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MATERIAL PROPERTIES OF BRITTLE BONES

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INTRODUCTION

Osteogenesis imperfecta (OI) is a genetic disorder of type I collagen that results in bone fragility. This fragility is believed to stem from a combination of bone mass deficiency and compromised bone material properties [1-3]. Little data, however, is yet available to describe bone material properties in individuals with OI. This study presents the first characterization of bone material strength and toughness in children with OI.

Previous studies have measured the elastic modulus (E) of bone specimens from children with OI using nanoindentation [3-5]. At that scale, E was found to be higher in children with severe OI vs. age-matched controls [3], and this property was also found to be slightly higher in children with mild vs. severe OI [5]. Nanoindentation measurements of E obtained along the long bone axis did not differ significantly from those obtained in the transverse direction, indicating that, compared to normal bone, OI bone exhibit more isotropy [4]. Bone properties in OI, however, have not yet been characterized at the mesoscale, and it is therefore not clear whether these observations from nanoindentation persist at a larger scale.

The first objective of this study was to measure the flexural properties of cortical bone from children with OI, and to compare those properties when loaded longitudinally vs. transversely to the long bone axis. The second objective was to investigate the relationships among cortical bone porosity and flexural properties.

METHODS

Eleven cortical bone specimens were collected from long bones of nine children with OI (Table 1). These specimens were obtained during routine orthopaedic surgeries at Shriners Hospitals–Chicago under informed consent and IRB approval (Rush #10101309, Marquette #HR-2167).

The specimens were machined into a total of 19 miniature rectangular beams using a diamond saw. Beam depth and width were measured with a digital micrometer. Average depth and width were 678 μm (SD 70 μm) and 1014 μm (SD 50 μm). A minimum beam length of 5 mm was chosen based on the dimensions of the smallest specimen obtained. Each beam was machined such that its long axis was oriented longitudinally (N=10) or transversely (N=9) to the long axis of the donated specimen (Table 1).

Table 1: Description of donors and bone specimens.

Specimen	Donor	OI type*	Age	Gender	Site
1	1	I	7	F	tibia
2	2	I	11	F	femur
3	3	III	16	M	tibia
4	4	III	14	M	tibia
5	4	III	14	M	tibia
6	5	III	8	F	humerus
7	6	III	9	F	tibia
8	7	III	3	F	femur
9	8	III/IV	9	M	tibia
10	8	III/IV	11	M	tibia
11	9	IV	6	F	tibia

* Phenotype: I (mild); III (severe); IV (moderate) [6].

Each beam was loaded to failure on an electromechanical testing system (Model 3345, Instron, Norwood, MA), using a previously validated 3-point bending test method designed to characterize small osteotomy specimens [7]. Each test consisted of five cycles of preconditioning up to 1 N, followed by a ramp to failure at a displacement rate of 2 mm/min (strain rate of approximately 0.9%/s).

The following flexural properties were determined from the load-displacement data obtained during the ramp to failure [7]. Yield strength (σ_y) was defined using the 0.2% strain offset method. Flexural strength ($\sigma_{f,max}$) was defined as the maximum flexural stress before failure. Modulus (E) was calculated as the slope of the flexural stress-strain curve between one and two thirds of σ_y. Finally, toughness was estimated as the area under the stress-strain curve.

Following mechanical testing, the beams were imaged by microcomputed tomography using a synchrotron light source (Advanced Light Source, Lawrence Berkeley National Laboratory, Berkeley, CA). Cortical porosity was defined as the volume occupied by voids relative to the total volume (Ca.V/TV), and was determined from the scans using ImageJ software and the plug-in BoneJ [8].

To assess whether the measured material properties are anisotropic in OI bone, these properties were compared between the longitudinal and transverse beams using a linear mixed model with random specimen effect. Finally, simple linear regression analysis was used to predict each flexural property from the porosity for each group of beams, i.e., longitudinal and transverse.

RESULTS

Flexural stress-strain curves for all beams are shown in Figure 1. Flexural properties differed significantly ($p<0.001$) between the longitudinal and transverse beams (Table 2). More specifically, E, σ_y, $\sigma_{f,max}$, and toughness were, on average, 68%, 74%, 78% and 87% lower for the transverse beams than for the longitudinal ones.

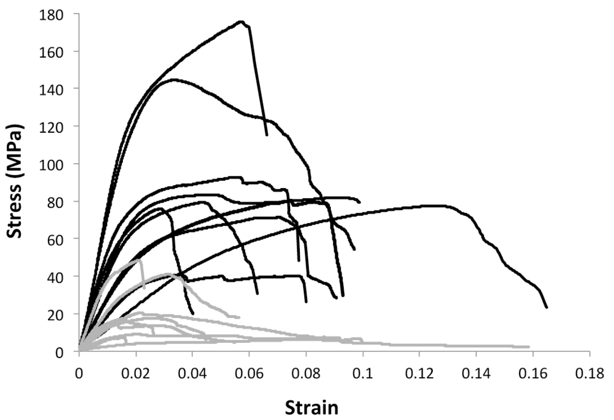

Figure 1: Flexural stress-strain curves for OI bone specimens oriented longitudinally (black) and transversely (grey) to the long bone axis.

Table 2: Flexural properties of longitudinal and transverse OI bone specimens relative to long bone axis. Mean (SD).

Orientation	E (GPa)	σ_y (MPa)	$\sigma_{f,max}$ (MPa)	Toughness (MJ/m^3)
Longitudinal	4.7 (2.0)	66.5 (28.3)	92.2 (39.0)	5.5 (2.8)
Transverse	1.5 (1.1)	17.0 (11.9)	20.4 (14.8)	0.7 (0.5)
P-value	<0.001	<0.001	<0.001	<0.001

The average porosity was 20.9% (SD 10.6%). This measure did not differ significantly between the longitudinal and transverse specimens (P=0.86). Analysis of association among flexural properties and cortical porosity is presented in Table 3 and Figure 2.

Table 3: Regression coefficients between the flexural properties of OI bone specimens and cortical porosity. P-values appear in parentheses. Asterisk (*) denotes P<0.05.

Property	Longitudinal	Transverse
E	-0.15 GPa/% (0.001)*	-0.06 GPa/% (0.135)
σ_y	-1.93 MPa/% (0.006)*	-0.59 MPa/% (0.163)
$\sigma_{f,max}$	-2.67 MPa/% (0.006)*	-0.68 MPa/% (0.202)
Toughness	-0.12 MJ/m^3/% (0.165)	-0.01 MJ/m^3/% (0.470)

DISCUSSION

Contrary to an observation made previously based on nanoindentation data [4], current results demonstrate that, similarly to normal bone, OI bone exhibits anisotropic properties at the mesoscale. Strength, E, and toughness were higher for specimens that were oriented longitudinally vs. transversely to the long bone axis.

Modulus results were lower than values measured by nanoindentation for pediatric OI bone [3-5]. This observation is not surprising, since bone specimens were dehydrated prior to nanoindentation, and nanoindentation tests are performed at a much smaller scale, which excludes the effect of pores, Haversian canals and other void spaces. Current results for longitudinal E and $\sigma_{f,max}$ were also smaller than values reported previously for normal pediatric and adolescent bone, i.e., 14-32 GPa [9] and 150-207 MPa [10], respectively. The lower E and $\sigma_{f,max}$ results in OI bone are likely attributed largely to substantial cortical porosity observed in these specimens. Regression analysis demonstrated that, for the longitudinal specimens, both E and $\sigma_{f,max}$ decreased with increasing porosity. Finally, for the two specimens having the lowest porosity, longitudinal E results (i.e., 7.3 and 8.5 GPa) were closest to normal values [9], while $\sigma_{f,mas}$ (i.e., 145 and 176 MPa) was within the normal range [10].

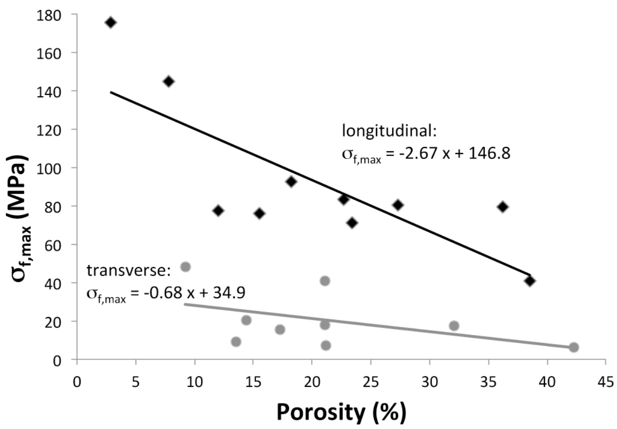

Figure 2: Relationships between flexural strength ($\sigma_{f,max}$) and porosity for OI bone specimens oriented longitudinally (black) and transversely (grey) to the long bone axis.

Surprisingly, porosity was not found to predict toughness, nor was it was found to predict flexural properties for the transverse beams. Further investigation into possible confounding factors, such as OI clinical phenotype, age, history of bisphosphonate treatments, and bone composition is warranted.

CONCLUSION

The current study presents the first characterization of bone material strength and toughness in OI. These results provide insight towards gaining a better understanding of bone fragility and the role of cortical porosity on the mechanical properties of bone in children with OI.

ACKNOWLEDGEMENTS

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