Fiscal Year:	FY 2011	**Task Last Updated:**	FY 06/08/2011
PI Name:	Bloomfield, Susan A. Ph.D.		
Project Title:	Maintaining Musculoskeletal Health in the Lunar Environment		
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		
PI Email:	sbloom@tamu.edu	**Fax:**	FY 979-862-1692
PI Organization Type:	UNIVERSITY	**Phone:**	979-845-2871
Organization Name:	Texas A&M University		
PI Address 1:	Department of Health & Kinesiology		
PI Address 2:	400 Harvey Mitchell Pkwy, Suite 300		
PI Web Page:			
City:	College Station	**State:**	TX
Zip Code:	77843-4375	**Congressional District:**	17
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2007 Crew Health NNJ07ZSA002N
Start Date:	06/01/2008	**End Date:**	09/30/2012
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	1	**No. of Master' Degrees:**	1
No. of Master's Candidates:	5	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	13	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 9/30/2012 (from 5/31/2012) per NSBRI (Ed., 1/24/2012)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Braby, Leslie (Texas Engineering Experiment Station) Hogan, Harry (Texas A&M University) Fluckey, James (Texas A&M University) Wang, Suojin (Texas A&M University)		
Grant/Contract No.:	NCC 9-58-MA01602		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The over-arching goal of this project is to determine if the usual bone and muscle loss observed during planetary missions will be exacerbated by exposure to space radiation. Using the partial g mouse model originally developed at MIT/Harvard by Drs. Wagner and Bouxsein (the "partial g mouse"), we first performed experiments to verify whether the partial loading provided by a crew member's body weight (1/6 g), or by body weight with spacesuit weight included (~1/3 g), would be enough to mitigate losses of bone and muscle. Additional analyses (micro-CT, histomorphometry, mechanical testing of bone) on tissues collected from our Experiment 1 in Year 1 were finalized this project year, enabling preparation of a manuscript to be submitted soon. These results confirm our original findings that 1/3 g is partially protective of cortical but not cancellous bone and that, for most bone outcomes, 1/6 and 1/3 BW loading do not prevent decrements in bone integrity observed with full hindlimb unloading (simulating, e.g., low-earth orbit). The major animal protocol work in Project Year 3 started with an intensive 5 ½ week stay at Brookhaven National Laboratory in June 2010 conducting a 3-week animal experiment testing responses to simulated galactic cosmic radiation in weightbearing (1 g) and partial (1/6) weightbearing mice, using 28Si, 300 MeV at the NASA Space Radiation Space Laboratory (NSRL). At experiment's end, we harvested multiple tissues beyond bone and muscle in hopes of tissue sharing with other PI's, and have found at least one laboratory at NASA-JSC and another at Texas A&M interested in these extra tissues. The rest of this third project year focused on processing of these tissues as well as those from parallel x-ray experiments performed at Texas A&M late in Project Year 2. Preliminary results derived from micro-CT analyses of distal femur cancellous bone from these two experiments indicate the highest doses of both x-ray and 28Si did exacerbate bone loss in our 1/6 g mice; these groups had 24% and 7% lower cancellous bone volume (%BV/TV) than sham exposed partial g mice. Interestingly, fractionating that highest dose protected against further loss of bone mass in the x-ray-exposed, but did not for silicon-exposed, mice on partial g. Micro-CT analyses of cancellous bone microarchitecture will soon be complemented by traditional histomorphometry measures of bone formation rate on both cancellous and cortical bone envelopes. Consistent suppression of femoral neck strength (load at failure) was observed in all partial g mice; this suppression was exacerbated in only one group exposed to low-dose radiation (17 cGy 28Si). Analyses in progress will provide some answers to potential mechanisms for these combined effects of reduced weightbearing and modeled space radiation (decreased bone formation? increased bone resorption? apoptosis of osteocytes/ osteoblasts?) which will address IRP Risk Degen 2 ["What are the mechanisms of degenerative tissue risks in the heart, circulatory, endocrine, digestive, lens and other tissue systems?"]. We are also examining skeletal muscle alterations with partial weightbearing and modeled space radiation exposure ; these analyses address IRP Risk M23 ["Do factors in addition to unloading contribute to muscle atrophy during space flight (e.g., radiation, inflammation, hydration, redox balance, energy balance)?"] Analyses on 1/6 partial g mice reveal gastrocnemius muscle atrophy consistently occurring; some of this muscle loss is due to a reduced protein synthesis rate. However, there was no detectable additional effect of co-exposure to low dose x-rays on either loss of muscle mass or the reductions in protein synthesis rate. Western blot assessment of proteins that regulate peptide chain initiation vs. elongation will reveal mechanisms for any alterations in protein synthesis rates. Early results suggest that impairment in muscle protein metabolism with partial gravity may occur at the level of peptide-chain elongation. Upcoming assays will quantify BrdU-positive nuclei to indicate radiation-induced damage to satellite cells and, secondly, fiber-type specific changes in fiber cross-sectional area. In the end, we will have a rich data base of both bone and muscle outcomes from parallel experiments performed with reference x-ray radiation and the 300MeV 28Si, with the capability of providing some calculations of relative biological effectiveness (RBE) for a number of physiological/structural outcomes. These experiments were designed to answer IRP Risk Degen 7 ["Are there significant synergistic effects from other spaceflight factors (microgravity, stress, altered circadian rhythms, changes in immune responses, etc.) that modify the degenerative risk from space radiation?"] in addition to IRP Risk B11 ["What are the effects of radiation on bone?"] In Year 4 (starting 6/1/2011) we will complete these analyses, prepare multiple manuscripts and conduct our final experiment to test whether acute high LET radiation exposure will impair the ability of bone and/or muscle to respond to a resistance-based training protocol administered during a 21-day period of partial weightbearing (at 1/6 g). To our knowledge, no other laboratories have tested this to date, so these data should be absolutely unique in the literature. NSRL beam time proposals were submitted to Brookhaven National Laboratory in February, 2010 and we await word of acceptance and scheduling, hopefully in the fall run, 2011. Mr. Brandon Macias, a senior doctoral student in Dr. Bloomfield's laboratory and NSBRI Pre-Doctoral Fellow at Texas A&M, will be attending NASA's Space Radiation Summer School in June 2011 at BNL, further enhancing our capabilities in radiation biology research.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Defining the impact of partial weightbearing (as opposed to complete non-weightbearing) has important implications for rehabilitative strategies applied to stroke or spinal cord-injured patients. Should the 1/6 or 1/3 g conditions in our experimental animals prove to mitigate the dramatic loss of mass and strength in both muscle and bone seen with zero load bearing (mimicking conditions of low-earth orbit, e.g.), then harness systems or walkers allowing for even minimal load bearing offer high potential for mitigating changes seen in muscle strength and bone integrity in these patients populations. Another population that stands to benefit from these data is composed of veterans returning home with traumatic brain injury, a major concern of the military these last 7 years. Our experiments focusing on effects of low-dose radiation on musculoskeletal structure and function will provide unique and novel data about the potential degenerative effects to be expected by those humans living in areas with high natural background radiation (e.g., Ramsar, Iran); by individuals who accumulate high occupational exposures to ionizing radiation (e.g., commercial airplane crews); and by patients accumulating multiple medical irradiation exposures over time. A growing literature is documenting surprising and deleterious effects on bone with low-level radiation (as opposed to the high doses used in radiotherapy for cancer patients); very little is known at the present time about the impact on these low doses on maintenance of normal muscle protein synthesis and muscle mass. Our experiments directly address these issues.

Task Progress:	Specific Aim 1 [does modeled Lunar gravity, with or without additional weight of EVA spacesuit, protect against decrements in musculoskeletal structure and/or function]: A manuscript comparing is nearly ready for submission by 5/31/2011; target journal is Bone. Poster presentations including these data were made at the Oct 2010 meetings of the American Society of Bone & Mineral Research. A separate manuscript detailing muscle outcomes (muscle protein synthesis, satellite cell BrdU incorporation, histological assessment of fiber cross-sectional areas) is in preparation. Specific Aim 2 [impact of low-dose radiation simulating galactic cosmic radiation on the musculoskeletal response to partial weightbearing]: Our Experiment 2 (performed 6/09-3/10) was a comprehensive pilot experiment testing the impact of low doses of reference x-ray radiation. These results have been reported in poster presentations at the Oct 2010 meetings of the American Society of Bone & Mineral Research (ASBMR) (Lima et al., JBMR 2010) and a manuscript is in preparation for submission to Radiation Research by July 1, 2011. Experiment 3, testing the combined effect of reference x-ray radiation (50 and 100 cGy) and partial weightbearing (1/6 g), was completed in Year 2; much of the current project year has been devoted to analysis of tissues collected (histomorphometry analyses, mechanical testing, immunostaining). Muscle protein synthesis assays are nearly complete; histological assays for BrdU incorporation and fiber-type specific cross-sectional areas are in progress. Experiment 4 was performed entirely on site at Brookhaven's NSRL in June 2010 at start of Year 3 to test the combined impact of high LET radiation (17 and 50 cGy of 28Si, 300 MeV) and partial weightbearing (1/6 g), parallelling as closely as possible Experiment 3 described above. The balance of our year has been spent in processing tissue analyses from bone and muscle collected during this experiment and in planning for our final Year 4 experiments; beam time and animal use proposals submitted to BNL 2/11 for fall 2011 run). Preliminary results from Experiments 3 and 4 have been presented at the April 2011 IAA Humans in Space Symposium (Houston, TX) and May 2011 joint meetings of the European Calcified Tissue Society and the International Bone and Mineral Society in Athens, Greece. Additional abstracts were submitted for presentation at the September 2011 meetings of the American Society of Bone & Mineral Research (San Diego, CA). Muscle protein synthesis assays are nearly complete; histological assays for BrdU incorporation and fiber-type specific cross-sectional areas are in progress.
Bibliography Type:	Description: (Last Updated: 05/28/2021)
Abstracts for Journals and Proceedings	Lima F, Swift JM, Greene ES, Allen MR, Cunningham DA, Braby L, Bloomfield SA. "Effect of low dose ionizing radiation on bone microarchitecture and bone marrow progenitor differentiation." Presented at the 2010 American Society of Bone and Mineral Research Annual Meeting; Toronto, Ontario, Canada, October 15-19, 2010. J Bone Miner Res 2010 Sep; 25(Suppl 1):SU0091. Available at: http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=1f73ef75-f01a-4539-94ae-344ffa8b3616 ; accessed 6/09/2011. , Sep-2010
Abstracts for Journals and Proceedings	Lima F, Swift JM, Macias BR, Greene ES, Kupke JS, Shirazi-Fard Y, Allen MR, Hogan HA, Bloomfield SA. "Weight bearing in simulated 1/6th and 1/3rd gravity does not prevent bone loss." Presented at the 2010 American Society of Bone and Mineral Research Annual Meeting; Toronto, Ontario, Canada, October 15-19, 2010. J Bone Miner Res 2010 Sep;25(Suppl 1):MO0094. Available at: http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=98e55093-2296-42ea-9899-5654faad070c ; accessed 6/09/2011. , Sep-2010
Abstracts for Journals and Proceedings	Swift JM, Swift S, Allen M, Lima F, Bloomfield SA. "Beta-1 adrenergic administration mitigates negative changes in cancellous bone microarchitecture and inhibits osteocyte apoptosis during disuse." Presented at the 2010 American Society of Bone and Mineral Research Annual Meeting; Toronto, Ontario, Canada, October 15-19, 2010. J Bone Miner Res 2010 Sep;25(Suppl 1):SA0319. Available at: http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=a8043d81-b402-419b-a6ed-81ba8c2104b9 ; accessed 6/09/2011. , Sep-2010
Abstracts for Journals and Proceedings	Swift JM, Swift SN, Bouse SD, Hogan HA, Bloomfield SA. "Alendronate inhibits bone formation response to simulated resistance training during disuse." American College of Sports Medicine 57th Annual Meeting, Baltimore, MD, June 2-5, 2010. Medicine & Science in Sports & Exercise 2010 May;42(5 Suppl):704. http://dx.doi.org/10.1249/01.MSS.0000386048.59831.72 , May-2010
Articles in Peer-reviewed Journals	Swift JM, Gasier HG, Swift SN, Wiggs MP, Hogan HA, Fluckey JD, Bloomfield SA. "Increased training loads do not magnify cancellous bone gains with rodent jump resistance exercise." J Appl Physiol. 2010 Dec;109(6):1600-7. PubMed PMID: 20930128 , Dec-2010
Articles in Peer-reviewed Journals	Swift JM, Swift SN, Nilsson MI, Hogan HA, Bouse SD, Bloomfield SA. "Cancellous bone formation response to simulated resistance training during disuse is blunted by concurrent alendronate treatment." J Bone Miner Res. 2011 Sep;26(9):2140-50. Epub 2011 Apr 20. http://dx.doi.org/10.1002/jbmr.407 ; PMID: 21509821 , Sep-2011
Articles in Peer-reviewed Journals	Carpenter RD, Lang TF, Bloomfield SA, Bloomberg JJ, Judex S, Keyak JH, Midura RJ, Pajevic PD, Spatz JM. "Effects of long-duration spaceflight, microgravity, and radiation on the neuromuscular, sensorimotor, and skeletal systems." The Human Mission to Mars: Colonizing the Red Planet. Journal of Cosmology 2010 Oct- Nov;12:3778-80. http://journalofcosmology.com/Mars147.html , Oct-2010
Awards	Macias B. "NSF Graduate Fellowship, September 2010." Sep-2010
Awards	Bloomfield SA. "Armstrong Research Scholar Award (Health & Kinesiology, TAMU), May 2011." May-2011
Awards	Shirazi Y. "Graduate Student Poster Award (5th), IAA Humans in Space Symposium, April 2011." Apr-2011
Dissertations and Theses	Kupke JS. "Characterization of the Femoral Neck Region's Response to the Rat Hindlimb Unloading Model through Tomographic Scanning, Mechanical Testing and Estimated Strengths." MS Thesis, Texas A&M University, December, 2010. , Dec-2010