

<b>Fiscal Year:</b>	FY 2016	<b>Task Last Updated:</b>	FY 06/02/2016
<b>PI Name:</b>	Pennline, James Ph.D.		
<b>Project Title:</b>	Digital Astronaut: Bone Remodeling Model		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>			
<b>Program/Discipline--Element/Subdiscipline:</b>			
<b>Joint Agency Name:</b>	<b>TechPort:</b>	Yes	
<b>Human Research Program Elements:</b>	(1) <b>HHC:</b> Human Health Countermeasures		
<b>Human Research Program Risks:</b>	(1) <b>Bone Fracture:</b> Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (2) <b>Osteo:</b> Risk Of Early Onset Osteoporosis Due To Spaceflight		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Comments:</b>			
<b>Project Type:</b>	GROUND	<b>Solicitation / Funding Source:</b>	Directed Research
<b>Start Date:</b>	04/01/2011	<b>End Date:</b>	09/30/2017
<b>No. of Post Docs:</b>	0	<b>No. of PhD Degrees:</b>	0
<b>No. of PhD Candidates:</b>	0	<b>No. of Master' Degrees:</b>	0
<b>No. of Master's Candidates:</b>	0	<b>No. of Bachelor's Degrees:</b>	0
<b>No. of Bachelor's Candidates:</b>	0	<b>Monitoring Center:</b>	NASA JSC
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<b>Flight Program:</b>			
<b>Flight Assignment:</b>	NOTE: Extended to 9/30/2017 per D. Griffin/GRC (HRP monitor)--Ed. 10/9/15		
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Mulugeta, Lealem ( Universities Space Research Association )		
<b>Grant/Contract No.:</b>	Directed Research		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>	<p>Background</p> <p>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. The most commonly used countermeasure against bone loss in microgravity has been prescribed exercise. However, data has shown that existing exercise countermeasures are not as effective as desired for preventing bone loss in long duration spaceflight. This spaceflight related bone loss may cause early onset of osteoporosis to place the astronauts at greater risk of fracture later in their lives. Consequently, NASA seeks to have improved understanding of the mechanisms of bone demineralization in microgravity in order to appropriately quantify this risk, and to establish appropriate countermeasures.</p>		

	<p>In this light, NASA's Digital Astronaut Project (DAP) is working with the NASA Bone Discipline Lead to implement well-validated computational models to help predict and assess bone loss during spaceflight, and enhance exercise countermeasure development. More specifically, computational modeling is proposed as a way to augment bone research and exercise countermeasure development to target weight-bearing skeletal sites that are most susceptible to bone loss in microgravity, and thus at higher risk for fracture.</p> <p><b>Methods</b></p> <p>The model consists of three major research areas: (1) the orthopedic science or mechanics of the removal and replacement of bone packets via remodeling units, (2) the biology and physiology of cellular dynamics of remodeling units, and (3) mechanotransduction which describes the function of skeletal loading and its role in maintaining bone health. The basic biological assumption used in the cellular physiology can be stated as such: Cell proliferation or anti-proliferation is respectively either directly proportional or inversely proportional to receptor occupancy ratio.</p> <p>In implementation, the bone remodeling model is based on a first principles physiological and mathematical description of the components of bone physiology, including responses by the endocrine, biochemical, autocrine, and paracrine systems. The model mathematically formulates the key elements based on well-accepted knowledge and experimental studies of bone. In particular, the model uses the RANK-RANKL-OPG signaling pathway to describe the cellular dynamics. For skeletal loading, the model includes the effects of nitric oxide (NO) and prostaglandin E2 (PGE2). In the computational model, reduced skeletal loading triggers a decrease in NO and PGE2, which in turn triggers an imbalance in the pathway in favor of resorption. This leads to a decrease in mineralized volume M and osteoid volume O, and hence a decrease in bone volume fraction (BVf). The loading portion of the model is based on the concept of a minimum effective strain stimulus, which takes into consideration strain rate as opposed to strain magnitude only.</p> <p><b>Specific Aims</b></p> <ol style="list-style-type: none"> <li>1. For individuals in the age range of the astronaut corps, predict changes in trabecular and cortical volumetric bone mineral fraction and density as a function of time since measurement, gravity level, and applied loads</li> <li>2. Support the bone fracture standard by accepting and providing data in the same form as that of a Quantitative Computed Tomography (QCT) scan.</li> </ol>
<p><b>Task Description:</b></p>	<p>This research is directed because it contains highly constrained research, which requires focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal. This task meets the requirements for being tightly coupled with NASA efforts and therefore not amenable to solicitation because it:</p> <ol style="list-style-type: none"> <li>1. Must be tightly coupled with integrated exercise biomechanical/device models that NASA is currently developing in-house. Otherwise, the bone remodeling model will have little utility for NASA because it will not be able to predict the time course change of vBMD in reduced gravity as a function of time and how exercise prescription can be optimized to counteract bone loss.</li> <li>2. Must be tightly integrated with the QCT-based NASA bone strength standard. The bone remodeling model will provide valuable additional data via "forward prediction" simulations for during and after spaceflight missions to be used as input to the new bone strength FE analysis method to gain insight on how bone strength may change during and after flight. The bone remodeling model will be particularly be useful for providing data for time periods where QCT is not available, such as during flight. Under such cases, the model will be used to estimate the time course change of vBMD during an exploration mission and between the scans astronauts undergo after they return to Earth. This information can also be useful to help optimize exercise countermeasure protocols to minimize changes in bone strength during flight, and improve regain of bone strength post-flight.</li> </ol>
<p><b>Rationale for HRP Directed Research:</b></p>	<p>The discoveries made through this work can have spin-off benefits to terrestrial healthcare by providing fundamental methods that can be further built upon to:</p> <p>(1) Gain further insight on the mechanisms and influence on the bone remodeling process and its implications in bone health and other health risks to patients who are bed-ridden or immobilized due to:</p> <p>* Long term illnesses; * Post-op surgery; * Limb fractures; and/or * Spinal injury, to name a few</p> <p>(2) Design exercise prescriptions for patients who have experienced bone demineralization from bed -ridden or immobilized disuse indicated in 1, in order to help them recover bone and minimize bone fracture.</p> <p>(3) Investigate the level of regular activity or exercise people should be engaged in to ensure healthy bones throughout their lives, particularly in minimizing or preventing age related osteoporosis.</p>
<p><b>Research Impact/Earth Benefits:</b></p>	<p>Significant progress has been made with regard to the plan outlined in the 2014 report for building in the effects of exercise induced loading on preserving bone mineral density (BMD) with initial focus on the femoral neck. First, let's review the previous progress accomplishments. DAP completed work on a mathematical model of bone physiology that was able to predict the amount of bone lost during a period of skeletal unloading in bed rest up to 180 days. While that provided an understanding of bone loss in the absence of any exercise countermeasure in microgravity, further development of the computational model was required to incorporate the effects of skeletal loading via exercise. During the last year, DAP delivered an updated model that both improves the accuracy of the original model and includes a Daily Load Stimulus (DLS) algorithm that predicts the effect of physical activity on BMD. In conjunction with the DLS algorithm, a finite element model (FEM) of the proximal femur was integrated into the computational modeling framework for a higher fidelity prediction of the three-dimensional stress-strain environment in bone due to exercise loading, which in turn drives the bone remodeling process. Since we focused on the femoral neck, a level one approach was used in which the stress values in the femoral neck were averaged to obtain an effective strain. Currently, the DLS algorithm has been verified and validated for predicting the cumulative effect of normal walking and running on the bones of healthy adults in Earth gravity, as well as for astronauts following long-duration spaceflight. Overall, the simulation results instill high confidence in the model's capability to correctly predict bone maintenance from</p>
<p><b>Task Progress:</b></p>	

	<p>walking and running both for the normal and post-flight astronaut populations for up to one year.</p> <p>As a result of this work, NASA now has a computational bone physiology simulation framework that can predict bone loss in the absence of skeletal loading for up to 180 days and bone preservation from gait loading with a focus on the femoral neck. This framework sets a firm foundation towards establishing a physiologically based model that can help NASA researchers to design optimal exercise protocols that can preserve the long-term bone health of astronauts. Our recent and future work has now turned to extending and developing the computational model for the total proximal femur. This involves gathering together additional data for the total proximal femur. This will include data from a 90 day bed rest study as well as data from the 70 day and 120 day studies. The post flight data from a group of 16 astronauts who participated in 4 to 6 months flights will also be considered.</p>
<b>Bibliography Type:</b>	Description: (Last Updated: 09/10/2018)
<b>Abstracts for Journals and Proceedings</b>	<p>Pennline JA, Werner CR, Lewandowski BE, Sibonga JD. "Bone Model Development for Spaceflight Bone Physiology Analysis (Proximal Femur)." Presented at 2016 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 8-11, 2016.</p> <p>2016 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 8-11, 2016. , Feb-2016</p>