Characterization of Brittle Mechanical Phenotype in Amish G610C model of Osteogenesis Imperfecta

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INTRODUCTION

Osteogenesis imperfecta (OI) is a hereditary bone disease where genetic mutations affecting collagen result in small, brittle bones. Established mouse models of OI are often severe, and therefore prohibitive of mechanical testing without significant specimen loss. Amish G610C is a moderate OI model, but it has been bred on several strains, thus literature data is inconsistent. This study is a comprehensive mechanical and architectural characterization of Amish mice based on a pure C57BL/6 inbred strain.

HYPOTHESIS

Amish mice will exhibit a distinct, brittle phenotype, independent of sex and age, with minimal specimen loss.

METHODS

Specimen Harvesting

Male and female wild-type (WT) and heterozygous (G610C) mice were euthanized at 10 and 16 weeks (n = 13-16). Right tibiae (RT) were cleaned of soft tissue and frozen in saline-soaked gauze.

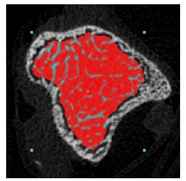


Figure 1. Sample trabecular ROI.

Micro-computed Tomography (µCT)

RT and hydroxyapatite phantoms were scanned via µCT (at 10 µm resolution) and analyzed for cortical and trabecular properties (Fig 1).

Mechanical Testing

RT were tested to failure in 4-point bending (Fig 2), at a displacement rate of 0.025 mm/s. µCT scans of failure sites were used to calculate mechanical properties.

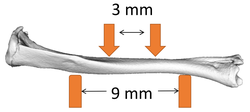
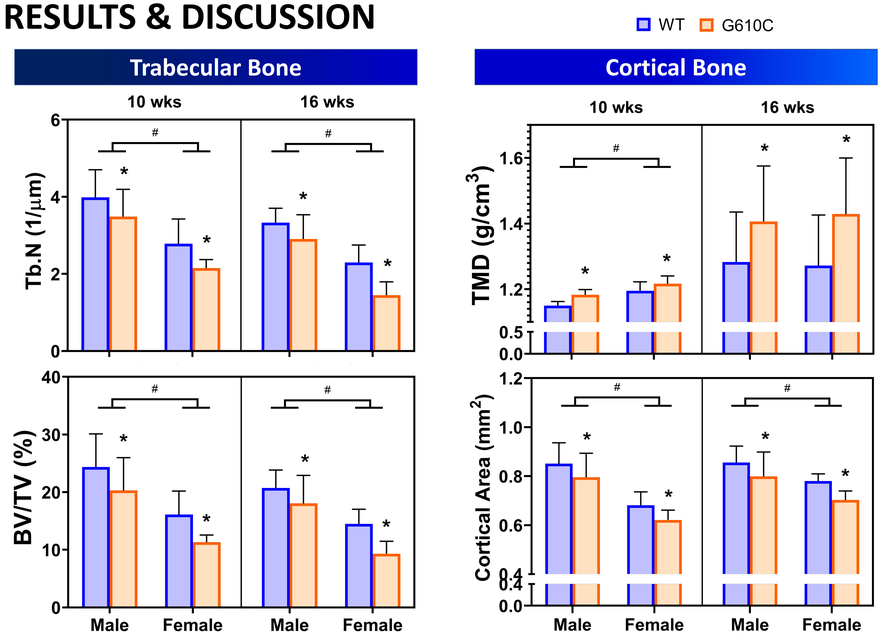


Figure 2. 4-pt bending test setup.

Statistical Analysis

Two-way ANOVA was performed with Tukey post-hocs for interaction.

RESULTS & DISCUSSION



Architecture analysis. Bars show average and standard deviation for trabecular number (Tb.N), trabecular bone volume % (BV/TV), cortical tissue mineral density (TMD), and cortical area, with main effects of sex (# p<0.05) and genotype (* p<0.05).

Bone Architecture

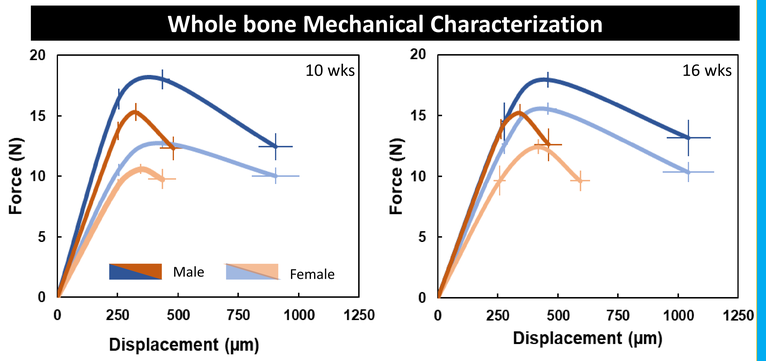
- *Small*: Less bone material in G610C bones (both trabecular and cortical)
- *Mineralized*: Higher tissue mineral density

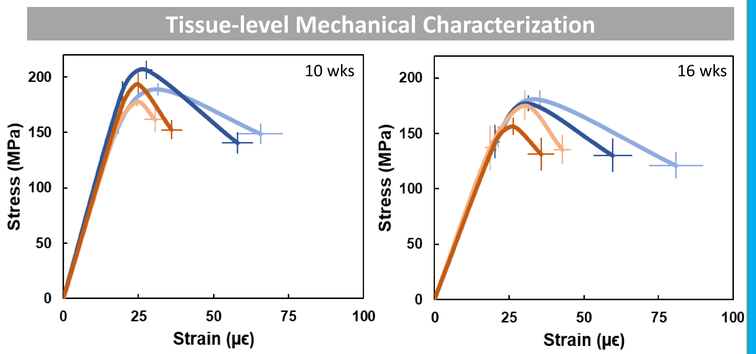
Mechanical Properties

- *Weak*: lower ultimate load, stress, and displacement
- *Brittle*: lower work, strain, and toughness

Summary

Architectural and mechanical properties are affected in both sexes and at both developmental (10 wks) and adult (16 wks) age points, demonstrating a main effect of genotype. Further, there were no spontaneous fractures noted in any bones harvested from the Amish mice.





Mechanical analysis. (above) Average force-displacement and stress-strain plots.

Summary Table. (below) Mechanical properties that are reduced in G610C mice.

Whole-bone	Tissue-level
Displacement (Postyield and Total) Work (Postyield and Total) Yield Force Ultimate Force Stiffness	Total Strain Toughness

LAB CONTACT

ACKNOWLEDEGEMENTS

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CONCLUSION

Despite being a moderate OI model, the Amish G610C mouse model maintains a distinctly brittle phenotype and is well-suited for use in treatment, loading, and mechanical analysis studies.

Jackson Laboratory C57Bl/6 mouse

FUTURE WORK

To more fully demonstrate this brittle phenotype, work is ongoing to analyze femurs and vertebrae in fracture toughness and compression tests, respectively.