Fiscal Year:	FY 2014	**Task Last Updated:**	FY 12/24/2013
PI Name:	Lau, Anthony G Ph.D.		
Project Title:	Whole Joint Health: Investigating Modeled Spaceflight Changes in Mice		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Musculoskeletal Alterations Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	NOTE: As of Fall 2015, Dr. Lau is at The College of New Jersey. Previously at University of North Carolina at Chapel Hill while NSBRI postdoc.		
Project Type:	Ground	**Solicitation / Funding Source:**	2012 NSBRI-RFA-12-02 Postdoctoral Fellowships
Start Date:	11/01/2012	**End Date:**	10/31/2014
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Bateman, Ted (MENTOR/ University of North Carolina)		
Grant/Contract No.:	NCC 9-58-PF03003		
Performance Goal No.:			
Performance Goal Text:			

POSTDOCTORAL FELLOWSHIP
(1) Original Aims

Aim 1: Further develop the image analysis technology for assessing changes to mouse knee joint soft tissue with microCT, including cartilage, meniscus, ligaments, and tendons.

Aim 2: Assess whole-joint changes in the knee, including bone and soft tissues, from both unloading and reloading using the established HLU model. This will be accomplished with two studies:

Aim 2a: Study the effects of hindlimb unloading on integrated joint properties, mimicking the STS-135 Space Shuttle

Task Description:	flight profile. Hypothesis: Degradation of bone strength, as assessed by computational FEA, will be similar to that observed in mice flown on STS-135 (13-days of unloading). Similarly, degradation of meniscus volume and density will also be observed with few changes in tendon and ligaments. Aim 2b: Study the effects of longer-term unloading followed by reloading on whole-joint structural and functional properties. Hypothesis: Longer periods of unloading cause greater degradation in bone volume and strength, as well as larger changes in the connective soft tissues. There will be limited recovery after 4-weeks of reloading. (2) Key Findings The development of the computational methods were performed on the bone tissues from mice flown on STS-135 and to investigate changes in the knee joint of hemophilic mice. FEA of the Proximal Femur of the STS-135 mice found significant reduction in femoral neck stiffness (-12%), which was prevented from sclerostin anti-body treatment. FEA of the Lumbar Vertebrae (L5) of the STS-135 mice found a significant reduction in L5 compressive stiffness (-20%) and a -4% reduction in bone structural efficiency (stiffness/amount of bone). In addition, in the non-loading L5 vertebrae, bone volume was an excellent indicator of bone stiffness using linear regression ($P<0.01$, $R2=0.992$) across all specimens. Imaging analysis of the knee joint in hemophilic mice found significant loss of bone in the proximal tibia and mineralization of the joint soft tissues (tendons, ligaments, menisci, cartilage) 2-weeks after induced joint bleeding. (3) Impact of Key Findings The findings from FEA of the proximal femur suggest that we reconsider the boundary conditions used in the mechanical testing of femoral neck strength for future studies. Mechanical loading of the femoral head must consider the lower density bone regions of the femoral head when attempting to characterize the strength of the femoral neck. The findings from FEA of the Lumbar vertebrae shed some insight to the difference gravitational unloading has between weight bearing (femur, tibia) and the non-weight bearing L5 vertebrae. Further investigation should consider the differences in bone morphology and how that affects the individual bone's relationship between bone volume, structure, and bone stiffness. The finding of bone loss and identification of rapid joint soft-tissue mineralization has implications to osteoarthritic degradation following joint injury and inflammation. (4) Proposed research plan In the coming year, we propose to use the analytical methods developed over the past year to analyze tissue samples from a study using hind limb unloading (HLU), modeling the STS-135 experiment profile of disuse, in mice already performed by Mary Bouxien's group at Harvard. In addition, the information gained from the Harvard study will help guide our 13-day HLU and 4-week HLU with reloading studies. In collaboration with CASIS and the pharmaceutical company Novartis, our lab plans to launch mice on SpaceX-4, which will be an excellent opportunity to use all the developed assays to look at skeletal and joint degeneration from longer term spaceflight. Mice will be exposed to at least 21 days of microgravity, with planning in progress for 60-day exposure on SpaceX-6. The microCT analysis to obtain bone morphometry, bone strength through FEA, and soft tissue properties will continually be refined as we apply them to the studies.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	In addition to providing information about functional changes in bone strength and joint degradation, the computational methods developed provide a framework for analysis of human CT Scans. These microCT methods provide important information about bone strength for the femoral neck and lumbar vertebrae, which are both clinically relevant sites. A better understanding of the relationship between bone volume and density to bone strength in these regions is important as most clinical tests (DXA scans) can only measure bone volumetric density. The findings of rapid bone loss and mineralization of joint soft tissues in hemophilic mice not only benefit patients with hemophilia, but also have implications to people with osteoarthritis. In addition, these findings give a better understanding of joint degradation following injury resulting from injury and inflammation. The hemophilic mouse model, which creates an environment that can rapidly mineralize joint tissues, serves as a platform for studying the initiation of osteoarthritic degradation after injury as well as its application to regenerative medicine for growing bone from soft connective tissues.
Task Progress:	Research highlights for this first year include: Developed methodology for assessing femoral neck stiffness using Finite Element Analysis and employed methodology for mice flown on STS-135. Results from Finite Element Analysis followed trend of the corresponding mechanical testing of the femoral neck, which makes this computational method a possible alternative to the complex mechanical testing to test the femoral neck. Developed methodology for assessing compressive stiffness of the L5 lumbar vertebrae using Finite Element Analysis. Discovered that the non-weight bearing L5 vertebrae responded much differently to spaceflight and sclerostin antibody treatment than the weight bearing proximal tibia. In addition, the bone volume and bone stiffness had a very linear correlation in the L5 vertebrae, regardless of the exposure to spaceflight or sclerostin antibody, which was not the case in the proximal tibia. Methods for imaging of the mouse knee with microCT were applied to a study looking at joint degradation in hemophilic mice. The finding of acute bone loss and mineralization of joint soft tissues from joint bleeding has many implications to osteoarthritic degradation. Post-Doctoral Training: In addition to research this past year, I participated in the science outreach and undergraduate student mentoring. For community outreach, I created and presented a Bone and Space exhibition for 3rd grade science students at a rural elementary school. In the spring, I led and coordinated our lab's research exhibit at UNC's Science Expo during North Carolina's Science Festival. This summer, I served as a Mentor for lab shadowing for UNC's Summer High School Apprenticeship Program. I also mentored two undergraduate research students over the past year. The first was an undergraduate BME student from UNC who worked with me during the spring and summer on a research project, and is on in the fall and spring semesters for her senior thesis. The second student worked in our lab during the summer through the Meredith Cooperative Research Program. For this program, I submitted a project proposal which was selected and matched to a student from Meredith College. The purpose of this program is to allow their students, who are at a small, all-girls teaching university, to participate in research at a larger institution. This

	student is continuing to work in our lab in the fall and spring semesters for research credit. I have also taken the opportunity to gain teaching experience at the undergraduate and graduate level this past year through the Joint Department of Biomedical Engineering at UNC and NC State. In the spring, I was a co-instructor for the biomechanics course with Dr. Ted Bateman at UNC Chapel Hill and taught a 3-week module on experimental biomechanics. This fall, I am a co-instructor with Dr. Peter Mente for his Biomechanics course over at NC State.
Bibliography Type:	Description: (Last Updated: 03/30/2016)
Awards	Lau AG. (Anthony G. Lau) "National Space Biomedical Research Institute (NSBRI) Dr. David Watson Post-doctoral Fellow Poster Award (Runner-up), February 2013." Feb-2013