Fiscal Year:	FY 2019	**Task Last Updated:**	FY 02/09/2019
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:**	01/31/2021
No. of Post Docs:	2	**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**No. of Master' Degrees:**	1
No. of Master's Candidates:	2	**No. of Bachelor's Degrees:**	5
No. of Bachelor's Candidates:	5	**Monitoring Center:**	NASA JSC
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
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Flight Program:	ISS		
Flight Assignment:	NOTE: Extended to 1/31/2021 per NSSC information (Ed., 10/16/18)		
Key Personnel Changes/Previous PI:			
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 Spaceflight Associated Neuro-ocular Syndrome (SANS)" (previously called "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 We do not know the etiological mechanisms and contributing risk factors for ocular structural and functional changes seen in-flight and postflight (SANS1) [previoulsy 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 strong 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 on possible mechanisms of Spaceflight Associated Neuro-ocular Syndrome (SANS); all approvals were received and experimental schedules were finalized, tested, and optimized. We have updated and submitted our project NNX13AJ12G entitled "Fluid Distribution before, during, and after Prolonged Space Flight" NASA Experimental Document and its revision. Likewise, we have updated and renewed our University of California - San Diego (UCSD) Institutional Review Board (IRB) approval.
Data collection is progressing; a total of 13 ISS crewmembers have been enrolled including the One-Year mission crewmembers. Preflight data from 10 crewmembers have been completed and are now being analyzed. Inflight data from 10 of the 13 crewmembers have been collected along with post-flight data from most crewmembers. We expect that all inflight data collection will be completed and analysis well underway by the end of 2019. 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 Spaceflight Associated Neuro-ocular Syndrome (SANS).

Our team continues the bi-weekly Fluid Shifts (FS) team telecons, coordinated and led by our new flight project coordinator, Alonso Fuentes.

Our team attended and presented data in numerous scientific sessions during the Human Research Program (HRP)

	meeting in Galveston in January 2019. Please see Bibliograpy section below for additional publications. At UCSD we have conducted IRB-approved, whole body tilt 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 HDT). These tests were valuable in order to verify data from tests on actual crew members. The data demonstrate that short duration exposures to HDT increase choroidal thickness and IOP.
Bibliography Type:	Description: (Last Updated: 06/30/2025)
Articles in Peer-reviewed Journals	Becker RL, Siamwala JH, Macias BR, Hargens AR. "Tibia bone microvascular flow dynamics as compared to anterior tibial artery flow during body tilt." Aerosp Med Hum Perform. 2018 Apr;89(4):357-64. https://doi.org/10.3357/AMHP.4928.2018 ; PubMed PMID: 29562965 , Apr-2018
Articles in Peer-reviewed Journals	Vico L, Hargens A. "Skeletal changes during and after spaceflight." Nat Rev Rheumatol. 2018 Mar 21;14(4):229-45. Review. https://doi.org/10.1038/nrrheum.2018.37 ; PubMed PMID: 29559713 , Mar-2018
Articles in Peer-reviewed Journals	Siamwala JH, Moossazadeh DG, Macaulay TR, Becker RL, Hargens RH, Hargens AR. "Aging decreases hand volume expansion with water immersion." Front Physiol. 2018 Feb 14;9:72.https://doi.org/10.3389/fphys.2018.00072 ; PubMed PMID: 29491839; PubMed Central PMCID: PMC5817426 , Feb-2018
Articles in Peer-reviewed Journals	Wilson MH, Hargens AR, Imray CH. "Effects of spaceflight on astronaut brain structure." N Engl J Med. 2018 Feb 8;378(6):581. https://doi.org/10.1056/NEJMc1716067 ; PubMed PMID: 29419272 , Feb-2018