Fiscal Year:	FY 2018	**Task Last Updated:**	FY 12/12/2018
PI Name:	Parsons-Wingerter, Patricia Ph.D.		
Project Title:	Mapping by VESGEN of Blood Vessels in the Human Retina Undergoing Bed Rest for Improved Understanding of Visual Impairments and Increased Intracranial Pressure		
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) **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:	Moffet Field	**State:**	CA
Zip Code:	94035-1000	**Congressional District:**	18
Comments:	NOTE: Formerly at NASA Glenn Research Center until summer 2014		
Project Type:	Flight,Ground	**Solicitation / Funding Source:**	2012 Crew Health NNJ12ZSA002N
Start Date:	10/01/2013	**End Date:**	06/30/2018
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	1
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	3	**Monitoring Center:**	NASA JSC
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Flight Program:	Pre/Post Flight		
Flight Assignment:	NOTE: End date changed to 6/30/2018 per discussion with PI (Ed., 3/26/18) NOTE: End date changed to 10/01/2017 per A. Allcorn/JSC and PI (Ed., 7/31/17) NOTE: End date changed to 4/08/2017 per PI (Ed., 1/30/17) NOTE: End date changed to 1/08/2017 (originally 9/30/2014 and subsequently 9/22/2015 and 10/1/2016 and 4/8/2017, which is actually supposed to be due date for final reporting), per PI (Ed., 5/17/16) NOTE: End date changed to 4/08/2017 (originally 9/30/2014 and subsequently 9/22/2015 and 10/1/2016), per PI (Ed., 10/20/15) NOTE: End date changed to 10/01/2016 (originally 9/30/2014 and subsequently 9/22/2015), per PI (Ed., 10/20/15) NOTE: End date changed to 9/22/2015 (originally 9/30/2014), per R. Brady/HRP (Ed., 7/17/14) NOTE: Gap change per IRP Rev E (Ed., 3/19/14)		
Key Personnel Changes/Previous PI:	August 2017 report: Co-Investigator Dr. Rob Ploutz-Snyder is no longer with the team.		
COI Name (Institution):	Vizzeri, Gianmarco M.D. (University of Texas Medical Branch at Galveston) Young, Millennia H. Ph.D. (NASA Johnson Space Center) Zanello, Susana B. Ph.D. (KBRWyle)		
Grant/Contract No.:	Internal Project		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The hypothesis proposed for our investigation of vascular contributions to Spaceflight Associated Neuro-ocular Syndrome (SANS) is that blood vessels within the retina, particularly the microvasculature, necessarily remodel to accommodate the cephalad fluid shifts and associated ocular changes incurred in microgravity and terrestrial head-down tilt (HDT) bed rest. Arterial and venous patterns were therefore analyzed in Heidelberg Spectralis 30° infrared (IR) images using NASA's VESsel GENeration Analysis (VESGEN) software. Results for the trends in pre to post status of vascular patterning within the retinas of Crew Members and HDT subjects are opposite. By two confirming measures of vascular branching complexity, the fractal dimension and length density of small vessels, the space-filling capacity of arterial and venous trees decreased for a majority of Crew Members following six-month missions to the International Space Station (ISS). As predicted, the length density of larger vessels remained relatively constant. The assignment of vascular branching generations into large and small vessels by VESGEN further confirmed that vascular adaptations to microgravity occurred primarily at the level of the smaller arteries and veins. In contrast, vascular densities increased by these same parameters for a majority of subjects following 70 days of HDT. Differing trends of arterial and venous response to cephalad fluid shifts after HDT and the ISS may have resulted from a long-duration adaptation phenomenon (6 months compared to 70 days), or from the presence of a gravity vector in HDT compared to microgravity on the ISS. Results further suggest the importance of individual variability (susceptibility) of vascular adaptations in Crew Members.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Results on vascular decreases in the retinas of ISS Crew Members support further investigation of vascular patterning as a potential biomarker of early SANS susceptibility. The one clinically diagnosed case of SANS by optic disk edema displayed the greatest decrease in vascular density. Smaller vascular decreases in most of the other Crew Member retinas were identified that could precede subsequent secondary vascular effects such as cotton wool spots, choroidal folds, and edemas of the optic disc and retinal/choroidal layers. The role of VESGEN vascular mapping and quantification as a useful research and technology (R&T) discovery tool was therefore validated. Fractal-based vascular patterning could offer a new, insightful biomarker of progressive, vascular-dependent pathologies such as SANS that is sensitive to the detection of subtle, early-stage remodeling, especially of smaller vessels. Results on opposite trends in retinal vascular remodeling in Crew Members and Bed Rest Subjects may contribute to better understanding and countermeasures development for SANS. The VESGEN vascular analysis is relevant to the study of other Human Research Program (HRP) risks such as cardiovascular response to radiation. The vascular analysis is being applied to another HRP study on rodent hindlimb unloading, an experimental model of cephalad fluid shifts resulting from microgravity. Increased knowledge and innovations from this investigation will benefit similar studies for terrestrial diseases such as diabetic retinopathy (DR), the major blinding retinal disease of working-aged adults, and other vascular-dependent diseases such as tumors.
Task Progress:	Two Specific Aims were proposed to support the microvascular hypothesis that addresses NASA solicitation requirements for an 'accelerated, new scientific approach to produce novel scientific knowledge and deliver initial proof-of-concept mappings.' The proposal further addressed HRP Risk 'Microgravity-induced Visual Alterations and Intracranial Pressure' by investigation of the HRP Gap 'VIIP1 What is the etiology of visual acuity and ocular structural and functional changes in-flight and post-flight?' ('VIIP' is now designated as Spaceflight Associated Neuro-ocular Syndrome (SANS)). The study further addressed the first objective of the NASA solicitation, quantification of crew health and performance risks. Below are the aims proposed for the study. The second aim was accepted by NASA, resulting in expansion of the original study design. Aim 1—Alterations in vascular patterning of the human retina responding to fluid shifts incurred by long-duration head-down tilt bed rest will be mapped and quantified. Aim 2—Alterations in the retinal vascular patterning of astronauts before and after spaceflight will be mapped and quantified, should NASA decide to provide additional resources to support this Aim. Work proposed for the study is now complete, including insightful biostatistical and ophthalmic correlations. Arterial and venous branching were analyzed by VESGEN in the retinas of eight Crew Members before and after six-month flight to the ISS, and of six subjects before and after 70-day 6° HDT Bed Rest. Trends in pre to post status within the retinas of Crew Members and HDT subjects measured by the VESGEN analysis are opposite. By two confirming measures of vascular branching complexity, the fractal dimension (Df) and length density of small vessels (Lv=5), the space-filling capacity of arterial and venous trees, decreased for a majority of Crew Members. In contrast, vascular densities increased by these same parameters for a majority of HDT subjects. As predicted, the length density of larger vessels (Lv1-4) remained relatively constant. The assignment of vascular branching generations into large and small vessels by VESGEN further confirmed that vascular adaptations to microgravity and HDT occurred primarily at the level of the smaller arteries and veins. One of 16 Crew Member retinas was found by NASA to display early SANS using a clinical optic disc edema (ODE) measure. A subclinical vascular pathology index (SVPI) was therefore calculated to compare the magnitude of vascular change measured by VESGEN in the SANS retina with the 15 other retinas assessed as clinically normal by clinical ocular measures that include ODE and total retinal and choroidal thicknesses. By the SVPI, twelve retinas displayed vascular decreases from 6% to 76%, compared to the SANS retina. Relationships of vascular change to other parameters such as globe flattening and total retinal and choroidal thickness were investigated as mixed effects. For example, vascular decreases were associated with increased total retinal and retinal nerve fiber layer thicknesses. Results of this first proof-of-concept VESGEN study support further investigation of vascular patterning as a potential biomarker of early vascular changes related to SANS etiology and susceptibility.
Bibliography Type:	Description: (Last Updated: 11/30/2021)
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