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EXPANDING WOLFF'S LAW: VARIANT & INVARIANT STRAIN STIMULI IN BONE ADAPTATION AND MAINTENANCE

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Introduction: Recent data have demonstrated consistent differences in predominant collagen fiber orientation (CFO) between "tension" and "compression" cortices of long bones [1,3,6,7,8]. These data, and the absence of differences along neutral axes (NA, "shear"), support the hypothesis that specific forms of variant (i.e., vectorial) mechanical stimuli are important in the *attainment* of bone tissue organization. Such variant stimuli are not presently considered important in most modern algorithms of bone adaptation, which are strongly biased toward the consideration of invariant (i.e., scalar) strain stimuli (e.g., absolute magnitudes of strain: strain energy density). This stems from the conventional view of bone as an adaptable *structure*, wherein the following criteria are modifiable: longitudinal curvature, cross-sectional shape, cortical thickness, and trabecular alignment and apparent density. This approach has historically emphasized strength and stiffness criteria while minimizing the potential biomechanical relevance that regional *material* variations have in affecting toughness and fatigue resistance. There is a growing body of data suggesting that greater emphasis be placed on the biomechanical relevance of a bone organ's regional *material* organization. These variables include regional and developmental variations in CFO, secondary osteon population density (OPD), osteon cross-sectional size and shape, and mineral content. The turkey ulna (a "tension/compression" bone) was selected to further explore this idea because it is one of the best-characterized bones in terms variant/invariant strain distributions [4]. During normal wing flapping, the turkey ulna exhibits preferential bending in the dorsal-ventral direction; the dorsal cortex receives primarily "compression" strains and the ventral cortex receives primarily "tension" strains. We have speculated that stimuli associated with vectorial components of principal strain (e.g., tension, compression, shear) might be relatively more influential during development than are the invariant strains that are considered important in the maintenance of skeletal mass [2].

Materials and Methods: Ulnae were obtained from 11 skeletally mature and 11 skeletally immature domestic turkeys. Two 5.0mm segments were cut transversely at mid-diaphysis. The 50% segment was embedded in polymethyl methacrylate and prepared for backscattered electron (BSE) imaging [7]. The dorsal (D), ventral (V), cranial (Cr), and caudal (Cd) cortices of the 60% sections of mature specimens were ashed at 550°C for mineral content (%ash) [7]. Two 200X BSE images were obtained from each of the D, V, Cr, and Cd cortices of immature bones; four 200X images (two endosteal and two periosteal) were obtained from each cortex of the mature specimens. Images were examined for: 1) OPD, 2) fractional area of secondary bone (FASB), 3) porosity, 4) osteocyte lacuna population density (OLPD), 5) new remodeling events (NREs = resorption spaces and newly forming osteons), and 6) predominant CFO [7]. CFO data were quantified as mean graylevels from circularly polarized light images of 100μ ultramilled sections of the 50% segments [1] (where "compression" = D, D-Cr, D-Cd, "tension" = V, V-Cr, V-Cd, and the neutral axis = Cr, Cd).

Results: The "compression" (dorsal) cortex exhibited relatively more oblique-to-transverse CFO than the "tension" cortex in both age groups (immature bones: 171.1+/-13.1 vs. 126.0+/-11.9; p<0.0001; mature bones: 185.0+/-11.4 vs. 153.7+/-15.0; p<0.0001). Cranial vs. caudal comparisons showed no differences in either age group (p > 0.25). Multiple regression analysis in mature bones (see Table) suggest that CFO is a primary adaptation, i.e., it is not linked to BMU remodeling. No secondary osteons were found in immature specimens, although porosity and OLPDs were significantly greater in immature specimens (1506.6+/-333.0 vs. 1202.2+/-215.4; p<0.0001). Apart from CFO data, the only significant regional differences existed in the caudal cortex (NA, shear) of mature specimens, which demonstrated greater cortical thickness (p<0.01) and higher OPD (p<0.01), OLPD (p<0.01), FASB (p<0.01) and porosity (p<0.01) when compared to other cortices. The caudal cortex also demonstrated lower %ash (caudal 68.9, cranial 70.2, dorsal 70.0, ventral 70.1) (p<0.05).

Table: Mature bones (R values)

	CFO	FASB	OPD	Porosity	OLPD	NREs
CFO	----	----	----	----	----	----
FASB	-.482+	----	----	----	----	----
OPD	-.495+	.987+	----	----	----	----
Porosity	-.387+	.534+	.450+	----	----	----
OLPD	-.709+	.349*	.378*	.183	----	----
NREs	-.309*	.456+	.400+	.698+	.124	----
ASH	-.332*	-.335*	-.328*	-.290	-.130	-.187

* p < 0.05, + p < 0.01

Discussion: These regional strain-mode(variant)-related CFO variations are consistent with data in various other bones [1,3,6,7] including the proximal human femoral diaphysis [8]. Recent studies suggest that these variations are adaptive – CFO has a significant role in differentially affecting regional bone toughness in tension and compression cortices across habitual neutral axes [5,9]. The organization of the caudal cortex of mature bones may be associated with shear strains, which, in this region, are more prevalent and localized than in the other cortical locations.

Empirical analyses demonstrate a *causal* role for variant-related stimuli in differentially adapting such regionally heterogeneous predominant CFO [10]. Variant-related attributes critical to the attainment of such adapted tissue morphology may include strain mode, direction and gradient, and related phenomena such as directional fluid flow. A dichotomous view of bone adaptation may eventually emerge from these data: 1) variant stimuli may be relatively more influential in the *attainment* of bone material organization, and 2) invariant stimuli may be more influential in the *maintenance* of skeletal mass. These hypotheses are amenable to experimental investigation. An important clinical challenge is to optimize such biophysical stimuli for preventive/therapeutic modalities that are aimed at curbing age-related skeletal senescence.

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