Fiscal Year:	FY 2016	**Task Last Updated:**	FY 01/23/2017
PI Name:	Ethier, Christopher Ph.D.		
Project Title:	Microgravity-driven Optic Nerve/Sheath Remodeling Simulator (MONSTR Sim)		
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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Zip Code:	30332-0363	**Congressional District:**	5
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2012 Crew Health NNJ12ZSA002N
Start Date:	10/01/2013	**End Date:**	09/30/2016
No. of Post Docs:	2	**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:**	NASA GRC
Contact Monitor:	Griffin, DeVon	**Contact Phone:**	216-433-8109
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	none		
COI Name (Institution):	Gleason, Rudolph (Georgia Institute of Technology) Myers, Jerry (NASA Glenn Research Center) Samuels, Brian (Indiana University) Nelson, Emily (NASA Glenn Research Center)		
Grant/Contract No.:	NNX13AP91G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Visual Impairment/Intracranial Pressure (VIIP) syndrome occurs in a significant fraction of astronauts undergoing long-duration space flight. VIIP is characterized by a spectrum of ophthalmic changes, including optic nerve sheath distention and kinking, optic disc edema, choroidal folds, and flattening of the posterior eye globe. Most significantly, astronauts with VIIP can suffer permanent loss of visual acuity. The cause(s) of VIIP are not well understood, but the syndrome has ophthalmic features similar to those seen in patients with idiopathic intracranial hypertension, strongly suggesting that elevations in intracranial pressure and/or reductions in intraocular pressure play an important role in VIIP. Notably, observations in VIIP are consistent with a major alteration in the pressure difference across the lamina cribrosa. Given the probable role of these altered pressures in VIIP, any VIIP computational model should include biomechanical models of the relevant ocular tissues. Importantly, VIIP develops slowly (over weeks); further, the anatomic changes observed in ocular connective tissues (e.g., the optic nerve sheath) appear to be permanent in some cases. This strongly suggests that tissue remodeling is an important aspect of VIIP, and thus any attempt to understand VIIP must consider remodeling effects. In view of the above, we hypothesize that cephalad fluid shifts in microgravity affect intracranial pressure (ICP) and intraocular pressure (IOP), leading to altered biomechanical loads on the tissues of the posterior globe and optic sheath. This altered biomechanical environment in turn causes connective tissue remodeling, an important contributing factor to vision changes in the VIIP syndrome. We will develop modeling tools to allow the above hypothesis to be tested, and which will provide a test bed for identification of which clinically observable attributes play key roles in the development of the VIIP syndrome. These tools will be developed through 4 specific aims: SA1: Develop validated tools for computing IOP and ICP in microgravity. These tools will be based on modeling of fluid shifts between the eye and various compartments in the cardiovascular, cerebrospinal and lymphatic systems. SA2: Develop validated finite element-based tools for computing the biomechanical environment and subsequent connective tissue remodeling in the optic nerve head, optic nerve sheath, and posterior globe. These tools will be complemented by a model of the eye's optical performance. SA3: Integrate the models from SA1 and SA2 to produce a unified, open, and extensible software package that can predict ocular biomechanics and ocular connective tissue remodeling under microgravity conditions. SA4: Use the integrated model of SA3 to study clinically observable attributes and determine the role they may play in the development of VIIP. This proposal directly addresses an explicit requirement of NASA Research Announcement NNJ12ZSA002N, namely to "… develop and deliver numerical model(s) of the visual system quantifying the biomechanical pathways by which gravitational unloading could affect the distribution of hydrodynamic pressures within the CVS and CNS, and their impact on the structure of the eye." Our models will provide a powerful platform for better understanding VIIP and, eventually, for suggesting VIIP screening and mitigation strategies, thus contributing to astronaut health. Our team has highly complementary skills that together address all relevant aspects of this complex, interdisciplinary problem. In addition to Ethier (Principal Investigator at Georgia Tech; expertise in modeling optic nerve head and ocular biomechanics), co-investigators include Myers, Best, and Nelson (NASA Glenn; expertise in cephalad fluid shift models and space physiology); Samuels (Indiana; expertise in clinical ophthalmology and neuroscience); and Gleason (Georgia Tech; expertise in soft tissue biomechanics and tissue remodeling).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This research helps understand the pathology underlying idiopathic intracranial hypertension (IIH).
Task Progress:	This grant investigates potential factors in Visual Impairment/Intracranial Pressure (VIIP) syndrome, with the eventual goal of identifying mitigation strategies. Our aim was to develop multiple computational models to simulate fluid shifts in the body. These computational models inform a finite element model (FEM) that simulates the biomechanical environment of the posterior eye and optic nerve sheath (pia mater and dura mater), since biomechanical factors are hypothesized to play an important role in VIIP. Accomplishments: Over the course of this proposal we have made accomplishments on all of our computational and experimental approaches. Specifically, we have developed 3 lumped parameter models: one each of the cardiovascular system, central nervous system, and eye. We have also further developed our FEM of the posterior eye and optic nerve head (ONH). We have worked towards integrating these lumped parameter models with our ocular biomechanics finite element code to understand how different environment conditions impact the deformation at the posterior eye. We have also made direct measurements of the tissue mechanical properties of the optic nerve sheath and collagen structure. Lastly, we have taken clinical imaging of patients with elevated intracranial pressure.
Bibliography Type:	Description: (Last Updated: 11/26/2021)
Articles in Peer-reviewed Journals	Feola AJ, Myers JG, Raykin J, Mulugeta L, Nelson ES, Samuels BC, Ethier CR. "Finite element modeling of factors influencing optic nerve head deformation due to intracranial pressure." Invest Ophthalmol Vis Sci. 2016 Apr;57(4):1901-11. http://dx.doi.org/10.1167/iovs.15-17573 ; PubMed PMID: 27088762 , Apr-2016
Articles in Peer-reviewed Journals	Raykin J, Forte TE, Wang R, Feola A, Samuels BC, Myers JG, Mulugeta L, Nelson ES, Gleason RL, Ethier CR. "Characterization of the mechanical behavior of the optic nerve sheath and its role in spaceflight-induced ophthalmic changes." Biomech Model Mechanobiol. 2017 Feb;16(1):33-43. Epub 2016 May 28. http://dx.doi.org/10.1007/s10237-016-0800-7 ; PubMed PMID: 27236645 (Note reported originally in January 2017 as "2016 May 28. [Epub ahead of print]") , Feb-2017
Articles in Peer-reviewed Journals	Nelson ES, Mulugeta L, Feola A, Raykin J, Myers JG, Samuels BC, Ethier CR. "The impact of ocular hemodynamics and intracranial pressure on intraocular pressure during acute gravitational changes." J Appl Physiol (1985). 2017 Aug 1;123(2):352-63. Epub 2017 May 11. https://doi.org/10.1152/japplphysiol.00102.2017 ; PubMed PMID: 28495842 , Aug-2017
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Articles in Peer-reviewed Journals	Feola AJ, Coudrillier B, Mulvihill J, Geraldes DM, Vo NT, Albon J, Abel RL, Samuels BC, Ethier CR. "Deformation of the lamina cribrosa and optic nerve due to changes in cerebrospinal fluid pressure." Invest Ophthalmol Vis Sci. 2017 Apr 1;58(4):2070-8. https://doi.org/10.1167/iovs.16-21393 ; PubMed PMID: 28389675 , Apr-2017

Articles in Peer-reviewed Journals	Nelson ES, Myers JG Jr, Lewandowski BE, Ethier CR, Samuels BC. "Acute effects of posture on intraocular pressure." PLoS One. 2020 Feb 6;15(2):e0226915. https://doi.org/10.1371/journal.pone.0226915 ; PMID: 32027692; PMCID: PMC7004359 , Feb-2020