Fiscal Year:	FY 2015	**Task Last Updated:**	FY 10/14/2014
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		
Space Biology Cross-Element Discipline:	None		
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) Hamilton, Doug (Wyle Integrated Sciences and Engineering Group)		
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 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, IIH, or shunt malfunction, or (3) clinically indicated need for 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, (2) insertion of a 25-gauge needle into the shunt reservoir and fluid-coupled external transducers for		

Task Description:	patients with shunt malfunction, and (3) CSF-infusion testing, 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 TMD method and DPOAE. Key Findings: To date, 15 subjects have been evaluated during CSF infusion testing in Umea, Sweden. Statistical analysis of both DPOAE and TMD results in relation to invasive ICP is in progress. Visual analysis of the raw data suggests that a linear relationship between invasive ICP and the noninvasive ICP methods may exist, but significant inter-individual variation exists. No conclusions should be reached regarding the accuracy or precision of the noninvasive ICP methods until the statistical analysis is complete. Impact: If, after statistical analysis is completed, a linear relationship between either DPOAE or TMD and invasive ICP is demonstrated, then either method may have the potential to detect change in ICP noninvasively. Proposed Research Plan for Year 3: The team in Baltimore plans to recruit 5 or 6 subjects in Year 3 for recording of spontaneous ICP to determine whether DPOAE and TMD can detect naturally-occurring ICP changes in sleep and wakefulness in patients with disorders of CSF pressure. The entire research team will complete the statistical analysis of the DPOAE and TMD data and submit the resulting manuscripts for peer-reviewed publication.
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 2 moved forward as desired following the difficulty we encountered in Year 1 with our attempted FDA application to bring the Likvor Celda device to the U.S. as an investigational new device. With approval of the NSBRI, we changed our research plan so that subjects could be investigated in Umea, Sweden, where use of the Likvor Celda device for infusion testing is a standard of care. The PI spent 1 week in Umea in September 2013 for formal training in the infusion technique. With co-investigators Jan Malm and Anders Eklund, the research protocol was translated to Swedish and submitted to the Ethical Review Committee, and approval was received in early November 2013. All patients evaluated for INPH with infusion testing at Umea between November 18 and November 29, 2013 were eligible to enroll in the protocol. The PI was present for this time period and performed all noninvasive ICP testing while the team in Umea performed the standard-of-care infusion testing and served as consultants. Eight of eight subjects were enrolled. The investigators encountered hardware/software incompatibility with the Marchbanks TMD device in the first week that resulted in incomplete data collection on some subjects. With input from Rob Marchbanks and the engineering team in Umea, we resolved the incompatibility by the beginning of the second week, and data collection for TMD and DPOAE methods proceeded. The nature of this incompatibility and its "fix" were shared with other NSBRI and NASA investigators using the same device. The TMD instrument was returned to the UK for repairs and upgrades, and then sent back to the PI. The PI returned to Umea and enrolled an additional 7 subjects between March 17 and March 28, 2014. Data analysis was begun in May 2014 and another software incompatibility with the Marchbanks device was discovered, rendering the machine unable to display on the video monitor except in "Safe Mode", which could not be used to run the instrument. Eventually the Marchbanks team sent a software fix, which, again, was shared with other NSBRI and NASA investigators using the same device. Processing of the TMD and DPOAE data from the Swedish subjects was completed before the ICP data was unblinded. The research team is presently running statistical analysis on both the TMD and DPOAE data sets. Working drafts of 2 manuscripts have been started. In Year 3, the team in Baltimore plans to recruit 5 or 6 subjects in Year 3 for recording of spontaneous ICP to determine whether DPOAE and TMD can detect naturally-occurring ICP changes in sleep and wakefulness in patients with disorders of CSF pressure.
Bibliography Type:	Description: (Last Updated: 08/24/2020)