Introduction

Raloxifene (RAL) is a FDA-approved pharmacological agent that has been clinically used to decrease fracture incidence in post-menopausal women. Recent work has shown that RAL improves bone quantity and quality. In this study, we investigated the effects of RAL on Osteogenesis Imperfecta (OI) mice.

Hypothesis

Raloxifene will produce beneficial effects on bone mechanical properties in a mouse model of OI.

Materials and Methods

Experiment Design #1: Ex vivo effects of Raloxifene

Animals and Sample Preparation

- Paired tibiae from 12-week-old homozygous OIM (B6C3F1a/a-Col1a2oim/Col1a2oim) and WT (B6C3F1a/J a/a) female mice
- Soaked in either PBS (left tibiae) or 2 μM raloxifene (right tibiae) for 13 days
- Incubated at 37° C
- Supplemented with 1% Pen/Strep

Mechanical Testing

- Four-point bending to failure
- 9 mm bottom support; 3 mm loading span
- Displacement rate of 0.025 mm/sec

Fracture Assessment

- # of fractures with raloxifene treatment

Cortical Architecture

- Measurement of bone volume fraction (BV/TV)
- Trabecular number and thickness
- Trabecular separation
- BMD

Cancellous Architecture

- OIM resulted in:
  - Decreased mechanical properties (both pre- and post-yield)
  - Reduced bone volume fraction (BV/TV)
  - Increased trabecular number and thickness
  - Reduced trabecular separation
  - Increased BMD

Conclusion

In accord with previous data, Osteogenesis Imperfecta is characterized by smaller, weaker bones with decreased mechanical integrity. Raloxifene treatment resulted in decreased fracture incidence and improved post-yield mechanical properties. Raloxifene significantly reduced the number of fractures in OI mice, providing initial framework for an alternative approach to treating OI.