**The Digital Astronaut Project Bone Remodeling Model**

J.A. Pennline¹, L. Mulugeta², B.E. Lewandowski¹, W.K. Thompson¹, and J.D. Sibonga³

¹NASA Glenn Research Center, Cleveland, Ohio, James.A.Pennline@nasa.gov

²Universities Space Research Association, Houston, Texas

³NASA Johnson Space Center, Houston, Texas

**INTRODUCTION:** Under the conditions of microgravity, astronauts lose bone mass at a rate of 1% to 2% a month, particularly in the lower extremities such as the proximal femur [1]. The most commonly used countermeasure against bone loss has been prescribed exercise [2]. However, current exercise countermeasures do not completely eliminate bone loss in long duration, 4 to 6 months, spaceflight [3,4], leaving the astronaut susceptible to early onset osteoporosis and a greater risk of fracture later in their lives. The introduction of the Advanced Resistive Exercise Device, coupled with improved nutrition, has further minimized the 4 to 6 month bone loss. But further work is needed to implement optimal exercise prescriptions [5]. In this light, NASA’s Digital Astronaut Project (DAP) is working with NASA physiologists to implement well-validated computational models that can help understand the mechanisms of bone demineralization in microgravity, and enhance exercise countermeasure development.

**METHODS:** The objective of the DAP computational modeling effort is to enable simulations in time of changes in bone mineral density (BMD) and Bone Volume Fractions (BVF) under the conditions of skeletal unloading and changes in physiological processes encountered in microgravity. Since the geometry of the remodeling units or bone packets that are removed and replaced during remodeling differ, separate modules for trabecular bone and cortical bone are developed. Key elements of the computational model include: Bone resorption (formation) rate varies with activation density, volume of remodeling unit removed (replaced), and active osteoclast (osteoblast) population. The active osteoblast and osteoclast populations vary according to the cellular dynamics mediated by hormones, proteins, ligands and receptors. The well-known adaptive response theory of Frost drives the bone response to variations in skeletal loading. Within the expressions for rates of changes of the cellular populations, assumptions for the ligand and receptor expressions are modeled in accordance with the American Society of Bone and Mineral Research educational literature.

**INITIAL MODEL DEVELOPMENT** The model’s initial development focuses on the femoral neck. Remodeling unit dimensions for the femoral neck (particular for cortical bone) were identified in the literature to make the model specifically applicable to the femoral neck, although many other model parameters were based on general bone knowledge. For model validation, we used BMD changes of control subjects in the current 70 day bed rest study and available data from the 17-week bed rest studies conducted in the past (Figure 1). Volumetric bone densities for the 70 day bed rest were obtained at pre and post bed rest via Quantitative Computed Tomography (QCT). However, bone densities from past bed rest studies were obtained via Dual-energy X-ray Absorptiometry (DXA). Given that DXA is 2-D integrated cortical and trabecular, and the computational model tracks BVF changes, the DXA values were mapped to equivalent QCT integral volumetric density values in order to run simulations with the DXA data. Our poster will discuss in detail how the model tracks BVF and the preliminary model validation results.

**DISCUSSION AND FUTURE WORK:** Our results show that a good foundation has been laid for establishing a physiologically accurate bone remodeling model. For example, mean BMD data for the 70-day bed rest is well within the 95% confidence interval of the model prediction. Future work will integrate the bone remodeling model with DAP’s biomechanical exercise models to predict the benefits of exercise induced load stimulus from different exercise prescriptions for maintaining bone at the femoral neck. The model will also be extended to include predictions for the lower lumbar spine, calcaneus, trochanter and the integrated proximal femur.

The Digital Astronaut Project Bone Remodeling Model

J.A. Pennline¹, L. Mulguta², B.E. Lewandowski³, W.K. Thompson¹, and J.D. Sibonga¹

¹NASA Glenn Research Center, Cleveland, Ohio, James.A.Pennline@nasa.gov
²Universities Space Research Association, Houston, Texas
³NASA Johnson Space Center, Houston, Texas

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 HBC address Bone Gap Factor. We don’t know the contribution of each ride factor to bone loss and recovery of bone strength and which factors are the key drivers for countermeasure application and efficacy. We need to identify options for mitigation of early onset osteoporosis before, during, and after spaceflight.

- Skeletal loading, along with substrate regulation and local mechanical loading, act to drive the physiological remodeling of bone, responsible for maintaining bone.
- Exercise induced loading, with appropriately designed protocols, allows us to take advantage of specific exercise programs and feedback to evaluate the beneficial or counterproductive effects.

Bone Remodeling Model Implementation Plan

Modeling the Influence of Skeletal loading

The most likely intermediate that enable sensor cells to trigger effectors cells is NO and PGE-2 [11].

- PGE-2 stimulates differentiation of osteoblasts (e.g. by TGF-β), stimulates proliferation of osteoblasts.
- NO inhibits production of RANKL.
- The model follows the level of expression of NO and PGE-2 according to the level of bone apposition or bone resorption suggested by the daily strain in a First Mechanism Theory as outlined below.

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

Model Representation of Bone Loss Due to Insufficient Mechanical

Converting Experimental Data to Model Variables

Preliminary Validation Results for Bone Deconditioning Simulations

Future Work

NOTE: Doses are generally unknown to be the sensor cells.

- Production rate of NO and PGE-2 per cell are defined to be proportional to SL.
- The model follows the level of expression of NO and PGE-2 according to the level of bone apposition or bone resorption suggested by the daily strain in a First Mechanism Theory as outlined below.

Modeling the Influence of Skeletal loading

The most likely intermediate that enable sensor cells to trigger effectors cells is NO and PGE-2 [11].

- PGE-2 stimulates differentiation of osteoblasts (e.g. by TGF-β).
- Stimulates proliferation of osteoblasts.
- The model follows the level of expression of NO and PGE-2 according to the level of bone apposition or bone resorption suggested by the daily strain in a First Mechanism Theory as outlined below.

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

Model Representation of Bone Loss Due to Insufficient Mechanical

Converting Experimental Data to Model Variables

Preliminary Validation Results for Bone Deconditioning Simulations

Future Work

Test Types

- Develop an algorithm to daily load factor for quantifying exercise induced loading and test against exercise treated subjects (e.g. CFT-5 study).

Legend

- Develop system for transforming force data from biomechanics modeling of specific exercise device, into-strain input.
- Integrate the compartmental model with Finite Element Method.
- Validate model using QCT data from spaceflight research.
- Develop model for predicting bone adaptation for therapeutic, total proximal femur and lower lumbar.
- Bone adaptation prediction for more than 180 days of spaceflight exposure with exercise countermeasures.

Acknowledgements

This work is funded by the NASA University Research Program, managed by the NASA Johnson Space Center. Specifically, this work is part of the Digital Astronaut Project (DAP), which directly supports the Human Health and Countermeasure Element. The DAP project is managed by the NASA-Glenn Research Center (GRC) via Debra W. Griffin, Ph.D., and section Chief of USRA Houston serves as the DAP Project Scientist.

References