Measured Cortical Bone Strain during Muscle Contraction in a Mouse Model of Osteogenesis Imperfecta

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Introduction

Osteogenesis Imperfecta (OI)

- Heritable bone disease caused by mutation in genes encoding Type I collagen
- Characterized by small, weak bones
- Typically also have weakened muscles (sarcopenia)
- OI murine (OIM) model recapitulates sarcopenia and osteoporosis [1, 2]

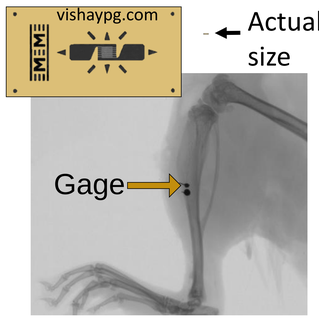
1) Bone responds to the strains engendered on it
2) Muscle contraction is one contributor to bone strain

Is weakened muscle able to engender strain on weakened bone?

Methods

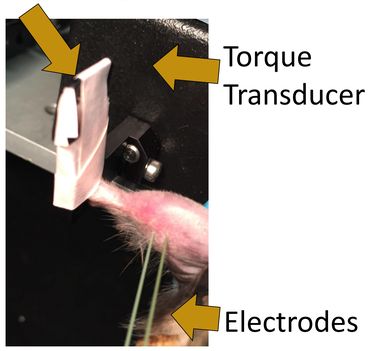
Animal Model

- OIM male mice on a C57BL/6J background
- Age: 16 weeks



Strain Gage Attachment

- Surgically attached to the anteromedial portion of the midshaft tibia using cyanoacrylate adhesive



Muscle Stimulation

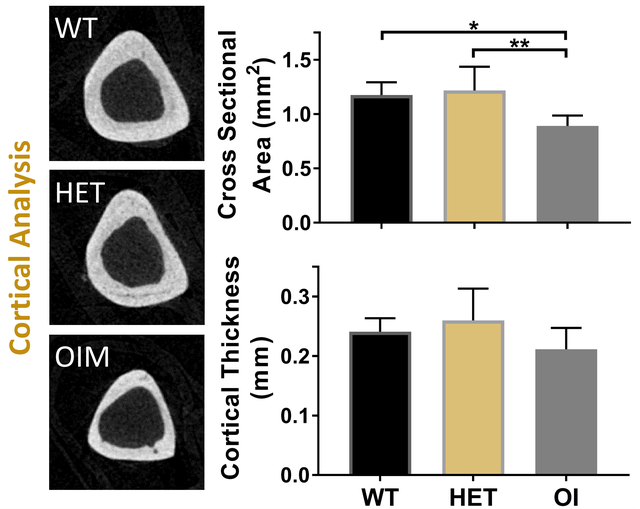
- Mouse moved from surgical suite to muscle stimulation machine
- Stimulation protocol
  - Frequency Range: 25 – 300 Hz
  - Pulse Width: 0.5 msec
  - Stimulation Length: 200 msec
- Measured muscle torque and bone strain simultaneously

Ex vivo Computed Tomography (CT)

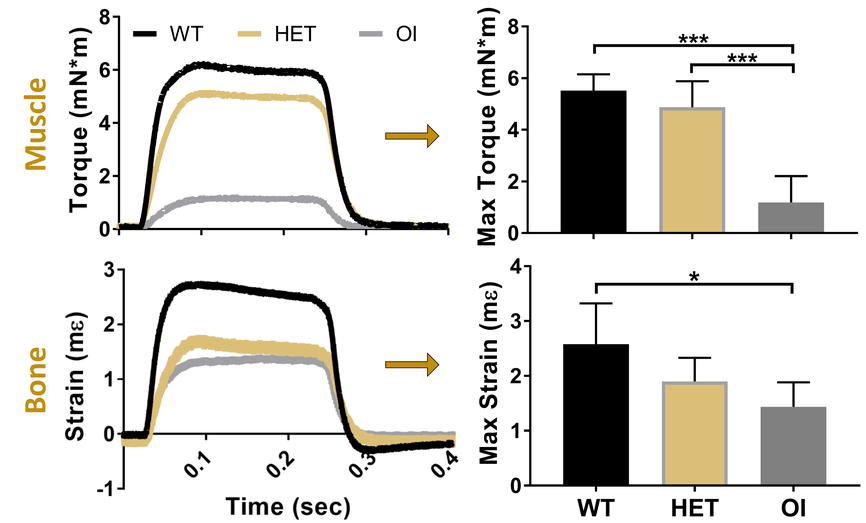
- 10 µm voxel size
- Cancellous Analysis - 1-mm ROI in the proximal metaphysis
- Cortical Analysis - 1-mm ROI centered at 50% of bone length

Results

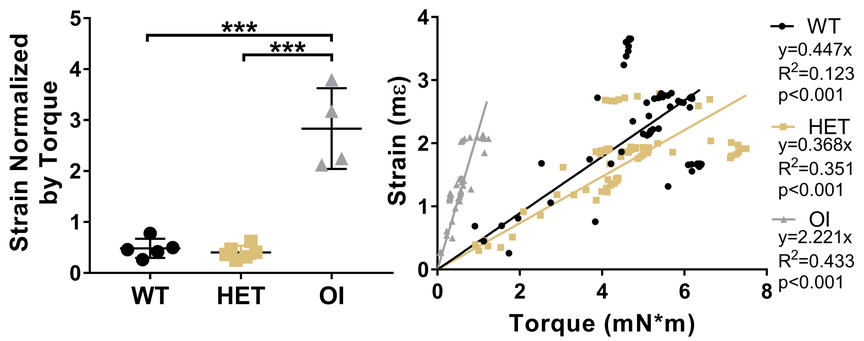
Bone Properties



Muscle Stimulation



Combined Effect



Although OIM muscles were weaker, because the bone was smaller and less stiff, the OI mice required far less muscle torque to engender strain on bone.

The OI mice required far less muscle torque to engender strain on bone. In addition, the average strain engendered on OI bone during muscle contraction was 1400 µε, which is within the range of strains shown to induce bone formation. This suggests that muscle stimulation may be a viable means to induce bone formation in this OI mouse model.

References

[1] Gentry BA, et al. *Matrix Bio.* 2010;29(7):638-644.
[2] Bart, ZR, et al. *Connective tissue research.* 2014;55:4-8.

Acknowledgements

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