Fiscal Year:	FY 2015	**Task Last Updated:**	FY 10/14/2014
PI Name:	Globus, Ruth Ph.D.		
Project Title:	Simulated Space Radiation and Weightlessness: Vascular-Bone Coupling Mechanisms to Preserve Skeletal Health		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Musculoskeletal Alterations Team		
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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PI Organization Type:	NASA CENTER	**Phone:**	650-604-5247
Organization Name:	NASA Ames Research Center		
PI Address 1:	Bone and Signaling Laboratory		
PI Address 2:	Space Biosciences Research Branch		
PI Web Page:			
City:	Moffett Field	**State:**	CA
Zip Code:	94035-1000	**Congressional District:**	18
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2010 Crew Health NNJ10ZSA003N
Start Date:	10/01/2011	**End Date:**	09/30/2016
No. of Post Docs:	2	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	3	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2016, per NSBRI (Ed., 8/26/15)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Alwood, Joshua (NASA Ames Research Center) Castillo, Alesha (Veterans Affairs Palo Alto Health Care System) Delp, Michael (Florida State University) Limoli, Charles (University of California, Irvine)		
Grant/Contract No.:	NCC 9-58-MA02501		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	(1) Original project aims/objectives. Long term spaceflight leads to extensive changes in the musculoskeletal system attributable to unloading in microgravity, although with future exploration outside the protection of Earth's magnetosphere, space radiation also may have adverse, long term effects. Acute, whole body irradiation at high doses can cause significant depletion of stem/progenitor cell pools throughout the body as well as inflammation associated with prompt tissue degradation. To date, little is known about the combined effects of weightlessness and space radiation on the musculoskeletal system and its associated vasculature. Radiation can increase cancellous osteoclasts, leading to rapid bone loss, which can be mitigated in the short term by treatment with a potent anti-oxidant (alpha-lipoic acid). Furthermore, simulated weightlessness in adult mice exacerbates the adverse effects of space-relevant radiation on cancellous tissue, mechanical properties, and osteoprogenitors, as well as long-term responses during recovery from disuse. If weightlessness undermines the capacity to mount radio-protective mechanisms, then potentially irreversible oxidative injury and persistent skeletal damage to stem and progenitor populations may ensue. Deficits in vascular-perfusion coupling also can lead to profound bone loss and may contribute to spaceflight-induced osteopenia. Together, these findings support a two-pronged approach for countermeasure development; one focusing on preventing acute bone loss and another on protecting cell populations needed for skeletal remodeling in the long term. Our long term goals are twofold--define the mechanisms and risk of bone loss in the spaceflight environment and facilitate the development of effective countermeasures if needed. Our working hypothesis is that prolonged musculoskeletal disuse and radiation together cause cumulative, adverse changes in the structure and function of bone and its vasculature resulting from oxidative stress, and prevent recovery from unloading by damaging the stem and progenitor cells needed for subsequent recovery. The rationale for this research is that a better understanding of the mechanisms and long-term risks posed by exposure to weightlessness and space radiation will improve the development and application of countermeasures for future exploration-class missions. (2) Key findings were: • Both weightlessness and ionizing radiation) caused rapid but transient increase in skeletal expression levels of the global antioxidant transcription factor, nrf2 expression, indicating that weightlessness and radiation pose an acute oxidative challenge to skeletal tissue. • Total-body irradiation (gamma or heavy-ion) caused temporal, concerted regulation of gene expression within both marrow and mineralized tissue for select, osteoclastogenic cytokines and markers of bone resorption; this is likely to account for the rapid and progressive deterioration of cancellous microarchitecture observed following exposure to ionizing radiation. • A dietary countermeasure with high antioxidant activity showed an impressive ability to maintain the integrity of their bone structure after high LET irradiation, making it a strong candidate to mitigate radiation-induced tissue damage. • High LET radiation did not completely impair ability of the bone to respond to a potent anabolic mechanical stimulus, rest-inserted axial loading. • Simulated weightlessness and iron radiation each impaired peak endothelium-dependent vasodilation and the combination of HU and IR further impaired endothelium-dependent vasodilation. (3) Impact of key findings on hypotheses, technology requirements, objectives, and specific aims of the original proposal. • Further experiments and analysis of tissues from the dietary intervention and mechanical stimulation experiments needed. • Results from the iron radiation experiment support the theory of a bone-vascular coupling for bone remodeling in response to simulated spaceflight. (4) Proposed research plan for the coming year. In the coming year, we plan to complete analysis of tissues and bones from recent extensive experimentation conducted at NASA Space Radiation Laboratory/Brookhaven National Lab (Aim 1 and 2). We also will conduct experiments at both NSRL/BNL and ARC for this coming year that will: 1) evaluate the effects of the new dietary intervention on vascular reactivity and bone structure following 2 wks of simulated weightlessness alone and combined with simulated space radiation (protons + iron) (Aim 2); 2) define the ability of bone and vascular responses to recover over the long term (2-6 mos) from the adverse effects of protons + iron on a standard vs. supplemented diet (Aim 2, 3) determine the time- and radiation- dependence of anabolic mechanical loading during recovery from simulated space radiation (Aim 1, 3).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our research project focuses on the effects of spaceflight environmental factors, such as microgravity and irradiation, on the skeleton. Through use of an antioxidant as a potential countermeasure to the effects of spaceflight could provide Earth-based benefits in areas including radioprotection, mitigation of oxidative stress, disuse osteoporosis, and fracture healing. Findings are relevant to biomedical concerns including skeletal degeneration such as those caused by radiotherapy, spinal cord injury, or prolonged bedrest.
Task Progress:	We are entering the last year of our four-year grant. We have successfully completed the majority of the first two Aims of the grant, and this coming year will focus on recovery and countermeasures. By the grant completion, our results will inform the design of a flight experiment utilizing antioxidants or dietary supplements as a countermeasure to spaceflight-induced bone loss and established the relevance of changes in vascular reactivity to simulated spaceflight-induced bone loss. We are also using models of mechanical loading as an anabolic stimulus to bone after exposure to ionizing radiation.
Bibliography Type:	Description: (Last Updated: 06/04/2025)
Articles in Peer-reviewed Journals	Prisby RD, BehnkeBJ, Allen MR, Delp MD. "Effects of skeletal unloading on the vasomotor properties of the rat femur principal nutrient artery." Journal of Applied Physiology. Pending review as of August 2014. , Aug-2014
Awards	Schreurs A-S. "NASA Postdoctoral Program (NPP) Fellowship, Year 2, August 2014." Aug-2014

Awards	Schreurs A-S. "Travel grant awarded to attend Association of Radiation Research, 6/29-7/2/2014 Brighton, UK, June 2014." Jun-2014
Awards	Alwood J. "2012 Presidential Early Career Award for Scientists and Engineers (PECASE), announced Dec. 23, 2013." Dec-2013