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| **Fiscal Year:** | FY 2016 | **Task Last Updated:** | FY 02/03/2017 |
| **PI Name:** | Dentinger, Aaron Ph.D. | | |
| **Project Title:** | Non-Invasive Monitoring of Intracranial Pressure (ICP) with Volumetric Ophthalmic Ultrasound | | |
| **Division Name:** | Human Research | | |
| **Program/Discipline:** | NSBRI | | |
| **Program/Discipline--Element/Subdiscipline:** | NSBRI--Smart Medical Systems and Technology Team | | |
| **Joint Agency Name:** | | **TechPort:** | Yes |
| **Human Research Program Elements:** | (1) **HHC**:Human Health Countermeasures | | |
| **Human Research Program Risks:** | (1) **Medical Conditions**:Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures<br>(2) **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:** | 12309-1027 | **Congressional District:** | 21 |
| **Comments:** | | | |
| **Project Type:** | Ground | **Solicitation / Funding Source:** | 2011 Crew Health NNJ11ZSA002NA |
| **Start Date:** | 10/01/2012 | **End Date:** | 09/30/2016 |
| **No. of Post Docs:** | 0 | **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:** | 0 | **Monitoring Center:** | NSBRI |
| **Contact Monitor:** | | **Contact Phone:** | |
| **Contact Email:** | | | |
| **Flight Program:** | | | |
| **Flight Assignment:** | NOTE: End date changed to 9/30/2016 per NSBRI (Ed., 4/26/16)<br>NOTE: End date changed to 3/31/2016 per NSBRI report submission (Ed., 5/8/14)<br>NOTE: Risk/Gap changes per IRP Rev E (Ed., 3/18/14) | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | Jagannathan, Srinivasan ( GE Global Research )<br>Sargsyan, Ashot ( Wyle Laboratories )<br>Patwardhan, Kedar ( GE Global Research )<br>Ebert, Douglas ( Wyle Laboratories )<br>Melton, Shannon ( Wyle Laboratories )<br>Garcia, Kathleen ( Wyle Integrated Sciences and Engineering Group )<br>Mills, David ( GE Global Research ) | | |
| **Grant/Contract No.:** | NCC 9-58-SMST02803 | | |
| **Performance Goal No.:** | | | |

**Performance Goal Text:**

**Task Description:**

Further research is needed to understand the role elevated intracranial pressure (ICP) plays in visual impairment observed during and following space missions. The long-term objective of this research is to noninvasively monitor ICP using 3-D ultrasound imaging by detecting changes in ocular structures and functioning of the eye that are correlated with elevated ICP. The project will lead to the development of tools to quantify inflight ocular changes, and thereby assess ICP. The new volumetric ultrasound imaging capability will provide user independent views of the entire ocular anatomy in a single scan with minimal crew time and ground guidance during image capture. A simplified ocular scan and new ocular metrics will provide the ability to track the short-term and long-term time course of ICP, determine the correlation of ICP with visual acuity changes in response to microgravity, and investigate effectiveness of potential countermeasures.
In the first two years of the grant, hardware was developed for 3-D ophthalmic imaging on the portable, high-resolution ultrasound platform (GE Vivid q) currently on board the International Space Station (ISS). A prototype mechanical 3-D ultrasound probe for ophthalmic scanning through a closed eyelid was integrated onto the Vivid q and several 2-D and Doppler imaging modes were implemented that control the acoustic output to remain below the FDA (Food and Drug Administration) limits for ophthalmic scanning. An external motor control unit was designed and fabricated to enable 3-D imaging with minimal changes to the Vivid q's hardware and software. Visualization and analysis tools were developed to automatically detect ocular structures within the ultrasound volumes, enhance standard and render new views of the ocular anatomy, enable new 3-D measurements, and align the ultrasound volumes with magnetic resonance images (MRI). These new capabilities were tested during ground-based human subject and animal studies in collaboration with a team from Wyle Integrated Science and Engineering with experience in the operational use of ophthalmic ultrasound. Safety tests were completed on the 3-D acquisition hardware at an external lab and the protocol for the human subjects' study was approved by NASA's IRB (Institutional Review Board).

An in vivo human subject study was conducted at Wyle's facility in Houston. In the first phase of the study, MRI and 3-D ultrasound data were acquired on 5 healthy volunteers. In the second phase of the study, 3-D ultrasound data were acquired on 11 healthy volunteers during head-down tilt (HDT) experiments. During the final year of the grant, the automatic image analysis and reconstruction algorithms were further refined, new structural and dynamic metrics were investigated, the animal study was completed, and the data from this study and the human study were analyzed. The computer algorithms automatically detect the optic nerve centerline and retina boundary within the 3-D ultrasound data. Knowledge of these anatomical landmarks enabled the contrast of the optic nerve sheath in standard longitudinal views to be enhanced and new cross-sectional views of the optic nerve to be generated. Additionally, new quantitative 3-D metrics of globe flattening were investigated to improve the repeatability of this traditionally subjective and highly user dependent metric when done solely with 2-D images. The image analysis algorithms were applied to both ultrasound and MRI volumes from the human study to demonstrate the ability to spatially align ocular structure across imaging modalities. Finally, new parameters related to intracranial dynamics were developed that quantify the periodic motion of structures near the optic nerve using tissue Doppler ultrasound. Analysis of the head-down tilt (HDT) data from the human study validated the 3-D ultrasound metrics, highlighted the individual variation in ONSD response to HDT even within the small number of healthy volunteers, and showed that 3-D globe flattening measures did not significantly change during the acute experiment. The elevated ICP animal study data demonstrated the feasibility to measure pulsatile motion of tissue near the optic nerve with ultrasound and allowed comparison of changes in the amplitude with mean ICP and ICP pulse pressure.

An advanced technology demonstration (ATD) of the 3-D ophthalmic ultrasound was conducted at the Space 4 Biomedicine to the National Space Biomedical Research Institute (NSBRI) leadership, the NSBRI user panel, and several NASA Johnson Space Center (JSC) researchers. The ATD provided the opportunity to walk the stakeholders through both the 3-D acquisition and the automated processing steps including some time for hands on scanning with the device during the demonstration. The team received helpful feedback on the usability of the technology in the space applications and applicability to the Vision Impairment and Intracranial Pressure (VIIP) problem from the group of experts.

**Rationale for HRP Directed Research:**

**Research Impact/Earth Benefits:**

The Earth-based clinical applications for volumetric ophthalmic ultrasound include non-invasive ICP assessment at the point of care and 3-D diagnostic imaging of ocular structures. Acute, noninvasive monitoring of ICP in traumatic brain injury patients has the potential to identify primary injuries in the emergency room and prevent secondary injuries in critical care units. 3-D ultrasound acquisitions coupled with automatic image analysis will provide easy-to-use, user-independent tools for rapid ICP assessment. Volume scanning with a portable ultrasound system provides the opportunity for frequent assessment of ocular structures at the point of care, eliminating the need to transport patients to an imaging suite and scanning by an expert sonographer. Automatic analysis of the 3-D ultrasound data will improve image quality, reduce review times, and ultimately provide automatic measurements. These new imaging tools have the potential to enhance existing ultrasound assessment of trauma in critical care settings, such as augmenting the extended-FAST exam used to locate free fluid as the result of internal bleeding and detect pneumothoraxes. The use of the technology to quantify 3-D ocular shapes and track changes in the ocular anatomy over time has applications to the diagnosis and treatment monitoring of patients with disorders affecting the ocular structure, such as high-myopia and staphyloma. Volumetric ultrasound provides a lower cost imaging alternative that could be acquired in a physician's office and allow multiple views of the anatomy to be acquired under a larger range of conditions for more detailed diagnoses.

The progress toward the aims to enhanced operation innovation for medical needs are summarized below.
Aim 1 – The prototype 3-D acquisition hardware and visualization and analysis tools for enhanced ocular scanning were demonstrated to members of the NSBRI and NASA research communities. This included a 3-D optic nerve sheath measurement workflow consisting of a single button press for the 3-D acquisition on the Vivid q, semi-automated image analysis of ultrasound 3-D volumes to produce multiple optic nerve sheath views with improved image quality and contrast, and integration with GE EchoPAC review software for optic nerve sheath diameter and area measurements. The 3-D information enabled multiples longitudinal views and new cross-sectional views of the optic nerve anatomy to be generated from a single 3-D ultrasound acquisition.

Aim 2 – The 3-D image analysis algorithms developed are applicable to both 3-D ultrasound and MRI ocular scans. The

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| **Task Progress:** | image analysis algorithms were used to spatially align ultrasound and MRI volumes acquired on a healthy volunteer to demonstrate the complementary structural information across imaging modalities from co-registered data sets.<br><br>Aim 3 – The optic nerve measurements with the prototype 3-D acquisition hardware and reconstruction software were validated with measurements from the current 2-D protocol in healthy subjects during moderately elevated ICP (n=11). The feasibility to use the results of the image analysis to generate 3-D posterior globe flattening metrics was demonstrated on data from the same healthy volunteers.<br><br>Aim 4 – The feasibility of a new ultrasound-based measure related to the pulsatility of the intracranial dynamics was demonstrated in an elevated ICP animal study. A response with ICP level was observed in the initial animal study (n=4) with further research needed to repeat the measure in human subjects and understand the clinical utility of the new parameter. |
| **Bibliography Type:** | Description: (Last Updated: 09/05/2020) |
| **Abstracts for Journals and Proceedings** | Dentinger A, MacDonald M, Ebert D, Garcia K, Sargsyan A. "Volumetric Ophthalmic Ultrasound for Inflight Monitoring of Visual Impairment and Intracranial Pressure." 16th International Symposium on Intracranial Pressure and Neuromonitoring, Massachusetts Institute of Technology, Cambridge, MA, June 28-July 2, 2016.<br>16th International Symposium on Intracranial Pressure and Neuromonitoring, Massachusetts Institute of Technology, Cambridge, MA, June 28-July 2, 2016. ICP Program Booklet, p. 37-38. , Jun-2016 |
| **Articles in Peer-reviewed Journals** | Dentinger A, MacDonald M, Ebert D, Garcia K, Sargsyan A. "Volumetric ophthalmic ultrasound for inflight monitoring of visual impairment and intracranial pressure." Acta Neurochir Suppl. 2018;126:97-101.<br>https://doi.org/10.1007/978-3-319-65798-1_21 ; PubMed PMID: 29492541 , Mar-2018 |