Fiscal Year:	FY 2014	**Task Last Updated:**	FY 09/08/2014
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:**	07/31/2016
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:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	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:	This report covers the 10-month period from project initiation in October 2013 to the end of June 2014. --Original project aims/objectives: 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. 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. Aim #3: Identify individuals with common intracranial venous variants, and study them using the protocol outlined in Aim #2. --Key findings/developments: Work in the past year has focused on constructing the model (Aim #1), and developing the protocols, hardware and experimental designs needed for Aim #2. For Aim #1, the key developments since October have been to (a) evaluate and select the best software for the modeling needed in the project, and (b) use the software to design a numerical model for the circulatory system that includes gravitational forces and the effects of gravity on tissue weight/tissue compliance. We are using the Simscape modeling environment. The primary strengths of this environment are the ability to leverage (a) MATLAB's robust set of solvers for systems of differential equations, (b) Simscape's automatic construction of the overall set of differential equations based on the variable relationships defined in each component block, and (c) the existing fluid component models available in the Simscape and SimHydraulics libraries. A lumped parameter circulatory system has been developed. The system includes a gravity dependent pressure drop element to capture the effects of changing orientation within a gravitational field on flow systems with multiple flow loops and branch points (such as the circulatory system). The model also includes flexible tubes that change size according to external pressure differences (i.e. modeling the effects of collapsing veins such as the internal jugular veins). Work on the overall modeling design for the circulatory system is also applicable to the CSF circulation model. Data from the studies in Aim #2 and existing data from NASA will be used to test the model. For Aim #2, several elements are under development to permit the MRI imaging studies planned for year 2. An MRI compatible LBNP device has been constructed, and is beginning initial trials within the MRI magnet. This device will be important for producing fluid shifts for the MRI imaging studies. MRI imaging protocols are being tested to optimize the tradeoff between measurement accuracy and test time. The current protocol will assess vascular anatomy, as well as venous, arterial, and CSF flows in and out of the head. Sequences are also included to provide information on eye flow, and sequences to measure regional brain tissue compliance will be assessed. The MRI studies will be complemented by ocular measurements made in different body positions, with and without fluid shifts, outside of the magnet. These posture studies have been advanced significantly by the acquisition of a Heidelberg Spectralis Optical Coherence Tomography device in the past year. This new device will greatly enhance the data collection for the postural studies beyond what had been proposed initially. A similar device is being used on the ISS to evaluate astronauts. An additional advance has been progress in obtaining existing data from NASA that can be used to help build the model. To date, we have received data from a bed rest study, and just recently received approval to receive deidentified OCT, MRI, and other astronaut data. ---Impact of key findings on hypotheses, technology requirements, objectives, and specific aims of the original proposal. The model development is a core objective of the project. The development of a model including gravitational and tissue compressive forces is novel, and will be essential for predicting microgravity effects. Work over the past 10 months has developed the major scaffolding for the circulatory system model. The primary subsystems are represented and the model includes both body orientation and gravitational effects. Further refinement of model parameters is needed to fine-tune the system to represent the circulatory flow system more accurately. From there, detail and complexity will be added to the model as needed to capture the effects of blood flow and pressures on the eye fluid system. To complete this work we developed custom units within Simscape to incorporate gravity dependence and custom compliance inputs. These custom units allow us to construct flow loops with branch points sensitive to body orientation. We plan to extend this work during the next reporting period by completing development of the shared pressure boundary unit and fluid exchange units to create model coupling between the CSF and circulatory system, the CSF and eye, and the circulatory system and aqueous humor regulatory system. The LBNP device and MRI protocols will be essential for completing the objectives planned for year 2 of the project. --Proposed research plan for the coming year. In the remainder of the existing year and in the coming year, we will increase the complexity of the model and extend it to the CSF circulation. In the next year we will begin the MRI studies that include both changes in gravitational orientation (supine/prone) and fluid shifts (LBNP/LBPP).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	While the numerical model we are developing in Aim #1 targets visual changes associated with microgravity, the model is also a tool for studying other instances where changes in intraocular, intracranial, or venous pressures affect vision. For example, the microgravity changes are similar in some aspects to changes seen on Earth in conditions such as idiopathic intracranial hypertension (IIH), psuedotumor, or prolonged prone positioning (i.e. during surgery). Our model has the potential to improve the understanding of how these conditions affect vision. The model is also applicable for studying intraocular pressure changes in glaucoma, and could be a useful tool for understanding this common disease. In Aims #2 and #3, we are developing novel MRI sequences for measuring cranial venous flow that may be useful for diagnosing cranial venous insufficiency. Cranial venous insufficiency has been proposed as a possible etiology (or associated factor) for symptoms seen in acute mountain sickness, obstructive sleep apnea, jugular outflow obstruction syndrome, multiple sclerosis, and IIH. The model and the MRI imaging sequences may be useful in studying these conditions.
Task Progress:	1. Evaluated software for performing the modeling needed in the project. Selected the Simscape modeling environment. 2. Developed a lumped parameter cardiovascular system model with custom modules for gravitational effects and tissue compliance. 3. Designed and built MRI-compatible LBNP/LBPP device 4. Tested MRI imaging protocols for angiography, CSF flow/volume, venous/arterial flow, and pressure. 5. Acquired a Heidelberg Spectralis Ocular Coherence Tomography device to enhance the data collection during the postural studies (a similar device is currently on the ISS). 6. Received NASA IRB approval to obtain astronaut data from long-duration missions.
Bibliography Type:	Description: (Last Updated: 03/18/2024)

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