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THE INFLUENCE OF OSTEOCYTES ON SURFACE AREA/VOLUME RELATIONSHIPS IN SECONDARY OSTEONS: CHALLENGING PARADIGMS BASED ON HUMAN RIB DATA

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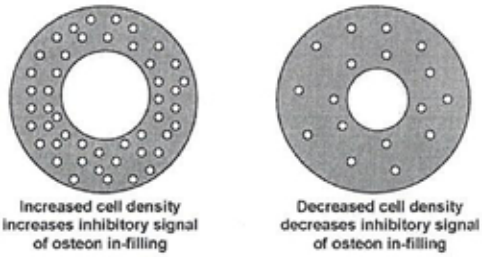
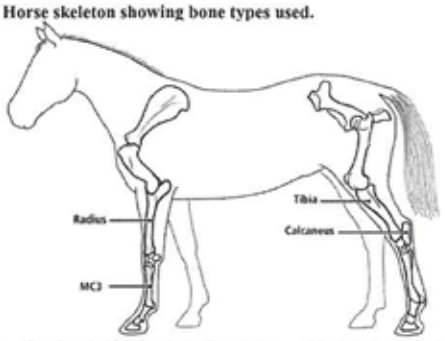
Introduction: The basic multicellular units (BMUs) that form secondary osteons are the most important entities for ensuring healthy bones in adult humans. Consequently, a large body of work has focused on determining how the formation of BMUs is regulated. The implications for osteoporosis (e.g., incomplete osteon in-filling) are obvious. An important concept proposed by Martin and Marotti describes osteocytes as interconnected networks that serve to repress remodeling (i.e., renewal by BMUs) [1]. De-repression of the network ensues when the cellular network is perturbed, which can result from microdamage or hormonal influences. In a recent study of human ribs, Qiu et al. [2] report data suggesting that, in this repression/de-repression context, osteocytes strongly influence the attainment of the final osteonal central canal area. We are dubious that this finding is broadly applicable since ribs have notable differences when compared to appendicular long bones; ribs 1) are derived from sclerotomes of the somites, in contrast to limb bones that are derived from lateral plate mesoderm, 2) are phylogenetically primitive, appearing in the fossil record well before limb bones, 3) are metabolically more active and sensitive to hormonal changes such as during lactation, and 4) receive frequent, low-strain loading; e.g. even when the animal is recumbent. In view of theses issues, the present study tests the hypothesis presented in Fig. 1 below, which shows two osteons.



Methods: 50X backscattered electron (BSE) images were obtained from mid-third diaphyses of 10 mature (ages 2-10) equine third metacarpals (MC3s) and radii (MC3s: in eight radial sectors: dorsal, dorsal-lateral, palmar-lateral, palmar, palmar-medial, medial, and dorsal-medial; Radii: cranial "tension" cortex, caudal "compression" cortex, and medial/lateral "neutral axis" cortices), and from mid-third diaphyses of 7 mature, horse, elk and sheep calcanei. As was done by Qui et al. [2], we quantified: osteon area (On.Ar), osteonal bone area (B.Ar), central (Haversian) canal area (Hc.Ar) and perimeter (Hc.Pm), number of osteocyte lacunae per osteon (Lc.N/On) and osteonal bone area (Lc.N/B.Ar), and the Haversian canal perimeter to osteonal bone area ratio (Hc.Pm/B.Ar). The 2D parameters (B.Ar and Hc.Pm) in osteons can be defined as the 3D bone surface to bone volume (BS/BV) ratio. Thus Hc.Pm/B.Ar is equivalent to (BS/BV) ratio. These data are compared to rib data reported by Qiu et al. [2].

Fig. 2 Horse skeleton showing bone types used.



Results: Equine MC3 and radius data. Similar to the human rib, On.Ar in the equine MC3 strongly positively correlated with Hc.Ar and Hc.Pm ($r = 0.79, 0.72$; $p < 0.01$ respectively). However, in contrast to the human rib, Lc.N/On showed little, if any, correlation to Hc.Ar and Hc.Pm ($r = 0.01, 0.10$; $p < 0.01$ respectively) in the MC3. Equine radii showed lower correlation (but still positive and statistically significant) of On.Ar to Hc.Ar and Hc.Pm ($r = 0.47, 0.49$; $p < 0.01$ respectively) than human ribs. Furthermore, radii showed lower Lc.N/On correlation of Hc.Ar and Hc.Pm ($r = 0.34, 0.36$; $p < 0.01$ respectively) than human ribs. Analysis of all data in each bone revealed that BS/BV (Hc.Pm/B.Ar) was highest in the MC3, next highest in horse radii and all calcanei, and lowest in human ribs ($p < 0.001$ for each paired comparison). Additionally, Lc.N/On was significantly lower in the MC3 than in the horse radius, all calcanei and the human rib ($p < 0.001$). Calcaneus data. Horse calcanei showed lower correlation (but still positive and statistically significant) of On.Ar to Hc.Ar and Hc.Pm ($r = 0.48, 0.48$; $p < 0.01$ respectively) than ribs; and lower Lc.N/On correlation to Hc.Ar and Hc.Pm ($r = 0.45, 0.44$; $p < 0.01$ respectively) than ribs. Elk and sheep calcanei showed poor correlation of On.Ar with Hc.Ar and Hc.Pm ($r = 0.32, 0.33$; $p < 0.01$; $r = 0.04, -0.04$; $p > 0.5$ respectively), and poor correlation of Lc.N/On with Hc.Ar and Hc.Pm ($r = 0.17, 0.19$; $p < 0.01$; $r = -0.001, -0.005$; $p > 0.5$ respectively).

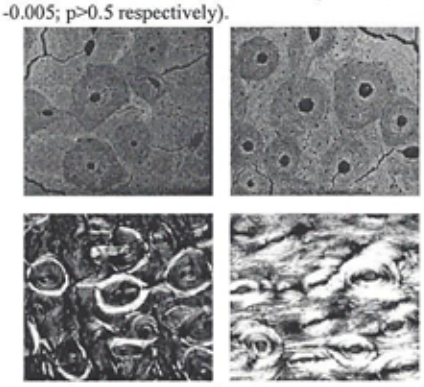


Fig. 3 BSE images: horse radius (HR, top left) and MC3 (top right); CPL images showing different osteon "morphotypes" in HR (lower left) and MC3 (lower right). Images are at same magnification and illumination.

Discussion: These results suggest that the putative coordination between the formation of an "optimal" Haversian canal and osteocytes found in human ribs [2] is present but weak in horse radii and calcanei and virtually non-existent in the MC3s as indicated by the low correlation coefficients comparing Lc.N/On to Hc.Ar and Hc.Pm. These relationships may not exist in bones where there are large regional variations in strain gradients and/or a highly non-uniform strain distribution, which produce relatively greater regional variations in trans-cortical fluid flow. For example, the MC3 exhibits dramatic trans-cortical strain gradients; the dorsal-lateral cortex experiences ~50x less strain than the palmar-medial cortex [3]. Regions of bones experiencing high strain gradients may also have more efficient nutrient delivery, which may explain why the MC3s have greater Hc.Pm/B.Ar but lower Lc.N/On than horse radii and human ribs. Beyond interspecies differences, there may be other important considerations when attempting to extrapolate human rib data to other mammalian appendicular bones. For example, it is possible that thresholds for metabolic activity of bone cells in ribs are probably fundamentally different when compared to appendicular bones; ribs are exquisitely sensitive to hormonal changes associated with lactation and appendicular bones are not. Although this is gender specific (i.e., occurs in females) it illustrates how metabolic demands can affect osteonal histomorphology in some regions differently than others. Additionally, different osteon "morphotypes" (Fig. 3) can confound these issues since they might not have equivalent lacuno-canalicular geometries. Nevertheless our results do point out that histomorphometric BS/BV vs. cell density data considered "optimal" in ribs might not apply to other mammalian appendicular bones.

References: **1)** Martin, RB., 2000. Bone. 26:1; **2)** Qiu et al., 2003. Anat. Rec. 272A:520; **3)** Gross et al., 1992. J. Biomech. 25:1081.