Introduction: A number of risk factors for stress fracture have been identified including poor physical fitness, external hip rotation, body height, body weight, age, race, level of physical activity, motivation, prior training history, footwear, smoking, and family history of osteoporosis [1]. Currently, having a narrow tibia relative to body mass is one of the best predictors of stress fracture risk and fragility [2]. However, the reasons why individuals with more slender bones for their body size are at increased risk of stress fracture are not fully understood. Understanding the mechanisms underlying this risk factor should lead to better identification of those at risk and, ultimately, to early diagnosis, treatment, and modification of training regimens.

Based on studies of bone morphology and bone quality in genetically distinct inbred mouse strains [3], mice with slender bones had increased mineral content suggesting that bone morphology and quality might be biologically coupled to satisfy mechanical demands imposed by weight bearing. Although increased mineral content may have compensated for the smaller morphology by increasing tissue stiffness and strength, the increased mineral had the adverse effect of being associated with increased bone brittleness and poor tissue damageability under fatigue loading. The possibility that slender bones may be associated with material level variation that ultimately leads to more damageable material than larger bones has not been considered in the human skeleton. To determine whether whole bone geometry is a predictor of tissue fragility we conducted a biomechanical and compositional evaluation of the tibiae from young adult males.

Methods: Tibiae from 17 male donors (age 17-46 yrs) with no known orthopaedic pathologic conditions were obtained and measures of bone morphology including cortical area (CrAr), AP and ML width, moments of inertia (IAP, ISL), and polar moment of inertia (I = IAP+ISL) were determined from mid-diaphyseal cross-sections at 30, 50, and 70% of the total tibia length. A slenderness index (S) was defined as the inverse ratio of the section modulus (J/width) to tibia length and body weight:

\[ S = 1/[(J/\text{width})/(L*BW)] \]

(1) where L = tibia length (cm) and BW = body weight (kg).

A total of 8 cortical bone samples (2.5mm x 5mm x 55mm) were machined from the diaphysis of each bone and split into 2 tests groups. First, monotonic failure properties were assessed by loading to failure in 4-point bending. Load and deflection were converted to stress and strain using equations which take yielding into consideration [4]. Mechanical properties measured were modulus (E), strength, work, and post-yield strain (PYe) as a measure of brittleness. Second, tissue damageability was assessed using a fifteen-cycle damage accumulation protocol in 4-point bending similar to that described previously [5]. The overall damage was the sum of each damage cycle plus interaction between existing damage and the increased applied load. The overall damage accumulation (D) was calculated by comparing the stiffness of the first and last diagnostic tests such that:

\[ D = 1 - S1/S0 \]

(2) where S1 is the stiffness of the last diagnostic cycle and S0 is the average stiffness of the first two diagnostic cycles and the first damage cycle.

The density, ash content, and water content were determined for each sample retrieved from the monotonic tests. Specimen volume, submerged weight, hydrated weight, dry weight, and ash weights were determined using Archimedes’ principal as described previously [6].

To determine whether bone morphology was related to tissue level material properties, partial correlation coefficients were determined between each morphological and compositional parameter (CrAr, width, IAP, ISL, J, S, Ash content) and each tissue level mechanical property (E, strength, PYe, work, D) while taking age into consideration.

Results: Significant correlations (p < 0.05) were only observed between post-yield properties and bone size and morphology (Table 1). AP width correlated with PYe and work indicating that the tissue of individuals with narrow tibiae was less ductile (Fig. 1). Further, there was a significant correlation between tissue damageability and tibia slenderness (p = 0.05) consistent with the mouse model suggesting that slender bones accumulate more cracks under equivalent loading conditions (Fig. 2). The relationship between mechanical properties and morphology could not be explained by differences in composition, as age corrected ash content did not correlate with any mechanical or geometric parameter (Table 1).

Discussion: This data indicated that not all bone is made the same way. Post-yield material properties related to damageability and fragility were also related to bone morphology. Having a more slender tibia was associated with tissue that was less ductile and more susceptible to damage accumulation. However, unlike the mouse model, increased mineral content was not associated with whole bone morphology and therefore not a strong explanatory variable of the variation in tissue fragility. Physical conditioning, which along with having a narrow tibia is a risk factor for stress fracture [7], is related to bone remodeling and ultimately affects microstructure. It has been reported that stiff and strong skeletons are not only developed by mineralizing collagen, but also by orienting the spatial disposition of the microstructural elements within the mineralized material [8]. Thus, under extreme loading conditions (e.g., military training), variation in bone quality, specifically tissue damageability, may be a contributing factor for increased stress fracture risk in individuals with a more slender bone.

Table 1. Pearson correlation coefficients are shown with p-values in parentheses. Data corrected for age based on linear regression method. Significant correlations in bold.

<table>
<thead>
<tr>
<th>Material Property</th>
<th>CrAr</th>
<th>Work</th>
<th>PYe</th>
<th>D</th>
<th>Ash Content</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>E (MPa)</strong></td>
<td>0.24</td>
<td>0.00</td>
<td>0.30</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Strength (MPa)</strong></td>
<td>0.35</td>
<td>0.00</td>
<td>0.32</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>PYe (MPa)</strong></td>
<td>0.40</td>
<td>0.00</td>
<td>0.50</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>D (MPa)</strong></td>
<td>0.38</td>
<td>0.00</td>
<td>0.40</td>
<td>0.00</td>
<td>0.03</td>
</tr>
</tbody>
</table>


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