Fiscal Year:	FY 2016	**Task Last Updated:**	FY 03/10/2016
PI Name:	Williams, Michael A. M.D.		
Project Title:	Comparison of Continuous Non-Invasive and Invasive Intracranial Pressure Measurement		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Smart Medical Systems and Technology 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		
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Space Biology Special Category:	None		
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Zip Code:	98104-2499	**Congressional District:**	7
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	10/01/2012	**End Date:**	10/31/2015
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 10/31/2015 per NSBRI (Ed., 11/5/15)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Voss, Susan (Smith College) Ebert, Douglas (Wyle Laboratories)		
Grant/Contract No.:	NCC 9-58-SMST02802		
Performance Goal No.:			
Performance Goal Text:			
	Original Aims/Objectives: Determine the validity, reliability, accuracy, and precision of two noninvasive methods of intracranial pressure (ICP) measurement (tympanic membrane displacement [TMD, Marchbanks Measurements Systems, UK] and distortion product otoacoustic emissions [DPOAE]) in comparison to a reference standard, invasive ICP measurement, in human subjects undergoing diagnostic ICP monitoring. Methods: This is a prospective research protocol involving human patients. Eligibility criteria include (1) adults ages 18-75 years, (2) clinically indicated need for continuous ICP monitoring for the diagnosis of hydrocephalus, idiopathic intracranial hypertension (IIH), or shunt malfunction, or (3) clinically indicated need for cerebral spinal fluid (CSF)-infusion testing for the diagnosis of hydrocephalus or IIH. Invasive ICP methods include (1) spinal catheter insertion and fluid-coupled external transducers for patients with hydrocephalus, IIH, and (2) CSF-infusion testing,		

Task Description:	which will use a standardized automated system, Likvor Celda System (http://www.likvor.com) that has been validated in clinical use in Sweden. Noninvasive ICP methods include the TMD method and DPOAE. Key Findings: In subjects evaluated during CSF infusion testing, as ICP increases, systematic and significant changes in the DPOAE measurements are seen. In particular, for frequencies from 800 to 1700 Hz the DPOAE angle shows significant increases when ICP is ~12 mm Hg above baseline. Statistical analysis of TMD results during infusion testing suggest a relationship between Vm and ICP; however, the subject population had impaired hearing which places the reliability of some measurements into question. Specifically, if the subject's acoustic reflex threshold is too high, then the acoustic stimulus required for the TMD will not be strong enough (in dB) to elicit a consistent tympanic membrane reflex. Re-analysis with subjects sorted according to acoustic reflex threshold is in progress. Impact: The DPOAE results confirm that changes in DPOAE angle and magnitude seen with change in ICP are physiologically based, and suggest that it should be possible to detect pathological ICP elevation using noninvasive DPOAE measurements. The TMD results may be promising, and in general are consistent with the studies performed by other groups; however, further subgroup analysis is required. Neither the DPOAE nor the TMD method is capable of providing a numeric estimate of ICP, but should be capable of showing relatively large changes in ICP. Furthermore, both methods require sampling over a period of 60 to ~120 seconds, and thus, at best, provide an estimate of the mean ICP during the sampling period, but do not provide information about the variability of ICP during the sampling period, which is a notable shortcoming because the same mean ICP can be seen in subjects with either normal or abnormal intracranial compliance. Additionally, neither method is suitable for noninvasive ICP monitoring during sleep, which is when pathologic ICP waveforms are most likely to appear in subjects with disorders of ICP. Should TMD or DPOAE not reveal significant changes in ICP during awake measurements on astronauts on the International Space Station (ISS), it will not be possible to conclude that ICP is normal on the ISS. Such a conclusion can be reached with continuous ICP monitoring during sleep using a method that is capable of sampling fast enough to permit analysis of beat-to-beat variability in ICP, which is necessary to provide a reliable estimation of whether intracranial compliance is normal or abnormal.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The outcome of this research program will have widespread benefits and Earth-based applications. The validation of reliable, portable, noninvasive methods of ICP measurement will dramatically change evaluation and management practices for thousands of children, adults, and elderly who have chronic disorders of CSF circulation, including idiopathic intracranial hypertension (IIH), hydrocephalus, shunt malfunction, and spontaneous intracranial hypotension. Currently, only invasive methods exist for accurately assessing whether ICP is normal or abnormal in these patients; however, their invasive nature limits their usage. As a result, many patients are managed with woefully imprecise methods, such as CT or MRI scans, assessment of clinical signs and symptoms, or empiric decisions to insert, remove, or revise shunts. Noninvasive ICP measurement will provide rapid reassurance to patients, parents, and physicians when a child with hydrocephalus becomes ill and it must rapidly be determined whether the illness represents shunt obstruction with elevated ICP or merely a systemic illness such as a cold or the flu that can cause similar symptoms. In the elderly with shunts for normal pressure hydrocephalus, the ability to routinely and noninvasively assess ICP before and after shunt surgery will offer reassurance that the shunt is functioning and that the patient is adequately treated. Alternately, noninvasive ICP measurement can help to determine if a shunt pressure setting is too low, putting the patient at risk for overdrainage with subdural fluid collections or hematomas. Additionally, patients with acute ICP elevation, such as those with stroke, brain tumor, intracerebral hemorrhage, or traumatic brain injury, would benefit from the rapid availability of noninvasive ICP measurement.
Task Progress:	Year 3 was spent with analysis of data collected in Year 2 in Umea (CSF infusion cohort) and enrolling subjects for continuous ICP monitoring at Sinai Hospital of Baltimore. Enrollment for continuous ICP monitoring was below expectation, primarily because of diminishing number of patients admitted for medically-indicated continuous ICP monitoring. Overall, 4 subjects provided consent; however, only 3 were able to participate in the protocol. One subject could not be included because reliable TMD and DPOAE signals could not be obtained during fitting and initial testing of the instruments. Of the 3 subjects who participated in the protocol, none was able to fall asleep while wearing the DPOAE ear tip. TMD was not attempted during sleep in this cohort because the acoustic stimulus would have awakened them. Analysis of data collected in Year 2 in Umea is in progress. One manuscript that describes the relation between DPOAE and ICP has been submitted for peer-reviewed publication. Analysis of the TMD cohort remains in progress due to the need for subgroup analysis of subjects whose acoustic reflex threshold was sufficiently low that the acoustic stimulus for TMD elicited reliable tympanic membrane reflexes. The Principal Investigator traveled to National Space Biomedical Research Institute (NSBRI) Headquarters to provide an Advanced Technology Demonstration on November 9, 2015.
Bibliography Type:	Description: (Last Updated: 08/24/2020)
Articles in Peer-reviewed Journals	Williams MA, Malm J, Eklund A, Horton NJ, Voss SE. "Distortion product otoacoustic emissions and intracranial pressure during CSF infusion testing." Aerosp Med Hum Perform. 2016 Oct;87(10):844-51. https://doi.org/10.3357/AMHP.4572.2016 ; PMID: 27662346 [Note reported originally in March 2016 as "Submitted, as of March 2016"] , Oct-2016