Our data show the oxidative state of articular cartilage is important in determining the effect of mechanical compression on production of inflammatory mediators. Therefore it is important to consider the avascularity and hence low oxygen tension, characteristic of articular cartilage, in our understanding of inflammation and mechanical loading of cartilage.

Disclosures: ***B. Fermor, NIH AR47920 2; NIH AR48182 2; NIH AG15768 2; VA Research 2.***

SU076

Gender Differences in Long Bone Fatigue using a Rat Model. L. D. Moreno*[1], A. M. Cheung[2], M. D. Grynpas[1]. [1]Samuel Lunenfeld Institute, Mount Sinai Hospital, Toronto, ON, Canada, [2]Osteoporosis program, University Health Network and Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada.

Stress fractures can occur because of prolonged exercise and are associated to cyclic loading. This is of special concern for athletes and army recruits. Understanding bone fatigue behavior may give insight into the mechanisms of bone fragility. Existing literature shows that the rates of stress fracture for female athletes and army recruits are higher than for their male counterparts. The objective of this work was to perform a comparative study of the fatigue response of female and male rat tibia. Young 16 weeks Sprague-Dawley rats were used for this study. Excised tibias were loaded at different strains from 0.5% to 1% ε to determine the strain versus cycles to failure curve (S/N curve) at physiological frequency of 2Hz. A set of tibias from male and female rats were monotonically loaded at different stages of the fatigue life (N_f) and the mechanical properties (stiffness, work to fracture and ultimate strength) were determined to assess bone mechanical properties deterioration. A set of tibias that were not fatigued were used as controls. The secant modulus of the tibias was fairly constant throughout the fatigue test; loss of stiffness and cyclic softening was reported only in the later stages of the fatigue life (>90%N_f). Male tibias undergo loss of stiffness for longer periods before fracture. From the S/N curves we inferred the endurance limit. We found that the tibias of the male rats have a higher endurance - about 17% higher. From the cumulative creep data, i.e. from the strain-time curve we found that ε_f (strain-to-failure) of both female and male are not significantly different ($p>0.05$), but for a given non-dimensional stress _/E_0 the female bones deteriorate at higher rate than the males (e.g. for an initial peak strain of 0.007_ the steady-state strain rate was 0.035 μ/s and 0.18μ/s for male and females respectively). The results of this rat model suggest that extensive training session with high intensity, even if scaled down to female strength levels would have a detrimental effect on their bones, hence shorter training sessions for females might help to reduce the rates of stress fractures in female athletes.

Disclosures: ***L.D. Moreno**, None.*

SU077

Young's Modulus of C57BL/6J Cortical Bone Is Less Than That of Outbred *Col1a1*^{oim} Heterozygotes or Their Wild-Type Littermates. G. E. Lopez Franco[1], D. S. Stone*[2], R. D. Blank[3]. [1]Medicine, University of Wisconsin-Madison, Madison, WI, USA, [2]Materials Science and Engineering, University of Wisconsin-Madison, Madison, WI, USA, [3]Geriatrics Research, Education, and Clinical Center, William S. Middleton Veterans' Hosptital, Madison, WI, USA.

One must distinguish the inherent mechanical properties of the bone tissue from the contributions of bone mass and bone architecture to bone strength in order to understand bone's mechanical performance fully. Nanoindentation provides a means of calculating hardness and Young's modulus independently of the sample's geometry.

Mice harboring the *Col1a2*^{oim} mutation (*oim*) are a well-studied mouse model of osteogenesis imperfecta arising from α2(I) chain deficiency. Mice homozygous for the mutation produce type I collagen composed of α1 homotrimers and suffer from marked skeletal fragility. Mice heterozygous for the mutation suffer reduced type I collagen synthesis and have a much more subtle biomechanical defect.

We performed nanoindentation to compare the hardness and Young's modulus of cortical bone from animals heterozygous for the *oim* mutation, wild-type littermate control, and C57BL/6J, an inbred mouse strain with low bone mineral density and low Young's modulus. Cortical bone from either the tibia or femur was polished from the periosteal surface prior to testing. We performed nanoindentation in conjunction with atomic force microscopy using a Hysitron TriboScope and a diamond Berkovich tip at loads between 3000 and 8000 μN. Comparison among genotypes was performed by ANOVA and Tukey's test.

Cortical Bone Nanoindentation

	C57BL/6J	*oim*/+	+/+
Young's Modulus (GPa, Mean ± SEM)	20.6 ± 0.8	29.0 ± 1.8*	30.6 ± 1.8**
Hardness (GPa, Mean ± SEM)	1.06 ± 0.08	1.45 ± 0.13	1.48 ± 0.18

*P =0.00309 *v* C57BL/6J, **P = 0.00053 *v* C57BL/6J, *oim*/+ *v* +/+ = NS

The results are summarized in the table. C57BL/6J bone had a lower Young's modulus than either *oim*/+ or +/+ littermates. The 3 genotypes did not differ significantly in hardness.

It therefore appears that neither decreased bone modulus nor decreased bone hardness is the source of skeletal fragility in *oim*/+ mice. It is worth noting that the *oim* mutation is maintained on an outbred B6C3 background. Our data suggest that the collective influence of the segregating background genes has a greater impact on Young's modulus of cortical bone than does heterozygosity for the *oim* allele of *Col1a2*.

Disclosures: ***G.E. Lopez Franco**, None.*

SU078

QTL Mapping of Bone Quality Measured Using Nanoindentation Technology. Y. Jiao*[1], Z. Fan*[2], H. Chiu*[3], H. Yang*[1], E. C. C. Eckstein*[3], J. Rho*[3], W. G. Beamer[4], W. Gu[1]. [1]Department of Orthopedic Surgery-Campbell Clinic, Univ. of Tennessee Health Science Center, Memphis, TN, USA, [2]Orthopedic and Rehabilitation Engineering Center, Marquette University, Marquette, WI, USA, [3]Department of Biomedical Engineering, University of Memphis, Memphis, TN, USA, [4]The Jackson Laboratory, Bar Harbor, ME, USA.

Using nanoindentation technology to identify QTLs that regulate bone quality represents a novel approach to improving our understanding of molecular mechanisms that control bone matrix properties. So far, nanoindentation appears to be the superb technology for measurement of bone quality. In this study, we investigate the use of nanoindentation measurements in identification of QTLs that regulate bone quality.

Mouse tibiae for comparison of different ages were from C57BL/6J and C3H/HeJ and for QTL mapping were from a F2 population derived from C57BL/6J and C3H/HeJ (provided by WGB at Jax). Those tibiae were from the same population used for the analysis of QTLs of bone mineral density. All tibiae were embedded in epoxy resin without infiltration at room temperature. After using silicon carbide abrasive papers with progressively finer grit sizes, they were polished on micro cloths with a 0.05 μm aluminum suspension. A Triboindenter (Hysitron, Inc. Minneapolis, MN) was used to conduct all indentation tests. The Oliver-Pharr method was used to determine the elastic modulus. Genome scan was performed in The Jackson Laboratory. QTL mapping was conducted using Map Manager QTX software. The analysis procedure followed the instructions in the text at (http://mapmgr.roswellpark.org/mmQTX.html; http://webqtl.roswellpark.org)

We obtained the following results: 1) Mice at 4, 8, 16, 32, and 40 weeks were used for the nanoindentation tests. The data at 16 weeks of age shows a moderated variation among mice within a strain compared with older ages. The data suggest that 16 weeks is sufficient time for mouse tibia to mature; 2) We examined 800 tibiae from F2 mice and compared the data to the two progenitors. Data shows that both Er (stiffness) and Hr (hardness) modulus appears normal distributions, suggesting that multiple genetic factors control the bone quality; and 3) Four QTLs for hardness (chr. 9, 12, 13, and 16) and three for stiffness (two on chr. 12 and one on chr. 16) have been identified. Among the QTLs detected from nanoindentation, the one on chromosome 13 has a similar location with the QTL of bone density. The others are new QTLs that have not been detected.

Our study suggests that using nanoindentation technology to identify QTLs that regulate bone quality represents a novel approach to improving our understanding of molecular mechanisms that control the matrix properties of bone.

Disclosures: ***Y. Jiao**, None.*

SU079

63. Prevalence of Atypical Osteon Characteristics May Reflect Adaptations in Bending Environments and During Growth. S. M. Sorenson*, N. H. Jenson*, J. G. Skedros. University of Utah, Utah, UT, USA.

Basic multicellular units (BMUs) produce 2nd osteons, which mediate microdamage repair, mineral mobilization, and the introduction of interfaces. Since fatigue behavior of cortical bone is significantly different in tension, compression, and shear strain *modes*, histologic adaptations are expected since many limb bones receive consistent tension/compression/shear distributions. BMU-mediated adaptations include variations in 2nd osteon densities and collagen fiber orientation (CFO). Additional important BMU characteristics might include 'atypical' secondary osteons (zonal, connected canal, mature and active drifting, elongated, dumbbell, and multiple canal). If these characteristics correlate with strain-related parameters, then regional variations in these not-often-quantified osteon characteristics (O.C.) may reveal mechanisms (e.g., increasing microstructural complexity/interfaces) that serve to "toughen" bone for relatively more deleterious loading environments (e.g., prevalent tension and shear). O.C. were examined in bones loaded habitually in bending for strain-mode-related correlations. Specimens included mid-third diaphyseal sections of a growth series of calcanei of wild mule deer (older fawns to adults). This model is useful for examining strain-related relationships with microstructural adaptation since the cranial (Cr) cortex receives prevalent compression, the caudal (Cd) cortex receives tension, and the medial/lateral (M/L) cortices receive prevalent shear since they are in proximity of the neutral axis. Regional variations in O.C. were evaluated in backscattered electron images and expressed as "osteon heterogeneity index" (OHI = O.C./total 2nd osteons). Kruskal-Wallis analyses of spatial OHI variations revealed no significant differences among the four cortices in fawns. Sub-adults *and* adults showed these significant differences: Cd vs. L, Cr vs. L, and M vs. L. Although OHI in the whole section (i.e., all cortices) vs. bone length was poorly correlated, the total no.of O.C./area increased with age ($r = 0.538$, $p=0.005$). The increase in these atypical osteon characteristics occurs during the phase of development when osteons may generally serve to enhance toughness and fatigue resistance. The differences between the M cortex and other locations may reflect the fact that the neutral axis is oblique, placing the M cortex in prevalent/predominant shear *and* compression. CFO in this region is also known to be highly oblique, consistent with adaptation for shear/compression. These observations may help understand the mechanisms mediating regional and age-related cortical histologic changes in the complexly loaded human femoral neck.

Disclosures: ***S.M. Sorenson**, None.*