INTRODUCTION: Mechanical properties of cancellous bone are primarily dependent upon its apparent density. However, the variation of cancellous bone microstructure at a given volume fraction level results in stiffness and strength variations much higher than those observed in most other cellular solids. The complex interaction of volume fraction and microstructure compounded by other issues such as increasing deviation from continuum mechanics principles (e.g. highly osteoporotic samples), loading direction, anatomic site and intraspecimen variations in addition to artifacts associated with mechanical testing protocols have hindered efforts to reach a consensus on the nature of the relationship between bone mechanical properties and its failure behavior. This is especially important for specimens from osteopenic patients, where bone volume fraction (BV/TV) is considerably lower than those observed in normal bone. This results in greater specimen inhomogeneity and further reduces the ability to average the microscopic indices to describe failure behavior. To this end, we aim to show that the mechanical behavior of a specimen at the lower range of the BV/TV scale manifests itself differently from that of an average or high density specimen, where instead the BV/TV of the weakest sub-region is a better predictor of failure than average BV/TV, and that a combination of microstructural indices from sub-regions of failure incorporated in a statistical model could be used to increase the predictive power of failure for such bones.

METHODS: A group of 25 human vertebral cancellous bone specimens were cored parallel to the anatomical axis from thoracic and lumbar regions of two donors. The specimens were assessed using image guided failure assessment (IGFA), a technique combining step-wise micro-compression and micro-computed tomography (μCT). IGFA was used to generate animations in order to visually identify the region(s) of failure (FX) and non-failure (NF) for each specimen. Conventional 3D morphometry was applied to all specimens to compute BT/TV, bone surface density (BS/TV), connectivity density (Conn.D), structure model index (SMI), trabecular spacing (TB.Sp), degree of anisotropy (DA), trabecular thickness (TB.Th), trabecular separation (TB.Sp) and mean intercept length (MIL) vectors (H1, H2, H3). Bone volume fraction was computed for the full specimens as well as for ten equal subregions along the loading axis. Multivariate stepwise logistic regression based on maximum likelihood estimation (MLE) was used to identify significant predictors of failure using the aforementioned morphometric indices as candidate variables tested in the model. Model fit was evaluated by the Hosmer-Lemeshow statistic using a chi-square distribution. Probability of failure was derived for combinations of the multivariate predictors using an exponential logistic equation with the fitted regression coefficients based on MLE.

RESULTS: Average bone volume fraction for the 25 specimens ranged from 4.2% to 12.3%, whereas the volume fraction range for the weakest sub-region ranged from 3.1% to 7.4% only. A power law model with BV/TV as the independent parameter described only 38% of the variation in the yield strength; however, the predictive power was increased to 56% when the BV/TV of the weakest sub-region for each specimen was considered as the independent parameter. Statistical analysis yielded significant differences in 8 morphometric indices between FX and NF regions. These indices included: BV/TV, BS/TV, Conn.D (all p<0.01) and SMI, TB.Sp, H1, H2, and H3 (all p<0.05). Multivariate logistic regression with the candidate variables consisting of the 8 significant parameters from univariate analysis resulted in a final model including 3 independent predictors. These parameters included: BV/TV, H1, and Conn.D (Likelihood ratio test (LRT) = 11.69, 12.91 and 21.31 respectively, all p<0.001). Coefficients from the logistic regression equation were used to derive a failure probability model (FPM) using the 3 independent variables (Equation 1). Varying the BV/TV values from 5-15%, the Conn.D from 1-4 and from 1-4, four graphs were generated to predict fracture (Figures 1-a, 1-d). As the range of Conn.D is increased from 1 to 4, the probability of failure is decreased dramatically for all H1 and BV/TV values.

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FPM = \frac{(2-1.2\text{Conn.D} - 0.4\text{H}_1)}{(2-1.2\text{Conn.D} - 0.4\text{H}_1)}
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(Discussion) The specimens in this study represent the lower range of the volume fraction scale for human cancellous bone. The volume fraction range for the weakest sub-regions is noticeably smaller than the BV/TV range for the average specimens, suggesting that failure of the chain occurs at its weakest link. This notion is further strengthened by the significant increase in the predictive power of yield strength when BV/TV of the weakest sub-region is used instead of the average specimen BV/TV. The low predictive power of yield strength in these specimens, in comparison to previously reported data, might be partially explained by the low range of specimen BV/TV, causing deviation from continuum mechanics principles. Statistical analysis of morphometric indices obtained in this study suggested that 8 indices yielded significant differences between the FX and NF regions. However, further multivariate logistic regression revealed that only three indices yielded independent significant differences between the FX and NF regions. These indices, BV/TV, Conn.D and H2, were used to derive a failure probability model to help better predict failure in specimens in the lower BV/TV spectrum, an area where traditional average specimen parameters do not yield high predictive powers. We have shown that sub-regions with the lowest bone volume fraction values are better suited to predict mechanical failure in cancellous bone. This predictive power is augmented even more by taking into consideration additional microstructural indices, in an effort to generate a failure prediction model based on bone volume fraction and microstructural distribution of cancellous bone specifically in areas where failure is most likely to occur.

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