Fiscal Year:	FY 2018	**Task Last Updated:**	FY 02/05/2018
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:**	01/31/2021
No. of Post Docs:	3	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	1
No. of Master's Candidates:	2	**No. of Bachelor's Degrees:**	4
No. of Bachelor's Candidates:	5	**Monitoring Center:**	NASA JSC
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:	ISS		
Flight Assignment:	NOTE: Extended to 1/31/2021 per NSSC information (Ed., 10/16/18)		
Key Personnel Changes/Previous PI:	February 2018: Removed Hanns Christian Gunga as CoInvestigator; Changed: Brandon Macias (Institution changed from University of California, San Diego to KBRwyle). Added CoInvestigators: Michael Stenger, NASA; Douglas Ebert, KBRwyle; and Lonnie Petersen, University of California, San Diego.		
COI Name (Institution):	Arbeille, Phillipe M.D., Ph.D. (CERCOM) Chang, Douglas M.D., Ph.D. (University of California, San Diego) Liu, John Ph.D. (University of California, San Diego) Macias, Brandon Ph.D. (KBRWyle/NASA Johnson Space Center) Stenger, Micheal Ph.D. (KBR Wyle/NASA Johnson Space Center) Ebert, Douglas Ph.D. (KBRWyle/NASA Johnson Space Center) Petersen, Lonnie M.D., Ph.D. (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 crewmembers 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 a 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 Vision Impairment and Intracranial Pressure (VIIP) 1: 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, 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 as 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 crewmembers 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 a 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 crewmembers 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 head-ward 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.
Task Progress:	We have made significant progress over the past year. All Institutional Review Board (IRB) approvals and Consents were obtained, and experimental protocols were finalized, optimized, and performed on International Space Station (ISS) crews. We have updated our "Fluid Shifts" NASA IRB documents. Moreover, we have updated and renewed our University of California - San Diego (UCSD) IRB protocol. Data collection has been performed on a total of 10 ISS crewmembers preflight, including the One-Year mission crewmembers. Preflight data from all 10 crewmembers have been completed and were analyzed. Inflight data from 7 of the 10 crewmembers have been collected along with post-flight data from 6 crewmembers. We expect that all inflight data collection will be completed and analysis well underway by 2018. Current regulations preclude us from publishing any specific data at this point, but initial analysis demonstrates reliable and reproducible data. Preliminary results indicate individual differences in acute responses to head-ward fluid shifts during transition from upright to supine and head down tilt (HDT) postures such as jugular venous engorgement, choroidal swelling, and increases in noninvasive estimates of ICP. Reversal of these changes with LBNP is also subject dependent. These data are useful in identifying pathophysiological mechanisms behind the VIIP syndrome. Because we are missing jugular vein pressure data on three early ISS crew members, we were approved to study three more ISS crew members, giving us a total of 13 ISS crew members. Our preliminary results to date are: 1) increased jugular vein dimensions and pressure, 2) increased total retinal thickness and choroidal engorgement by optical coherence tomography (OCT), and 3) no evidence of pathologically high ICP. These preliminary results were recently reported by Dr Mike Stenger at the 2018 Human Research Program (HRP) Workshop. At UCSD we have conducted IRB-approved, whole body tilt studies to further investigate short-term changes to choroidal layer of the eye (OCT) along with measurements of IOP and systemic cardiovascular responses to both

	augmented and attenuated gravitational stress (by head-up tilt and head-down tilt, HDT). These tests provided unique insights and helped verify data from tests on actual crewmembers. The data demonstrate that short duration exposures to HDT increase choroidal thickness and IOP. We have involved UCSD graduate and undergraduate student in projects using ground-based, Lower Body Negative Pressure (LBNP) chambers and Leg Negative Pressure chambers related to fluid-shift countermeasure studies. These projects involve various LBNP chambers, LBNP pants, limb and foot blood flow and sensation with various pressures and development of better waist seals for LBNP.
Bibliography Type:	Description: (Last Updated: 10/31/2023)
Articles in Peer-reviewed Journals	Zhang LF, Hargens AR. "Spaceflight-induced intracranial hypertension and visual impairment: Pathophysiology and countermeasures." Physiol Rev. 2018 Jan 1;98(1):59-87. Review. https://doi.org/10.1152/physrev.00017.2016 ; PubMed PMID: 29167331 , Jan-2018
Articles in Peer-reviewed Journals	Challa ST, Hargens AR, Uzosike A, Macias BR. "Muscle microvascular blood flow, oxygenation, pH, and perfusion pressure decrease in simulated acute compartment syndrome." J Bone Joint Surg Am. 2017 Sep 6;99(17):1453-9. https://doi.org/10.2106/JBJS.16.01191 ; PMID: 28872527; PMCID: PMC5685422 , Sep-2017
Articles in Peer-reviewed Journals	Howden M, Siamwala JH, Hargens AR. "Bone microvascular flow differs from skin microvascular flow in response to head-down tilt." J Appl Physiol. 2017 Oct 1;123(4):860-6. Epub 2017 Jun 29. https://doi.org/10.1152/japplphysiol.00881.2016 ; PMID: 28663380. , Oct-2017
Articles in Peer-reviewed Journals	Watkins W, Hargens AR, Seidl S, Clary EM, Macias BR. "Lower-body negative pressure decreases noninvasively measured intracranial pressure and internal jugular vein cross-sectional area during head-down tilt." J Appl Physiol (1985). 2017 Jul 1;123(1):260-6. https://doi.org/10.1152/japplphysiol.00091.2017 ; PubMed PMID: 28495841; PubMed Central PMCID: PMC5538811 , Jul-2017
Articles in Peer-reviewed Journals	Siamwala JH, Macias BR, Lee PC, Hargens AR. "Gender differences in tibial microvascular flow responses to head down tilt and lower body negative pressure." Physiol Rep. 2017 Feb;5(4):e13143. https://doi.org/10.14814/phy2.13143 ; PubMed PMID: 28242824; PubMed Central PMCID: PMC5328775 , Feb-2017
Articles in Peer-reviewed Journals	Macaulay TR, Siamwala JH, Hargens AR, Macias BR. "Thirty days of spaceflight does not alter murine calvariae structure despite increased Sost expression." Bone Rep. 2017 Aug 18;7:57-62. eCollection 2017 Dec. https://doi.org/10.1016/j.bonr.2017.08.004 ; PubMed PMID: 28875158; PubMed Central PMCID: PMC5574818 , Aug-2017
Awards	Petersen L. "American Physiological Society Exercise & Environmental Physiology Section's National Space Biomedical Research Institute Postdoctoral Research Award for paper 'Effects of Gravity and Lower Body Negative Pressure on Intracranial Pressure; Implications for Astronauts and Patients on Earth,' Experimental Biology, Chicago, IL, April 2017." Apr-2017
Awards	Khieu K. "Received a 2017 USRA Frederick A. Tarantino Memorial Scholarship Award. She was selected from among 112 eligible applicants for one of 6 USRA scholarships. June 2017." Jun-2017
Awards	Petersen L. "Human Research Program Workshop Postdoctoral Research Award for abstract and poster 'Mobile Negative Pressure Suit as an Integrated Countermeasure,' 25 Jan 2018." Jan-2018
Awards	Hargens AR. "Kjell Johansen Award and Invited Lecture 'What can Giraffes on Earth Teach Astronauts in Space?' University of Aarhus, Denmark, 2016." Mar-2016
Awards	Hargens AR. "Recognition Award from Southwest American College of Sports Medicine, October 2017." Oct-2017
Awards	Hargens AR. "Received the NASA Distinguished Public Service Medal (NASA's highest form of recognition that is awarded to any non-Government individual or to an individual who was not a Government employee during the period in which the service was performed, whose distinguished service, ability, or vision has personally contributed to NASA's advancement of United States' interests), June 2017." Jun-2017