Fiscal Voar	FY 2017	Task Last Undated.	EV 07/03/2017
PI Name:	Hargens, Alan R. Ph.D.	Task Last Opuatou.	110//03/2017
Project Title:	Spinal Structure and Function after 90 D	Days Long-Duration Simulated S	pace Flight and Recovery
σ	1		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline Element/Subdiscipline:	HUMAN RESEARCHBiomedical cou	intermeasures	
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	(1) <b>HHC</b> :Human Health Countermeasur	res	
Human Research Program Risks:	<ol> <li>Bone Fracture: Risk of Bone Fracture</li> <li>Osteo: Risk Of Early Onset Osteoport</li> </ol>	re due to Spaceflight-induced Cl rosis Due To Spaceflight	hanges to Bone
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	ahargens@ucsd.edu	Fax:	FY
PI Organization Type:	UNIVERSITY	Phone:	858-534-7837
Organization Name:	University of California, San Diego		
PI Address 1:	Altman Clinical and Translational Resea	arch Institute	
PI Address 2:	9452 Medical Center Drive/0863		
PI Web Page:			
City:	La Jolla	State:	CA
Zip Code:	92037-0863	Congressional District:	52
Comments:			
Project Type:	Ground	Solicitation / Funding Source:	2013 HERO NNJ13ZSA002N-Crew Health (FLAGSHIP & NSBRI)
Start Date:	08/01/2014	End Date:	12/31/2018
No. of Post Docs:	2	No. of PhD Degrees:	
No. of PhD Candidates:	1	No. of Master' Degrees:	
No. of Master's Candidates:		No. of Bachelor's Degrees:	1
No. of Bachelor's Candidates:	2	Monitoring Center:	NASA JSC
Contact Monitor:	Norsk, Peter	<b>Contact Phone:</b>	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End datd changed to 12/31/2018	8 per NSSC information (Ed., 7/1	18/17)
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Ferguson, Adam Ph.D. (University of California at San Francisco) Lotz, Jeffrey Ph.D. (University of California at San Francisco) Macias, Brandon Ph.D. (NASA Johnson Space Center) Masuda, Koichi M.D. (University of California at San Diego)		
Grant/Contract No.:	NNX14AP25G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The vertebral bodies and flexible intervertebral discs are important, weight-bearing tissues that have adapted to gravitational stress. Consequently, the absence of gravitational axial loads during exposure to microgravity likely disrupts normal spine physiology. Throughout longer space flight missions, deconditioning of the intervertebral discs and spinal muscles poses a serious injury risk upon re-exposure to upright posture in a gravitational environment. We will use state-of-the-art technologies to quantify morphology, biochemistry, and kinematics of spines (including the vertebrae, intervertebral discs, and spinal muscles) of rats at defined time points as described in the NASA research announcement. After successful completion of our investigation, we will deliver a comprehensive database of simulated microgravity-induced spinal adaptations (type and magnitude). The overarching goal of these proposed studies are to develop a long-duration space flight ground based model of spine function and structure. In addition, this research project will afford the opportunity to examine possible gender differences in spinal structure and function. Our research group is in a unique position to leverage our past rodent space flight experience on STS-131, STS-133, STS-135, and BION M-1 missions and directly compare to this ground based model of simulated microgravity. Moreover, we are also uniquely positioned to compare this 90-days hindlimb suspension model to those changes that occur in our currently funded project to test crew members before and after 6-month International Space Station (ISS) missions. Our project directly addresses Critical Path Roadmap Risks and Questions regarding disc injury (Integrated Research Plan (IRP) Gap-B4)): Is damage to joint structure, intervertebral discs, or ligaments incurred during or following microgravity exposure? Our research will improve understanding of the underlying pathophysiology of spinal deconditioning induced by simulated microgravity, and mechanisms of spinal adaptatio
Rationale for HRP Directed Research	1:
Research Impact/Earth Benefits:	To our knowledge, this study is the first to examine the effects of 90-days simulated space flight on spinal deconditioning in rats and to compare this model of simulated microgravity with actual space flight. The vertebral bodies and flexible intervertebral discs are important, weight-bearing tissues that have adapted to gravitational stress. Our research will aid understanding of spinal deconditioning during simulated microgravity and of the higher incidence of disc prolapse or herniation following re-exposure to 1-G with a long-term view to prevent such spinal deconditioning with exercise or other physiologic countermeasures. This research may aid understanding of spinal deconditioning during inactivity such as after spinal cord injury and bed rest in human patients on Earth.
	<ul> <li>Introduction: Astronauts are at increased risk for spinal fractures and disc herniation because of the lack of loading during space missions, which can cause bone mineral density (BMD) decline and micro-architectural changes in structural integrity [1-3]. It may take several years to achieve complete BMD recovery [4]. The underlying mechanism and magnitude of BMD, bone morphology and intervertebral disc (IVD) changes remain unclear [5]. To study these effects, the hindlimb unloading model, a ground-based model that mimics cephalic fluid shifts and bone volume density losses of a microgravity environment [6-7], was utilized because of the limited pool of human subjects and the resource restrictions that a space flight animal study would require.</li> <li>In this model, we hypothesized that lumbar spines would experience a significantly greater decline in BMD, bone morphological parameters, and IVD height with longer exposure to hindlimb unloading and that these changes are restorable with a recovery period. A 90-day hindlimb unloading study previously reported a loss in BMD and IVD height [8]. However, there are no data that encompass multiple time points or investigate the extent of recovery under the normal gravity conditions after unloading. The purpose of this study was to investigate the extent of recovery under the normal gravity conditions after unloading. The purpose of this study were subjected to hindlimb unloading, is BMD and IVD height at different time points.</li> <li>Methods: Thirty-seven Long Evans rats (3 months old) were separated into two groups, hindlimb-unloaded (HLU) group and weight-bearing control (WBC) group. Rats in the HLU group were subjected to hindlimb unloading, as reported by Morey-Holton and Globus, for 14 days (n=7, 14D), 90 days (n=8, 90D), and 90 days with 28 days of recovery (n=3, 90D/Recov) [6]. The hindlimb unloading was removed during the 2-day recovery period. The WBC group was not subjected to the unloading but was similarly divided into groups of 1</li></ul>
	PLSD post hoc tests (p<0.05). Level, group, and time point were treated as independent factors.
	Results: There were no significant changes among all WBC groups for all levels, groups, and time points.
	BMD analysis: Group and time significantly affected BMD. BMD of the 14D HLU and 90D HLU groups were significantly lower than those of the 14D WBC and 90D WBC groups, respectively (both, p<0.05). BMD of the 90D group was significantly lower than that of the 14D HLU group (p<0.01); however, BMD of the 90D/Recov HLU group was significantly higher than that of the 90D HLU and 14D HLU groups (p<0.01 for 90D HLU, p<0.05 for 14D HLU).
Task Progress:	Bone morphological analysis: Similarly, group and time significantly affected BV/TV, Tr. Th, and Tr. Sp. The 14D HLU and the 90D HLU groups had a significantly lower BV/TV than those of corresponding WBC groups (vs. 14D WBC, vs. 90D WBC, respectively, both $p<0.01$ ). There was no significant progression of BT/TV decrease between the 14D HLU and 90D HLU groups after the initial decrease; importantly, BV/TV of the 90D/Recov HLU group was significantly greater than that of 90D HLU group ( $p<0.01$ ). Tr. Th of the 14D HLU group was significantly lower than that of the 14D HLU groups ( $p<0.01$ ), respectively). The 90D/Recov HLU group had a significantly higher Tr. Th those of the 14D HLU, 90D HLU, and 90D/Recov WBC groups ( $p<0.01$ for all). For Tr. Sp, the 90D HLU group was significantly higher separation than that of 90D WBC group ( $p<0.01$ ). Tr. Sp of the 90D HLU group was significantly greater than of the 14D HLU group ( $p<0.01$ ); no significant difference was observed between the 90D

	HLU and the 90D/Recov HLU groups.
	DHD analysis: Group and time significantly affected DHD. DHD of the 90D HLU group was significantly lower than that of the 90D WBC group ( $p<0.01$ ). DHD differences were not significant in the HLU and WBC groups of the 14D and 90D/Recov time point. The 14D HLU DHD was a significantly higher than that of the 90D HLU and 90D/Recov groups ( $p<0.01$ for both). Importantly, there were no significant differences in DHD between the 90D HLU and the 90D/Recov HLU groups.
	Discussion: BMD analysis revealed a significant decrease in the 90D HLU group compared to the 14D HLU group and a significant recovery in BMD in the 90D/Recov group compared to the 90D HLU group. The initial decrease in BMD agreed with previous studies that revealed a similar decrease in mice sent on a 15-day space mission [12]. BMD and bone morphological parameters generally showed a significant difference between the 90D HLU and the 90D/Recov HLU groups. Furthermore, the lack of significant differences between the HLU and WBC groups of the 90D/Recov time point in BMD, BV/TV, Tr. Th, and Tr. Sp suggest that a recovery period can aid in bone recovery to baseline conditions. To examine the extent of bone recovery after hindlimb unloading, future analyses of the bone recovery at different time points will be needed. For IVD changes, significant DHD decreases were observed, especially in the lower lumbar regions of the 14D and 90D HLU groups. This agreed with previous data that reported a significant decrease in DHD in four-week himdlimb unloaded rats [13]. The lack of significant changes in DHD between the 90D HLU group and the 90D/Recov group indicated that removal of the microgravity environment may not be enough to aid in IVD recovery.
	Significance: Extended unloading of the hindlimb results in decreased BMD, bone morphological parameters, and progressive decrease in IVD height. The 28-day recovery period, where the hindlimb unloading was removed, aided in bone recovery but was ineffective in IVD height restoration.
	References:
	(1) Johnston+. Aviat Space Environ Med, 81(6):566, 2010. (2) Orwoll+. JBMR, 28(6):1243, 2013. (3) Lang+. JBMR, 19(6):1006, 2004. (4) LeBlanc+. Bone, 22(5 Suppl):113S, 1998. (5) Turner+. J Appl Physiol, 89(2):840, 2000. (6) Morey-Holton+. J Appl Physiol, 92, 1367, 2002. (7) Canciani+. JMBBM, 51:1, 2015. (8) Cheng+, ORS Trans; 0696, 2015. (9) Tavella+. PLoS ONE, 7(3): e33179, 2012. (10) Buie+. Bone, 41(4):505, 2007. (11) Wantanabe+. Eur Spine J, 21(5):946, 2012. (12) Blaber+. PLoS One, 8(4):e61372, 2013. (13) Holguin, Aviat Space Environ Med, 81(12):1078
	Other tests such as biomechanics and histomorphology will be delayed due to the unexpected slow arrival of samples.
Bibliography Type:	Description: (Last Updated: 06/30/2025)
Abstracts for Journals and Proceedings	Huang J, Cheng K, Kato K, Sah RL, Akeda K, Macias B, Inoue N, Hargens A, Masuda K. "28-Day Recovery After Microgravity Conditions Restored Rodent Bone Quality But Not Intervertebral Disc Height." Presented at 63rd Annual Meeting of the Orthopaedic Research Society, San Diego, CA, March 19-22, 2017. 63rd Annual Meeting of the Orthopaedic Research Society, San Diego, CA, March 19-22, 2017. , Mar-2017
Articles in Peer-reviewed Journals	Hargens AR, Vico L. "Long-duration bed rest as an analog to microgravity." J Appl Physiol (1985). 2016 Apr 15;120(8):891-903. Review. <u>http://dx.doi.org/10.1152/japplphysiol.00935.2015</u> ; PubMed <u>PMID: 26893033</u> , Apr-2016