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GENETIC DIFFERENCES IN BONE RESPONSE TO *IN VIVO* LOADS IN MICE. MP Akhter, T Satterfield*, DM Cullen, DB Kimmel. Creighton University; Omaha, NE.

Differences in the bone response to external loading in low (C57BL/6J) and high peak bone density (C3H/HeJ) mice were examined. The general concept of an *in vivo* tibial four-point bending device used for rats was miniaturized for mice. *In vivo* strain during loading was measured directly in six adult mice of each breed through uniaxial strain gages attached to the right tibial lateral surface, in the center of the loaded region, 3mm proximal to the tibio-fibula junction. Next, the right legs of six C57BL/6J and five C3H/HeJ mice were externally loaded in the device for 36 cycles/d@2Hz, 6d/wk for two wks by 9.5±0.9N force, inducing 1540±497$\mu\varepsilon$ in both breeds. Both tibiae were measured for marrow area (Ma.Ar), cortical area (Ct.Ar), total area (Tt.Ar), periosteal and endocortical woven bone surface (Wo.B/BS), and total formation surface (FS/BS). Differences due to breed and loading were tested by two way ANOVA.

	C57BL/6J		C3H/HeJ	
Variable	Loaded	NonLoad	Loaded	NonLoad
Ma.Ar(mm^2)	0.44±0.08	0.44±0.14	0.17±0.03[b]	0.13±0.03[b]
Ct.Ar(mm^2)	0.63±0.08	0.58±0.12	0.56±0.05	0.56±0.05
Tt.Ar(mm^2)	1.07±0.10	1.01±0.25	0.73±0.06[b]	0.70±0.06[b]
pWo.B/BS(%)	78±12[a]	0±0	54±44[a]	0±0
eWo.B/BS(%)	45±20[a]	0±0	8±14[b]	0±0
pFS/BS(%)	78±12[a]	10±7	58±46[ab]	42±32
eFS/BS(%)	75±13[a]	12±10	30±23[b]	31±29

[a]diff due to loading; [b]diff due to breed (P<.02)

Marrow area and total area were greater in C57BL/6J than in C3H/HeJ. Periosteal woven bone and formation surface were higher due to loading in both breeds. However, breed influenced the endocortical formation response to loading, C57BL/6J being greater than C3H/HeJ. We conclude that the response to external loading of equal force is more robust in the low peak bone density breed (C3H/HeJ).

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UNIFORM OSTEOCYTE LACUNA POPULATION DENSITIES IN A LIMB BONE WITH NON-UNIFORM CUSTOMARY STRAIN MILIEU AND HETEROGENEOUS MATERIAL ORGANIZATION J.G. Skedros, K.C. Deitch*, M.D Zirovich*, and M.W. Mason* U. South. Cal. and Penn. State Depts. of Orthopaedics, L.A., CA and Hershey, PA; & DVA Med. Ct., Salt Lake City, UT

Osteocytes embedded within bone tissue may be the "sensors" which transduce stimuli relevant in bone organ homeostasis and adaptation. If modifications in the sensitivity of this network is required, then it is likely that this is accomplished by adjusting cell numbers. To examine this hypothesis, osteocyte lacuna population densities (OLPDs) were quantified in cortical locations of the horse radius. In vivo measurements have demonstrated that during functional loading the cranial cortex receives predominantly tension strains with peak magnitudes of approximately 1000 microstrain, and the caudal cortex receives compression strains of approximately 1250 microstrain. Two 5mm thick segments were cut from the mid- to proximal-third diaphysis of one radius from each of 10 skeletally mature standard breed horses. Segments were embedded in polymethyl methacrylate, and two 50X backscattered electron images were obtained in each of the periosteal (P), middle (M), and endosteal (E) regions at the cranial, caudal, medial, and lateral cortical locations. Secondary osteon population density (SOPD), fractional area of secondary osteon bone (FASB), and porosity (central canals and other vascular channels) were quantified using point counting techniques. Osteocyte lacunae were counted individually. Mineral content (ash fraction) was determined in each cortex by ashing (550C) bone specimens from adjacent segments. Three-way ANOVA (section, cortical location, region) showed no statistical differences in OLPD between the two segments ($p = 0.20$), and all possible comparisons of the 12 regions ($p = 0.34$). Fisher's PLSD post-hoc tests showed that OLPD per mm^2 bone in the cranial cortex is statistically lower than in the caudal ($p = 0.013$) and lateral ($p = 0.002$) cortices (cranial 478±137; caudal 522±152; medial 512±129; lateral 532±125). However, these differences represent only approximately a two micron difference in the distance between any two neighboring osteocytes. The caudal cortex has nearly two-fold greater SOPD and FASB than the cranial cortex ($p < 0.01$). Linear regression analysis showed poor correlation between OLPD and SOPD ($r^2 = 0.039$), FASB ($r^2 = 0.033$), and porosity ($r^2 = 0.009$). Less than 1% difference in ash fractions and equivalent numbers of resorption spaces between cortices suggests uniformity of regional remodeling (renewal) rates. It is possible that the variation in the customary strain milieu is not sufficient to require regional adjustments in the sensitivity of the "sensor" network. However, the heterogeneous material organization and relatively uniform cell densities may reflect both the achievement of optimal tissue construction and cell distribution for both cell-matrix and cell-cell interactions.

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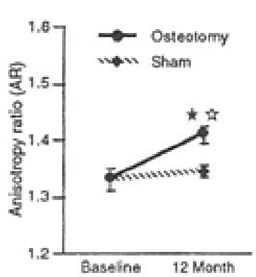
ELASTIC ANISOTROPY OF OSTEONAL BONE IS DEPENDENT ON THE MECHANICAL STRAIN DISTRIBUTION. Y. Takano, C.H. Turner, D.B. Burr, Departments of Anatomy and Orthopaedic Surgery, Indiana University, Indianapolis, IN 46202.

The relationship between mechanical strain and elastic anisotropy of osteonal bone was investigated using an acoustic microscope. Ulnar osteotomies were performed on three adult foxhound dogs. Three more dogs received a sham surgery. The dogs were allowed normal kennel activity for 12 months, after which, three rosette strain gages were placed on the midshaft of the radius and in vivo surface peak strains and strain distributions were measured. Osteotomy caused the neutral axis of the bending strains to be rotated and changed the surface peak strains. After strain measurements, the dogs were euthanized and radii were removed and embedded in plastic. Cross-sectional and longitudinal 500 mcm thick sections were cut from the anterior, posterior, medial and lateral regions of each radius. Acoustic velocity (AV) was measured for each section using an acoustic microscope. From AV measurements, an elastic anisotropy ratio (AR) was calculated. AR was significantly positively correlated with strain ($r=0.8$, $p<0.0001$) such that the highest AR were in regions of bone loaded predominantly in tension and the lowest AR were in compressive regions. In the osteotomy group, we identified a region that had very low strains previous to osteotomy, but had high tensile strains after osteotomy. In this region, AR was significantly higher in the osteotomy group than the corresponding region in the sham group ($n=3$, $p<0.05$) and the corresponding region in a baseline control group ($n=3$, $p<0.05$). Altering the strain environment caused changes in the bone tissue making it more anisotropic. The new bone appeared to have more longitudinally oriented collagen fibers under polarized light. In conclusion, the tissue 'quality' of bone may depend upon its mechanical loading environment.



★ : Significantly different from the baseline group

☆ : Significantly different from the sham group

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THE RELATIONSHIP OF STREAMING POTENTIAL MAGNITUDE TO STRAIN AND PERIOSTEAL MODELING IN THE LOADED ULNA.
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Medial Tibial Stress Syndrome (MTSS) is an overuse condition of the tibia which may result from periosteal modeling induced by repetitive impact loads. Improved understanding of the biomechanical signalling relevant to bone modeling may, therefore, facilitate the development of more effective treatment modalities for MTSS than are currently available.

Tibial loading results in the development of both axial and bending strains in the tissue, and it has been suggested that the initiation of the modeling response may be due to the bone or periosteal tissue deformation. However, sub-periosteal bone formation induced in response to loading has frequently been observed to occur away from the sites of maximum strain. This observation indicates that an alternative transduction process, such as streaming potentials, may link mechanical loading to the bone modeling response.

Streaming potentials were measured at the sites of maximum and minimum strain on the mid-diaphysis of 6 functionally isolated turkey ulnae under two distinct loading conditions (axial and bending loads), at 19 loading frequencies, from 0.1 to 100 Hz. Significant streaming potentials were observed under all recording conditions, with magnitudes which increased with loading magnitude, and which also exhibited a dependence on frequency of loading. Streaming potential magnitudes observed at the high and low strain sites were found not to be significantly different under either bending or axial loading conditions (Table 1). However, at the higher strain levels, bending loads gave rise to a significantly higher average streaming potential measurement than axial loads. The demonstration of significant streaming potentials occurring at sites of minimal strain lends support to the hypothesis that load-induced streaming potentials, or the corresponding fluid pressures or flows, may transduce mechanical information to induce periosteal modeling. Further, the remarkable uniformity of the potential measurements suggests that some mechanism of spatial integration may play a role in the signal transduction pathway through which mechanical stimuli influence bone adaptation.

	Axial (±s.d.)	Bending (±s.d.)
High strain site	99±46 µV	230±130 µV
Low strain site	98±50 µV	170±130 µV

Table 1. Representative potential measurements obtained across ulna cortex under 1 Hz axial and bending loading conditions (N=6 animals). Inter-animal variability is seen to be substantial. Peak induced strains were 300-600 µε.