

The Mechanical Relevance of Secondary Osteon "Morphotypes": Implications for Accommodating Non-Uniform Strains and the Etiology of Stress Fractures

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Disclosures:

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Introduction: Important toughening mechanisms in cortical bone are variations in the distribution of secondary osteon collagen/lamellar "morphotypes". These microstructural variations correspond to the nonuniform strain distributions that are linked to habitual bending, which is typically experienced by many bones [1]. For example, significant regional variations in osteon morphotypes occur in the proximal femoral diaphysis (subtrochanteric region) where they are thought to help accommodate the nonuniform strain distribution of a high bending moment [2,3] (Fig. 1). These regional distributions of specific osteon morphotypes likely help curb deleterious differences in the incidence of microdamage that can occur between different regions of a bone as a result of habitual differences in prevailing strain mode (e.g., compression in the medial vs. tension in the lateral subtrochanteric region). Age- or drug-related (e.g., bisphosphonates) degradation of the maintenance of these regional microstructural variations are suggested to contribute to atypical or fragility fractures that occur in this and more proximal femoral locations [2]. In younger adults, osteon morphotypes help to avoid stress fractures by differentially toughening regions of the same bone for tension strains in some locations and compression strains in others. Nunamaker [4] suggested that failure to achieve this regional microstructural toughening as a result of race training leads to stress fractures in the third metacarpal (MC3) of thoroughbred horses. It is unclear what effect differences in the population densities of secondary osteon morphotypes have on bone mechanical properties. We used equine MC3s to test the hypothesis that osteon morphotypes enhance the energy absorption capacity of cortical bone to a greater extent than what has been described for more general regional variations in predominant collagen fiber orientation (CFO) [5].

Methods: Right and left MC3s from ten mature, non-elderly, horses with no racing history were tested in our prior study [5]. Briefly, six cubes (5mm/edge) for compression testing were cut from these regions: dorsal-lateral (D-L, n=2; 20 total specimens), lateral (L, n=1; 10 total specimens), palmar-medial (P-M, n=2; 20 total specimens) and dorsal-medial (DM, n=1; 10 total specimens). From contralateral bones, rectangular slabs were milled to dumbbell-shapes: two dorsal-lateral (D-L) and two palmar-medial (P-M) from each bone (Fig. 2). Cubic specimens were compressed to failure along the longitudinal diaphyseal axis (0.001/sec, strain-controlled). Tension data were obtained using an extensometer attached to each specimen while loaded to failure at 0.01/sec. Fractured specimens were analyzed for secondary osteon morphotypes in circularly polarized light (CPL) [1,5], and predominant CFO that was expressed in terms of weighted mean gray levels (WMGL) in CPL images [1]. For each image, secondary osteon morphotype scores (MTSs) were quantified [1] (Fig. 3). Additional data obtained from our prior study [5] included the population density of secondary osteons (OPD), osteon cross-sectional area, porosity, and percent ash (mineral) content. Pearson correlations were used to detect significant relationships between the material characteristics with six mechanical properties: Young's elastic modulus, yield stress, ultimate stress, pre-yield energy absorption, post-yield energy absorption, and total energy absorption (pre-yield + post-yield).

Results: Osteon MTS and predominant CFO were moderately correlated ($r = 0.58$ in compression tests; $r = 0.60$ in tension tests; $r = 0.63$ for all tests; $p < 0.01$). When considering all data: (1) osteon MTS correlated weakly with OPD ($r = 0.31$, $p < 0.01$) and ash content ($r = 0.25$, $p = 0.3$), and (2) CFO was only, and moderately, correlated with OPD ($r = 0.57$, $p < 0.001$). In tension tested specimens, neither osteon MTS nor CFO correlated with the mechanical properties. By contrast, in compression tested specimens osteon MTS or CFO showed the highest correlations when compared to all of the other material characteristics in terms of energy absorption: (1) osteon MTS was the second strongest correlate with total energy absorption ($r = 0.31$, $p = 0.03$); (2) CFO was the strongest correlate with pre-yield energy ($r = 0.30$, $p = 0.03$), post-yield energy ($r = 0.39$, $p < 0.01$), and total energy ($r = 0.47$, $p < 0.01$) absorption. These correlation coefficients improved by ~ 0.2 when considering compression tests of specimens from the regions that are naturally subject to higher levels of compression.

Discussion: Different osteon collagen/lamellar "morphotypes" modulate and optimize energy absorption for the locally prevalent strain mode [6-8]. Over time (months/years), different cortical regions can become highly populated with different morphotypes [1]. If the natural remodeling process is perturbed (e.g., excessive harsh/repetitive loading; bisphosphonate treatment), then it is hypothesized that non-specific microdamage can accumulate in some regions, in addition to the general reduction in the formation of 'beneficial' osteon morphotypes [2]. Our data show that distributions of specific osteon morphotypes have an important role in the post-yield behavior in compression, which is the habitual loading mode of the equine MC3 [9]. However, predominant CFO was an even stronger correlate in this context, and also with respect to pre- and post-yield energy absorption. This difference can be explained by the fact that approximately 40-60% of the regions analyzed were not remodeled with secondary osteons, which makes these equine bones different from the more highly remodeled secondary osteonal bone of adult humans. Consequently, a significant proportion of the regional CFO variations across the

equine MC3, including the more fracture prone dorsal-lateral cortex of racing animals, is only partially mediated by secondary osteons. In other words, the primary bone also exhibits preferred CFO (which *is* accounted for in CFO data but *not* MTS data). We speculate that regional variations in osteon morphotypes will have substantial greater mechanical relevance in bones that are more highly remodeled, including human bones prone to stress fracture (tibia, metatarsals, tibia). Our finding that osteon MTS and predominant CFO are only moderately correlated, and that each of these characteristics correlate much less strongly with OPD, are important considerations when attempting to extrapolate the pathogenesis of stress fractures in equine MC3s to stress fractures in human bones. We speculate that in more highly remodeled human limb bones regional variations in osteon morphotypes play a significant role in accommodating and regulating microdamage formation that is linked to behaviors of bone that we did not consider (e.g., fatigue, and initiation and propagation toughness). Additional studies are needed to test this hypothesis using specimens from human bones where stress and fragility fractures are known to occur as the result of harsh/repetitive activity or bisphosphonate use.

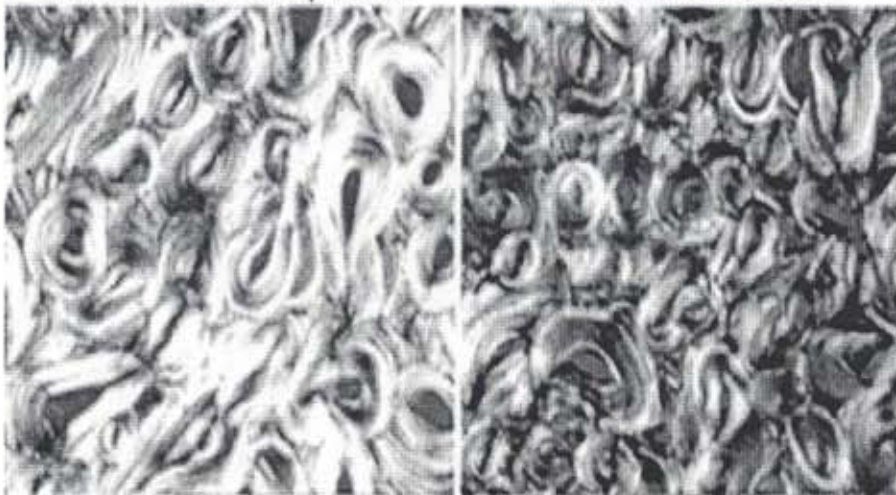
Significance: Regional differences in the microstructural organization of bone, especially secondary osteon morphotypes, have important functions in helping avoid fatigue and fragility fractures.

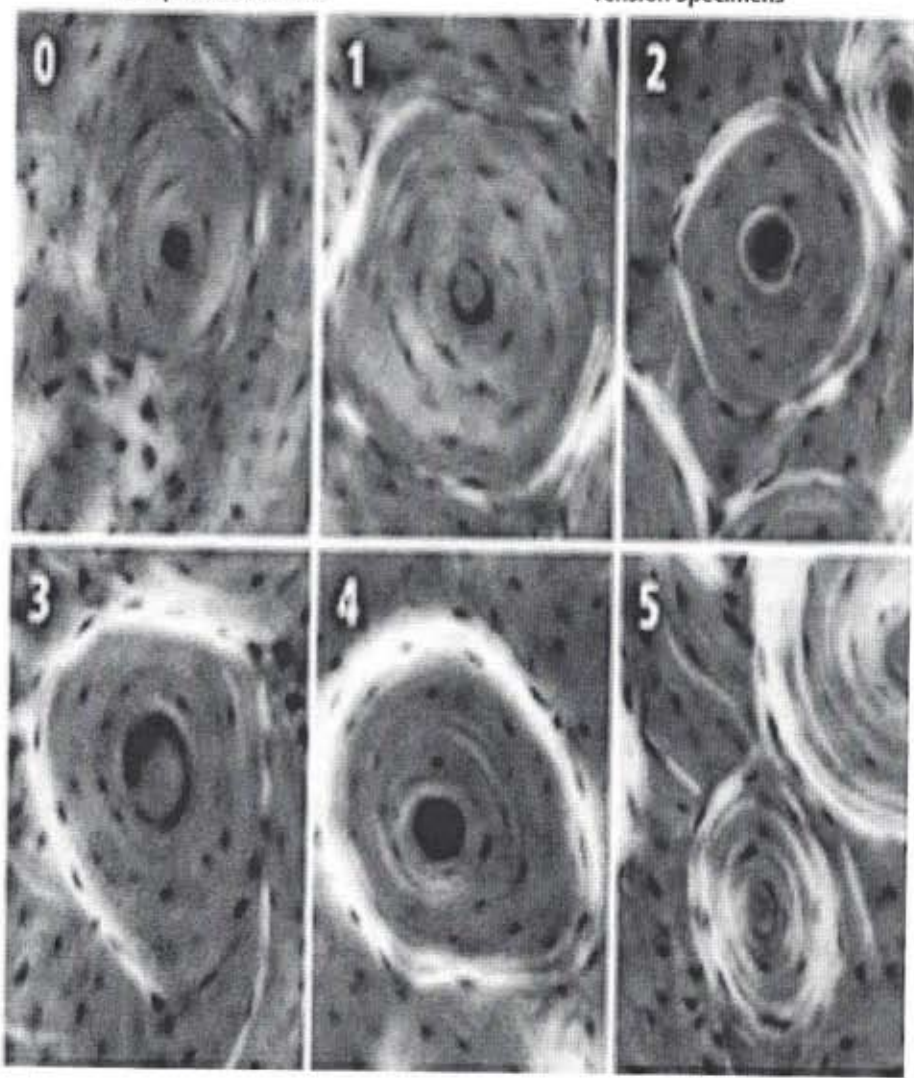
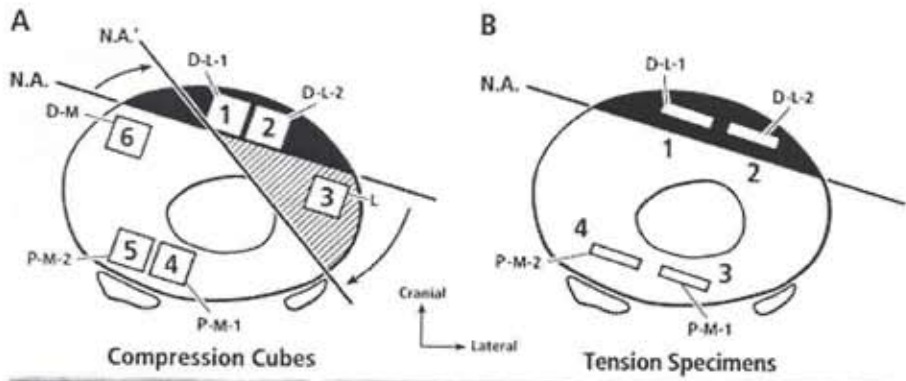
Acknowledgments:

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