Background

Why Quantifying Change in Bone via Bone Remodeling is Objective of NASA Digital Astronaut Project (DAP)

- One of the main objectives is to provide a tool to help HHC address Bone Gap
- Exercise induced loading
- Hernández, C.
- One effort is underway to evaluate
- Develop/formulate a daily load formula for quantifying exercise
- A bone remodeling formulation that quantifies dynamic changes in bone has the potential of tracking changes in
- Compare
- Time
- Group
- \( \epsilon \)
- Develop model for predicting bone adaptation for trochanter, total
- LeBlanc, A.
- Integrate the computational model with Finite Element Method

Bone Remodeling Model Implementation Plan

- Simulation of Bone Mineral Changes
- Predict Bone Strength Changes
- Help reduce lifetime bone health risks to astronauts
- Insight into efficacy of exercise protocols to maintain bone

Modeling the Influence of Skeletal loading

Some likely intermediaries that enable sensor cells to trigger effector cells are NO and PGE2 [5].

Expression for Osteoprotegerin (OPG). RANKL and the ligand receptor complexes are derived via mass balance equations. The complete detailed set of cellular dynamics is a considerable modification of the work of

Lemarie et al. [2] and Pronskova et al. [3] with the addition of effectors related to skeletal loading.

Sensing strength or response level (SL) defined in relation to bone strain

\[ SL = f(\epsilon) = \frac{-\epsilon^2}{2} + 1 \]

Complete Unloading \( \epsilon = 0 \)

Remodeling Balance \( \epsilon = \epsilon_0 \)

\[ SL = 1 \]

NOTE: Osteocytes are generally understood to be the sensor cells

Production rate of NO and PGE2 per cell are defined to be proportional to SL

<table>
<thead>
<tr>
<th>State Variables and Definitions</th>
<th>Mathematical System and Equations</th>
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</thead>
<tbody>
<tr>
<td>( B_{0} ) Bone Volume Fraction</td>
<td>( \dot{B} = \dot{B}_{0} ) Bone Volume Fraction</td>
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<tr>
<td>( a_{0} ) Average Activity</td>
<td>( \dot{a} = a_{0} ) Average Activity</td>
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<tr>
<td>( \alpha ) Density of Mineralized Bone</td>
<td>( \dot{\alpha} = \alpha ) Density of Mineralized Bone</td>
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<tr>
<td>( \beta ) Density of Osteoid</td>
<td>( \dot{\beta} = \beta ) Density of Osteoid</td>
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<tr>
<td>( \gamma ) Density of Unmineralized Osteoid</td>
<td>( \dot{\gamma} = \gamma ) Density of Unmineralized Osteoid</td>
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<tr>
<td>( \delta ) Rate of Unmineralization</td>
<td>( \dot{\delta} = \delta ) Rate of Unmineralization</td>
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<tr>
<td>( e ) Rate of Formation</td>
<td>( \dot{e} = e ) Rate of Formation</td>
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<tr>
<td>( \theta ) Mass of Bone ash</td>
<td>( \dot{\theta} = \theta ) Mass of Bone ash</td>
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<tr>
<td>( \psi ) Mass of Bone Total</td>
<td>( \dot{\psi} = \psi ) Mass of Bone Total</td>
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<tr>
<td>( \phi ) Mass of Bone Mineral</td>
<td>( \dot{\phi} = \phi ) Mass of Bone Mineral</td>
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<td>( \chi ) Mass of Bone Organic</td>
<td>( \dot{\chi} = \chi ) Mass of Bone Organic</td>
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<tr>
<td>( \rho ) Mass of Bone Water</td>
<td>( \dot{\rho} = \rho ) Mass of Bone Water</td>
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Converting Experimental Data to Model Variables

- Ash density \( \rho_{\text{ash}} = \frac{m_{\text{ash}}}{V_{\text{total}}} \)
- Apparent (dry) density \( \rho_{\text{app}} = \frac{m_{\text{dry}}}{V_{\text{total}}} \)
- Ash fraction \( \alpha = \frac{\rho_{\text{app}}}{\rho_{\text{ash}}} \)
- Density of Mineralized Bone \( \alpha_{\text{m}} = \frac{\rho_{\text{ash}} - \rho_{\text{water}}}{\rho_{\text{ash}}} \)

Preliminary Validation Results for Bone Deconditioning Simulations

- Seven:
  - A Pre-Bed Rest QCT BMD value.
  - A Bed Rest Duration of N days.
  - A Post-Bed Rest QCT value.

  1. (a) Convert \( \rho_{\text{ash}} \) to \( \rho_{\text{app}} \) (e.g. Keyak regression)
  2. (b) Compute initial ash fraction \( \alpha_{0} = \frac{\rho_{\text{app}}}{\rho_{\text{ash}}} \)
  3. Initial value \( M_{\phi} = \rho_{\text{ash}} / (\phi + \rho_{\text{water}}) \)
  4. Solve for initial value \( O \) using \( \theta = \frac{\psi - \phi}{\phi + \rho_{\text{water}}} \)
  5. Run computational simulation subject to loading history (i.e. bed rest) for N days to track change in \( M_{\phi} \) at \( \rho_{\text{app}} = \rho_{\text{ash}} \) (BMD), and BFP
  6. Compare BMD to QCT BMD

References


Future Work

Near Term:
- Develop/deliver a daily load formula for quantifying exercise induced loading and test against exercise treated subjects (e.g. CF7W study)
- Long Term:
  - Develop method for transforming force data from biomechanics modeling of specific exercise devices into stress/strain input
  - Integrate the computational model with Finite Element Method
  - Validate model using QCT data from spaceflight research
  - Develop model for predicting bone adaptation for trochanter, total proximal femur and lower hamber
- Bone adaptation prediction for more than 180 days of spaceflight exposure with exercise countermeasure

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