Fiscal Year:	FY 2024	**Task Last Updated:**	FY 09/30/2023
PI Name:	Adler, Robert M.D.		
Project Title:	Magnetic Resonance Imaging (MRI) to Assess Changes to Trabecular Microarchitecture of the Hip		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
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		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Richmond	**State:**	VA
Zip Code:	23249-0001	**Congressional District:**	4
Comments:	Contact Co-PI email for communications.		
Project Type:	Ground	**Solicitation / Funding Source:**	2021 HERO NNJ21ZSA001N-FLAGSHIP, Appendix A: NASA Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions
Start Date:	12/01/2022	**End Date:**	11/30/2025
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Brocato, Becky	**Contact Phone:**	
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	Ed. Note: The name of Dr. Adler's institution has changed; the former McGuire Research Institute, Inc. is now known as the Richmond Veterans Affairs Medical Center. Update: Chamith Rajapakse, Ph.D. (University of Pennsylvania) was added to the project in May, 2023. Dr. Rajapakse is a subject matter expert in magnetic resonance imaging (MRI) and HR-pQCT. Dimitri Martel, Ph.D. (New York University Langone) has also been added to the investigation; Dr. Martel performs the analysis of the hip scans by MRI. (Ed., 9/30/23)		
COI Name (Institution):	Sibonga, Jean Ph.D. (NASA Johnson Space Center) Gorgey, Ashraf Ph.D. (Richmond Veterans Affairs Medical Center) Chang, Gregory M.D. (New York University Langone) Young, Millennia Ph.D. (NASA Johnson Space Center) Rajapakse, Chamith Ph.D. (University of Pennsylvania) Martel, Dimitri Ph.D. (New York University Langone)		
Grant/Contract No.:	80NSSC23K0382		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	New Task Description (Ed., 9/30/23) Background. Studies of bone loss in ISS astronauts, using quantitative computed tomography (QCT) of the hip and spine and high-resolution-peripheral QCT (HRpQCT) of the lower leg, describe losses of trabecular bone mineral density (Trb vBMD) that are not detectable by the clinical test for age-related osteoporosis (Op), i.e., areal bone mineral density (aBMD) measured by dual-energy X-ray absorptiometry (DXA). Both QCT and HRpQCT revealed losses in Trb vBMD immediately following long duration (LD) spaceflight and continuing in some individuals even after recovery periods of a year or more. We reported rapid rates of spaceflight hip QCT Trb vBMD loss, relative to terrestrial aging rates. In a pilot study, hip QCT showed lack of recovery of hip Trb vBMD to baseline in 4 of 10 astronauts evaluated 2 years after return to Earth. Analyses of serum and urine collected during spaceflight showed significant in-flight elevation of bone resorption (BR) markers in the 4 astronauts who did not recover Trb vBMD vs. the 6 astronauts who did; a biomarker for bone formation (BF) remained stable until ~120 days into the flight. Biochemical assays consistently show BR exceeding BF during spaceflight accounting for a rapid loss of Trb vBMD which could also increase the risk for disrupted trabecular connectivity. While the efficacy of an oral bisphosphonate to mitigate spaceflight bone loss has been substantiated in an astronaut flight study, there is reduced willingness in some stakeholders to use a pharmaceutical countermeasure. Hence, there is a concern for the risk of irreversible losses in trabecular connectivity in the absence of an anti-resorptive countermeasure. Such trabecular disruptions are associated with skeletal fragility and fractures in other populations undergoing bone loss but have not been characterized in astronaut hips because of prohibitive radiation exposures needed for high-resolution imaging of deeply embedded bone. HRpQCT has low radiation and sufficient resolution to study microarchitecture, but only for peripheral sites such as the lower leg and wrist. Hence, it is critical to apply a technology with no ionizing radiation such as MRI to safely define the effect size of spaceflight on hip trabecular microarchitecture, particularly with the observation of delayed or no recovery in hip Trb vBMD. Hypothesis. We hypothesize that 1) LD astronauts will have an increased risk for bone fractures because of disruptions in Trb uArch of the hip and 2) a 3-Tesla (3T) MRI scanning protocol can detect disruptive changes in Trb uArch, some of which could be irreversible. Specific Aims: We will investigate this hypothesis by addressing the following Specific Aims (SA): Specific Aims: 1) Identify and consent individuals with SCI to assess the effects of prolonged unloading to the hip; 2) Apply a previously-validated 3T MRI protocol to characterize serial changes in hip trabecular microarchitecture of SCI subjects at 0 and 12-mo following injury; 3) Compare the ability of 3T MRI to discriminate loss of trabecular connectivity between subjects with SCI (Aim 1) and age- and sex-matched ambulatory controls for the hip and ankle; 4) Evaluate the ability of MRI to discriminate changes in trabecular connectivity at the hip and ankle (by MRI serial testing 12 months apart) and the subsequent effects on trabecular bone strength (by the analysis of Finite Element models of serially acquired trabecular microarchitecture data).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Disruptions in trabecular bone microarchitecture is part of the definition of Osteoporosis: “…a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration with a consequent increase in bone fragility with susceptibility to fracture …” Am. J. Med.1991. Currently, there is no test in terrestrial medicine used to assess trabecular bone microarchitecture in deeply embedded bones. Evidence acquired would substantiate that individuals with rapid loss of aBMD at the hip, including astronauts, could be at risk for irreversible loss of trabecular connectivity and would provide compelling evidence to prescribe anti-resorptive therapy. The proposed study of an MRI protocol at New York University Langone (Langone) will assess its sensitivity to detect irreversible changes in trabecular bone microarchitecture of the deeply embedded hip bone. The protocol will be assessed, using a Siemens 3T MRI Vida (models at both Richmond Veterans Affairs Medical Center / Richmond and Langone), in the non-weightbearing hips of patients following SCI. The non-weightbearing hips of the SCI will serve as an analog for the accelerated hip bone loss that occurs in astronaut hips during spaceflight. We will consent newly admitted patients to the SCI unit who are matched in age, sex and physical characteristics of astronauts as well as to matched to able-bodied controls. The effects of twelve months hip unloading following SCI will be evaluated and compared to able-bodied controls.
Task Progress:	PROGRESS UPDATE (Ed., 9/30/23) SA 1) Use spinal cord injury (SCI) to model the skeletal effects of LD spaceflight on hip trabecular bone microarchitecture (Trb uArch). a) Houston and Richmond Co-PIs finalize the NASA Shared Services Center (NSSC) budgets and funds for base award (March 2023) and for augmented budget award (June 2023) to Richmond Veterans Affairs Medical Center (VAMC), formerly known as Hunter Holmes McGuire VA Medical Center. b) Richmond Co-PI hires Research Administrative Assistant/Study Coordinator to prepare required documents for study implementation and conduct chart reviews to survey annual admissions of SCI patients. c) Siemens 3T MRI Vida (the same model as used at New York University Langone) is installed and operating at Richmond VAMC (Summer 2023); suitability of the MRI coil accompanying the Vida will be confirmed by the Langone Co-I. d) Richmond Co-PI completes and submits Institutional Review Board (IRB) protocol to Richmond IRB (Sept. 2023). Upon Authorization-to-Proceed by Richmond IRB, recruitment of study SCI and Control subjects is initiated in FY24. e) Final preparation and submission of Study Protocol to NASA Johnson Space Center (JSC); IRB will attach an approved Richmond protocol when available. f) Integration of MRI after-hours use for research study being coordinated with Richmond Dept of Radiology. SA 5) Compare estimates of trabecular bone strength (as a surrogate for fracture risk) at the hip and the ankle by Finite

	Element modeling of Trb uArch data, including verification and validation processes informed by data. Data of Trb uArch are derived from serial testing (12-mth apart) of hip and ankle in study subjects (controls and SCI) by 3T MRI and HR-pQCT. a) Purchase of HR-pQCT instrument to integrate skeletal measurements of the ankle (by MRI and HR-pQCT) in Study Subjects of Hip Bone Microarchitecture (SCI and Able-bodied controls). b) Acceptance by Dr. Chamith Rajapakse (April 2023) to join the investigative team, where his expertise in MRI and HR-pQCT will ensure optimal analyses of the ankle (and hip) measurements. c) Delivery of crated HR-pQCT to Richmond VAMC (August 2023). d) Remodeling (re-wiring) commences of room at Richmond VAMC to house the HR-pQCT instrument (September 2023). Once completed, ScanCo engineer will travel to Richmond to uncrate and install HR-pQCT.
Bibliography Type:	Description: (Last Updated:)