SU066

Do BMUs Adapt Osteon Cross-Sectional Shape for Habitual Tension vs. Compression Loading? J. G. Skedros. Dept. of Orthopaedic Surgery, University of Utah, Ogden, UT, USA.

Mechanically relevant local variations in bone tissue organization are often interpreted in the context of stiffness and strength criteria. However, basic multicellular units (BMUs), which dictate osteon size and shape, may also affect local toughness and fatigue resistance by adjusting osteon population density and cross-sectional shape. Such adaptations may be most evident between regions habitually loaded in a different prevalent strain mode (tension, compression, shear) -- cortical bone mechanical properties substantially differ in these loads. To examine this idea, osteon cross-sectional shapes were quantified in "tension" and "compression" cortices of 7 of each adult bones: calcanei of sheep (S.C.), deer (D.C.), and horses (H.C.), radii of sheep (S.R.) and horses (H.R.), and sheep tibiae (S.T.). Compression regions of horse third metacarpals (H.M.) served as controls. Transverse mid-diaphyseal sections were embedded in methacrylate, milled to 100µm, and two to four 50X images (2.3mm^2/img) were obtained at mid-cortex. Osteon "shape factors" were determined from perimeter (p) tracings of pixel edges [= $4\pi a/p^2$; a = area of a circle (πr^2), $p=2\pi r$ (Image 1, Universal Imaging Corp., West Chester, PA)]; range from 0.0 to 1.0 (perfect circle). Results are not consistent with the hypothesis of such tension/compression adaptation [Table: means & (S.D.)]. But it is possible that osteon morphologic adaptations exist in medial-lateral cortices where shear strains predominate.

	S.C.	D.C.	H.C.	S.R.	H.R.	S.T.	H.M.
Cranial	0.87 (.09)	0.87 (.08)	0.90 (.10)	0.87 (.08)	0.87 (.08)	0.87 (.09)	0.89 (.10)
Caudal	0.86 (.10)	0.83 (.10)	0.83 (.14)	0.85 (.10)	0.91 (.09)	0.90 (.04)	0.90 (.10)

Cranial=compression in calcanei, and tension in radii and tibiae. Only D.C., H.C., and H.R. show significant differences ($p<0.01$).

SU067

36. **Uniform Osteocyte Lacuna Population Densities in a Limb Bone with Highly Non-Uniform Strain Milieu.** J. G. Skedros, K. J. Hunt,* E. N. Attaya,* M. D. Zirovich.* Dept. of Orthopaedic Surgery, University of Utah, Ogden, UT, USA.

Osteocytes may have distinct effects in appraising mechanical signals and regulating bone adaptation. The possibility that regional differences in sensitivity of the osteocyte network is accomplished by adjusting cell numbers was examined by quantifying osteocyte lacuna population densities (OLPDs) in the horse third metacarpal. *In vivo* measurements demonstrated that functional loading produces a broad range of compressive strain magnitudes across the mid-diaphysis. One 5 mm thick segment was cut transversely from this region in 9 adult horses. Segments were embedded in methacrylate, and two 50X backscattered electron images were obtained in each of the periosteal, middle, and endosteal regions at 8 sector locations: cranial (Cr.), caudal (Cd.), medial (Med.), lateral (Lat.), Cr.-Lat., Cd.-Lat., Cr.-Med., and Cd.-Med. Secondary osteon population density (SOPD; no./sq. mm), fractional area of secondary osteon bone (FASB), and OLPD (no./sq. mm) were quantified. Predominant collagen fiber orientation (CFO) was estimated in each region using circular polarized light. Strain data were obtained from a finite element mesh based on *in vivo* measurements. OLPD ranged from 425±101 (Cd.) to 533±88 (Cr.) ($p=0.09$). Although there were a few instances of statistical differences in OLPD, these represent, at most, a 6 µm increased distance between two adjacent osteocytes. No or low positive correlation was shown between OLPD and SOPD ($r=0.108$, $p=0.1$), FASB ($r=0.347$, $p<0.0001$), CFO ($r=0.408$, $p<0.0001$), normal strain ($r=0.323$, $p<0.0001$), shear strain ($r=0.306$, $p<0.0001$), and peak and summed strain energy density ($r=0.190$, $p=0.006$; $r=0.06$, $p=0.4$). The relatively uniform cell densities in this highly non-uniform strain milieu may reflect the probability that nutritional constraints are vastly more important than any spatially determined communication between osteocytes.

SU068

Trabecular Bone Adaptation in Rabbit Femora Using a Novel *In Vivo* Loading Device. M. Bostrom,[1] X. Yang,*[1] M. C. H. van der Meulen,[2] T. G. Morgan,*[2] T. Baldini,*[1] H. Weinans,*[3] T. Wright.*[1] [1]Hospital for Special Surgery, New York, NY, USA, [2]Cornell University, Ithica, NY, USA, [3]Erasmus University, Rotterdam, Netherlands.

Purpose: While the importance of mechanics in the growth and development of the skeleton is well accepted, the mechanisms of bone adaptation are not well understood and our ability to predict trabecular adaptation is very limited. In particular, we need to understand the influence of mechanical load magnitude, duration and frequency. The goal of this study was to understand how quantifiable mechanical forces modulate trabecular bone mass. **Methods:** A loading device was developed to apply controlled compressive loads to trabecular bone. The device consists of a stationary based mounted on the lateral femoral condyle with a movable core and top. When the top is twisted percutaneously, the 5-mm diameter core slides within the base and compresses the underlying bone with a known load. Implantable loading devices were inserted bilaterally into the distal femurs of 15 New Zealand White rabbits (6-9 months old). Each experimental animal served as its own internal control. The right side was subjected to compressive loads (LOAD) while the left had the device implanted but not subjected to any load (NO LOAD). The devices were manually loaded to 1 MPa at 0.5 Hz for four weeks starting the day of surgery. The animals were divided into three groups of 5 animals and loaded for 10, 25, and 50 cycles/day respectively. The loading parameters were confirmed in selective animals using an instrumented core. Four weeks after surgery, the animals were sacrificed. Micro-CT scans of the LOAD and NO LOAD condyles were obtained and the region below the device core was analyzed. **Results:** The Micro-CT showed a greater area bone fraction under the LOAD cores than the NO LOAD cores in specimens loaded for 50 cycles/day. The trabecular bone fraction was 30.9+7.4% for LOAD and 21.0+4.6% for NO LOAD ($p=0.006$). No difference was present between LOAD and NO LOAD for the groups loaded for 10 or 25 cycles/day. **Conclusions:** These preliminary studies showed a significant difference between LOAD and NO LOAD for 1 MPa applied for 50 cycles/day; however, no difference was detected in the animals subjected to the same load for a lower number of daily cycles. This device offers the opportunity to systematically vary loading parameters to improve our understanding of the factors controlling trabecular bone adaptation to mechanical loading. **Acknowledgments:** This study was funded by grants from the Oxnard Foundation, NIH and NSF.

SU069

Mechanical Loading Response in EP2 Receptor Knockout Mice. D. M. Cullen, A. C. Peyton,* M. P. Akhter, G. Gong. Medicine, Creighton University, Omaha, NE, USA.

The bone loading response is partially mediated by PGE_2. The EP2 receptor stimulates cAMP and is associated with osteoblast differentiation and bone formation. This study compared the bone formation response to loading in EP2 knockout (KO) and wild type (WT) control mice (Dr. Pan, Pfizer Central Research). The right tibia of all mice were loaded in four-point bending 3 days/wk for 3 wks, at 5 N, 36 cycles, and 2Hz. The left (noLoad) and right (Load) tibiae were collected from 20 mice/breed and processed for histomorphometry. Two sections (70mm) from the loaded region were measured for periosteal (Ps) and endocortical (Ec) mineralizing surface (MS), woven bone (WoB), mineral apposition rate (MAR), and bone formation rate (BFR=MS*MAR+WoB). Differences within animal (L v nL) and between breed were tested by GLM repeated measures (SPSS). Results are reported in the table.

Mice	Leg	Ps.BFR (µm/yr)	Ec.MS (%)	Ec.MAR (µm/d)
WT	nL	177 (126)	30 (10)	0.96 (0.24)
	L	2907 (1541)^a	22 (10)^a	1.32 (0.32)^a
KO	nL	145 (113)	36 (15)	1.17 (0.17)
	L	2185 (1013)^{ac}	22 (13)^a	1.26 (0.29)^{ab}

Mean (SD) Load different from noLoad ^{a} $P<0.05$, KO response (Load-noLoad) different from WT ^{b} $P<0.03$, ^{c} $P=0.09$

We conclude that formation parameters in EP2 KO are not different from WT in non-loaded legs, and show a significant increase with loading. However, the loading response (L-nL) tends to be smaller in KO than WT mice. The EP2 receptor may be involved in the loading response, but is not essential at high forces.