Tech4POD TECHNOLOGIES FOR PEDIATRIC ORTHOPAEDIC DISABILITIES
Marquette University Rehabilitation Research Center

BONE MODULUS IN OSTEOGENESIS IMPERFECTA BY NANOINDENTATION

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Introduction

Osteogenesis imperfecta (OI) is a genetic disorder that primarily affects type I collagen and leads to bone fragility. This fragility stems in part from bone mass deficiency [1]. Bone material properties are also believed to be compromised by the impaired collagen network and abnormal mineralization observed in OI [2,3]. However, little data is yet available to describe bone material properties in OI. The objective of this study was to compare the elastic modulus (*E*) of bone from young individuals with mild and severe OI.

Methods

Per an IRB approved protocol (MU HR-2167), eleven osteotomy specimens were collected from lower extremity long bones of ten individuals (ages 7-16 yrs) with OI: five with each mild and severe OI. The specimens were dehydrated in ethanol and embedded in resin (Figure 1).

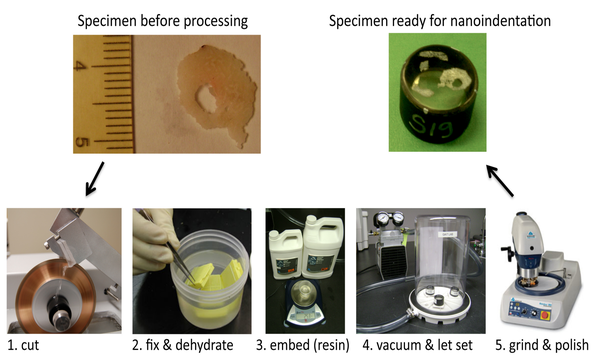

Figure 1. Processing of bone specimen prior to nanoindentation: cutting with a diamond saw, fixing and dehydrating in ethanol, embedding in resin, setting under vacuum, and polishing.

The polished cross-sections were indented with a nanoindenter (XP, MTS, MN), using a continuous stiffness measurement approach (45Hz, amplitude 2 nm, strain rate 0.05 s^{-1}) up to a depth of 1600 nm. Twenty indents were attempted in lamellar bone per specimen. In an attempt to explain the wide range of *E* observed within each specimen, lamellar microstructure was identified at each indent site as either osteonal or interstitial (Figure 2).

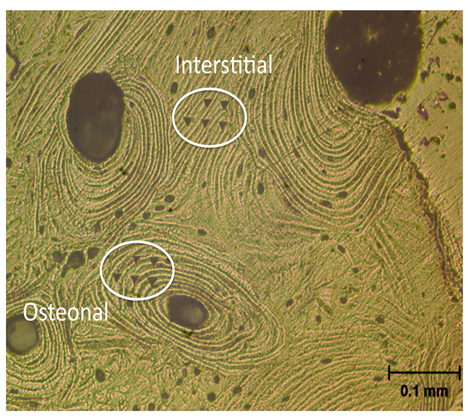

Figure 2. Typical indentation sites. The specimen shown was obtained from the femur of a 12-year-old girl with severe OI.

Table 1. Specimen Descriptions.

Specimen	OI type	Age	Gender	Anatomic site	Bisphosphonate use	# indents osteonal	# indents interstitial
1	I	16	M	Tibia	Yes	10	10
2	I	7	F	Tibia	Yes	11	0
3*	I	14	F	Tibia	Yes	9	3
4	I	13	M	Femur	Yes	7	9
5*	I	11	F	Femur	Unknown	8	10
6	I	15	M	Femur	Yes	0	8
7	III	12	M	Tibia	No	5	9
8	III	12	M	Tibia	No	2	14
9	III	14	M	Tibia	Yes	14	5
10	III	7	F	Tibia	No	5	6
11	III	12	F	Femur	Yes	13	10

*Specimens 3 and 5 were from the same subject.

The effects of OI severity (mild/severe) and lamellar microstructure (osteonal/interstitial) on *E* were analyzed using a linear mixed model. Four covariates were explored: age, gender, anatomic site (femur/tibia), and history of bisphosphonate treatment. Only covariates and interactions that were found to be significant ($p<0.05$) were included in the final model.

Results

OI severity, microstructure and anatomic site had significant effects on *E* (Table 2). Individuals with severe OI had lower mean *E* than those with mild OI by 1.2 GPa (7%). Osteonal regions on average had lower *E* than interstitial regions by 2.2 GPa (3%). Finally, *E* was higher in the tibia than the femur by 1.4 GPa (8%).

Table 2. Linear Mixed Model Results for *E*.

	Coefficient (GPa)	SE (GPa)	P value
Intercept (Mild OI, Interstitial, Femur)	17.5	0.5	<0.001
OI severity = Severe	-1.2	0.5	0.024
Microstructure = Osteonal	-2.2	0.3	<0.001
Anatomic site = Tibia	1.4	0.6	0.014

Discussion

A previous study found that *E* was higher in bones from children with severe OI than in age matched controls [4]. In the current study, *E* was slightly lower in severe than mild OI (Figure 3). This difference may be attributed to a lower collagen quantity in mild OI.

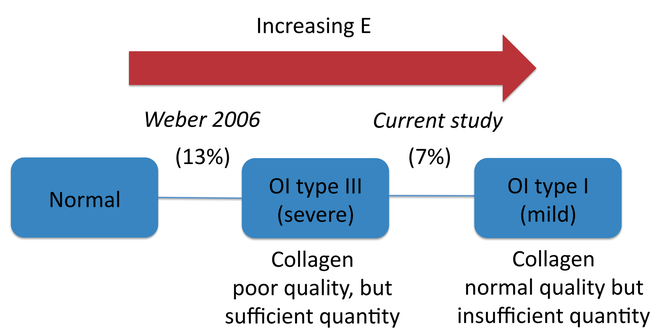

Figure 3. Comparison of bone elastic modulus (*E*) in children with and without OI.

Modulus was also lower in osteonal than interstitial bone regions. This difference is likely the result of a lower local degree of mineralization in osteonal bone. However, bisphosphonate treatments, which have become common in children with OI, did not have a significant effect on *E*.

A limitation of this study is that strength and toughness were not measured. Future research is therefore needed to determine how bone tissue strength and toughness are affected in OI, and whether those properties are compromised by bisphosphonate treatment.

Acknowledgements

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References

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