Fiscal Year:	FY 2014	**Task Last Updated:**	FY 03/11/2014
PI Name:	Hargens, Alan R. Ph.D.		
Project Title:	Fluid Distribution before, during and 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) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes (2) **SANS**:Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	La Jolla	**State:**	CA
Zip Code:	92037-0863	**Congressional District:**	52
Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	04/05/2013	**End Date:**	09/30/2018
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	1
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	3	**Monitoring Center:**	NASA JSC
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Flight Program:	ISS		
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Arbeille, Phillipe (CERCOM) Chang, Douglas (University of California, San Diego) Gunga, Hanns-Christian (CHARITE - UNIVERSITATSMEDIZIN BERLIN) Liu, John (University of California, San Diego) Macias, Brandon Richard (University of California, San Diego)		
Grant/Contract No.:	NNX13AJ12G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Editor's Note (4/24/2013): NOTE THIS IS A CONTINUATION OF FUNDING FOR NNX12AL66G WITH THE SAME TITLE AND PRINCIPAL INVESTIGATOR. We will use state-of-the-art, non-invasive technologies to quantify upper-body compartmental volumes and pressures in crew members before, during, and after prolonged space flight. Importantly, we will correlate these data with vision deficits that occur in order to establish pathophysiologic 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, head-ward volume and pressure changes (type and magnitude) and a prioritization of these changes as to their deleterious effects on vision in crewmembers during and after prolonged space flight. We are proposing a well-documented and validated battery of non-invasive or minimally-invasive, image-based tests developed to identify and quantify microgravity-induced, head-ward volume and pressure changes. We hypothesize that prolonged microgravity-induced, head-ward volume and pressure shifts are responsible for elevating intracranial pressure (ICP) and producing deficits in crewmembers' vision. Our project directly addresses Critical Path Roadmap Risks and Questions regarding "Risk of Microgravity-Induced Visual Alterations and Intracranial Pressure", specifically Integrated Research Plan (IRP) Gap Cardiovascular (CV)7: How are fluids redistributed in-flight? and IRP Gap VIIP1: What is the etiology of visual acuity and ocular structural and functional changes seen in-flight and post-flight? Our first specific aim is to study periocular fluid volumes, intraocular pressure (IOP), upper-body compartment volumes before, during, and after prolonged microgravity exposure. The second specific aim is to measure jugular vein dimensions and blood flow using ultrasound before, during, and after prolonged microgravity exposure. The third specific aim is to quantify ventricular and cerebrospinal volumes using ultrasound before, during, and after prolonged microgravity exposure. A fourth specific aim is to perform retinal imaging to observe retinal venous distension in space. Tests of ocular structure will include optic nerve head tomography, nerve fiber layer thickness, axial length, and orbital retrolaminar subarachnoidal space. Tests of ocular function will include visual acuity, total retinal blood flow, and capillary blood flow in the optic nerve head and macula. Finally, changes in ICP, intraocular pressure (IOP), and ocular structures and functions will be investigated while applying a purely-mechanical countermeasure of low-level lower body negative pressure or thigh cuffs to counteract the head-ward fluid shift in space. To our knowledge, this study will be the first to provide detailed and non-invasive measures of compartmental volume and pressure changes in the upper body induced by prolonged microgravity and to correlate these specific changes with decrements in vision for crewmembers. The proposed techniques represent the best available, state-of-the-art tools to quantify and document features that are clinically suspected as vision deficit generators. By correlating volume and pressure changes with vision problems, we expect to identify factors that will later motivate targeted development of effective physiologic countermeasures such low-level lower body negative pressure exposure or thigh cuffs in space. This project has the potential to prevent loss of vision in crewmembers exposed to prolonged space flight and upon return to Earth. NOTE: This study was merged with investigations from Dr. Michael Stenger (Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance) and Dr. Scott Dulchavsky (Microgravity associated compartmental equilibration) resulting in a comprehensive study titled "Fluid Shifts Before, During and After Prolonged Space Flight and Their Association with Intracranial Pressure and Visual Impairment" (short title: Fluid Shifts).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our proposed tests represent a comprehensive set of state-of-the-art, noninvasive technologies to quantify upper-body compartmental volumes and vascular parameters in crew members before, during, and after prolonged space flight. Importantly, we will correlate these data with vision deficits that occur in order to establish pathophysiologic mechanisms that will serve as basis for future countermeasure development. After successful completion of our investigation, we will deliver a database of microgravity-induced, head-ward volume and vascular changes (type and magnitude) and a prioritization of these changes as to their deleterious effects on vision in crew members during and after prolonged space flight. Finally, our project includes use of lower body negative pressure (LBNP) which is known to sequester fluid in lower body tissues and counteract headward fluid shifts. Importantly, these procedures have the potential to reduce intracranial pressure and counteract papilledema, even if the proposed countermeasure acts transiently. This research has immense Earth benefits such as development and validation of a noninvasive ICP device and greater understanding of glaucoma using the latest technology for measuring intraocular and intracranial pressures.
	We have made significant progress over the past year preparing applications and receiving approvals from the NASA-Johnson Space Center (JSC) Institutional Review Board (IRB). Moreover, we also made significant progress with optimizing and scheduling our pre-, in-, and post-flight tests to maximize their scientific value and to minimize impacts and risks to International Space Station (ISS) crew members. The "Fluid Shifts: Space Flight Study" was approved by the NASA JSC IRB on 1/28/2014. In addition, we submitted a Phase I: Feasibility Study of five subjects to test the integration of all of our planned ground-based measures. This Phase 1 feasibility study is currently under review; and we expect approval soon. We do not anticipate any delays in approval since the Flight project was approved and this feasibility study consists of the same measures. We have submitted the approved NASA-JSC IRB to our University of California San Diego (UCSD) IRB office. Erik Hougland, our flight project manager, has been coordinating our bi-weekly FS team telecons. At the request of the NASA Element office we have merged three flight projects. Following our flight definition phase, we have worked to integrate our proposed ground and flight measures among the research team (Stenger and Dulchavsky). We have been in frequent contact to develop a final draft of the NASA Experimental Document. We visited the upright magnetic resonance imaging (MRI) facility to brief the Fonar and MRI personnel on our proposed MRI measures and develop MRI protocols for our cerebral spinal fluid flow tests. The Cerebral Cochlear Fluid Pressure (CCFP) Marchbanks device received a CE mark and the NASA unit was shipped 1/30/2014. With this final hardware item set to arrive JSC next week we have blocked the week of March 3rd to start our integration and Phase I feasibility study. We are in frequent contact with collaborators Philippe Arbeille and John HK Liu, to coordinate their travel and participation in these tests. Our study will utilize the Russian Chibis device; we have been in close contact with our Russian collaborators, Irina Alferova and Zhanna Yarmanova, to coordinate ISS Chibis operations and study implementation. We have scheduled March 18-20 for a meeting at NASA JSC to collaborate with them on Chibis operations and study protocols. Over the past year other important milestones were met. We helped finalize the NASA informed consent briefing for the

Task Progress:	first one-year astronaut. We provided Professor Arbeille's in-flight and ground ultrasound procedures to the NASA JSC in preparation for our feasibility and flight studies. We provided feedback on the acquisition of the research Spectralis OCT device with anterior segment module. We provided feedback on the acquisition of a iCARE intraocular pressure measurement devices. Also, we provided feedback on acquisition of the Marchbanks CCFP unit. We have held conferences with Drs. Mike Williams and Bob Marchbanks to gain lessons learned from their experiments and building of our CCFP units to facilitate implementation of the CCFP hardware into our ISS flight project. At UCSD we have conducted IRB-approved, whole body tilt and lower body negative pressure (LBNP) studies to determine optimal head-down tilt angles for our ground-based ISS flight project. Seven normal healthy, non-smoking volunteers participated in this study (mean age: 36 years). Right and left intraocular pressure (IOP), intracranial pressure (ICP) by non-invasive ultrasound pulse phase lock loop, arm blood pressure, and heart rate were measured during the last minute of each testing condition. Subjects were positioned supine (5 mins), sitting (5 mins), 15-degrees head-down tilt (HDT) (5 mins), and ten minutes of HDT with LBNP (25 mmHg). The order of HDT and HDT+LBNP tests were balanced. Right and left IOP values were averaged and used for statistical analysis (significance accepted at $p<0.05$). The change from supine was calculated for IOP values. IOP significantly decreased from supine to sitting posture by 2.4 ± 0.7 mmHg, and increased by 1.3 ± 2.4 mmHg from supine to the HDT position. LBNP during head-down-tilt significantly lowered IOP to supine levels (difference from supine, 0.1 ± 0.8 mmHg). In addition, added LBNP during HDT significantly decreased ICP pulse amplitudes by 2.8 ± 4.3 microns. Mean blood pressure and heart rate did not change significantly across all conditions. The times for each test were within the limits which we cited in our NASA and UCSD IRB applications; and the tests were valuable in order to optimize tests on actual crew members planned for next year. These data demonstrate that short duration exposures to HDT increase IOP and ICP significantly and further, that LBNP counteracts these elevations of IOP and ICP. Therefore, space flight countermeasures that simulate hydrostatic pressure gradients may mitigate vision problems.
Bibliography Type:	Description: (Last Updated: 10/31/2023)
Abstracts for Journals and Proceedings	Macias BR, Liu JHK, Hargens AR. "Altered Ocular Structure/Function and Mitigation of Peri-optic Nerve Edema during Simulated Microgravity." 2013 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-14, 2013. 2013 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-14, 2013. , Feb-2013
Abstracts for Journals and Proceedings	Hargens A. "Overcoming Cardiovascular Challenges of Interplanetary Flight: May the Force of Pressure be with You." Presented at the 29th American Society for Gravitational and Space Research and 5th International Symposium for Physical Sciences in Space, Orlando, FL, November 3-8, 2013. 29th American Society for Gravitational and Space Research and 5th International Symposium for Physical Sciences in Space, Orlando, FL, November 3-8, 2013. Program and abstracts, p. 101-102. , Nov-2013
Abstracts for Journals and Proceedings	Macias BR, Hargens AR, Liu JHK. "Lower Body Negative Pressure Counters Short-Duration Head-Down-Tilt Induced Elevation in Intraocular Pressure." Presented at the 29th American Society for Gravitational and Space Research and 5th International Symposium for Physical Sciences in Space, Orlando, FL, November 3-8, 2013. 29th American Society for Gravitational and Space Research and 5th International Symposium for Physical Sciences in Space, Orlando, FL, November 3-8, 2013. Program and abstracts, p. 108. , Nov-2013
Abstracts for Journals and Proceedings	Stenger M, Hargens A, Dulchavsky S, Ebert D, Lee S, Sargsyan A, Martin D, Liu J, Macias B, Arbeille P, Platts S. "Fluid Shifts." Presented at 2014 Human Research Program's Investigators' Workshop, Galveston, TX, February 12-13, 2014. 2014 Human Research Program's Investigators' Workshop, Galveston, TX, February 12-13, 2014. http://www.hou.usra.edu/meetings/hrp2014/pdf/3174.pdf , Feb-2014