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	Astronauts may develop bone loss in space as a result of environmental challenges such as exposure to weightlessness and ionizing radiation. Oxidative
	Astronauts may develop hole hosts in space as a result of environmental equiption of the radicals and the ability of cells to counteract their harmful effects at the molecular level. To date, little is known about the combined effects of weightlessness and space radiation on the musculoskeletal system, the cardiovascular system, and how these two systems interact in maintaining bone health. The overall objectives of our National Space Biomedical Research Institute (NSBRI)-supported research project were to define mechanisms and risks of bone loss in space, to explore the relationship between microvessel function and bone loss due to weightlessness and radiation exposure, and to help develop effective ways to prevent bone loss. Our NSBRI-supported research project can be considered quite productiveseven peer-reviewed primary papers have been published to date, one published review article, and numerous talks and posters were presented at national and international scientific conferences. Two of the published papers garnered considerable public interest and exposure in the popular press, while one was the subject of both a commentary and a recent article in JAMA. A new manuscript is now in review at a journal (Radiation Research). Three additional primary research papers acknowledging this grant's support are still in preparation (all experimental work complete), and a review article is also being prepared that integrates both our new findings over the life of this project and the contributions of others to this field of research. In the course of this grant. Further, results obtained in the course of executing this grant's research contributed key preliminary results to two new grants that were awarded recently by NASA. Thus, considerable scientific advances and leverage were realized as a consequence of this NSBRI award.
Tel Descision	Using mice to simulate weightlessness and space-relevant radiation, results from the series of studies supported by this grant demonstrate that both of these environmental conditions interact to induce early impairment of endothelium-dependent vasodilation and cancellous bone loss. However, the only sustained vascular endothelial cell dysfunction is that mediated by exposure to High-Z-High Energy ions (HZE) and not by simulated weightlessness. If such results translate to the human condition, then long-term dysfunction of the vascular endothelium induced by HZE particles could be a major contributor to the development of atherosclerotic cardiovascular disease in astronauts, as well as contribute to the long-term bone loss.
Task Description:	We find that simulated weightlessness causes decrements in both slow-turnover cortical bone tissue and high turnover cancellous tissue, whereas ionization radiation (0.5-2Gy) causes decrements only in cancellous tissue. Whereas the radiation-induced deficits in skeletal microarchitecture diminish over a period of 6-7 months due to age-related bone loss in control animals, dysfunction in cell populations persists. HZE but not protons or gamma (<2Gy) cause defects in osteoblastogenesis from bone marrow derived stem cells and progenitors. This defect can be attributed to persistent deficits in progenitor cell proliferation and colony growth, whereas the capacity to differentiate into osteoblast-like cells and mineralize an extracellular matrix (the hallmark of osteoblasts) is retained. In addition, bones from HZE-irradiated animals can respond later to anabolic loading stimulus with improved bone formation, although there is some evidence from analyses by dynamic histomorphometry and gene expression that there may be persistent deficits in osteoprogenitor cell populations localized to regions adjacent to the periosteal surfaces of bone tissue. Together, these findings on marrow-derived progenitors and periosteal cell behavior lead us to predict that fracture healing and perhaps other wound healing processes that depend mesenchymal stem cells derived from the marrow and/or periosteal bone surfaces or regenerative medicine in space, thus represents a potentially important area for future study. With respect to prevention, either mechanical stimulation (resembling vigorous exercise) or feding a diet containing dried plum, can improve bone structure despite prior exposure to HZE. In contrast, treatment with antioxidants that have displayed at least some radioprotective properties (lipoic acid injections, anti-oxidant cocktail, or treatment with an anti-inflammatory (Ibuprofen)) failed to prevent radiation-induced bone loss. These findings imply treatment with antioxidants alone are unlikely to prove fully protective t
	In sum, findings from our studies show that in the short term, ionizing radiation and simulated weightlessness cause greater deficits in blood vessels when combined compared to either challenge alone. In the long term, HZE but not unloading, can lead to persistent, adverse consequences for bone cell and vessel function, possibly due to oxidative stress-related pathways. Novel countermeasures to radiation-induced damage to the skeleton identified in the course of this project include both mechanical stimulation and a dietary supplement.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	A better understanding of the mechanisms and long-term risks posed by exposure to weightlessness and radiation in space is needed to help protect the skeletal health of astronauts during and after long duration, exploration class missions. We hypothesize that countermeasures to unloading and radiation-induced bone loss that target cells responsible for bone formation and bone's vascular supply will be useful for limiting continued bone loss in space and preserving subsequent recovery. Cellular and molecular mechanisms that contribute to the formation of new bone (stem cells, osteoprogenitors, and osteoblasts) will be defined, using ground-based rodent models for simulating space radiation and weightlessness. On the basis of the mechanistic insight gained, potential anti-oxidant countermeasures will be tested in the following specific aims. Aim 1: Determine how prolonged weightlessness and space radiation (simulated spaceflight) cause functional and structural changes in skeletal vascular dysfunction. Aim 3. Determine how low dose space radiation influences later skeletal recovery from prolonged weightlessness. Aim 4. Determine if transient treatment with countermeasures protects from bone loss caused by weightlessness and radiation during subsequent aging. These studies will provide important new insight into the bone loss that is caused by musculoskeletal disuse and radiation during subsequent aging. These studies applications to Earth (e.g., radiotherapy, accidental exposures), as well as space.
Task Progress:	Astronauts may develop bone loss in space as a result of environmental challenges, such as exposure to weightlessness and ionizing radiation. Oxidative stress results from an imbalance between production of free radicals and the ability of cells to counteract their harmful effects at the molecular level. The overall objectives of our research are to define the mechanisms and risks of bone loss in space and to help develop effective ways to prevent that bone loss. We hypothesize weightlessness and radiation together cause oxidative stress, adversely affecting both bone and the blood vessels that feed muscle and bone. This last year, four published papers describe results from our experiments with mice testing various aspects of our hypothesis. We examined the effects of radiation and/or simulated weightlessness by hindlimb unloading on bone and blood vessel function either after a short period or at a later time after transient exposures. In short term studies the combination of weightlessness and heavy ion radiation. With respect to prevention, either mechanical stimulation (resembling vigorous exercise) or feeding a diet containing dried plum, can improve bone structure despite prior exposure to heavy ion radiation. In sum, recent findings from our studies show that in the short term, ionizing radiation, but not unloading, can lead to persistent, adverse consequences for bone and vessel function, possibly due to oxidative stress-related pathways.
Bibliography Type:	Description: (Last Updated: 06/04/2025)
Articles in Peer-reviewed Journals	Ghosh P, Behnke BJ, Stabley JN, Kilar CR, Park Y, Narayanan A, Alwood JS, Shirazi-Fard Y, Schreurs AS, Globus RK, Delp MD. "Effects of high-LET radiation exposure and hindlimb unloading on skeletal muscle resistance artery vasomotor properties and cancellous bone microarchitecture in mice." Radiat Res. 2016 Mar;185(3):257-66. <u>http://dx.doi.org/10.1667/RR4308.1</u> ; PubMed <u>PMID: 26930379</u> , Mar-2016
Articles in Peer-reviewed Journals	Delp MD, Charvat JM, Limoli CL, Globus RK, Ghosh P. "Apollo lunar astronauts show higher cardiovascular disease mortality: Possible deep space radiation effects on the vascular endothelium." Sci Rep. 2016 Jul 28;6:29901. <u>http://dx.doi.org/10.1038/srep29901</u> ; PubMed <u>PMID: 27467019</u> ; PubMed Central <u>PMCID: PMC4964660</u> , Jul-2016
Articles in Peer-reviewed Journals	Globus RK, Morey-Holton E. "Hindlimb unloading: rodent analog for microgravity." J Appl Physiol (1985). 2016 May 15;120(10):1196-206. Review. http://dx.doi.org/10.1152/japplphysiol.00997.2015 ; PubMed

Articles in Peer-reviewed Journals	Alwood JS, Shahnazari M, Chicana B, Schreurs AS, Kumar A, Bartolini A, Shirazi-Fard Y, Globus RK. "Ionizing radiation stimulates expression of pro-osteoclastogenic genes in marrow and skeletal tissue." J Interferon Cytokine Res. 2015 Jun;35(6):480-7. <u>http://dx.doi.org/10.1089/jir.2014.0152</u> ; PubMed PMID: 25734366; PubMed Central PMCID: PMC4490751, Jun-2015	
Articles in Peer-reviewed Journals	Prisby RD, Alwood JS, Behnke BJ, Stabley JN, McCullough DJ, Ghosh P, Globus RK, Delp MD. "Effects of hindlimb unloading and ionizing radiation on skeletal muscle resistance artery vasodilation and its relation to cancellous bone in mice." J Appl Physiol (1985). 2016 Jan 15;120(2):97-106. Epub 2015 Oct 15. <u>http://dx.doi.org/10.1152/japplphysiol.00423.2015</u> ; PubMed <u>PMID: 26472865</u> , Jan-2016	
Articles in Peer-reviewed Journals	Prisby RD, Behnke BJ, Allen MR, Delp MD. "Effects of skeletal unloading on the vasomotor properties of the rat femur principal nutrient artery." Journal of Applied Physiology. 2015 Apr 15;118(8):980-8. Epub 2015 Jan 29. <u>http://dx.doi.org/10.1152/japplphysiol.00576.2014</u> ; PubMed <u>PMID: 25635000</u> ; PubMed Central <u>PMCID: PMC4398884</u> , Apr-2015	
Articles in Peer-reviewed Journals	Schreurs AS, Shirazi-Fard Y, Shahnazari M, Alwood JS, Truong TA, Tahimic CG, Limoli CL, Turner ND, Halloran B, Globus RK. "Dried plum diet protects from bone loss caused by ionizing radiation." Sci Rep. 2016 Feb 11;6:21343. <u>http://dx.doi.org/10.1038/srep21343</u> ; PubMed <u>PMID: 26867002</u> ; PubMed Central <u>PMCID: PMC4750446</u> , Feb-2016	
Articles in Peer-reviewed Journals	Shirazi-Fard Y, Alwood JS, Schreurs AS, Castillo AB, Globus RK. "Mechanical loading causes site-specific anabolic effects on bone following exposure to ionizing radiation." Bone. 2015 Dec;81:260-9. Epub 2015 Jul 18. <u>http://dx.doi.org/10.1016/j.bone.2015.07.019</u> ; PubMed <u>PMID: 26191778</u> , Dec-2015	
Articles in Peer-reviewed Journals	Alwood JS, Tran LH, Schreurs AS, Shirazi-Fard Y, Kumar A, Hilton D, Tahimic CGT, Globus RK. "Dose- and ion-dependent effects in the oxidative stress response to space-like radiation exposure in the skeletal system." Int J Mol Sci. 2017 Oct 10;18(10):E2117. <u>https://doi.org/10.3390/ijms18102117</u> ; PubMed <u>PMID: 28994728</u> ; PubMed Central <u>PMCID: PMC5666799</u> , Oct-2017	
Articles in Peer-reviewed Journals	Schreurs AS, Torres S, Truong T, Moyer EL, Kumar A, Tahimic CGT, Alwood JS, Globus RK. "Skeletal tissue regulation by catalase over-expression in mitochondria." Am J Physiol Cell Physiol. 2020 Oct 1;319(4):C734-C745. Epub 2020 Aug 12. <u>https://doi.org/10.1152/ajpcell.00068.2020</u> ; <u>PMID:</u> 32783660, Oct-2020	
Awards	Schreurs A-S. "American Society for Bone and Mineral Research (ASBMR) young investigator travel award, September 2016." Sep-2016	
Awards	Schreurs A-S. "HRP-IWS (Human Research Program-Investigators' Workshop), travel award, February 2016." Feb-2016	
Awards	Globus R. "NASA Ames Honor Award, September 2016." Sep-2015	
Awards	Globus R. "NASA Scientific Achievement Medal, July 2015." Jul-2015	
Awards	Shirazi-Fard Y. "American Society of Bone and Mineral Research Young Investigator Travel Grant, September 2015." Sep-2015	
Awards	Shirazi-Fard Y. "Radiation Research Society Scholar in Training Travel Award, September 2016." Sep-2016	
Significant Media Coverage	Kaplan S. "Studying heart disease in astronauts yields clues but not conclusive evidence. Coverage of PI Globus' paper: Delp MD, Charvat JM, Limoli CL, Globus RK, Ghosh P. Apollo lunar astronauts show higher cardiovascular disease mortality: Possible deep space radiation effects on the vascular endothelium. Sci Rep. 2016 Jul 28;6:29901. "Washington Post feature article, July 28, 2016. https://www.washingtonpost.com/news/speaking-of-science/wp/2016/07/28/studying-heart-disease-in-astronauts-yields-clues-but-not-conclusive-evidence/, Jul-2016	