A Human Model of Bone Adaptation: Effects of Short-Term Mechanical Loading

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INTRODUCTION

Bone responds to novel mechanical loads by adapting to best resist those loads. This concept provides a theoretical basis for developing mechanical-loading-based interventions to preserve or enhance bone mass and bone strength.
To optimize this approach it is necessary to link the exact mechanical conditions experienced by the bone with the resulting adaptation. Animal loading models such as the turkey ulna, rat ulna, and mouse tibia loading models have been used for this purpose.[1,2,3]

Although the fundamental biological processes of bone apposition and resorption are preserved between species, large differences in metabolism and size exist between these animals and humans.

Our purpose was to develop a human model of bone adaptation and measure the adaptive response due to controlled and known mechanical loading conditions.

METHODS

Subjects

- 25 young women (age: 23±4 years, height: 163±8 cm, mass: 65±10 kg) separated into 3 groups (10, 10, and 5 women each)

Intervention

- Subjects applied a 300 N force to the non-dominant radius by leaning onto the hand (Figure 1)
- 50 loading cycles per day, 3 days per week*
- Target frequency: 0.5 Hz (sound cues provided)

Data Collection

- Dual Energy X-ray Absorptiometry (DXA) at serial time points
- Computed Tomography (CT) pre/post in select subjects

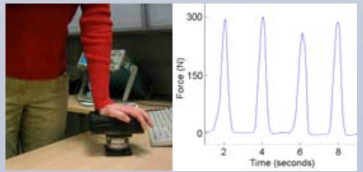

Figure 1 Loading set-up and actual force recording. A subject loads her wrist by leaning on it until the target force is reached. Forces are recorded by a computer that provides real-time visual feedback to the subject. A sound cue is provided every 2 seconds.

*Group 1 (10 subjects) loaded only 2 days per week.

** Open source software *IA-FEMesh* and *FEBio* were used to generate and run all finite element models.

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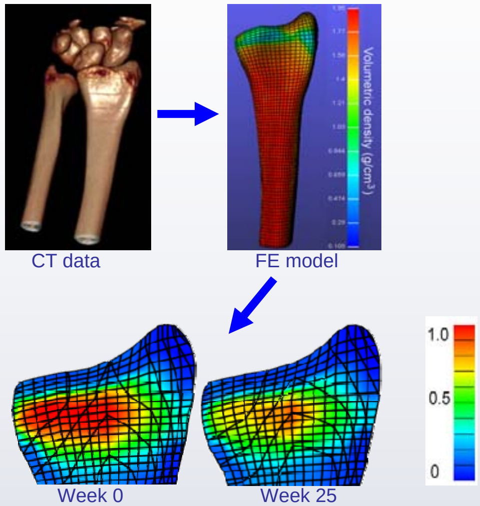

Figure 2 FE Model generation (top) and results (bottom). The bottom figures show a cut-away of the FE model loaded to 1900 N showing failure criterion (1=failure) for loaded wrist at week 0 and week 25

DATA ANALYSIS

DXA

- Data were collected every 7-14 weeks for both radii; unloaded (dominant) radii were considered a within-subject control
- Bone mineral content (BMC) of the ultra-distal region (15 mm proximal to subchondral plate) was analyzed
- Paired t-tests compared week 0 to week *n* for the loaded (dominant) and unloaded (non-dominant) radius
- Single-sample t-test (versus zero) compared percent change from week 0 to week *n* for each radius

CT

- Data were collected on one subject at week 0 and 25
- Voxel size: 625 x 231 x 231 microns
- Calibration phantom included
- 15-mm transverse ultra-distal region analyzed for:
  - Mineralized tissue volume (mm^3 of thresholded voxels)
  - Mean Hounsfield Unit of tissue (HU)
  - I_{min} of distal-most 5 mm transverse slices

Models

- 4 subject-specific finite element (FE) models were created based on CT data (loaded and unloaded, 0 and 25 weeks)**
- Continuum material properties were assigned based on HU
- Radii were fixed proximally and compressed axially to simulated failure as determined by distortion energy failure criterion (Figure 2)[4,5]

RESULTS

DXA

- Loaded radius BMC decreased 7, 13, and 14 weeks after beginning the intervention ($p<0.05$)
- Loaded radius BMC returned to baseline after 25-33 weeks
- No change in control radius at any time point

CT *(week 25 vs. 0, loaded / unloaded)*

- Mineralized tissue volume ↑ 6.1% / ↓ 1.0%
- Mean HU of tissue ↑ 9.1% / ↔ 0%
- Failure strength ↑ 36% / ↓ 6.2%
- I_{min} ↑ 13.3% / ↓ 7.4%

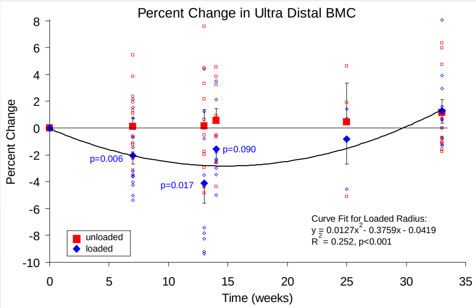

Figure 3 Percent change in BMC from baseline to each time point, for a total of 25 subjects. Solid symbols show the group mean; hollow symbols show each individual data point. Error bars show the standard error. P-values indicate means that are different from 0% at select time points.

DISCUSSION

We have developed methods to induce and measure bone adaptation due to controlled mechanical loading in young women. With this model we have shown that novel mechanical loads cause a temporary decrease in BMC in young women at 7-14 weeks after initiating the regime.

After 25 weeks there was no significant change in BMC compared to the baseline value, but subject specific models estimated a 36% increase in fracture strength due to mechanical loading in one pilot subject. This increase is functionally and clinically relevant and indicates that a mechanical loading intervention may be a plausible means to prevent distal radius fractures.

Current work with this model focuses on quantifying mechanical changes during the 7-14 week time period, expanding the model to other populations, and determining the effect of loading-signal specifics.

References: **[1]** Gross TS, Srinivasan S, Liu CC et al. J Bone Miner Res 2002;17(3):493-501. **[2]** Hsieh YF, Silva MJ. J Orthop Res 2002;20(4):764-771. **[3]** Rubin CT, Lanyon LE. J Orthop Res 1987;5(2):300-310. **[4]** Troy KL, Grabiner MD. J Biomech 2007;40(8):1670-1675. **[5]** Keyak JH, Rossi SA. J Biomech 2000;33(2):209-214.