Fiscal Year:	FY 2012	**Task Last Updated:**	FY 10/11/2012
PI Name:	Hogan, Harry Ph.D.		
Project Title:	Contributors to Long-Term Recovery of Bone Strength following Exposure to 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) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (2) **Osteo**:Risk Of Early Onset Osteoporosis Due To Spaceflight		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	College Station	**State:**	TX
Zip Code:	77843-3123	**Congressional District:**	17
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2007 Crew Health NNJ07ZSA002N
Start Date:	05/20/2008	**End Date:**	11/19/2012
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**No. of Master' Degrees:**	1
No. of Master's Candidates:	3	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	6	**Monitoring Center:**	NASA JSC
Contact Monitor:	Maher, Jacilyn	**Contact Phone:**	
Contact Email:	jacilyn.maher56@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: New end date is 11/19/2012 per NSSC information (Ed., 6/01/2012) NOTE: New end date is 5/19/2012 per NSSC information (Ed., 5/31/2011)		
Key Personnel Changes/Previous PI:	Collaborator added: Dr. Stefan Judex, Stony Brook University		
COI Name (Institution):	Bloomfield, Susan (Texas A&M University) Martinez, Daniel (University of Houston)		
Grant/Contract No.:	NNX08AQ35G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The project uses the adult male hindlimb unloaded (HU) animal model with three specific aims and associated experiments. The first aim addresses the observed "discordant recovery dynamic" reported for astronaut data (Lang et al., JBMR 21:1224, 2006) and will characterize bone mass, bone mineral density (BMD), and bone strength relationships after HU and during various periods of recovery. Additional outcome measures include bone biochemistry and gene expression. A major emphasis is to compare detailed dynamics between the animal model and astronaut data. The animal model also permits direct comparison of calculated/estimated bone strengths with measured strengths. The second aim examines multiple mission scenarios and will use HU, recovery for a period, and then a second HU exposure. The third aim will also follow the two-exposure protocol but with resistance exercise added during the recovery period. The cross-cutting area, or element, of the Bioastronautics Critical Path Roadmap (CRP) that this research project addresses is Human Health & Countermeasures (HHC). The specific health risk is the Risk of Accelerated Osteoporosis as identified in the Bioastronautics Roadmap (Risk No. 1, Bone Loss, p. 19 of NASA/SP–2004–6113) and the Human Research Program (HRP) Integrated Research Plan (Risk 14.0). The Gaps addressed, as defined in the HRP-IRP, are: B1 (Is bone strength completely recovered with recovery of BMD) B10 (Time-course of bone degradation during missions) The 2007 NASA Research Announcement (NNJ07ZSA002N) to which the proposal for this project responded included the following specific solicitation wording for Gap B1: "There are preliminary indications that overall bone quality/strength does not recover at the same rate that bone mineral density recovers after spaceflight. It is not known if there is a long term health effect related to this discordant recovery dynamic." {emphasis added} Research proposals are solicited that directly address this relationship. The specific topic solicited is: Novel research that defines the precise relationship between long term recovery of bone mineral density and bone strength/quality, including the effects of multiple spaceflights." {emphasis added} The research conducted as part of this project will provide unique data addressing these issues through well-controlled animal studies. The wide range of outcome variables will provide a comprehensive set of results that will give rise to new insights at the basic and applied levels.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Results from this project will provide fundamental understanding of the way bone responds to mechanical unloading and how it recovers when mechanical loads are restored. Insights gained should be applicable to the clinically relevant case of aging adults with reduced activity levels, in addition to the effects of long term exposure to microgravity for crew members. Further, many of the same basic mechanisms overlap considerably with the broader health problem of osteoporosis and increased fracture risk in aging humans. It is widely known that bone mineral density (BMD) is not an accurate predictor of fracture incidence despite its wide use as a screening tool for osteoporosis. The findings of the research being conducted in this project will help to better define the relationships between BMD and other important factors, such as bone mineral content (BMC, i.e., bone mass), bone tissue quality, and most importantly bone strength. In addition, the project will identify which anatomic sites in the rat provide the closest correspondence to bone loss and recovery characteristics in humans (astronauts in this case). These results should bolster the utility and robustness of rodent animal models and linking their findings to clinical cases. Finally, the project will generate new and unique data on the effects of resistance exercise in restoring skeletal integrity during recovery from mechanical unloading. This information should be directly applicable to corresponding efforts aimed at using exercise to combat age-related losses from osteoporosis or related pathologies.
Task Progress:	[Editor's note 10/11/2012: No Task Book report received. Progress section and Bibliography compiled from PI's Annual Technical Report dated June 2012] The results and findings from Year 4 can be summarized in terms of several highlights. The microCT of the proximal tibia metaphysis results for the double-HU study follow similar trends as densitometric results from pQCT. Namely, BV/TV shows an age-related decline for control animals, a significant drop due to the 1st HU, but little effect of the 2nd HU. In contrast, both trabecular thickness and cortical shell thickness show significant decrements due to both the 1st and 2nd HU exposures. At the femoral neck (FN), both total BMC and total vBMD were negatively affected by both HU exposures. For total vBMD, however, values recovered faster after HU exposures. Biomechanical strength of the femoral neck also showed significant reductions due to both HU exposures. Recovery was even faster than vBMD though, particularly for the FN strength under axial loading. Adding exercise during recovery between HU exposures revealed impressive and powerful benefits for the vast majority of variables measured. For in vivo pQCT results, both total BMC and total vBMD showed significantly enhanced recovery with the exercise added. Values not only recovered completely to control levels, but the exercise also engendered an apparent "protective" effect, as the losses for the 2nd HU were milder. At the femoral neck, however, the results were slightly different. Specifically, exercise produced benefits for total BMC only, with no appreciable effect on total vBMD. For total BMC, however, the benefits were much more dramatic, as the exercise produced "super-recovery," which is defined to indicate that mean values actually exceeded control animal values at the end of the exercise+recovery period. As was true at the proximal tibia, both BMC and vBMD exhibited a protective effect for the 2nd HU at the femoral neck. Perhaps the most dramatic effects of exercise were reflected by the mechanical strength of the FN. Both axial and lateral loading cases yielded super-recovery, with the maximum force for axial loading 35% higher than age-matched controls, and the maximum force for lateral loading 20% higher. A protective effect was also generated for maximum force at the FN, as the 2nd HU had not significant effect (no statistically significant changes pre- to post-HU). These results effectively illustrate the value and usefulness of this ground–based animal model, particularly for studying repeated exposures to simulated microgravity in a controlled fashion. Results for the initial HU exposure, and recovery there from, compare quite favorably to recent results on ISS crew members.
Bibliography Type:	Description: (Last Updated: 01/11/2021)

Abstracts for Journals and Proceedings	Shirazi-Fard Y, Morgan DS, Shimkus KL, Boudreaux RD, Gonzalez E, Davis JM, Fluckey J, Bloomfield SA, Hogan HA. "Effects of Exercise During Recovery Between Two Bouts of Simulated Microgravity on Bone and Muscle in Adult Male Rats." 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
Abstracts for Journals and Proceedings	Gonzalez E, Morgan DS, Kupke JS, Shirazi-Fard Y, Bloomfield SA, Hogan HA. "Densitometric and Biomechanical Properties of the Femoral Neck in Response to Exercise During Recovery Between Unloading Bouts in Adult Male Rats." 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
Abstracts for Journals and Proceedings	Morgan, DS, Davis JM, Kupke JS, Shirazi-Fard Y, Bloomfield SA, Hogan HA. "The Effects of Age on Changes in the Densitometric and Mechanical Properties in the Femur of the Hindlimb Unloaded Adult Rat." Orthopaedic Research Society Annual Meeting 2012, San Francisco, CA, February 4–7, 2012. Orthopaedic Research Society Annual Meeting 2012, San Francisco, CA, February 4–7, 2012. Poster 0548. , Feb-2012
Abstracts for Journals and Proceedings	Shirazi-Fard Y, Kupke JS, Davis JM, Morgan DS, Lima F, Greene ES, McCue AM, Thompson JV, Marchetti JM, Bloomfield SA, Hogan HA. "Previous Exposure to Microgravity Does Not Adversely Affect Second Exposure in the Tibia of Hindlimb Unloaded Adult Male Rats." 33rd Annual Meeting of the American Society for Bone and Mineral Research, San Diego, California, September 16-20, 2011. 33rd Annual Meeting of the American Society for Bone and Mineral Research, San Diego, California, September 16-20, 2011. Available at: http://www.abstracts2view.com/asbmr/view.php?nu=ASBMR11L_A11007383-148 ; accessed 9/18/2012. , Sep-2011
Abstracts for Journals and Proceedings	Kupke JS, Davis JM, Morgan DS, Shirazi-Fard Y, Marchetti JM, McCue AM, Bloomfield SA, Hogan HA. "Effects of Multiple Exposures to Microgravity on the Femur of Adult Male Hindlimb Unloaded Rats." 33rd Annual Meeting of the American Society for Bone and Mineral Research, San Diego, California, September 16-20, 2011. J Bone Miner Res 2011 Sep;26(Suppl 1):Poster SA0040. http://www.abstracts2view.com/asbmr/view.php?nu=ASBMR11L_A11007698-52 ; accessed 9/18/2012. , Sep-2011
Awards	Gonzalez E. "First Place Award, Graduate Student Poster Competition, for 'Densitometric and Biomechanical Properties of the Femoral Neck in Response to Exercise During Recovery Between Unloading Bouts in Adult Male Rats.' 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012." Feb-2012
Awards	Shirazi-Fard Y. "Second Place Award, Graduate Student Poster Competition, for 'Effects of Exercise During Recovery Between Two Bouts of Simulated Microgravity on Bone and Muscle in Adult Male Rats.' 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012." Feb-2012
Papers from Meeting Proceedings	Shirazi-Fard Y, Gonzalez E, Kupke JS, Morgan, DS, Davis JM, Bloomfield SA, Hogan HA. "Exercise Following Disuse Enhances Bone Recovery and Moderates Effects of a Second Bout of Disuse in Adult Rats." Orthopaedic Research Society Annual Meeting 2012, San Francisco, CA, February 4–7, 2012. Orthopaedic Research Society Annual Meeting 2012, San Francisco, CA, February 4–7, 2012. Paper 0120. , Feb-2012