Fiscal Year:	FY 2014	**Task Last Updated:**	FY 10/16/2013
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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Organization Name:	NASA Ames Research Center		
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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:**	09/30/2015
No. of Post Docs:	3	**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:**	0
No. of Bachelor's Candidates:	5	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
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 (University of Florida) 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. Substantial progress was made in completing Aims 1 and 2 of the original proposal. A standard protocol for simulating the spaceflight factors of space radiation (dual-ion; proton+iron) and weightlessness (hindlimb unloading) was established, and the influence of possible nutritional countermeasures (antioxidant cocktail and flaxseed) tested. The following provides a summary of key findings. • Dietary supplementation of male, 16wk old C57Bl/6J mice with an antioxidant cocktail or flaxseed did not prevent decrements in cancellous bone volume and microarchitecture caused by exposure to ionizing radiation. • Gamma irradiation and hindlimb unloading each reduced endothelium-dependent vasodilation of the gastrocnemius feed artery, which correlated well with cancellous tissue decrements. Signaling pathways in addition to those related to nitric oxide (NO) release may contribute to observed changes in vascular reactivity during simulated spaceflight. (3) Impact of key findings on hypotheses, technology requirements, objectives, and specific aims of the original proposal. • Further analysis of tissues and results from the dietary intervention strategies tested to date are needed before definitive conclusions can be drawn and impact on hypotheses and aims determined. Results obtained to date lead us to focus on evaluating tissues at the mRNA and biochemical levels for evidence of both oxidative damage and the impact of the dietary countermeasures. • Results from the gamma 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 the dietary countermeasure experiments using ionizing radiation (Aim 1 and 2). We also will conduct experiments at both NSRL/BNL and ARC for this coming year that will: continue analysis of tissues and data from vascular reactivity experiments using simulated space radiation at NSRL/BNL with Dr. Delp's team and perform additional in-depth experiments to evaluate vascular responses (Aim 1); analyze skeletal gene expression after exposure to simulated space radiation (Aim 1 and 2); determine the influence of dietary antioxidants on skeletal responses to simulated weightlessness (Aim 2); assess the ability of axial loading to stimulate bone formation after exposure of the mice to simulated space radiation in recovery experiments (Aim 3); perform additional follow-on experiments to determine the ability of dietary countermeasures to prevent bone loss caused by simulated spaceflight (Aim 2, 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 our research could provide Earth-based benefits in areas including radioprotection, mitigation of oxidative stress, and disuse osteoporosis. Findings are relevant to biomedical concerns including skeletal degeneration such as those caused by radiotherapy, spinal cord injury, or prolonged bedrest.
Task Progress:	During this reporting period, we performed series of experiments at the NASA Space Radiation Laboratory at Brookhaven, NSRL-BNL, using iron (56Fe) or a sequential exposure to protons / iron / protons, and separate experiments at NASA Ames Research Center (ARC), using 137Cs. Analysis of samples is still in progress from the recent NSRL experiments, which focused on dietary and mechanical countermeasures to radiations and skeletal unloading. Analysis of an experiment that focused on the effects of gamma irradiation and disuse on the vascular reactivity showed impaired vasodilation in gastrocnemius muscle feed arteries. It is likely that both skeletal disuse and radiation causes diminished vascular capacity. Initial results revealed that dietary interventions (an antioxidant cocktail or flaxseed) did not protect cancellous tissue from ionizing radiation; further experiments are in progress.
Bibliography Type:	Description: (Last Updated: 06/04/2025)