DECREASED BONE MATERIAL STRENGTH IN SEVERE OSTEOGENESIS IMPERFECTA (OI)

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INTRODUCTION
Osteogenesis imperfecta (OI) is a disorder of bone fragility caused by genetic mutations that affect type I collagen. Severity varies widely, from mild to lethal in the perinatal period. The most severe form in children who survive the neonatal period, OI type III, can lead to several fractures over a lifetime.

Bone fragility in OI is believed to result from a combination of bone mass deficiencies and compromised material properties of the bone tissue. Little data, however, is available to describe bone material properties in individuals with OI. At the sub-microstructural scale, nanoindentation studies have found that the elastic modulus (E) of bone tissue is lower in children with severe OI (type III) than in normal controls [1], and that this property is slightly higher in mild vs. severe OI [2]. Bone material properties at the mesoscale, including strength and toughness, however, have not yet been characterized in individuals with OI.

The objectives of the current study were to measure the longitudinal and transverse flexural properties of cortical bone in individuals with severe OI and to compare these values with those of normal adults.

METHODS
Osteotomy specimens were collected from the tibial diaphyses of four adolescents (ages 13.5 ± SD 2.0, three males and one female) with OI type III (OI Group, N=4). These specimens were obtained during routine orthopaedic surgeries at Shriners Hospitals–Chicago, under an approved IRB protocol (Rush University Medical Center #10101309, Marquette University #HR-2167) and with informed consent from the donors. Control group specimens (N=4) were obtained from the mid-diaphyses of four cadaveric tibiae from adults (two males and two female donors, aged 50.5 ± SD 4.4) with no known musculoskeletal conditions.

The specimens were machined into rectangular beams using a low speed diamond saw. Each beam was machined such that its long axis was either longitudinal or transverse to the long tibial axis. A total of 1 to 6 beams per specimen were obtained in each the longitudinal and transverse directions. Beam depth and width were measured with a micrometer. Average depth and width were 628 µm (SD 49 µm) and 1018 µm (SD 43 µm). Beam lengths were 5-6 mm.

The beams were subjected to three-point flexural testing, using a validated method designed to characterize small bone specimens [3]. Yield strength (σy) was calculated using the 0.2% strain offset method. E was defined as the slope of the linear region of the flexural stress-strain curve, between 33% and 66% of σy. Flexural strength (σf,max) was determined as the maximum flexural stress. Toughness was estimated as the area under the stress-strain curve.

For each specimen, longitudinal properties were calculated as the average value over all available beams. The same was done for the transverse properties. Within-group (longitudinal vs. transverse orientation) and between-group (OI vs. control) comparisons were made using paired and unpaired t-tests, respectively.

RESULTS AND DISCUSSION
Representative flexural stress-strain curves for each group and each specimen orientation are shown in Fig. 1.

Within each group, all measured properties were significantly lower for transverse beams than longitudinal ones, p<0.04 (Table 1). In the control group, transverse properties were on average 60–96% lower than longitudinal ones. Similarly, in the
OI group, average transverse properties were 38-53% lower than those in the longitudinal direction.

![Graph](image.png)

**Figure 1:** Flexural stress-strain curves for typical specimens in the OI (grey) and control (black) groups. Within each group, longitudinal and transverse specimens are shown as thick and thin lines, respectively.

It has been suggested, based upon nanoindentation data, that the properties of OI bone tissue may be less anisotropic than those of normal bone [4]. The current results, however, demonstrate that, similar to normal bone, OI bone exhibits anisotropic material behavior at the mesoscale.

Compared with the control group, longitudinal properties were significantly lower in the OI group, with average differences of 74-83% (Table 1). Transverse E, σy and σf,max were also lower in the OI group by 46-65%. Toughness in the transverse direction, however, was not significantly different between the two groups.

In the control group, E and σf,max were similar to longitudinal values published previously for normal adult cortical bone, e.g., 15 GPa and 220 MPa, respectively [5,6]. For the OI group, however, σf,max was much lower than values reported for normal adolescent bone, i.e., 184-205 MPa [5].

Finally, although the two groups of donors in this study were not age-matched, similar σf,max values have been reported between normal adolescent and adult bones [5]. Therefore, the large decrease in strength observed in the OI (vs. control) group may be attributed primarily to the genetic disorder rather than to age differences between the groups.

**CONCLUSIONS**

The results of this study provide insight into the mechanisms of bone fragility in OI. More specifically, the results support the assertion that compromised tissue properties play a part in the structural fragility of bones in individuals with OI.

**REFERENCES**


**ACKNOWLEDGEMENTS**

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**Table 1:** Longitudinal and transverse flexural cortical bone properties for each group. Means (SD).

<table>
<thead>
<tr>
<th>Group</th>
<th>Orientation</th>
<th>E (GPa)</th>
<th>σy (MPa)</th>
<th>σf,max (MPa)</th>
<th>Toughness (MJ/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OI</td>
<td>longitudinal</td>
<td>3.7 (1.6) *</td>
<td>53 (21) *</td>
<td>67 (25) *</td>
<td>3.0 (0.5) *</td>
</tr>
<tr>
<td></td>
<td>transverse</td>
<td>2.3 (1.4) †</td>
<td>30 (18) *†</td>
<td>37 (21) *†</td>
<td>1.4 (0.7) †</td>
</tr>
<tr>
<td>Control</td>
<td>longitudinal</td>
<td>16.2 (0.7)</td>
<td>205 (6)</td>
<td>261 (10)</td>
<td>17.2 (5.2)</td>
</tr>
<tr>
<td></td>
<td>transverse</td>
<td>6.5 (1.2) †</td>
<td>64 (8) †</td>
<td>69 (7) †</td>
<td>1.3 (0.4) †</td>
</tr>
</tbody>
</table>

* p ≤ 0.05 compared with control group (between group comparisons)
† p ≤ 0.05 compared with longitudinal beams (within group comparisons).