Fiscal Year:	FY 2015	**Task Last Updated:**	FY 12/12/2014
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		
PI Email:	LauA@tcnj.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	609-771-2644
Organization Name:	College of New Jersey		
PI Address 1:	Department of Biomedical Engineering		
PI Address 2:	2000 Pennington Rd, P.O. Box 7718		
PI Web Page:			
City:	Ewing	**State:**	NJ
Zip Code:	08618-1104	**Congressional District:**	12
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:**	10/31/2015
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:	3	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 10/31/2015 per NSBRI submission (Ed., 12/12/14)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Bateman, Ted Ph.D. (MENTOR/ University of North Carolina)		
Grant/Contract No.:	NCC 9-58-PF03003		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	POSTDOCTORAL FELLOWSHIP 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 hindlimb unloading (HLU) model. This will be accomplished with two studies: Aim 2a: Study the effects of hindlimb unloading (HLU) on integrated joint properties, mimicking the STS-135 Space Shuttle flight profile. Hypothesis: Degradation of bone strength, as assessed by computational finite element analysis (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. Key Findings STS-135 Data Results from the HLU study had similar overall trends that were observed in spaceflight. One major difference is that while both HLU and spaceflight caused a 17% decline in proximal tibia bone volume, HLU caused a 22% decline in bone strength, compared to the 34% decline from spaceflight. Impact of Key Findings 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 comparison between the spaceflight and HLU study suggests that the established HLU animal model may not be a good representation of the loss of bone strength experienced during spaceflight. The HLU model does not result in the same decline in bone structural efficiency observed in spaceflight, which is hypothesized to be an indicator of the ability to recover upon reloading. Therefore, we have decided not to move forward with a longer duration HLU study, but analyze bone changes from spaceflight on mice flown on SpaceX-4. The FE modeling provides a more detailed assessment of bone health compared to the traditional microCT analysis and should be considered in future assessments of bone quality. The finding of bone loss and identification of rapid joint soft-tissue mineralization has implications to osteoarthritic degradation following joint injury and inflammation. Proposed research plan for the coming year Over the past two years, I have developed a framework that provides new detailed information about bone health at multiple skeletal sites. The unique changes caused by spaceflight in bone structural efficiency are an area for future research. In collaboration with CASIS (Center for the Advancement of Science in Space) and the pharmaceutical company Novartis, Dr. Bateman's Lab will receive hind limbs and animal carcasses from the Rodent Research-1 project flown on the SpaceX-4 flight. This will be the first study to fly mice for the longer duration of 30 days. This will be an excellent opportunity to use all the developed assays to look at skeletal degeneration from longer term spaceflight. In addition to microstructural bone strength analysis with FE modeling, we plan on investigating changes of bone material properties at the tissue level from the longer exposure to microgravity with micro/nano indentation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The microCT and computational modeling provide important information about bone strength changes in the femoral neck and proximal tibia in the Hind Limb Unloading (HLU) mouse animal model. The differences in skeletal changes between the HLU model and spaceflight should be considered for future studies. Both spaceflight and HLU caused similar declines in bone volume, but different declines in bone strength and structural efficiency. The comparison between these two studies shows the deficiency in our current clinical assessments of bone health, which only measures bone density (or bone volume). The computational methods developed in these studies can be translated to assess humans as non-invasive clinical imaging improves. Developing these relationships between bone density and corresponding bone strength in the HLU model can provide information to help studies of humans on Earth undergoing disuse, such as during bed rest.
Task Progress:	This past year, we performed finite element modeling at the proximal tibia and femoral neck skeletal sites for mice undergoing 13-days of hind limb unloading (HLU), and evaluated the performance of a sclerostin-antibody countermeasure in this disuse model. These findings were compared to results from mice flown on Space Shuttle Mission STS-135 for 13 days, which also had a sclerostin-antibody countermeasure. Major differences between HLU and spaceflight were seen at the proximal tibia location. Both 13-days of HLU and spaceflight caused a similar decline in bone volume. However, Spaceflight caused a greater loss of bone strength compared to HLU. In addition, spaceflight caused a much larger decline in bone structural efficiency compared to HLU. Post-Doctoral Training: In addition to research this past year, I participated in the science outreach, undergraduate student mentoring, and teaching. For community outreach, I led and coordinated our lab's research exhibit at UNC's (University of North Carolina) Science Expo during the North Carolina Science Festival. This year, we developed a Space Radiation Game Exhibit where children could play a game throwing BBs at a toy astronaut and mouse in space and learn about the dangers of space radiation. I also mentored three undergraduate research students over the past year. The first was an undergraduate BME (Biomedical Engineering) student from UNC who worked with me during the spring and summer on a research project. She graduated and returned to the lab as a graduate student for the fall. 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, womens teaching university, to participate in

	research at a larger institution. This was the same student from last year, who continued to work in the lab during the academic year, and returned to the lab in the summer full time. The 3rd student is one of the BME department's Lucas Scholars, who joined the lab in the fall of 2013 and worked in the lab during the spring, summer, and fall of 2014. 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. In the spring, I was a co-instructor for the biomechanics course with Dr. Ted Bateman at UNC Chapel Hill and expanded my experimental biomechanics module to teach about 4 weeks of the course.
Bibliography Type:	Description: (Last Updated: 03/30/2016)
Articles in Peer-reviewed Journals	Lau AG, Sun J, Hannah WB, Livingston EW, Heymann D, Bateman TA, Monahan PE. "Joint bleeding in factor VIII deficient mice causes an acute loss of trabecular bone and calcification of joint soft tissues which is prevented with aggressive factor replacement." Haemophilia. 2014 Sep;20(5):716-22. Epub 2014 Apr 8. http://dx.doi.org/10.1111/hae.12399 ; PubMed PMID: 24712867 , Sep-2014
Awards	Lau A. "American Society for Bone and Mineral Research: Harold M. Frost Young Investigator Award, August 2014." Aug-2014
Awards	Lau A. "National Space Biomedical Research Institute (NSBRI) Dr. David Watson Post-Doctoral Fellow Poster Award: Best Poster, February 2014." Feb-2014
Awards	Lau A. "University of North Carolina- Chapel Hill: Postdoctoral Award for Research Excellence, November 2014." Nov-2014
Awards	Lau A. "University of North Carolina- Chapel Hill: Postdoctoral Scholar Award for Excellence in Mentoring, November 2014." Nov-2014