Fiscal Year:	FY 2015	**Task Last Updated:**	FY 10/19/2015
PI Name:	Buckey, Jay C. M.D.		
Project Title:	Role of the Cranial Venous Circulation in Microgravity-Associated Visual Changes		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Cardiovascular Alterations Team		
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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Zip Code:	03756-0001	**Congressional District:**	2
Comments:	Address updated 9/2008		
Project Type:	GROUND	**Solicitation / Funding Source:**	2012 Crew Health NNJ12ZSA002N
Start Date:	08/01/2013	**End Date:**	05/31/2017
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	4	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 5/31/2017 per NSBRI (Ed., 3/1/16) NOTE: Title change to "Role of the Cranial Venous Circulation in Microgravity-Associated Visual Changes" (original proposal title was "Ocular Venous Contributions to Spaceflight Visual Impairment")--Ed., 2/6/14		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Weaver, John (Dartmouth College) Knaus, Darin (Creare, Inc.) Deserranno, Dimitri (Creare, Inc.) Belden, Clifford (Dartmouth College) Kattamis, Nicholas (Creare, Inc.) Phillips, Scott (Creare, Inc.) Davis, Brynmor (Creare, Inc.) Zegans, Michael (Dartmouth College)		
Grant/Contract No.:	NCC 9-58-CA03401		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	We are developing a numerical model of the cerebral venous circulation and how it responds to both fluid shifts and changes in gravitational forces. We are validating this model using magnetic resonance imaging (MRI) to measure the responses of the cranial vascular and cerebrospinal fluid systems to fluid shifts in both the supine and prone positions. A companion set of ocular measures are also being taken using these same interventions outside of the MRI magnet. The likely anatomic differences that could alter the responses to a fluid shift will be identified. This model and supporting data will provide a means to develop hypotheses about how microgravity produces visual changes over time and may allow predictions about which subjects may be at risk for the visual deficits associated with microgravity. Aim #1: Develop a numerical model to estimate changes in intracranial venous flow, volume, compliance, and pressure in response to a fluid shift and changes in hydrostatic gradients. Include tissue compressive forces in the model. During this reporting period, we advanced and expanded the numerical model. Specifically, we introduced collapsible vessels, which allows behavior such as body-orientation-dependent flow shunting in the jugular veins (i.e., jugular vein collapse in the upright position) to be modeled. We also used transmural pressure across the boundaries of model components (e.g., vessels and fluid cavities) to capture the effects of tissue weights and the resulting gravity dependent impact on the circulatory and cerebrospinal fluid (CSF) systems. Finally, we targeted integration of the circulatory and CSF sub-models, providing mass and pressure communications between the two sub-models. Aim #2: Determine the cranial venous changes produced by fluid shifts and altered hydrostatic gradients. Use interventions that can produce fluid shifts (lower body negative pressure and lower body positive pressure) and alter hydrostatic gradients (supine and prone postures). These experiments are designed to provide data for validating and verifying the model developed as a part of Aim #1. During this reporting period, we developed the protocol to collect the data for this experiment. We conducted an experiment with 10 subjects and determined that ocular measures plateau after an average of 12 minutes upon entering the posture. This will be used to ensure consistent data for all subjects. We designed and built a MRI-compatible chamber to provide lower body positive and negative pressures, aimed at creating cephalad fluid shift similar to that experienced in space flight. The apparatus will be used in the MRI studies. We plan to finalize the apparatus and employ it in the test campaign during the next reporting period. The imaging protocol needed to collect our parameters for the model was established through an iterative process to establish the optimum trade-off between scan accuracy, data needed for the model, and subject acceptability. The analysis techniques for the MRI data were also established. We developed tools to aid hypothesis development of the etiology behind visual changes in long duration space flight. We developed graphical descriptions of the potential mechanisms for the microgravity-induced ocular and visual changes. We have acquired several devices to measure key parameters needed in the studies, such as an anterior segment module, episcleral venous pressure device, and a BIOPAC continuous, noninvasive blood pressure system. The data collected from these devices will be use to provide additional information for the model. Aim #3: Identify individuals with common intracranial venous variants, and study them using the protocol outlined in Aim #2. Aim 3 is an objective for our third year. The data collection methods have been established in this reporting period through our Aim 2 objectives. In our initial cohort of pilot subjects, we have identified subjects with anatomical variants--a primary interest of this experiment. Over the next reporting year, we will collect data from our experiments for Aims #2 and #3. These data will feed directly into the model. We provide tools to develop hypotheses about the etiology of microgravity induced visual changes. Our models will help predict which subjects may be at risk for the visual deficits associated with microgravity, and could help develop potential countermeasures in the future.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The model and experimental results will give a better understanding of cranial venous insufficiency. Cranial venous insufficiency results when venous outflow from the head is reduced or obstructed. This can be due to an increase in venous resistance from anatomical variations. The increased resistance to flow can produce headaches or vision changes. Venous insufficiency has been proposed as a possible etiology for symptoms in acute mountain sickness, obstructive sleep apnea, jugular outflow obstruction syndrome, multiple sclerosis, and idiopathic intracranial hypertension (IIH). Bilateral transverse sinus stenosis is found in 90% of IIH sufferers, and internal jugular vein stenosis occurs in 80% of IIH patients. Although numerical models of the circulatory system, cerebral venous system, and cerebral spinal fluid system exist (as do fluid models of the aqueous humor regulatory system and structural finite element models of the eye) the model developed on this project is the first comprehensive model that links the effects of all systems together. It could be used in the future to predict how surgical interventions, such as sagittal stenting, can improve an individual's symptoms.
Task Progress:	Aim #1: Develop a numerical model to estimate changes in intracranial venous flow, volume, compliance, and pressure in response to a fluid shift and changes in hydrostatic gradients. Include tissue compressive forces in the model. During this reporting period, we advanced and expanded the numerical model. We introduced collapsible vessels, which allow behavior such as body-orientation-dependent flow shunting in the jugular veins (i.e., jugular vein collapse in the upright position) to be modeled. We also used transmural pressure across the boundaries of model components (e.g., vessels and fluid cavities) to capture the effects of tissue weights and the resulting gravity dependent impact on the circulatory and CSF systems. Finally, we targeted integration of the circulatory and CSF sub-models, providing mass and pressure communications between the two sub-models. Aim #2: Determine the cranial venous changes produced by fluid shifts and altered hydrostatic gradients. Use interventions that can produce fluid shifts (lower body negative pressure and lower body positive pressure) and alter hydrostatic gradients (supine and prone postures). These experiments are designed to provide data for validating and verifying the model developed as a part of Aim #1. The main efforts this reporting period were to design and test the MRI-compatible LBNP/LBPP (lower body negative pressure/lower body positive pressure) chamber, test the MRI imaging protocols, and develop the MRI data analysis tools needed for the studies. We also conducted a posture experiment with 10 subjects and determined that ocular measures plateau after an average of 12 minutes upon entering a new posture (e.g., seating, supine, prone). This will be used to ensure consistent data for all subjects in the MRI studies. The MRI-compatible LBNP/LBPP chamber will be employed it in the test campaign during the next reporting period. The optimal parameters for collecting and analyzing MRI data were established, which involved examine the trade off between scan accuracy, data needed for the model, and subject acceptability. We developed tools to aid hypothesis development of the etiology behind visual changes in long duration space flight. We developed graphical descriptions of the potential mechanisms for the microgravity-induced ocular and visual changes. We have acquired several devices to measure key parameters, such as an anterior segment module, episcleral venous pressure device, and a BIOPAC continuous, noninvasive blood pressure system. The data collected from these devices will be use to provide additional

	information for the model. Aim #3: Identify individuals with common intracranial venous variants, and study them using the protocol outlined in Aim #2. Aim 3 is an objective for our third year. The data collection methods have been established in this reporting period through our Aim 2 objectives. In our initial cohort of pilot subjects, we have identified subjects with anatomical variants, the primary interest of this aim.
Bibliography Type:	Description: (Last Updated: 03/18/2024)
Abstracts for Journals and Proceedings	Anderson A, Fellows A, Buckey J. "Feasibility of dpoae mapping as an in-flight measure of intracranial pressure in space." 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. , Jan-2015
Abstracts for Journals and Proceedings	Anderson A, Fellows A, Babu G, Swan J, Phillips S, Kattamis N, Knaus D, Zegans M, Buckey J. "Ocular and cerebrovascular changes in microgravity." 86th Scientific Meeting of the Aerospace Medical Association, Lake Buena Vista, Florida, May 10-14, 2015. 86th Scientific Meeting of the Aerospace Medical Association, Lake Buena Vista, Florida, May 10-14, 2015. , May-2015
Abstracts for Journals and Proceedings	Swan JG, Phillips SD, Kattamis N, Knaus DA, Zegans ME, Fellows AM, Buckey JC. "Effect of posture and microgravity on the eye and cranial vascular system." 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. , Jan-2015
Abstracts for Journals and Proceedings	Phillips SD, Chepko A, Kattamis NT, Knaus DA, Swan JG, Zegans M, Buckey JC. "Modeling gravity dependence in the cranial venous circulatory system." 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. , Jan-2015
Abstracts for Journals and Proceedings	Phillips S, Kattamis N, Chepko AB, Knaus DA, Swan JG, Zegans ME, Buckey JC. "Modeling the ocular and cerebrovascular changes in microgravity." 86th Scientific Meeting of the Aerospace Medical Association, Lake Buena Vista, Florida, May 10-14, 2015. 86th Scientific Meeting of the Aerospace Medical Association, Lake Buena Vista, Florida, May 10-14, 2015. , May-2015
Awards	Anderson A. "NSBRI First Award Fellowship, October 2015." Oct-2015