## Anisotropy and Heterogeneity in Finite Element Models of Trabecular Bone Alters Expected Failure Outcomes

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INTRODUCTION: At the nanoscale bone is composed of aligned mineralized collagen fibrils organized into packets along the surface of trabecular bone creating an anisotropic tissue microstructure. Newer packets at the trabecular surfaces are usually less mineralized than older bone in the interior of the trabeculae, which along with irregular mineral deposition within packets, forms a heterogeneous material across the span of a trabeculae. However, finite element (FE) models of bone typically use homogenous isotropic material properties, because it is challenging to build anisotropy and heterogeneity into a model in a way that is applicable to the complex geometries of trabecular bone. Both the material anisotropy and heterogeneity may influence the stress state of trabecular bone, and it is important to understand the implications of such differences for determining bone biomechanical failure. It was hypothesized that taking into consideration both the tissue anisotropy and heterogeneity of bone's biomechanical properties would alter the expected failure locations by reducing tensile stress on near surface elements of an FE model of canine trabecular bone. The objective of this study was to test this hypothesis and to develop a method to apply anisotropic and heterogeneous material properties to a model automatically from micro-computed tomography (μCT) data.

METHODS: A vertebral body from a female beagle (part of a previously IACUC-approved study) was imaged with a Skyscan 1172 μCT using a voxel size of 5.88 μm. A mesh was generated from a 3.0 mm cube of trabecular bone using ScanIP, resulting in a FE mesh with over 6.8 x 10<sup>6</sup> linear tetrahedral elements. A custom MATLAB code, developed by the authors, was used to calculate (i) the surface normal, (ii) the distance to the closest surface, and (iii) the local coordinate system for each element of the model. Surfaces created on the edges of the isolated cube were excluded from the calculation to avoid associated artifacts. Based on the local directions computed, tissue anisotropy was then added by assigning transversely isotropic material properties to each element. The ratios of the in-plane to out-of-plane elastic modulus, Poisson's ratio, and shear modulus vere 2.0, 1.25, and 1.5, respectively, and reflect expected anisotropy levels. In-plane values were used for the isotropic cases. From the average grayscale value of each element, tissue heterogeneity was added to the model by scaling the in-plane elastic modulus to the calibrated material density. The average grayscale of the entire model was used to assign the moduli of the homogenous cases. Uniaxial compression of the virtual bone cube was simulated using ABAQUS FE-code. The principal stress with the largest absolute value (as a metric of failure onset) and the distance to the nearest trabecular surface was extracted at the centroid of each element. Cumulative distribution functions of the extracted stress were generated for elements within (a) 5 μm of the surface (1.7 x 10<sup>6</sup> elements) and (b) greater than 50 μm from the surface (2.7 x 10<sup>5</sup> elements). Four cases were compared: isotropic homogenous (IsoHmg), isotropic heterogeneous (IsoHtg), anisotropic homogenous (AnisoHtg).

RESULTS: Both cases incorporating mineral heterogeneity had a distribution shifted towards lower magnitudes of compressive and tensile principal stresses for the near surface elements (Fig. 1). However, adding heterogeneity shifted distributions to higher magnitudes of compressive stress for interior elements (Fig. 2). Incorporating anisotropy did not alter the principal stress distribution for either the homogenous or the heterogeneous case for the near surface elements (Fig. 1) and only slightly shifted the distribution of tension-dominated interior elements to lower values (Fig. 2). Anisotropy in the model reduced the maximum principal stress by 48%–68% for the near surface elements of both cases (Table 1). Heterogeneity in the model produced similar reductions of maximum principal stress for near surface elements. Interestingly, anisotropy and heterogeneity combined reduced the maximum principal stress by 81% compared to the homogenous isotropic case while also altering the location where that peak stress occurred.

DISCUSSION: Heterogeneity alone redistributed stress from the near surface elements to the presumably older bone located within the interior of the trabeculae due to the stiffer interior bone exerting a stress shielding effect for the weaker less mineralized surface. The lower stress experienced by the surface likely will reduce the volume susceptible to damage (Fig. 1 and Fig. 2). Anisotropy did little to change the overall spatial distribution of stress, but rather exerted its effects mainly through reducing the maximum principal stress near the trabecular surface with slight effects on minimal principal stress and interior stresses (Table 1). Heterogeneity also reduced maximum and minimum principal stress, but the effects were moderate for interior elements. Because bone is weaker in tension than compression, the predicted reduction of the maximum principal stress would be especially relevant for bone failure predictions. The importance of adding heterogeneity and anisotropy to trabecular bone models is apparent because changes to predicted stress values are large enough to reduce a peak tensile stress that would cause failure in the homogenous isotropic case to one that likely would not cause failure in the anisotropic heterogeneous case. Additionally, because the location of the peak tensile stress is also changing, anisotropy and heterogeneity are important factors for predicting where failure occurs. A limitation of this study is that actual failure mechanisms were not accounted for, so the redistribution of stress due to damage initiation is not yet predicted. This will be addressed in future studies along with the effects of anisotropy on damage propagation. Canine trabecular bone was selected for this study, and while similar outcomes are expected for other samples of trabecular bone, more work is needed to observe the impacts in other models, anatomical sites, and disease states with varying microarchitecture. The true anisotropic behavior of bone is more complicated than the transverse isotropy applied in the current study, and future work to refine the material definitions to better mimic bone is underway. In conclusion, this study demonstrates the importance of assigning anisotropic heterogeneous material properties to trabecular bone models when failure is expected, and we present how such information can be extracted automatically from μCT.

SIGNIFICANCE: FE models of bone typically assume homogenous isotropic material properties despite it being well appreciated that bone is anisotropic and heterogeneous. This study utilized a novel method to assign anisotropy and heterogeneity automatically from  $\mu$ CT data and assessed the effects on the stress distribution and peak stresses at the near surface and interior of trabeculae. Understanding the role these more complex material definitions play in determining possible failure zones and utilizing a method to automate their application is a critical next step to accurately predict damage accrual in bone.

## IMAGES AND TABLES:

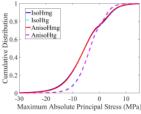


Figure 1. Near surface stress distributions

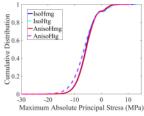


Figure 2. Interior stress distributions

Table 1. Maximum and minimum principal stress

	Near surface		Interior	
	Max (MPa)	Min (MPa)	Max (MPa)	Min (MPa)
Iso Hmg	247	-676	12	-33
Iso Htg	144	-427	15	-40
Aniso Hmg	132	-622	10	-29
Aniso Htg	46	-393	13	-36