(^,\)\(^6\)\(^,\)\(^,\)\(^,\)\(^,\)\(^3\)\(^,\)\(^,\)\(^3\)\(^,\)\(^,\)\(^,\)\(^,\)\(^4\) and may even be slightly higher in women,\(^5\)\(^,\)\(^6\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(\)
method used to assess “peripheral” properties (e.g., total strength – trabecular strength) ignores load sharing between the two compartments. A thorough analysis of load sharing between trabecular and cortical bone would require a high-resolution micro-CT-based analysis.\(^{(13)}\) Unfortunately, because of the resolution used to obtain the CT scans in this study, this type of analysis was not possible. However, the contributions of the individual compartments that we calculate with continuum models in the current study is consistent with what Eswaran reported with the micro-CT-based models, which suggests that by taking off the 2 mm of bone, we are effectively removing the cortical shell (about 0.4 mm thick) and adjacent trabeculae that would be unloaded upon removal of the cortical shell. Therefore, we conclude that removal of the outer 2 mm in the continuum models provides a good estimate of the results that would be obtained with removal of just the real cortical shell — because for the latter, the adjacent trabeculae become unloaded since there is no cortical shell to transmit load in the vertical direction to and from these trabeculae.\(^{(13)}\)

**Conclusions**

Decreases in vertebral strength occur differently with age for men and women, particularly in the peripheral (cortical) compartment. Whereas women lost bone mass and bone strength in both the cortical and trabecular compartments with age, men primarily lost bone mass and strength from the trabecular compartment, while cortical bone properties did not decrease with age. Combined with the increased mechanical role of the cortical compartment with age, this presents a potential mechanism that may contribute to the disparate incidence of vertebral fractures in women and men.

**Disclosures**

Tony Keaveny and David Kopperdahl have financial interests in O.N. Diagnostics. All the other authors state that they have no conflicts of interest.

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