Fiscal Year:	FY 2021	**Task Last Updated:**	FY 07/29/2020
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		
PI Email:	srutkove@bidmc.harvard.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	617-667-8130
Organization Name:	Beth Israel Deaconess Medical Center, Inc./Harvard Medical School		
PI Address 1:	330 Brookline Ave TCC-810		
PI Address 2:			
PI Web Page:			
City:	Boston	**State:**	MA
Zip Code:	02215-5400	**Congressional District:**	7
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
No. of Post Docs:	2	**No. of PhD Degrees:**	2
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:	0	**Monitoring Center:**	NASA ARC
Contact Monitor:	Griko, Yuri	**Contact Phone:**	650-604-0519
Contact Email:	Yuri.V.Griko@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Bouxsein, Mary Ph.D. (Beth Israel Deaconess Medical Center, Inc./Harvard Medical School)		
Grant/Contract No.:	80NSSC19K1598		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	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.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	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.
Task Progress:	During this initial funding period that began 10/1/2019, we have begun work on Aim 1: studying the impact of short-term reloading after exposure to hindlimb unloading (0g analog). For this paradigm, we first exposed male rats to 14 days of hindlimb suspension (HLS). We then placed the animals either at full loading (PWB100), Martian analog loading (PWB40), or Lunar analog loading (PWB20) for 4 or 24 hours. Muscle health and function were assessed weekly using limb girth, intra-muscular electrical impedance myography (EIM), nerve conduction studies, and grip force. In addition, many biological samples were collected including daily (food intake, body weight) and weekly (blood glucose level, plasmas, feces, urine). Muscles have been analyzed using immunohistochemistry to determine cross-sectional area, myofiber type, and to detect muscle injury. In terms of bone outcomes, we are acquiring peripheral quantitative computerized tomography data and tissue for gene expression studies. Thus far, 68 animals have completed the study. Due to the COVID-19 pandemic, animal studies were suspended from mid-March until mid-June 2020 and the lab focused on analysis and new manuscripts. However, animal research activities have recommenced and we are making steady progress toward the completion of Aim 1. Although data collection is underway for the 4 hours reloading groups, we are already quantifying the effects of 14 days of HLS using a pelvic harness and to determine the electrical impedance myography (EIM) parameters that are impacted by weightlessness. While preliminary, our data suggest that short-term reloading (4 and 24 hours) is able to impact muscle health as observed through EIM, grip force, muscle weight, and muscle architecture.
Bibliography Type:	Description: (Last Updated: 08/08/2024)
Articles in Peer-reviewed Journals	Semple C, Riveros D, Sung D-M, Nagy JA, Rutkove SB, Mortreux M. "Using electrical impedance myography as a biomarker of muscle deconditioning in rats exposed to micro- and partial-gravity analogs." Front Physiol. 2020 Sep 15;11:557796. https://doi.org/10.3389/fphys.2020.557796 ; PMID: 33041858; PMCID: PMC7522465 , Sep-2020