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POTENTIAL EVIDENCE OF MICROSTRUCTURAL, MINERAL, AND CROSS-SECTIONAL ADAPTATION TO SPECIFIC STRAIN FEATURES IN BONE

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Introduction Strain history is thought to provide epigenetic signaling for bone modeling and remodeling activities. Strain can be dissected into numerous components including mode and magnitude whose preeminence as an adaptive signal remains controversial. Strain gauge documentation of the equine third metacarpal reveals a neutral axis passing through the craniolateral cortex resulting in a narrow band of tension with the remainder of the cortex experiencing a wide range of compression magnitudes which are maximal in the caudomedial cortex (1). This predictable strain pattern provides a model for examining the hypothesis that strain mode, magnitude, and strain energy density (SED) are potential correlates to adaptive remodeling.

The objective of the present study is to examine the equine third metacarpal for correlations between microstructure, cortical thickness, mineral content, and the prevailing strain environment.

Methods Third metacarpal bones were obtained from ten skeletally mature standard breed horses. 5mm thick blocks cut immediately distal to 50% of bone length were embedded in polymethyl methacrylate and prepared for backscattered electron (BSE) imaging. Orientation lines were etched on each specimen defining cranial, craniolateral, lateral, caudolateral, caudal, caudomedial, medial, and craniomedial regions. Three cortical depths were imaged (50x; 1.6mm x 2.3mm) within each region representing the pericortical, middle, and endocortical envelopes. The micrographs were analyzed for the following variables using standard stereologic point-counting techniques: osteon population density (OPD); fractional area of secondary bone (FASB), fractional area of porosity, and fractional area of porosity corrected by excluding resorption spaces. The mineral content of each region was determined using the blocks cut proximal to the 50% level by dividing the weight of ashed bone (24h@550C) by the weight of the dried, defatted bone. Cortical thickness was measured to the nearest 0.01mm.

Results were compared using a two-way ANOVA design on ranks. Tukey's Studentized Range Test was employed in post hoc testing. Initial comparisons considered data from all regions. Subsequently, comparisons were made considering data only from tension and low compression regions of comparable strain magnitude.

Values of normal strain, shear strain, peak SED, and summed SED were obtained from finite element mesh data in a recent study on the in vivo mechanical milieu of the equine third metacarpal (1). The two elements in the mesh that coincided with the imaged regions were averaged and used to compute least mean square linear regressions comparing structural variables to normal strain, shear strain, peak SED, and summed SED. Values of normal strain were compared both as their respective positive (tension) and negative (compression) values and as absolute values.

Results FASB was significantly lower in the craniolateral region (32.1%±15) region than the caudolateral (46.6%±14) and caudal (44.2%±13) regions ($p \leq 0.006$). OPD (ost/mm2) did not differ significantly between cortical regions (range: craniolateral 13.5±6.3 to caudolateral 17.1±6.4) ($p \leq 0.3$). Porosity was marginally increased in the caudal cortices (range: lateral 4.4%±1.4 to caudal 6.9%±4.6) ($p \leq 0.1$). This tendency became more pronounced after excluding resorption space area from the porosity measurements ($p \leq .06$). Cortical thickness differed significantly around the cortex with the thinnest cortex in the caudal (5.8mm±0.6), caudomedial (6.5mm±0.5), and caudolateral (6.9mm±0.6) regions ($p \leq 0.0001$). The mineral content in each of the caudal regions was found to be significantly lower than all other cortices (range: caudolateral 66.7%+4.5 to craniomedial 72.3+11.6) ($p \leq 0.01$). Comparisons of tension and low magnitude compression regions also revealed similar differences in cortical structure.

The majority (80%) of correlations comparing the structural and microstructural parameters to the strain features reported in the literature were weak ($R<0.2$). The strongest correlations were seen between cortical thickness and shear ($R=-0.6$) and normal ($R=0.5$) strains.

Discussion These data suggest that there is increased remodeling of the caudal compression cortices relative to the remainder of the cortex. Conversely, the craniolateral tension cortex tends to be less remodeled than the remaining cortex. The FASB pattern demonstrates the least remodeled bone in the craniolateral cortex, becoming significantly greater in the caudal cortices. Differences in OPD were minimal between cortical regions, but notably paralleled the pattern of FASB. The caudal cortices contain significantly less mineral and are more porous than the remaining regions. These findings correspond to regions of high FASB and OPD which agrees with previous findings of decreased mineral and increased porosity of remodeled bone.

Linear regression analysis comparing these remodeling indices to literature magnitude values of normal strain, shear strain, peak SED, and summed SED patterns yielded weak and nonsignificant correlations. Additional regression analysis converting all strain magnitudes to their absolute values failed to strengthen the correlations. The regression plots did not show discernible steps consistent with threshold theories of remodeling . Therefore it seems unlikely that strain magnitudes, even over a wide range, represent the preeminent remodeling stimulus in this model unless site-specific differences exist.

That strain mode may influence remodeling activity in this model is supported by: 1) decreased remodeled bone in the craniolateral tension cortex, 2) relatively increased remodeled bone of the caudal compression cortices, 3) post hoc groupings of FASB which single out the craniolateral cortex as differing from all other regions, and 4) statistical differences between tension and compression areas of equal strain magnitude.

Recent authors have suggested that bending may engender some biologically beneficial level of strain, or that bending systems ensure a predictable distribution of strains during in vivo loading (2). The equine third metacarpal is harshly loaded and experiences substantial bending. It is provocative to consider how its structural elements may be arranged either to accentuate or attenuate bending through regional adjustments in elastic modulus and cortical thickness. Although the relative decrease of mineral and increase of porosity in the compressive cortices may simply be necessary by-products of remodeling, an alternative explanation is that they may contribute to a structural objective of bone adaptation. The relative thinness of the caudal cortices despite their experiencing large magnitude compression strains suggests that this strain is at least tolerated by, and may represent a goal of its adaptation as shown in other bones (3,4). Further investigations of these possibilities may help to improve our understanding of common orthopaedic problems of skeletal maintenance, repair, and adaptation.

References 1) Gross et al.: *J. Biomech.* 25:1081-87, 1992; 2) Rubin et al.: *J. Biomech.* 23(Supp.1):43-54, 1990. 3) Skedros et al.: *Anat. Rec.* Aug.,1994a,b; 4) Mason et al.: ORS abst., p.562, 1994.

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