INTRODUCTION

Bone and Type I Collagen

- Bone's hierarchical structure spans 10 orders of magnitude in length.
- Fundamental constituents: hydroxyapatite and Type I collagen (see below).

Osteogenesis Imperfecta (OI)

- Mutations in collagen compromise triple helix structure and quality.
- Detrimental impacts across length scales.
- Mutations lead to the production of α1 homotrimers.
- α1 homotrimers alter the mineralization process.

Multiscale Analysis

- Studies at various lengths scales have been performed in oim/+ and oim/oim mice.
- Limited work performed at multiple scales within same study.
- Goal: perform multiscale analyses in bone from oim/+ and oim/oim, maintaining samples close to physiological conditions as possible.

RESULTS AND DISCUSSION

Nanoscale Morphology and Tissue Chemistry

- Mean D-spacing ↓ in oim/+ and oim/oim vs. WT.
- Driven by kinking in tropocollagen molecules?
- Mean D-spacing distributions differed for all groups.
- oim/oim shifted ↓ for entire population vs. WT.
- oim/+ intermediate: due to the presence of both heterotrimers and homotrimers?
- Homotrimers may alter crosslinking and stability.

Bone

- Volumetric bone mineral density (vBMD) at 5 locations.
- Indentation to 2 N for 5 loading cycles.
- Cycle-by-cycle analysis using MATLAB script.

Whole Bone Mechanics (3 pt Bending)

- Displacement control, 0.3 mm/sec, posterior surface in tension.
- Stress/strain from beam bending equations.

MATERIALS AND METHODS

Animals

- 12 week female mice from Jackson labs:
  - wild type (WT), oim/+ and oim/oim
  - Femora used: n=15 per group

Atomic Force Microscopy (AFM)

- Right femur (n=5) mounted, polished, treated with 0.5M EDTA (pH=8).
- 3 anterior sites per bone, ~55 fibrils per bone analyzed by 2D FFT for D-spacing.

Raman Spectroscopy

- Right femur's (n=5-6): 5 locations along unprocessed posterior surface.

CONCLUSIONS

- OI-induced changes to the collagen triple helix modified the assembly of collagen fibrils.
- Disease-specific shift in D-periodicity caused by α1 homotrimers alters the mineralization process.
- Changes in the collagen/mineral composite impact mechanical properties of the tissue.
- Tissue deficiencies and altered structure result in weaker bone with decreased post-yield behavior.

Molecular changes to collagen due to OI altered both the organic and inorganic phases of bone causing defects throughout the bone hierarchy leading to architectural flaws, decreased strength and brittle behavior.