Fiscal Year:	FY 2012	**Task Last Updated:**	FY 04/30/2012
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:	2	**No. of PhD Degrees:**	1
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	3
No. of Bachelor's Candidates:	4	**Monitoring Center:**	NASA JSC
Contact Monitor:	Maher, Jacilyn	**Contact Phone:**	
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Flight Program:	Pre/Post Flight		
Flight Assignment:	ISS		
Key Personnel Changes/Previous PI:	Removal of two Co-Is (Alavi and Sayad-Shah) who are no longer involved in the study and addition of a new Co-I, Scott Parazynski, MD.		
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) Haughton, Victor (University of Wisconsin) Chang, Douglas (University Of California, San Diego) Allon, Moshe (Self) Garfin, Steven (University Of California, San Diego) Parazynski, Scott (The Methodist Hospital Research Institute) Riascos-Castaneda, Roy (University of Texas Medical Branch)		

Grant/Contract No.:	NNX10AM18G
Performance Goal No.:	
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 12 months streamlining our pre- and post-flight tests, consenting two ISS crew members, updating IRB applications, submitting amendments and receiving approvals from the UCSD and NASA-JSC Institutional Review Boards (IRBs). Moreover, we also made significant progress with optimizing and validating our pre- and post-flight tests to maximize their scientific and clinical value and to minimize impacts and risks to ISS crew members. In terms of tests, we improved the set-up and safety of the Biering-Sorensen Test and received approval for our Test Readiness Review on 17 Feb 2012. On June 2011 we submitted an Investigation Summary Form for our project which was officially approved as “IVD.” After responding to the NASA-JSC CPHS, we received official approval of our amended NASA protocol and consent form on 21 June 2011. The significant revisions are summarized below and reflect changes made to improve the science and reduce the time commitment and radiation risk to crew members. We added UTMB Victory Lakes MRI Facility as the supine MRI site to reduce travel time from JSC. Pre- and post-flight, crew will be imaged at Upright MRI in Clear Lake during supine posture and then upright posture with normal weight bearing and after donning a back pack with 10% body weight load. This weight-bearing procedure is more natural than supine loading at 50% body weight. Specific Aim 4 and all methods related to PET scan were deleted to reduce the time commitment and radiation risk to crew members. A pre-flight familiarization of the Biering-Sorensen trunk strength test was added. Prior to any test day, we requested a log of medications taken by the crew member over the previous 48 hours. Also, prior to any test day, we requested a log of exercises (type, intensity and duration) performed by the crew member over the previous 7 days. Moreover, we requested a log of all in-flight exercises performed by the crew member. We will also share muscle strength data with the JSC Exercise Physiology and Countermeasures Lab. One of our four testing sessions (formerly Session C) was deleted, reducing post-flight testing time from 345 min to 320 min not including travel time. We reduced total radiation dose from 30.9 mSv to 3.4 mSv. The Consent was revised to reflect the changes outlined above. We were selected for flight on 25 July 2011 and we received approval from the JAXA IRB on 27 May 2011. In Sept 2011, we briefed two ISS crews and received Consent from two crew members. In Nov-Dec 2011, we drafted an Intervertebral Disc Damage (IVD) Science Verification Test (SVT) Plan. This SVT plan outlined the IVD tests with specific steps regarding scheduling, test preparation, test completion, and data transfer to verify the experiment system was adequate to support the scientific objectives.

Task Progress:	On 6 Jan 2012 we submitted a renewal and amendment to our JSC-CPHS Protocol 10-072. The changes to our JSC-CPHS Protocol 10-072 (since it was initially approved on 7 Feb 2011) included the removal of two Co-Is (Alavi and Sayad-Shah) who are no longer involved in the study and addition of a new Co-I, Scott Parazynski, MD. We clarified that all pre-flight tests will be conducted within L-120 to L-60 days before the scheduled space flight. All post-flight tests will occur during the period R+1-7. However, it should be noted that the MRI and MRS tests will be repeated during the R+30-60 day period. The later MRI and MRS tests will monitor recovery of the discs. It was emphasized that no new tests are added. We also uploaded our Legacy protocol to the new NASA JSC CPHS web site and also, uploaded new Letters of Support and Conflict of Interest statements. In Nov 2011, UCSF graduate student Cory Laws presented a poster at the American Society for Gravitational and Space Biology (ASGSB) Annual Meeting entitled 'Increased risk of disc herniation following spaceflight: a biomechanical model'. These data represent work to develop analytical and experimental (human cadaveric) models that can be used to clarify mechanisms of microgravity-induced disc injury. These models will be used to help interpret data collected from crew members as well as develop potential countermeasures. Cory Laws was featured in the Student Spotlight in the most recent ASGSB newsletter (https://). In Dec 2011, Sayson, Lotz, Parazynski, and Hargens submitted a review paper "Back Pain in Space and Post-Flight Spine Injury: Mechanisms and Countermeasure Development," based on a presentation at the 2011 IAA Humans in Space meeting in Houston, TX. This paper was conditionally accepted for possible publication in Acta Astronautica. On 5 Feb 2012, Dr Jeff Lotz presented a talk at the Orthopaedic Research Society entitled "Spines in Space: Microgravity Effects on Spinal Discs." On 14 February 2012, Dr Alan Hargens presented a talk at the Human Research Program Investigators' Workshop entitled "Mechanism of Post-Flight Herniation of Intervertebral Discs." Following the Human Research Program Investigators' Workshop, we performed additional pilot studies of our upright MRI at the Upright MRI facility nearby NASA JSC. Based on our studies on 17 Feb 2012, we further amended our JSC-CPHS Protocol 10-072 to include the cervical spine and reduced the total scanning time for our upright MRI tests of ISS crews before and after flight. This modification reduced the risk (reducing overall scanning time from 80 min to 60 min and having the crew member sit in a fourth scan) and raised the benefit of our protocol by including the cervical spine which has the highest incidence of post-flight disc herniation. The risk of herniated vertebral discs was reported recently for 321 astronauts (Johnston et al., 2010). The incidence of disc herniation was the highest (41%) in the cervical spine, compared to 9% in matched controls. Our amendment was approved by the JSC-CPHS on 28 March 2012. During pilot studies on the PI last month, we were able to streamline the upright MRI studies of the lumbar spine to less than the proposed 80 minutes. We were also able to add scans of my cervical spine for a total scanning time of 60 minutes. On 13 March 2012, Dr. Jeff Lotz gave an invited presentation to the Department of Orthopaedic Surgery at the University of Hong Kong entitled "The Effects of Microgravity on the Human Lumbar Spine." On 24 April 2012 we briefed two additional crew members as well as conducted a full pilot study of the MRI and dynamic fluoroscopy studies to be performed at Victory Lakes. Two sets of studies were performed on two volunteers to both verify protocols and data integrity; and also to assess the ability to discriminate diurnal fluctuations in disc anatomy, biomechanics, hydration, and metabolic profile. For the first time, all of these data sets will be correlated within and across individuals. We had allotted 2 hours to both tests and were able to reduce the time by 15 minutes. With these extra 15 minutes, we plan to submit a modification to the CPHS, to include the cervical spine given the prevalence of disc herniations in this region. This will allow us to compare both upright and supine MRI.

Bibliography Type:	Description: (Last Updated: 07/09/2025)
Abstracts for Journals and Proceedings	Lotz J, Hargens AR. "Spines in Space: Microgravity Effects on Spinal Discs." Presented at 2012 Annual Meeting of the Orthopaedic Research Society, San Francisco, CA , February 4-7, 2012. Transactions of the 58th Annual Meeting of the Orthopaedic Research Society, 2012. , Feb-2012
Abstracts for Journals and Proceedings	Hargens AR, Lotz, J. "Mechanism of Post-Flight Herniation of Intervertebral Discs." 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. 2012 Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. , Feb-2012
Abstracts for Journals and Proceedings	Lotz J. "The Effects of Microgravity on the Human Lumbar Spine." Invited presentation to the Department of Orthopaedic Surgery, University of Hong Kong. Department of Orthopaedic Surgery, University of Hong Kong., 13 March 2012. , Mar-2012
Articles in Peer-reviewed Journals	Sayson JV, Lotz J, Parazynski S Hargens AR. "Back Pain in Space and Post-Flight Spine Injury: Mechanisms and Countermeasure Development. " Acta Astronautica-conditionally accepted, as of April 2012. , Apr-2012