Fiscal Year:	FY 2010	**Task Last Updated:**	FY 08/06/2010
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		
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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:**	05/31/2012
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	2	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	4	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
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)		
Grant/Contract No.:	NCC 9-58-MA01602		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The over-arching purpose of this project is to determine if the usual bone and muscle loss observed during spaceflight will be mitigated by the moon's partial (1/6 g) gravity, if radiation exposure exacerbates bone/muscle loss at this reduced loading level, and if exercise is effective in mitigating such losses under these conditions. This requires an effective model of the Lunar environment, simulating conditions during Lunar outpost missions. We will use a novel partial gravity mouse model to first determine the independent impact of 1/6 g on multiple bone and muscle outcomes, including direct determinations of bone breaking strength and other mechanical properties. We will then test the additional impact of low dose radiation modeling galactic cosmic radiation (GCR) during partial gravity conditions by exposing these mice to one acute dose, or 4 fractionated doses on a weekly basis, of ionizing radiation. Data from these experiments will be used to justify expanded experiments at the Brookhaven NASA Space Radiation Laboratory utilizing heavy iron ions to simulate galactic cosmic radiation. Finally, the impact of the Lunar environment (partial gravity plus modeled space radiation) on the musculoskeletal response to exercise countermeasures. Experiments supporting Specific Aim 1 [does partial weightbearing (~1/6 g) mitigate losses observed with full unloading (~ 0 g)] are just concluding in early June 2009, hence we are not yet able to report on key findings. We have made a "course correction" in the design of those first experiments. To simulate the additional loadbearing incurred by crew members locomoting on the Lunar surface due to the weight of EVA spacesuits, we elected to add one additional group of animals designated "1/3 g" (since current spacesuit design is roughly equivalent to one body weight, hence doubling the load bearing in the 1/6 g environment). This is easily accommodated by our partial g mouse model, since weightbearing can be titrated to whatever fraction of 100% body weight is desired. We are concurrently preparing to start Experiment 2 (supporting Specific Aim 2: does low-dose radiation exposure change the bone or muscle response to partial gravity). This is a dose-response study utilizing reference x-ray radiation to assess responses of bone and muscle at early (~3 days), "delayed" (~21 days) and "recovery" (~56 days) time points. To achieve the best sensitivity possible, we have added cell culture studies to this experiment at the earlier timepoints to assess the impact on osteoprogenitor cell populations in the marrow. Pilot experiments are in progress to verify our procedures with primary cell culture. Year 2 of this project will hence start with Experiment 2 (beginning July 2009) utilizing 108 mice (12 groups of 9 each) to test responses at the 3 time points listed above at 3 different radiation exposures. We will choose the lowest radiation dose producing detectable change in muscle protein synthesis and bone formation rate to use in the subsequent Experiment 3, commencing in February 2010, which will test the effects of x-ray exposure on the response to simulated partial gravity; in this experiment, mice subjected to 1/3 g (and weightbearing control mice) will be exposed to one acute dose of x-ray (low LET) radiation as well as 3 fractionated doses. Results of Experiment 2 will also be critical to constructing a beam time proposal for a repetition of Experiment 3 at Brookhaven National Lab during Year 3 of this project. The project PI (S. Bloomfield) is attending NASA's Space Radiation Summer School at Brookhaven National Laboratory in June 2009. Both the conceptual and practical knowledge gained will prove invaluable for the later preparation of a beam time proposal as well as preparing for the logistics of conducting 3-week long experiments with live animals at the NASA Space Radiation Laboratory facility.
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 the growing number of returning veterans with traumatic brain injury. 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 that 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 muscle.
Task Progress:	Specific Aim 1 [does modeled Lunar gravity protect, with or without additional weight of EVA spacesuit, protect against decrements in musculoskeletal structure and/or function]: The live animal experiments were completed in the first week of Year 2. Virtually all analyses from this Experiment 1 have been completed: pQCT data collected at days 0 and 21; micro CT scans of excised distal femurs; histomorphometric measures of cancellous bone microarchitecture and bone formation rate at cortical/cancellous bone sites; mechanical testing of tibiae and radii; fecal corticosterone levels to assess animal stress; TUNEL staining for osteocyte apoptosis; and muscle outcomes (wet weights, fractional protein synthesis rate, BrdU incorporation to assess satellite cells, gene expression of markers for protein anabolism). These outcomes were reported at 2010 Experimental Biology meetings (April, Anaheim, CA); first manuscripts are in progress. Specific Aim 2 [impact of low-dose radiation simulating galactic cosmic radiation on the musculoskeletal response to partial weightbearing]: We first completed a dose-response experiment to determine the best dose of x-ray radiation to use in Experiment 3, as well as timing of animal sacrifice after the radiation exposure. In the summer of 2009, mice were exposed to 0 (sham), 17, or 50 or 100 cGy of reference x-ray radiation; one group was sacrificed 3 days after exposure and a second group at 21 days. Micro-CT analyses of distal femurs, histological assessment of bone formation rate, were completed. A significant addition to this experiment was performance of primary cell culture studies of bone marrow stromal cells (BMSC) to assess radiation effects on BMSC proliferative and differentiation capabilities. An additional round of mice were irradiated in spring of 2010 to repeat cell culture experiments. Most analyses have been completed; preliminary results will be presented at the 2010 Skeletal Tissue Biology Workshop (Sun Valley, August, 2010) and at the American Society for Bone & Mineral Research (Toronto, October 2010). The main experiment for Specific Aim 2 (Experiment 3) was completed by April 2010; both weightbearing (1 g) and

	partial (1/6) g mice were exposed to sham irradiation or 1 dose of 17 or 50 cGy of x-ray radiation on Day 0. A fourth group was exposed to 3 fractionated doses (0.17 Gy at 1 week intervals, on Day 0, 7 and 14). Animals were sacrificed after 21 days; analysis of bone and muscle collected at sacrifice are on-going. April and May of 2010 has been dominated by planning for experiments at the NASA Space Radiation Laboratory at Brookhaven National Laboratory, which will expose weightbearing and partial (1/6) g mice to similar doses of a higher LET ionizing radiation (silicon). These experiments are scheduled for the Summer 2010 run, starting on May 31.
Bibliography Type:	Description: (Last Updated: 05/28/2021)
Abstracts for Journals and Proceedings	Lima F, Nilsson MI, Bouse S, Hogan HA, Swift SN, Bloomfield SA. "Alendronate inhibits disuse bone loss in dose-dependent manner in mature male rats." 31st Annual Meeting of the American Society for Bone and Mineral Research, Denver, CO, September 11-15, 2009. J Bone Miner Res. 2009 Sep;24(Suppl 1). Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=0ad3c165-74d5-452f-96e2-661da47b6166 , Sep-2009
Abstracts for Journals and Proceedings	Macias BR, Swift JM, Lima F, Greene ES, Allen MR, Bloomfield SA. "Weightbearing in simulated 1/6th and 1/3rd gravity does not prevent cancellous bone loss." Experimental Biology 2010, Anaheim, CA, April 24-28, 2010. FASEB J. 2010 Apr;4. , Apr-2010
Abstracts for Journals and Proceedings	Swift JM, Gasier HG, Wiggs MP, Swift SN, Bouse SD, Hogan HA, Fluckey JD, Bloomfield SA. "Increased strain magnitude during rodent voluntary dynamic exercise does not further enhance the anabolic skeletal response." 31st Annual Meeting of the American Society for Bone and Mineral Research, Denver, CO., September 11-15, 2009. J Bone Miner Res. 2009 Sep;24(Suppl 1). Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=af138fdb-3efd-49ab-a870-3e07ad059658 , Sep-2009
Abstracts for Journals and Proceedings	Wiggs MP, Fluckey JD, Swift JM, Lima F, Greene ES, Bloomfield SA. "The effect of simulated 1/6th and 1/3rd gravity on gastrocnemius muscle mass and fractional protein synthesis in mice." Experimental Biology 2010, Anaheim, CA., April 24-28, 2010. FASEB J 2010 Apr;24. , Apr-2010
Articles in Peer-reviewed Journals	Bloomfield SA. "Disuse osteopenia." Curr Osteoporos Rep. 2010 Jun;8(2):91-7. PMID: 20425616 , Jun-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." Bone. In press, 2010. , Aug-2010
Articles in Peer-reviewed Journals	Swift JM, Nilsson MI, Hogan HA, Sumner LR, Bloomfield SA. "Simulated resistance training during hindlimb unloading abolishes disuse bone loss and maintains muscle strength." J Bone Miner Res. 2010 Mar;25(3):564-74. PMID: 19653816 , Mar-2010
Awards	Swift JM. "Texas A&M Assoc. of Former Students Distinguished Graduate Student Excellence in Research Award, April 2010." Apr-2010
Awards	Wang S. "Editor-in-Chief, Journal of Nonparametric Statistics, November 2009." Nov-2009
Awards	Wang S. "Texas A&M System Teaching Excellence Award, October 2009." Oct-2009
Dissertations and Theses	Bouse S. "Investigation of transfer function analysis as a means to predict strain on rat tibiae from ankle torque waveforms." Thesis, Texas A&M University, December 2009. , Dec-2009
Dissertations and Theses	Lucas MW. "A novel method for the evaluation of mechanical properties of cancellous bone in the rat distal femur." Dissertation or Thesis, August 2009. , Aug-2009