**Fiscal Year:** FY 2018  
**Task Last Updated:** FY 02/22/2018

**PI Name:** Kernagis, Dawn Ph.D.  
**Project Title:** Cervical Lymphatic Function Quantification and Associated Molecular Changes in Response to Simulated Microgravity

**Division Name:** Human Research  
**Program/Discipline:**

**Program/Discipline--Element/Subdiscipline:**

**Joint Agency Name:**

**TechPort:** No

**Human Research Program Elements:** None

**Human Research Program Risks:** None

**Space Biology Element:** None

**Space Biology Cross-Element Discipline:** None

**Space Biology Special Category:** None

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**Congressional District:** 1

**Comments:**

**Project Type:** GROUND  
**Solicitation:** 2017 HERO NNJ16ZSA001N-TRIRT. Appendix C: Translational Research Institute for Space Health (TRISH) Research Topics

**Start Date:** 10/01/2017  
**End Date:** 09/30/2019

**No. of Post Docs:**  
**No. of PhD Degrees:**  
**No. of PhD Candidates:**  
**No. of Master’s Degrees:**  
**No. of Master's Candidates:**  
**No. of Bachelor's Degrees:**  
**No. of Bachelor's Candidates:**

**Contact Monitor:** TRISH  
**Contact Phone:**

**Contact Email:**

**Flight Program:**

**Flight Assignment:**

**Key Personnel Changes/Previous PI:**

**COI Name (Institution):**

Clark, Jonathan M.D. ( Florida Institute For Human And Machine Cognition Inc. )
Crandall, David Ph.D. ( Indiana University )
Sevick, Eva Ph.D. ( University of Texas Health Science Center )

**Grant/Contract No.:** NNX16AO69A-T0105

**Performance Goal No.:**

**Performance Goal Text:** An increased presence of white matter hyperintensities (WMH) has been previously described in astronauts; however,
An increased presence of white matter hyperintensities (WMH) has been previously described in astronauts; however, the underlying cause of this pathology is not clearly understood. Astronauts exposed to long-duration microgravity also develop varying degrees of visual change and signs of elevated intracranial pressure (ICP), which are thought to potentially be associated with the increased WMH seen in this population. Central nervous systems (CNS) changes associated with extreme environmental exposures, including increased WMH, have also been detected in high altitude aviators and professional SCUBA divers. There is growing evidence that a proportion of the cerebrospinal fluid drains from the cranium via the deep cervical lymphatic pathway. Recent literature has also revealed the existence of lymphatic vessels in the brain that serve to regulate fluid pressure and pathological clearance for surrounding tissue, and these vessels are connected to the peripheral lymphatics. Impairment of these drainage systems in other pathological models have demonstrated histological changes, including tau protein accumulation and white matter damage, in the brain. Changes in fluid dynamics with environmental exposures, such as microgravity or immersion, could lead to impairment of brain lymphatic drainage, resulting in accumulation fluid and elevated ICP, stasis of brain metabolic waste, and subsequent tissue damage and lesion development. At present, however, the effect of microgravity on deep cervical lymphatic function has not yet been characterized.

Impact: Understanding the effect of microgravity on cervical lymphatic function and outflow from the brain will provide insight into factors and potential mitigation strategies for dangerous training or mission-limiting physiological conditions, such as increased ICP and development of WMH, which could detrimentally impact astronaut performance both acutely and long-term. In addition, further refinement of lymphatic function monitoring technology could lead to its utilization in space as a diagnostic tool for crew members experiencing CNS symptoms.

The proposed study will address the following Specific Aims:

SA1: Refine the current near-infrared fluorescence lymphatic imaging (NIRFLI) system underwater lymphatic imaging.

SA2: Characterize and compare the effect of deep cervical lymphatic function in humans in response to two models of simulated microgravity: head-out immersion (HOI) and head-down tilt (HDT).

SA3: Develop a visual quantification software program for objectively measuring lymphatic function as captured by the device.

SA4: Evaluate targeted molecular biomarkers associated with impaired immune function and lymphatic clearance in response to the HOI and HDT models of simulated microgravity.

Approach: The proposed study will refine existing lymphatic imaging technology while addressing the hypothesis that simulated microgravity (HDT, HOI) in humans impairs lymphatic transit speed in the head/neck lymphatics as compared to baseline due to the associated increase in hydrostatic pressure on the lymphatic system while increasing lymphatic transit in a chest- and head-ward direction. Study participants will undergo dry baseline measurements of cervical lymphatic function using a novel, portable, low footprint method for assessing lymphatic function, followed by measurements conducted during and following simulated microgravity exposures. Each subject will undergo both HDT and HOI, separated by at least 48 hours. Venous blood samples will be collected for assessment of targeted biomarkers prior to baseline measurements and at the conclusion of each exposure. In parallel with study data collection, visual analysis and machine learning algorithms will be applied to develop a software program that automatically quantifies lymphatic function in conjunction with the measuring device.