Fiscal Year:	FY 2014	**Task Last Updated:**	FY 06/18/2014
PI Name:	Puttlitz, Christian Ph.D.		
Project Title:	Fracture Healing in Haversian Bone under Conditions of Simulated Microgravity		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (IRP Rev F)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Fort Collins	**State:**	CO
Zip Code:	80523-1374	**Congressional District:**	4
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2010 Crew Health NNJ10ZSA003N
Start Date:	08/24/2011	**End Date:**	06/30/2016
No. of Post Docs:	0	**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:**	0
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NASA JSC
Contact Monitor:	Gilbert, Charlene	**Contact Phone:**	
Contact Email:	charlene.e.gilbert@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: Extended to 6/30/2016 per NSSC information (Ed., 9/28/15) NOTE: Extended to 8/23/2015 per HRP and NSSC information (Ed., 10/21/2014)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Browning, Raymond (Colorado State University) Haussler, Kevin (Colorado State University) McGilvray, Kirk (Colorado State University) Santoni, Brandon (Foundation for Orthopaedic Research and Education) Palmer, Ross (Colorado State University) Easley, Jeremiah (Colorado State University)		
Grant/Contract No.:	NNX11AQ81G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	There is a need for information regarding hard and soft tissue healing in microgravity environments, and if impaired healing exists, what countermeasures can be called upon to enhance healing. Research on fracture healing using the rodent hindlimb suspension model shows healing is impaired in simulated microgravity, while clinical research shows that moderate, early mechanical loading caused by weight bearing induces osteogenesis and aids in repair of bone fracture. Further research is needed to determine what loads, if any, should be applied during spaceflight to promote fracture healing. Most ground-based microgravity models utilize rodent hindlimb suspension to simulate how reduced loading affects isolated physiologic systems. Unfortunately, results derived from these studies are difficult to directly translate to the human condition due to major anatomic and physiologic differences between rodents and humans. Specifically, the differences in rodent and human bone structures become increasingly important when studying orthopaedic issues such as bone maintenance and healing during spaceflight. For example, the basic microstructure of rodent bone, known as “plexiform” bone, lacks the osteons (Haversion systems) that are the main micro-architectural feature of human cortical bone. Furthermore, it is known that the osteogenic and healing potential of rodent bone far exceeds that of adult human tissue. Due to these limitations in current ground-based microgravity models, there exists a need to develop a ground-based, large animal model of fracture healing in simulated weightlessness that more closely approximates the human condition as has been done in the first year of this study. This animal model should be capable of simulating a wide spectrum of microgravity and able to investigate exercise protocols that may aid in the optimization of the fracture healing cascade. Four specific aims were defined to meet these goals: 1) Develop a ground-based large animal model of bone unloading in order to simulate full weightlessness; 2) interrogate the effects of a simulated microgravity environment on bone fracture healing in a large animal model; 3) develop a computational model of weightbearing in ovine bone under different experimental conditions in order to characterize the loads experienced by the fracture site; and 4) investigate possible countermeasures to the deleterious effects of weightlessness on fracture healing.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The data collected during the first year of this study clearly demonstrate that the ovine model of ground-based microgravity effectively simulates the bone loss experienced by astronauts in space and ground-based rodent hindlimb suspension. This model has a major advantage over rodent hindlimb suspension models in that the mature ovine bone structure is nearly identical to that of humans, and future studies utilizing this large animal model (i.e., how hard and soft tissues heal in a microgravity environment which will be executed in year two of this grant) will be easily translated to the human condition. Furthermore, the study of fracture healing will benefit from the use of a large animal model rather than a rodent model since the healing potential of sheep more closely matches that of humans than rodents. The ground-based experiments utilizing this large animal (ovine) model directly address the need to know how varying microgravity environments affect fracture healing, as well as determining the applied loads at the fracture healing site through inverse dynamics and finite element simulations. The fracture rehabilitation protocols explored within this study will also aid in determining which mechanical environment leads to enhanced bone healing under microgravity conditions. The data produced during this study will significantly advance the basic mechanobiology of fracture healing by discerning which mechanical signals and environments facilitate enhanced bone healing.
Task Progress:	Aim 1 (completed): To date, the work for Specific Aim 1 is 100% complete. The findings of Specific Aim 1 have been presented at the 2012 and 2013 NASA Human Research Program Investigators’ Workshops, the 2013 American Society of Mechanical Engineers Summer Bioengineering Conference, and have been submitted to the Journal of Biomechanics. Aim 2: To date, the work for Specific Aim 2 is 100% complete. The findings of Specific Aim 2 have been presented at the 2014 NASA Human Research Program Investigators’ Workshop, and have been submitted to the Journal of Biomechanics. Aim 3: Substantial progress has been made in the development of the musculoskeletal and finite element models of Specific Aim 3. To date, the musculoskeletal model has been validated and muscle forces have been incorporated in the finite element model. Additionally, the finite element model has successfully passed an in vitro and an in vivo validation process. Currently, external fixation and sham finite element models with mid-diaphyseal metatarsal fractures are being finalized. The final phase of Specific Aim 3 is ongoing and consists of utilizing the finite element models to predict the forces, stresses, and strains that are experienced at a simulated diaphyseal fracture site under varying degrees of microgravity. These predictions will be directly correlated with the histological data derived in Specific Aim 2 in order to delineate what specific mechanical signals (e.g., deviatoric stress, hydrostatic stress) are directing the fracture healing cascade under different microgravity environments. Aim 4: Work on Specific Aim 4 has commenced with the investigation of shock wave therapy as a countermeasure to the inhibited fracture healing of microgravity. The first experimental group is currently undergoing shock wave treatment, and the expected completion date for biomechanical, microCT, and histomorphometric analyses of this portion of Specific Aim 4 is no later than November, 2014. Additionally, the in vivo investigation of low-intensity pulsed ultrasound as a countermeasure to inhibited fracture healing will commence in September, 2014 with an anticipated completion date for all biomechanical, microCT, and histomorphometric analyses no later than May 2015.
Bibliography Type:	Description: (Last Updated: 03/25/2020)
Abstracts for Journals and Proceedings	Gadomski BC, Lerner ZF, Browing RC, Puttlitz CM. "Development and validation of a finite element model of the ovine hindlimb for the investigation of microgravity loading on skeletal tissue healing." 7th World Congress of Biomechanics, Boston, MA, July 6-11, 2014. 7th World Congress of Biomechanics, Boston, MA, July 6-11, 2014. , Jul-2014
Abstracts for Journals and Proceedings	Gadomski BC, McGilvray KC, Easley JT, Palmer RH, Puttlitz CM. "Evaluation of Haversian bone fracture healing in simulated microgravity." 2014 NASA Human Research Program Investigators’ Workshop, Galveston, TX, February 12-13, 2014. 2014 NASA Human Research Program Investigators’ Workshop, Galveston, TX, February 12-13, 2014. http://www.hou.usra.edu/ , Feb-2014

Abstracts for Journals and Proceedings	Gadomski BC, McGilvray KC, Easley JT, Palmer RH, Puttlitz CM. "An ovine model of simulated microgravity." 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. , Feb-2012
Articles in Peer-reviewed Journals	Gadomski BC, McGilvray KC, Easley JT, Palmer RH, Ehrhart EJ, Haussler KK, Browning RC, Santoni BG, Puttlitz CM. "An in vivo ovine model of bone tissue alterations in simulated microgravity conditions." J Biomech Eng. 2014 Feb;136(2):021020. http://dx.doi.org/ ; PubMed PMID: 24170133 , Feb-2014
Articles in Peer-reviewed Journals	Gadomski BC, McGilvray KC, Easley JT, Palmer RH, Ehrhart EJ, Haussler KK, Browning RC, Santoni BG, Puttlitz CM. "Gravity unloading inhibits bone healing responses in Haversian bone systems." Journal of Biomechanics, In Review, as of June 2014. , Jun-2014
Awards	Gadomski B, McGilvray K, Easley J, Palmer R, Puttlitz C. "1st Place Overall Doctoral Student Paper Competition for: BC Gadomski, K C Mcgilvray, JT Easley, RH Palmer, CM Puttlitz. 'Simulating microgravity in a large animal model.' American Society of Mechanical Engineers 2013 Summer Bioengineering Conference, Sunriver, OR, June 26-29, 2013." Jun-2013