Fiscal Year:	FY 2015	**Task Last Updated:**	FY 02/17/2015
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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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:	2	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:	1	**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 (University of California, San Diego)		
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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 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 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 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 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 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.
	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, the "Fluid Shifts" study has been approved by the University of California San Diego (UCSD) IRB. Moreover, we have received Japanese Space Agency (JAXA) IRB approval. Erik Hougland, our flight project manager, has been coordinating our bi-weekly FS (Fluid Shifts) team telecons. At the request of the NASA Element office we have merged three flight projects. We have successfully worked to integrate our proposed ground and flight measures among the research team (Hargens et al., Stenger et al., and Dulchavsky et al.). We have now finalized our research testing protocols for ISS crewmembers. We are currently working to update our "Fluid Shifts" 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. We have completed feasibility studies and determined that our proposed tests can be successfully completed within the allotted crew time. We have successfully captured pre-flight upright MRI data from two ISS crewmembers, and one back-up crewmember. The Cerebral and Cochlear Fluid Pressure (CCFP)- Marchbanks device received a CE mark and the NASA unit was shipped 1/30/2014. In addition, two of the CCFP flight units have arrived NASA-JSC on 12/29/2014. These flight units are currently being configured for flight and transported to ISS on SpaceX6. We are in frequent contact with our collaborators, to coordinate their travel and participation in ground-based tests. Our collaborators visited NASA-JSC during our ground feasibility tests to help successfully integrate vascular ultrasound and ocular measurements. A major milestone completed this year was acquisition and modification of an optical coherence tomography (OCT) arm for OCT measurements in the upright, supine, and head-down-tilt position. A

Task Progress:	Wyle team member did an excellent job retrofitting the OCT device for use in our experiment. We have worked with our flight project manager to set up remote ultrasound guidance capabilities. Our study will utilize the Russian Chibis device; we have been in close contact with our Russian collaborators to coordinate ISS Chibis operations and study implementation. We continue to have productive meetings to coordinate our planned physiological measures in the Russian ISS segment during Chibis operations at NASA-JSC this year. We are currently working with the OCT manufacture to finalize automated, quantitative, and objective measures of ocular structures. Testing and training have been initiated to enable “free-floating” of the OCT device for in-flight measurements. Over the past year other important milestones were met. We helped finalize the NASA informed consent briefing for the first one-year astronaut. We provided Professor Arbeille’s in-flight and ground ultrasound procedures to the NASA JSC in preparation for 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 an 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 learn lessons from their experiments and building of our CCFP units to facilitate implementation of the CCFP hardware into our ISS flight project. In addition, we have developed a CCFP data analysis protocol. Our team attended the National Space Biomedical Research Institute (NSBRI) VIIP Working Group Jan. 13th, 2015 during the NASA Human Research Program (HRP) Investigators’ Workshop in Galveston, TX. 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. Twenty-five 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. IOP significantly decreased from supine to sitting posture by 3.2 ± 1.4 mmHg (mean $\pm$ standard deviation), and increased by 0.9 ± 1.3 mmHg from supine to the HDT position. LBNP during HDT significantly lowered IOP to supine levels. In addition, LBNP significantly reduced transcranial ultrasound pulse amplitudes (noninvasive ICP) by 38% as compared to the HDT condition (n=9). 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 were published as the lead article in the Jan. 2015 issue of Aerospace Medicine and Human Performance. 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. These data are now published (Macias BR, Grande-Gutierrez N, JHK Liu, and AR Hargens. Intraocular and Intracranial Pressures during Head-Down-Tilt with Lower Body Negative Pressure. Aerospace Medicine and Human Performance, 86(1):3-7, 2015). More recently, seventeen normal healthy non-smoking volunteers participated in a Cerebral and Cochlear Fluid Pressure (CCFP, a noninvasive ICP surrogate) study. This CCFP study is currently in progress.
Bibliography Type:	Description: (Last Updated: 06/30/2025)
Articles in Peer-reviewed Journals	Macias BR, Liu JHK, Grande-Gutierrez N, Hargens AR. "Intraocular and intracranial pressures during head-down tilt with lower body negative pressure." Aerospace Medicine and Human Performance. 2015 Jan;86(1):3-7. PMID: 25565526 , Jan-2015
Awards	Macias BR. "Aerospace Medical Association Fellows Scholarship, January 2015." Jan-2015
Awards	Macias BR, Grande Gutierrez N, Hargens AR, Liu JHK. "National Space Biomedical Research Institute’s Gravitational Physiology Beginning Investigator Award, April 2014." Apr-2014
Awards	Macias BR, Grande Gutierrez N, Hargens AR, Liu JHK. "International Society for Gravitational Physiology & European Space Agency Young Researcher Award, June 2014." Jun-2014