INTRODUCTION
Osteogenesis imperfecta (OI) is a genetic disorder that affects the production of type I collagen. A major characteristic of OI is bone fragility, caused in part by bone mass deficiency [1]. Impaired collagen network and abnormal mineralization have also been observed in OI [2,3], suggesting that bone material properties are also compromised. Little data, however, is yet available to describe bone material properties in OI. The objectives of this study were to measure and compare intrinsic elastic modulus ($E$) of bone tissue from young individuals with OI types I (mild) and III (severe), and to examine how this property varies between osteonal and interstitial regions.

METHODS
Per an IRB approved protocol (MU HR-2167), eleven osteotomy specimens were collected from long bones of ten individuals (ages 7-16 years) with OI: five with OI type I and five with type III. The specimens were dehydrated in ethanol and embedded in resin. The polished cross-sections were indented with a Nanoindenter XP (MTS, MN, USA), using a continuous stiffness measurement approach, in which a low magnitude oscillating force was superimposed onto a quasi-static force ramp. Frequency, amplitude, and strain rate were set as 45 Hz, 2 nm, and 0.05 s$^{-1}$, respectively. $E$ was averaged between indentation depths of 800 to 1600 nm. Twenty indentations were attempted in each specimen. Bone microstructure was observed at each indent site using a reflectance microscope. Indent sites were divided into two groups: osteonal and interstitial bone (Figure 1).

Figure 1: Typical indentation sites. The specimen shown was obtained from the femur of a 12 year-old girl with OI type III.

The effects of OI severity (OI types I/III) and lamellar microstructure (osteonal/interstitial) on $E$ were analysed using a linear mixed model. Four covariates were explored: age, gender, site (femur/tibia), and history of bisphosphonate treatment (yes/no). Covariates and interactions that were found to be significant ($p<0.05$) were included in the final model.

RESULTS
Anatomic site (femur/tibia) had a significant effect on $E$, therefore this covariate was included in the final statistical model. Other covariates and interactions did not have a significant effect and these were not included in the model.

OI severity, microstructure and anatomic site had significant effects on $E$ (Table 1). Individuals with OI type III had lower mean $E$ than those with type I by 1.2 GPa (approximately 7%). Osteonal regions had lower $E$ than interstitial regions by approximately 13%. Finally, $E$ was higher in the tibia than the femur by approximately 8%.

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>17.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Severity = OI type III</td>
<td>-1.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Microstructure = Osteonal</td>
<td>-2.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Anatomic site = Tibia</td>
<td>1.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

DISCUSSION AND CONCLUSIONS
Little is known about the material properties of bones in OI. In particular, bone properties have not yet been characterized for the most common form of OI, type I. The results of the current study indicate that bone tissue $E$ is slightly lower in OI type III than in type I. Results also show that $E$ values are lower in osteonal than interstitial regions. This difference is likely attributed to variations in local degrees of mineralization between these regions.

Bisphosphonate treatments have become common in children with OI. In this study, patient history of such treatment was not found to have 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 if these properties are compromised by bisphosphonate treatment.

REFERENCES

ACKNOWLEDGEMENTS
This work was supported by US Department of Education NIDRR grants H133P080005 and H133E100007.