

Fiscal Year:	FY 2023	Task Last Updated:	FY 07/31/2022
PI Name:	Rutkove, Seward M.D.		
Project Title:	Approaching Gravity As a Continuum: Musculoskeletal Effects of Fractional Reloading		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline-- Element/Subdiscipline:			
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Musculoskeletal Biology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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Comments:			
Project Type:	Ground	Solicitation / Funding Source:	2018 Space Biology (ROSBio) NNH18ZTT001N-FG. App B: Flight and Ground Space Biology Research
Start Date:	10/01/2019	End Date:	09/30/2022
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No. of PhD Candidates:	0	No. of Master' Degrees:	0
No. of Master's Candidates:	0	No. of Bachelor's Degrees:	1
No. of Bachelor's Candidates:	1	Monitoring Center:	NASA ARC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	None		
COI Name (Institution):	Bouxsein, Mary Ph.D. (Beth Israel Deaconess Medical Center, Inc./Harvard Medical School)		
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Task Description:	<p>The effect of full mechanical unloading has been extensively studied in both rodents and humans using ground-based models. Recently, rodent partial weight bearing (PWB) models have revealed that partial gravity provides dose-dependent rescue of the musculoskeletal system as compared to full unloading. Separate work has also shown that after unloading, an abrupt mechanical reloading to 1g causes additional musculoskeletal injury. Here, we propose to employ both PWB and hindlimb unloading models sequentially to investigate gravity as a continuum and its impact on musculoskeletal adaptation to reloading. This work will have critical practical and scientific outcomes, and will provide for the first time, insights into the musculoskeletal responses to adult to fractional gravity after a period of microgravity (as would occur when traveling to Mars). It will also provide information on the mitigating effects of partial gravity after extended unloading. Our Specific Aims are: 1) To determine the physiological adaptations of the musculoskeletal system in males to the fractional gravity of either the Moon or Mars after experiencing microgravity in transit, 2) To determine the physiological adaptations of the musculoskeletal system in females to the fractional gravity of either the Moon or Mars after experiencing microgravity in transit, and 3) To investigate the potential musculoskeletal benefits of artificial gravity in-flight before returning to Earth. Specifically, we plan to investigate the resulting musculoskeletal alterations in transitioning from 2 weeks of 0g to 0.2, 0.4, and 0.7g, hypothesizing that there is a dose-dependence to the reloading, including recovery and associated injury. We will also assess the potential benefit of using these three levels of PWB as intermediate steps on the way to transitioning back to 1g. Thorough post mortem analyses, we will be able to identify the different processes that might be involved in reloading injury and its mitigation. Stress levels and metabolic/hormonal alterations will also be evaluated. Ultimately, we hope to provide the space biology community a deeper understanding of the musculoskeletal impact of fractional gravity in relation to both microgravity and Earth gravity.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	<p>Our research will have important implications for the improved understanding of the effects of prolonged disuse on bone and muscle due to bedrest or injury and the effects of rehabilitation. Specifically, lessons learned from this work may help us better understand the negative impact of the re-establishing normal activity after the development of disuse atrophy and the potential for applying graded rehabilitation approaches so as to ensure effective recovery.</p>
Task Progress:	<p>During the last year, all animal experiments have been finalized. Critically, we finished all experiments in males and females, aiming at understanding the acute and mid-term adaptation to mechanical reloading following disuse. Moreover, we assessed if partial gravity could be a useful countermeasure when implemented during a mission (by simulating different artificial gravity protocol on the Gateway station, for example).</p> <p>All in vivo and ex vivo analyses have been performed (including muscle function, force production, physiological measurements, muscle histomorphometry, gene expression using RTqPCR). Organs have been collected and stored for further analysis and for future shipping to the NASA Ames Life Sciences Data Archive (ALSDA) storage facility. Bone analysis has been performed using peripheral quantitative computed tomography (pQCT) and micro computed tomography (microCT), and serum levels of several bone biomarkers have been performed.</p> <p>Overall, our work demonstrates that males and females react differently to mechanical reloading following disuse, and that bone deconditioning seems to be dramatically impacted by biological sex, both during disuse and recovery. These data will bring valuable insights to better understand how males and females respond to gravity shifts and allow for the development of targeted countermeasures.</p> <p>While we have shown that exposure to partial weight-bearing (PWB) leads to a dose-dependent musculoskeletal deconditioning, our results suggest that this could be a useful avenue to explore for long missions (in males).</p> <p>Over the course of the year, the team has attended 5 conferences, been invited to give 2 seminars, and presented 3 podium talks and 4 posters. Another poster has been accepted for the European Low Gravity Research Association (ELGRA) meeting in Lisbon, Portugal that will take place in September 2022.</p>
Bibliography Type:	Description: (Last Updated: 08/08/2024)
Abstracts for Journals and Proceedings	<p>Rosa-Caldwell ME, Mortreux M, Sung DM, Schreurs S, Boussein ML, Kaiser U, Rutkove SB. "Sex differences in the etiology of micro-gravity induced musculoskeletal losses are not solely dependent on sex hormones." 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022.</p> <p>Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. , Feb-2022</p>
Abstracts for Journals and Proceedings	<p>Mortreux M, Rosa-Caldwell ME, Sung DM, Stiehl ID, Nagy JA, Rutkove SB. "Early muscular response to partial gravity following a bout of disuse in male and female rats." 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022.</p> <p>Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. , Feb-2022</p>