

Fiscal Year:	FY 2023	Task Last Updated:	FY 11/15/2022
PI Name:	Macias, Brandon Ph.D.		
Project Title:	Investigating Structure and Function of the Eye		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	(1) HHC: Human Health Countermeasures		
Human Research Program Risks:	(1) 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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Comments:	NOTE: Became civil servant fall 2020; previously KBR/NASA Johnson Space Center. Prior to that until 2016, was at the University of California, San Diego.		
Project Type:	FLIGHT	Solicitation / Funding Source:	2017-2018 HERO 80JSC017N0001-BPBA Topics in Biological, Physiological, and Behavioral Adaptations to Spaceflight. Appendix C
Start Date:	01/30/2019	End Date:	09/30/2033
No. of Post Docs:	0	No. of PhD Degrees:	0
No. of PhD Candidates:	0	No. of Master' Degrees:	0
No. of Master's Candidates:	0	No. of Bachelor's Degrees:	0
No. of Bachelor's Candidates:	0	Monitoring Center:	NASA JSC
Contact Monitor:	Stenger, Michael	Contact Phone:	281-483-1311
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2033 per HHC element/JSC (Ed., 12/16/21) NOTE: End date changed to 1/24/2026 per HHC element/JSC (Ed., 4/8/21) NOTE: End date changed to 9/30/2025 per PI (Ed., 12/21/19)		
Key Personnel Changes/Previous PI:	December 2022 report: Dr. Alan Hargens retired and has been removed from the project. In addition, Drs. Scott Greenwald, Laura Pardon, Jessica Jasien, and Karina Marshall Goebel obtained new employment and left the project and have been removed.		

COI Name (Institution):	Brunstetter, Tyson O.D., Ph.D. (NASA Johnson Space Center) Huang, Alex M.D., Ph.D. (Doheny Eye Institute) Karanjia, Rustum M.D., Ph.D. (Doheny Eye Institute) Laurie, Steven Ph.D. (KBR/NASA Johnson Space Center) Martin, Bryn Ph.D. (University of Idaho, Moscow) Sadda, Srinivas M.D. (Doheny Eye Institute) Smith, Scott Ph.D. (NASA Johnson Space Center) Zwart, Sara Ph.D. (University of Texas, Galveston) Lee, Stuart Ph.D. (KBR/NASA Johnson Space Center) Gibson, Charles O.D. (Coastal Eye Associates) Kramer, Larry M.D. (University of Texas Health Science Center, Houston) Lytle, Jason Ph.D. (KBR/NASA Johnson Space Center) Young, Millennia Ph.D. (NASA Johnson Space Center)
Grant/Contract No.:	Internal Project
Performance Goal No.:	
Performance Goal Text:	
Task Description:	This proposal will identify if ocular structure and function alterations occur at a greater frequency and magnitude during one-year missions compared to six-month and two-month expeditions and whether the recovery profile is dependent upon mission duration. In addition, this project will determine if changes in vascular structure and function are greater after one-year missions and if they contribute to alterations in ocular structure and function. The identification of structural and functional changes related to the development, progression, and recovery of Spaceflight Associated Neuro-ocular Syndrome (SANS) will provide NASA the information necessary to inform the risk posture for future interplanetary expeditions with duration of up to three years and to identify possible countermeasures. SPECIFIC AIMS: Conducting SANS research on two-month, six-month, and one-year crewmembers will enable us to objectively generate data to help NASA determine if and how SANS findings change with mission duration. Data from these missions will enable the development of a non-linear trend model that can be extrapolated to make predictions for spaceflights that are up to three years in duration. Therefore, the results of the "Investigating Structure and Function of the Eye" (iSAFE) study will help NASA to define the risk posture for future interplanetary expeditions and to identify possible countermeasures. Specific Aim 1: To determine if ocular structural changes develop to a greater degree (frequency or magnitude) during long-duration one-year spaceflight missions compared to findings during shorter length missions, and if recovery is prolonged after longer missions. Specific Aim 2: To determine if ocular vascular structure is altered to a greater degree during long-duration one-year spaceflight missions, and if recovery is more prolonged. Specific Aim 3: To determine if ocular function is altered to a greater degree during long duration one-year spaceflight missions, and the recovery profile. Specific Aim 4: To determine if measures of vascular structure and function are altered to a greater degree during long-duration one-year spaceflight missions, and if these vascular adaptations correlate with alterations in ocular structure and function. RELEVANCE AND MAP TO THE NASA HUMAN RESEARCH ROADMAP: This multi-project proposal is in response to NASA research announcement Human Exploration Research Opportunities (HERO), 80JSC017N0001-BPBA, Appendix C, Topic 1: Analyses of the Temporal Nature of Human Adaptation to Long-Duration Low-Earth Orbit Mission Virtual NASA Specialized Center of Research (VNSCOR). This proposal addresses multiple Human Research Program (HRP) Integrated Research Plan Gaps, including: • SANS101: Determine the relationship between fluid shifts (intravascular, interstitial, CSF) and ocular manifestations in astronauts during spaceflight. • SANS102: Determine the relationship between the fluid-shifts induced ocular changes and fluid shifts in the CNS, including whether elevated intracranial pressure or brain edema play a role.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The Investigating Structure and Function of the Eye (iSAFE) research study will advance NASA's understanding of Spaceflight Associated Neuro-ocular Syndrome (SANS), an important human health and performance risk. This goal will be accomplished by quantifying how ocular alterations develop, progress, and recover as a function of spaceflight duration and by identifying underlying mechanisms. Results from this study are anticipated to lead to a temporal model of SANS progression during long-term missions and to inform the development of countermeasures. Given the unique environment of the International Space Station, commonly used ophthalmic instruments are being implemented in novel operational environments (e.g., electroretinography (ERG), optical coherence tomography (OCT) angiography, pneumotonometry). This work may lead to the adoption of these new hardware, software, or protocol elements in clinical practice, benefiting patients on Earth. SANS shares characteristics with several terrestrial ophthalmic diseases, such as papilledema, and iSAFE study results could provide new insights into mechanisms underlying these conditions.
Task Progress:	• The iSAFE Principal Investigator (PI) team has continued to work with NASA Research Operations and Integration (ROI) Element to integrate this project into the Complement of Integrated Protocols for Human Research (CIPHER) complement of studies. This effort included providing inputs to the Scientific Research Document (SRD); the iSAFE SRD is now baselined for all mission durations: Short, Standard, and Extended. • The Test Readiness Review (TRR) was approved in May of 2022. • The iSAFE PI team supported the TRR for the Payloads Development Laboratory (PDL) in NASA Johnson Space Center Building 9, which is now approved. This TRR permits the use of the PDL for training crewmember operators to perform ERGs and pneumatonometry. • Supported the informed consent briefings (ICB) for 5 potential CIPHER subjects (3/1/2022, 4/6/2022, 4/28/2022, 8/4/2022, and 8/18/2022) and developed an iSAFE overview video that is being integrated into the CIPHER ICB presentation. • Two crewmembers (Crew-6 and 69S) signed informed consent documents and have agreed to participate in the iSAFE study. • Supported a hardware checkout of the ERG units designated for flight, flight backup, ground use by ROI, and for baseline data collection. • ERG and pneumatonometry flight/units hardware passed Science Verification Testing (SVT) and are now on the International Space Station. • Two iSAFE operators completed Telescience Center orientation in preparation for remote guidance activities, and remote guidance scripts were drafted for ERG and pneumatonometry. • Completed the Payloads Training Dry Run (PTDR) that was overseen by NASA Marshall Spaceflight Center, certifying proficiency of Cardiovascular and

	Vision Laboratory (CVL) personnel (Co-Investigator Greenwald) to train crewmember operators for ERG and pneumatonometry. Two additional CVL team members have been certified to lead the crew training classes. • During FY22, we supported 8 crewmember operator and subject “Training” sessions for ERG, ultrasound, and pneumatonometry. • Final preparations for baseline data collection have been completed in the Cardiovascular and Vision Laboratory in preparation for preflight BDC sessions. • The team verified functionality of the inflight OCT angiography software. • The Dynamic Vessel Analyzer hardware was received by the CVL and CVL personnel were trained by the vendor. • The iSAFE study was presented at the 2022 Human Research Program Investigators’ Workshop.
Bibliography Type:	Description: (Last Updated: 04/04/2024)
Abstracts for Journals and Proceedings	SH Greenwald, LP Pardon, JV Jasien, T Brunstetter, ND Mercaldo, A Hargens, A Huang, R Karanjia, SS Laurie, SMC Lee, K Marshall-Goebel, BA Martin, LA Kramer, S Sadda, SM Smith, SR Zwart, BR Macias. "Investigating structure and function of the eye (iSAFE)." Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-10, 2022. Virtual Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-10, 2022 , Feb-2022
Articles in Peer-reviewed Journals	Pardon LP, Greenwald SH, Ferguson CR, Patel NB, Young M, Laurie SS, Macias BR. "Identification of factors associated with the development of optic disc edema during spaceflight." JAMA Ophthalmol. 2022 Oct 27. https://doi.org/10.1001/jamaophthalmol.2022.4396 ; PubMed PMID: 36301519 ; PubMed Central PMCID: PMC9614681 , Oct-2022