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40. Regional Microstructural Heterogeneity in the Turkey Ulna: Implications for Understanding Fluid Flow Dynamics During Functional Loading. K. J. Hunt,*[1] J. G. Skedros.[2] [1]Orthopaedics, Univ. Utah, Salt Lake City, UT, USA, [2]Univ. Utah, Salt Lake City, UT, USA.

Recent evidence suggests that the mechano-sensitivity of osteocytes is mediated by fluid-flow through bone's lacunar-canalicular porosity. This idea has been examined in an analytical model of the turkey ulna [Srinivasan & Gross, Med. Eng. & Phys., 2000]. During normal loading this bone experiences circumferential strain gradients that are highest along the neutral axis, which typically traverses the cranial-caudal cortices. Additionally, regional differences in fluid-flow dynamics within the turkey ulna have been described. Intercortical and transcortical pressure gradients and fluid flux are largely dependent on matrix porosity. We speculate that heterogeneities in osteocyte lacuna density and non-lacuna porosity, in addition to other material characteristics, might be important considerations in understanding fluid-flow and related strain dynamics. A transverse segment was cut at mid-diaphysis of 11 skeletally mature domestic turkeys, and four 200X backscattered electron images (two endocortical and two pericortical; excluding circumferential lamellae) were obtained from cortical octants: D, D-Cr, Cr, D-Cd, Cd, V-Cd, V, V-Cr (D = dorsal, Cr = cranial, Cd = caudal, V = ventral). These images were examined for osteocyte lacuna population densities and non-lacuna porosity (primary and secondary canals, vascular channels). Secondary osteon population densities were quantified in cortical quadrants (D, V, Cr, Cd). Octant comparisons demonstrated more lacunae in the Cr and Cd cortices compared to the other locations ($p<0.001$) [Means: Cr 1,316.6/mm2; Cd 1,388.0; range in other regions: D-Cd 966.7 to V-Cr 1,100.1]. There was relatively greater porosity in Cd, V-Cd, and D-Cd regions ($p<0.05$). However, non-lacuna porosity and lacuna density were not correlated ($r = 0.008$). Quadrant comparisons showed significantly more secondary osteons in the caudal cortex. Previous data have shown that this region has significantly greater thickness and lower mineralization (%ash). Pericortical-endocortical comparisons showed more lacunae in the pericortical region (1,234.4 vs. 1,170.1, $p=0.05$) and greater non-lacunar porosity in the endocortical region ($p = 0.06$). These data demonstrate significant regional microstructural heterogeneity. In the context of fluid-flow analyses, it is important to recognize that regional variations in lacuna and non-lacuna porosities might not be correlated. These are important considerations in analytical models examining strains and fluid flow induced by anisotropy and architectural changes between the continuum and microstructural levels of bone matrix morphology.

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Interplay of Nitric Oxide Synthase (NOS), Cyclooxygenase (COX) and Lipoxygenase (LOX) Pathways in Response to Mechanical Compression of Articular Cartilage. B. Fermor,*[1] H. Bodduluri,[2] J. B. Weinberg,[3] D. S. Pisetsky,*[3] C. Fink,*[1] F. Guilak.*[1] [1]Duke University, Durham, NC, USA, [2]University of Louisville, Louisville, KY, USA, [3]VA and Duke University Medical Centers, Durham, NC, USA.

Mechanical signals play important roles in regulating the homeostasis of articular cartilage. Under abnormal conditions, however, mechanical stress maybe a critical factor in the onset and progression of arthritis. The pathways involved in mechanotransduction are not fully understood but are associated with increased nitric oxide (NO) production via NOS2. NOS inhibitors can prevent the onset and duration of arthritis in experimental models but their influence on other inflammatory mediators such as prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) (derived from the enzymes COX2 and LOX) are not fully understood. To test the hypothesis that physiological levels of mechanical stress may induce the formation of PGE2 or LTB4, articular cartilage explants from 2 year old female pigs were subjected to dynamic mechanical compression at 0.1 MPa, 0.5 Hz. This mechanical regimen has previously been shown to be associated with increased proteoglycan synthesis. Effects of the NOS2 selective inhibitor 1400W or the COX2 selective inhibitor NS398 were also tested. PGE2 and LTB4 levels in the media were measured by radioimmunoassay and expressed as percentage of control. COX1, COX2 and LOX proteins were determined by immunoblot.A 12-fold increase ($p <0.05$) in PGE2 occurred in response to mechanical compression which increased to 40 fold in the presence of 1400W ($p <0.001$). COX2 but not COX1 protein was detected. Mechanical compression plus NS398 diminished the PGE2 and NO induced by mechanical compression alone. LTB4 was not detected in response to compression alone but a 300-fold increase ($p < 0.001$) in LTB4 occurred in response to compression in the presence of 1400W, with increased LOX protein. These data indicate that inducible NO has an important negative feedback role in the COX and LOX pathways in articular cartilage. These findings may have important implications regarding the pathogenesis of arthritis and the development of new biophysical and pharmacological interventions for arthritis.