Fiscal Year:	FY 2011	**Task Last Updated:**	FY 04/29/2011
PI Name:	Hargens, Alan R. Ph.D.		
Project Title:	Risk of Intervertebral Disc Damage after Prolonged Space Flight		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Dynamic Loads**:Risk of In-Mission Injury and Performance Decrements and Long-term Health Effects due to Dynamic Loads (2) **IVD**:Concern of Intervertebral Disc Damage upon and immediately after re-exposure to Gravity [inactive] (3) **Medical Conditions**:Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures (4) **Renal Stone**:Risk of Renal Stone Formation		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	92037-0863	**Congressional District:**	52
Comments:			
Project Type:	Flight	**Solicitation / Funding Source:**	2009 Crew Health NNJ09ZSA002N
Start Date:	07/01/2010	**End Date:**	06/30/2013
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NASA JSC
Contact Monitor:	Baumann, David	**Contact Phone:**	
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Flight Program:	Pre/Post Flight		
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Lotz, Jeffrey (University Of California, San Francisco) O'Neill, Conor (Self) Sayson, Jojo (Ola Grimsby Institute, San Diego) Chiang, Stephen (Methodist Hospital) Alavi, Abass (University of Pennsylvania) Haughton, Victor (University of Wisconsin) Chang, Douglas (University Of California, San Diego) Allon, Moshe (Self) Garfin, Steven (University Of California, San Diego)		
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Performance Goal Text:	
Task Description:	Our proposal is a Flight Definition Study that will use state-of-the-art imaging technologies to quantify morphology, biochemistry, metabolism, and kinematics for lumbar discs of crew members before and after prolonged space flight. Importantly, we will correlate these data with low back pain that spontaneously arises in space so as to establish pain and disc damage mechanisms that will serve as basis for future countermeasure development. After successful completion of our investigation, we will deliver a comprehensive database of microgravity-induced intervertebral disc and vertebral changes (type and magnitude) and a prioritization of these changes as to their deleterious effects and risks for crew member injury based on clinical findings. We hypothesize that spontaneous space-flight back pain and disc herniation are due to biomechanical and biological pathomechanisms. First, microgravity leads to higher than normal physiologic disc swelling and increased disc height that may stiffen the lumbar motion segment and cause abnormal segmental movement patterns. These biomechanical changes increase risk for annular rupture, vertebral endplate microfracture, and facet joint capsule strain. Second, increased disc swelling may alter nuclear matrix osmotic pressure and nutrient transport from endplate capillaries in adjacent vertebra. These biological changes adversely affect disc cell metabolism, causing pain and inducing disc matrix degradation. Our project directly addresses the Critical Path Roadmap Risks and Questions for NASA regarding disc injury (IRP Gap-B4): Is damage to joint structure, intervertebral discs, or ligaments incurred during or following hypogravity exposure? The goal of this research is to characterize space-flight induced changes comprehensively in disc morphology, biochemistry, metabolism, and kinematics. These data will be correlated with measures of back pain intensity and disability. Crewmembers will be imaged pre-flight to establish baseline data and to characterize measurement repeatability. After long-term microgravity exposure (about 180 days on ISS), crewmembers will be studied while maintaining supine posture as soon as possible after return to 1-G in order to quantify the acute effects of prolonged space flight. Also, pre- and post-flight, they will be imaged supine and in standing upright posture at one body weight and again at 1.1 body weight so that MR images are obtained before and after axial body-weight loads. Pre-flight tests will be done within L-120 to L-60 days before the scheduled space flight. Post-flight tests will be undertaken1-7 days and 30-60 days after landing to investigate re-adaptation to 1-G and to distinguish immediate and longer-term recoveries. Our proposed measures represent a comprehensive set of tests that evaluate exposure severity, potential injury mechanisms, and pain generator localization. Our research will aid understanding of spinal pain and deconditioning during prolonged microgravity and of the higher incidence of disc prolapse or herniation following re-exposure to 1-G with a long-term view to prevent such spinal deconditioning with exercise or other physiologic countermeasures.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	We propose to use state-of-the-art, non-invasive imaging technologies to quantify morphology, biochemistry, metabolism, and kinematics for lumbar discs of crew members before and after prolonged space flight. Importantly, we will correlate these data with low back pain that spontaneously arises during prolonged microgravity and after re-adaptation to Earth gravity, so as to establish pathomechanisms that will serve as a basis for future countermeasure development. After successful completion of our investigation, we will deliver a comprehensive database of microgravity-induced intervertebral disc and vertebral changes (type and magnitude) and a prioritization of these changes as to their deleterious effects and risks for crew member injury based on clinical findings. Importantly, this research will have application to back-pain patients on Earth in general and specifically, to patients exposed to long-term bed rest or lack of mobility (spinal-cord injury patients as well as patients suffering lack of exercise, mobility and obesity). This research also has application to abnormal spinal curvature and pain suffered by children wearing heavy backpacks to and from school.
	We have made significant progress over the past 10 months preparing IRB applications and receiving approvals from the UCSD and NASA-JSC Institutional Review Boards (IRBs). Moreover, we also made significant progress with optimizing and scheduling our pre- and post-flight tests to maximize their scientific value and to minimize impacts and risks to ISS crew members. After receiving official notice on 7 April 2010 from the Human Research Program at NASA JSC that our proposal was selected as a “Flight Definition” project, we submitted an IRB application to UCSD. We received official approval for our IRB application from UCSD on 27 July 2010, back-dated to our “pending approval” date of 24 June 2010. Next, we submitted our approved UCSD protocol to the NASA-JSC CPHS on 29 July 2010. The NASA-JSC CPHS tabled their full review of our UCSD-approved protocol until their NASA Radiation Isotopes Subcommittee reviewed and approved it. After we were contacted in late August 2010 to provide more information on radiation dosages and to reduce dosages to levels as low as reasonably achievable, the NASA Radiation Isotopes Subcommittee met on 15 September 2010 to reconsider our protocol. After consideration of the reduced dosages and the impact upon astronaut career limits, the NASA Radiation Isotopes Subcommittee approved the proposal with the specification that the Consent Form be revised and individualized to provide astronauts with both career limit impact and health risks of combined space flight and scientific investigation induced-radiation exposures. Prior to an ISS Investigator Working Group meeting on 22 November 2010, the PI received feedback from Drs. Jan Meck and Scott Parazynski that the Astronaut Office thought that the radiation levels were too high and crew consent would be difficult to obtain. Thus, during a meeting of two Co-Is (Drs. Lotz and Chiang) and myself, we decided to delete the post-pre-flight PET test using Na-F and make all PET tests optional for crew members as follows: 1) Post-flight FDG of the whole spine only (10 mSv/0.42 mSv/day=24 extra days on ISS) 2) Pre- and Post-flight FDG scans of the whole spine (48 extra days on ISS) 3) Post-flight Na-F if abnormal post-flight MRI (7.5mSv/0.42mSv/day= 18 extra days on ISS) 4) No PET scans- minimal radiation from fluoroscopy only (3.4 mSv or 8 extra days on ISS) These four options would allow crew members to decide what radiation dosage best suits their career limits and helps them manage their individual risks. Also, following the ISS Investigator Working Group meeting on 22 November 2010, we moved our MRI and MRS testing site to UTMB Victory Lakes to reduce ISS crew transport times and evaluated the standard, back strength tests that are performed using the NASA JSC Biodex equipment. We decided that Biodex data will be of value to us, but we

Task Progress:	also need a form of endurance test in spine posture as the isometric endurance is more functional outcome for spinal fatigue. Below is a list of our action items from the ISS Investigator Working Group meeting on 22 November 2010, followed by our responses: 1. For IVD, SPRINT, ICV: a. Gather all MRI requirements. See attached NASA IRB application to be submitted tomorrow. b. Determine if Victory Lakes can accommodate all MRI requirements. Yes, we think so depending on NASA's negotiations with UTMB for use of their facilities. c. Determine to what degree, if any, MRI sessions can be combined. Not possible as far as we know as we request R+1 imaging. d. Determine washout time for tracers (how long between IVD and ICV MRI's). No washout time. 2. For FTT, SPRINT and IVD: a. Can any muscle function/strength measurements from SPRINT/FTT be shared with IVD? No, but we are checking is CSE tests are sufficient for our purposes. After responding to the NASA-JSC CPHS, we received official approval of our revised NASA protocol and consent form on 7 February 2011. Before and after this approval by the NASA-JSC CPHS, we have been coordinating and optimizing our protocol and pre- and post-flight crew-testing schedule with several personnel from the Biomedical Research and Countermeasures Projects Branch and the Bioastronautics Team of the International Space Station Medical Project at NASA JSC. On 12 April 2011, Sayson and Hargens presented a review paper "Back Pain Mechanisms in Space" at the IAA Humans in Space meeting in Houston, TX: J.V. Sayson, A.R. Hargens. Back Pain Mechanisms in Space. IAA 18th Humans in Space Symposium: "Integration and Cooperation in the Next Golden Age of Human Space Flight." April 11-15, 2011. On 14 April 2011, also at the IAA 18th Humans in Space Symposium, our team presented an abstract "STS-131: Effects of Microgravity on the Creep Behavior of Murine Intervertebral Discs." J.F. Bailey, K.K. Cheng, A.R. Hargens, K. Masuda, and J.C. Lotz. STS-131: Effects of Microgravity on the Creep Behavior of Murine Intervertebral Discs. IAA 18th Humans in Space Symposium: "Integration and Cooperation in the Next Golden Age of Human Space Flight." April 11-15, 2011. Following this meeting, we performed pilot studies of our upright MRI, spinal kinematics, MRI and MRS tests at facilities nearby NASA JSC. The times for each test were within the limits which we cited in our IRB applications; and the tests were valuable in order to optimize tests on actual crew members planned for next year. We plan to conduct another pilot test in San Diego 19 May 2011 in order to optimize further the back pack design and stability conditions for our upright MRI tests. Related to the tests of spinal kinematics, we noted an upright L5/S1 motion curve with three peaks in one of our investigators who served as a control subject. Our expert, Adam Deitz, compared the results multiple times with the raw images and confirmed that the graph was true to the motion in the video. We found that our control subject is highly mobile, especially in the upper lumbar region. Based on the recumbent flexion/extension data, it appears that his L5/S1 is the least stiff of all of his spinal segments, and that L3/L4 and L4/L5 are the most-stiff segments. These pilot studies demonstrate that dynamic fluoroscopy is a very sensitive tool for quantifying lumbar motion and should provide valuable information as to how long-duration space flight alters spinal movement patterns. Also, at the IAA Humans in Space meeting in Houston, our team was informed that our proposed PET/CT tests of spinal inflammation and injury were deleted because they were deemed to be insufficiently valuable from a benefit/risk ratio. We hope to receive a formal letter from NASA explaining this decision. We are finalizing a review paper "Back Pain in Space and Post-Flight Spine Injury: Mechanisms and Countermeasure Development" by J Sayson, J Lotz, S Parazynski and A Hargens for submission to Acta Astronautica within the next month. The next few months will include revising our UCSD and NASA IRB applications to incorporate changes related to the PET/CT scans and other minor adjustments which were derived from our pilot studies in April 2011.
Bibliography Type:	Description: (Last Updated: 06/30/2025)
Abstracts for Journals and Proceedings	Bailey JF, Cheng KK, Hargens AR, Masuda K, Lotz JC. "STS-131: Effects of Microgravity on the Creep Behavior of Murine Intervertebral Discs." Presented at the IAA 18th Humans in Space Symposium: "Integration and Cooperation in the Next Golden Age of Human Space Flight," Houston, TX, April 14, 2011. Proceedings, 18th IAA Humans in Space Symposium, 2011. http://www.dsls.usra.edu/meetings/iaa2011/pdf/2286.pdf , Apr-2011
Abstracts for Journals and Proceedings	Sayson JV, Hargens AR. "Back Pain Mechanisms in Space." Presented at the 18th IAA Humans in Space Symposium: "Integration and Cooperation in the Next Golden Age of Human Space Flight," Houston, TX, April 12, 2011. Proceedings, 18th IAA Humans in Space Symposium, 2011. http://www.dsls.usra.edu/meetings/iaa2011/pdf/2024.pdf , Apr-2011