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Effects of loading orientation on the morphology of the predicted yielded regions in trabecular bone

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Abstract

While the effects of bone mineral density and architecture in osteoporotic bone have been studied extensively, the micromechanics of yielding and failure have received less attention. However, understanding architectural features associated with failure should provide insight into assessing bone quality. In this study, microstructural finite element models were used to compute regions of tissue level yielding in ten bovine tibial trabecular bone samples. The morphology, number, and mean volume of the yielded regions were quantified for four apparent strains under two loading conditions. For on-axis loading, the mean aspect ratio of the tissue that yielded due to compressive strain increased with increasing apparent strain, expanding along the principal trabecular orientation. This suggests that tissue level yielding progresses along vertical trabeculae when a specimen is loaded on-axis. The number, but not the volume, of the regions yielded due to tensile strain increased with increasing applied load, consistent with relaxation and redistribution of stresses around the yielded regions. When the specimens were compressed perpendicular to the principal axis, the aspect ratio of the yielded regions was close to one, while the number, mean volume, and mean thickness of the yielded regions increased. This indicates that localized high strains consistent with bending rather than axial deformation of struts occur at the tissue level. Overall, the results provide new insight into trabecular bone failure, which is relevant to assessing diagnostic tests for fracture risk or evaluating osteoporosis treatments.

Keywords

trabecular bone; architecture; finite element analysis; morphology

Introduction

Trabecular bone mechanics play an important role in osteoporosis and increased fracture susceptibility. The mechanical properties of trabecular bone depend on both the volume fraction and the architecture, or physical arrangement of the solid bone tissue. It has been hypothesized that trabecular bone architecture adapts to have its principal material axes oriented along the most common loading directions.¹ This adaptation results in a morphologically and mechanically anisotropic structure. Theoretical relationships between the apparent elastic properties and morphological parameters that describe the architecture of trabecular bone, such as volume fraction and fabric, explain over 90% of the variation in the apparent elastic properties.^{2–6} Similar relationships between fabric and damage behavior have been proposed and validated.⁷ However, these relationships are phenomenological and, as such, do not fully explain the role of individual trabecular structures. Trabecular bone

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morphology changes with aging and bone density.^{8, 9} As such, understanding the relationship between trabecular architecture and failure progression could provide insight into the role of trabecular architecture in age-related bone diseases.

Micro-Finite Element Analysis (micro-FEA) has become a powerful tool for investigating damage and failure in trabecular bone. Regions of experimentally labeled microdamage corresponded to areas of high von Mises stress and strain calculated from micro-FEA.¹⁰ In nonlinear simulations, smaller volumes of tissue yielded during transverse vs. on-axis loading of trabecular bone,¹¹ and the effects on residual modulus were similarly smaller.¹² Due to thinning of trabeculae¹³ or conversion of trabecular plates to trabecular rods,⁸ strain magnitudes in osteoporotic bone are much higher and have greater variability than in healthy bone.¹⁴ *In vivo* microcrack density was related to the calculated range and variability of von Mises stress in human vertebral trabecular tissue.¹⁵ Recently, micro-FEA results were processed using a trabecular classification scheme to quantify the relative roles of plate-like and rod-like trabeculae in the elastic behavior of trabecular bone,¹⁶ and similar analyses could be applied to nonlinear models. Alternatively, morphological analysis of highly stressed or yielded regions could be used to statistically describe tissue level failure in trabecular bone.

While nonlinear finite element models can provide details of tissue level yielding in trabecular bone,^{17, 18} it is difficult to interpret the results in terms of biomechanics due to the geometric complexity, the heterogeneity of trabecular bone, and the quantity of data produced by the models. Morphological parameters exist to describe the orientation, shape, and size of structures. These parameters could be used to describe and interpret tissue level yielding in trabecular bone. Therefore, the objective of this study was to investigate the effects of loading orientation on the morphology of the predicted regions of tissue level yielding in trabecular bone. Specifically, 1) microstructural finite element models were used to identify regions of tissue level yielding in trabecular bone; 2) the morphology, number, and mean volume of the yielded regions were quantified; and 3) the results were compared for on-axis and transverse compression at four different apparent strain levels.

Materials and Methods

Ten cylindrical bovine proximal tibial trabecular bone specimens from a previous study¹⁹ were analyzed. The orientation of the specimens was controlled using micro-CT imaging to ensure that the principal trabecular orientation was aligned with the axis of the specimens.²⁰ The specimens were scanned at 20 μm resolution in a micro-CT scanner (μCT -80, Scanco Medical AG, Brüttisellen, Switzerland). The architecture of the samples was quantified using the analysis application from the micro-CT scanner (Scanco μCT Evaluation program V4.3, Table 1). The threshold used to segment the images was calculated by obtaining a volume fraction equal to that based on Archimedes' Principle. This has been shown to result in more accurate model behavior.²¹⁻²³

Microstructural finite element models were created for each specimen by directly converting bone voxels into eight-node finite elements.²⁴ Cuboid regions approximately $5 \times 5 \times 6 \text{ mm}^3$ in size were taken out of the cylindrical specimens. The images were region-averaged by assigning the mean value of each $2 \times 2 \times 2$ grouping of voxels to a single 40 μm isotropic voxel to reduce computational expense. The mean trabecular thickness of the samples was 184 μm , on average, giving an element size approximately one-fourth the mean trabecular thickness, as suggested for model convergence.^{21, 25, 26} The trabecular tissue was modeled as a homogenous isotropic material with a specimen-specific back-calculated tissue modulus based on previous experimental measurements of the modulus (Fig. 1).²⁷ Poisson's ratio was assumed to be 0.3. A bilinear elastic model with an asymmetric principal strain tissue yield criterion¹⁸ was applied with compressive and tensile yield strains of 0.83% and 0.41%, respectively.²⁸

This material model provides good prediction of the apparent level yield behavior of trabecular bone.^{12, 18, 28, 29} Each sample was analyzed twice, with boundary conditions corresponding to 1.2% on-axis compressive strain or 1.2% transverse compressive strain. On-axis loading is typical of the activities of daily living, in the sense of Wolff's law,¹ while transverse loading was chosen as an example of an off-axis, or abnormal, load. Geometric nonlinearity was not included, but the effects would be small for dense bone samples and low apparent strains such as those used here.²²

The tissue strains were found from the incremental solutions. At each of the apparent strain levels of interest, the tissue level strains in each voxel were output to a file. Due to the porosity and architecture of trabecular bone, bone tissue can yield due to either compressive strain or tensile strain under apparent compressive loading. The regions of tissue that yielded due to exceeding the compressive or tensile strain limits (0.83% or 0.41% strain) were identified and segmented at each of 0.6%, 0.8%, 1.0%, and 1.2% apparent strains. If the tissue strains were such that both limits had been exceeded, the limit that was exceeded by the greater proportion was assigned. Morphological analysis (IPL, Scanco Medical AG, Brüttisellen, Switzerland) was applied to the segmented images to obtain the fabric tensor, the Structure Model Index (SMI), and the mean thickness of the yielded tissue. The ratio of the largest to the smallest eigen value of this fabric tensor was used as an estimate of the aspect ratio of the yielded regions, and the mean orientation of the yielded regions was found from the eigen vectors of the fabric tensor.

Connected component labeling³⁰ was used to determine the number and mean volume of the yielded regions. Many small clusters of yielded voxels occur in the model, with the smallest likely due to numerical errors caused by the voxel based discretization. Within each sample, only regions containing more than 27 voxels (0.002 mm³) were analyzed, in order to improve the efficiency of the calculation. The analysis was repeated using a minimum region size of 16 voxels (0.001 mm³) to assess the effects of eliminating small regions.

The effects of both loading orientation and apparent strain on the morphology, number, and mean volume of the yielded regions were quantified. Linear regression was used to examine the relationships between the aspect ratio of the yielded regions with the architectural parameters of the samples. Relationships between the number and mean volume of the yielded regions and the architectural parameters of the samples were also examined. Statistical analysis was performed with Student's *t*-test in Microsoft Excel. The significance level was 0.05. The Tukey post-hoc test was used to identify groups with significant differences for ANOVA using JMP IN 5.1 (SAS Institute Inc., Cary, NC).

Results

The aspect ratio of the yielded regions depended on the loading direction. When the specimens were loaded on-axis, the aspect ratio of the regions that yielded due to compressive strain increased from 1.23 ± 0.08 (mean $\pm$ S.D.) at 0.8% apparent strain to 1.41 ± 0.11 at 1.2% apparent strain ($p < 0.001$, Fig. 2a). At 0.6% apparent strain, the data were not analyzed because the volume of the yielded regions was too small to obtain a fabric tensor. The aspect ratio of the regions yielded due to compressive strain was higher than that of those yielded due to tensile strain at all apparent strain levels ($p < 0.002$). On average, the regions of tissue that yielded due to tensile strain had an aspect ratio of 1.10 ± 0.04 , independent of the applied apparent strain ($p > 0.9$, Fig. 2a). During transverse compression, regions yielded due to both tensile and compressive had a mean aspect ratio of 1.19 ± 0.07 (Fig. 2b). This is nearly isotropic in comparison to the aspect ratio for on-axis loading, considering that aspect ratios less than 1.0 are not possible using this method. The aspect ratio of the regions yielded due to compressive

strain did not change with apparent strain, while a slight decrease was seen for regions yielded due to tensile strain.

The orientation of the yielded regions also differed between on-axis and transverse compression. At 1.2% apparent compressive strain along the principal axis, regions yielded due to compressive strain were oriented $3 \pm 3^\circ$ from the loading direction, in contrast to those yielded due to tensile strain, which were $46 \pm 17^\circ$ from the loading direction, on average ($p < 0.001$, Fig. 2c). At 1.2% apparent compressive strain in the transverse orientation, regions that yielded due to compressive strain were oriented $12 \pm 9^\circ$ from the loading direction, while those yielded due to tensile strain were $58 \pm 18^\circ$ from the loading direction, on average ($p < 0.001$, Fig. 2d). The yielded regions for transverse loading were within the transverse plane ($78 \pm 10^\circ$ from vertical), but they were not aligned with the second or third fabric eigen vector of the whole bone sample, which were not necessarily aligned with the loading direction.

Three-dimensional visualization was used to qualitatively characterize the yielded regions. For on-axis loading, tissue yielded due to compressive strain expanded along the vertical trabeculae with increasing apparent strain, while tissue yielded due to tensile strain expanded uniformly. For transverse compression, yielding appeared mainly at locations where trabeculae branch or merge (Fig. 3).

The architecture of the samples affected the aspect ratio of the yielded regions. The aspect ratio of the regions that yielded due to compressive strain was positively correlated with the degree of anisotropy of the samples for 1.2% apparent on-axis strain (Fig. 4), in contrast to 1.2% apparent transverse strain where the aspect ratio of the regions that yielded due to tensile strain was positively correlated with the degree of anisotropy of the samples. For both on-axis and transverse loading, the aspect ratio of the regions yielded due to compressive strain was positively correlated with trabecular thickness (Fig. 5) and volume fraction of the samples, while the aspect ratio of the regions yielded due to tensile strain was not.

Yielding was localized and, on average, did not progress across whole trabeculae. The SMI of the yielded regions ranged from 3.57 ± 0.09 to 4.92 ± 0.14 , indicating that the yielded regions were mostly connected or disconnected rod-like. In on-axis compression, the mean thickness of the tissue yielded due to compressive strain was less than one-third of the trabecular thickness at 0.6% apparent strain but increased to more than one-half of the trabecular thickness at 1.2% apparent strain. The mean thickness of the tissue yielded due to tensile strain was about one-third of the trabecular thickness at all apparent strain levels (Fig. 6). In contrast, for transverse compression, the mean thickness of all yielded regions was approximately one-third of the trabecular thickness at all apparent strain levels.

The volume of the tissue that yielded increased with increasing apparent strain, but through differing processes for on-axis vs. transverse loading. In on-axis compression, the number of regions that yielded due to compressive strain was unchanged, on average, as the apparent strain increased from 0.8% to 1.2% ($p > 0.05$). In contrast, the number of regions that yielded due to tensile strain was higher at successively higher apparent strain levels ($p < 0.01$, Fig. 7a). There was a six-fold increase in the volume of regions that yielded due to compressive strain and a two-fold increase in the volume of regions that yielded due to tensile strain (Fig. 7c). When subjected to transverse loading, the number of the regions yielded increased with increasing apparent strain ($p < 0.01$, Fig. 7b). Only approximately 15% more regions yielded due to tensile strain than due to compressive strain. The mean volume of both the compressively and tensilely strained regions also increased with increasing apparent strain ($p < 0.01$), with no difference between compressively and tensilely strained regions ($p > 0.59$, Fig. 7d). The equal number and volume of yielded regions is consistent with bending with superposed axial compression for the tissue level yield criterion employed in the models.

The elimination of small clusters of yielded voxels did not affect the results. Regardless of the criterion for ignoring small regions, the data showed the same trends.

Discussion

Understanding the failure mechanisms in trabecular bone can provide insight into bone fragility, and more importantly identify the mechanisms by which architectural features affect strength. Micro-FEA has become a standard tool for studying trabecular bone mechanics, but interpretation of the results is complicated due to the volume of data produced and the need to aggregate data across a population. We applied morphometric analysis to quantify, in a statistical manner, the results of micro-FEA analyses of initial material failure in trabecular bone compressed along two orthogonal axes. The degree of anisotropy, orientation, mean thickness, number, and mean volume of the yielded regions all showed distinct characteristics for the two loading modes. In axial compression along the principal material direction, the yielded tissue was oriented parallel to the principal trabecular orientation and loading axis. Although yielding was dominated by axial compression of trabeculae, the tissue yielding did not progress completely across the struts, indicating that trabeculae were subjected to bending, even in this ideal loading case. Regions of tensile yielding were small in volume, had uniformly distributed shapes, and the number of regions increased more than the volume with increasing apparent strain. As such, tensile yielding results in local relaxation of stresses and redistribution to other sites. When the apparent loading was normal to the principal trabecular orientation, neither the compressively nor the tensilely strained regions were clearly elongated, but they were generally within the transverse plane perpendicular to the vertical trabeculae. Moreover, the regions were less than one half of the mean thickness of the trabecular struts, and the number and mean volume of the yielded regions both increased uniformly with increasing apparent strain. Together these findings are consistent with bending of the trabeculae and the formation of plastic or damage “hinges”.³¹

The novelty of this study is the application of morphometric techniques to extract information from nonlinear micro-FEA models. By focusing on two loading modes from a single anatomic site, it was possible to investigate the transition from normal physiologic loading to an abnormal configuration. The normal loading produced axial deformation of the trabeculae, while the transverse load resulted in bending of trabeculae. In this way, morphometric features of the yielded regions consistent with both axial deformation and bending could be identified.

There are some limitations to the current results. For example, direct application to human bone, especially in the case of osteoporosis or aging, is limited. However, the results do provide insight into the expected behavior of human trabecular bone at locations such as the proximal femur where density and architecture are similar to these specimens. The tissue yield criterion used in the simulations was calibrated for human femoral trabecular bone tissue rather than bovine bone.²⁸ Indeed, although micro-FEA models have been widely applied to analyze trabecular bone mechanics, direct validation of tissue level stresses and yielding has not been performed. However, correlation of tissue level damage to high-stress regions in micro-FEA models,¹⁰ and the general agreement between models and experiments at the apparent level suggest that the aggregate data are valid. As such, the results are representative even though they were not directly validated. Finally, geometric nonlinearity was not considered in the simulation, but the effects are small for dense bone, especially at the low strains studied here.²²

Incorporation of tissue level heterogeneity based on mineralization levels could affect the model results.³²⁻³⁴ The young bovine bone used in this study was relatively homogeneous. As such, a single homogeneous modulus was defined. However, heterogeneous properties may be important for human bone.

Validation of the models by comparing the predicted regions of yielding to experimentally measured damage would be valuable. Histologically measured damage has been associated with highly stressed regions calculated by micro-FEA models.¹⁰ More recently three-dimensional techniques have been developed for quantifying microdamage in trabecular bone,^{35, 36} but these techniques are still under development and were not applied to the bone samples studied here.

The results provide insight into the mechanisms of microdamage formation in experimental studies. When samples were subjected to compressive overloading, the microcrack density and diffuse damage area were lower in specimens with greater trabecular thickness.³⁷ The morphological analysis found that the aspect ratio of the regions yielded due to compressive strain was higher in specimens with thicker trabeculae, which is consistent with greater axial deformation and less bending. Moreover, the greater aspect ratio is consistent with less variability in tissue level stresses, which was correlated with lower microdamage in experiments.¹⁵ Taken together, trabecular bending may increase susceptibility to microdamage. The information will be especially useful in studying microdamage generation and propagation in osteoporotic bone, since osteoporotic bone has thinner trabeculae¹³ which are more prone to bending.

The results also complement previous computational studies of trabecular bone failure. Models of equi-biaxial compression found that micromechanical failure mechanisms for on-axis and transverse loading are largely uncoupled.²⁹ This is reflected in the differing orientations of the yielded tissue that were found for the two loading cases. This may allow trabecular bone to tolerate damage from one loading direction without compromising its structural integrity along the perpendicular directions. The computational results are consistent with experiments that showed overloading in vertebral trabecular bone had little effect on the mechanical properties along an orthogonal axis.³⁸

Morphological analysis of the yielded regions from nonlinear micro-FEA simulations was found to be a valuable means for interpreting the large complex result sets that were produced by this method. Using mechanistic interpretations and comparing to previous experimental and analytical models, it is possible to gain insight into the development of tissue level failure with respect to the trabecular architecture. This technique provides a new tool for trabecular bone mechanical analysis that can be used to assess the progression of osteoporosis and the effect of treatments.

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(a)

(b)

Figure 1.

(a) Schematic of the bilinear tissue level constitutive model (not to scale). The elastic constants of the tissue were decreased isotropically when the principal strains exceeded either the tensile (0.41%) or compressive (0.83%) tissue yield strain. (b) A typical apparent level stress-strain curve for one of the specimens during on-axis loading.

Figure 2.

Mean aspect ratio (a, b, * $p < 0.002$) and principal orientation (c, d, * $p < 0.02$) of the yielded regions for on-axis and transverse loading. Error bars are one standard deviation ($n = 10$). Bars marked by the same letter are not significantly different ($p < 0.05$ ANOVA).

Figure 3.

Visualization of the yielded tissue regions. Blue regions indicate tissue yielded due to compressive strain and red due to tensile strain. Arrows indicate the apparent loading direction. The vertical direction corresponds to on-axis loading.

Figure 4.

At 1.2% apparent strain, the aspect ratio of the regions yielded due to compressive strain for on-axis compression and that of the regions yielded due to tensile strain for transverse compression were correlated with the degree of anisotropy of the samples.

Figure 5.

The aspect ratio of the tissue that yielded due to compressive strain was correlated with the trabecular thickness of the specimens for both on-axis and transverse loading. The aspect ratio of the tissue that yielded due to tensile strain was independent of trabecular thickness.

Figure 6.

The ratio of the mean thickness of the yielded regions to the mean trabecular thickness of the samples at each apparent strain level for on-axis and transverse loading. The ratio increased with increasing apparent strain for both loading modes ($p < 0.0001$). * indicates differences between compressive and tensile yielding within on-axis loading ($p < 0.05$), while + indicates differences between compressive and tensile yielding within transverse loading ($p < 0.05$). Error bars are one standard deviation ($n = 10$).

Figure 7.

The number (a, b) and mean volume (c, d) of the yielded regions at each apparent strain level for on-axis and transverse compression. Error bars are one standard deviation ($n = 10$). Bars marked by the same letter are not significantly different ($p < 0.05$, ANOVA). Note the different scales between on-axis and transverse loading. * indicates $p < 0.05$.

Table 1

Structural parameters of the samples (n = 10)

Parameters ^a	Mean	S.D.	Range
VF ^b	0.243	0.044	0.190 - 0.320
Tb.Th. (mm)	0.184	0.034	0.133 - 0.235
Tb.Sp. (mm)	0.606	0.080	0.467 - 0.700
SMI	0.568	0.391	-0.131 - 1.078
Conn.D. (1/mm ³)	5.410	2.674	2.611 - 11.449
DA	1.828	0.195	1.603 - 2.265

^aVF = volume fraction; Tb.Th. = trabecular thickness; Tb.Sp. = trabecular spacing; SMI = structure model index; Conn.D. = connectivity density; and DA = degree of anisotropy.

^bMeasured by Archimedes' Principle.