

<b>Fiscal Year:</b>	FY 2017	<b>Task Last Updated:</b>	FY 03/10/2017
<b>PI Name:</b>	Hayman née Anderson, Allison Ph.D.		
<b>Project Title:</b>	Feasibility of DPOAE Mapping as an In-Flight Measure of Intracranial Pressure in Space		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>	NSBRI		
<b>Program/Discipline--Element/Subdiscipline:</b>	NSBRI--Smart Medical Systems and Technology Team		
<b>Joint Agency Name:</b>		<b>TechPort:</b>	No
<b>Human Research Program Elements:</b>	None		
<b>Human Research Program Risks:</b>	None		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Comments:</b>	NOTE: name change to Hayman née Anderson (Ed., March 2025). PI moved to University of Colorado from Dartmouth College in early 2017.		
<b>Project Type:</b>	Ground	<b>Solicitation / Funding Source:</b>	2014 NSBRI-RFA-14-02 First Award Fellowships
<b>Start Date:</b>	11/01/2014	<b>End Date:</b>	10/31/2016
<b>No. of Post Docs:</b>	1	<b>No. of PhD Degrees:</b>	0
<b>No. of PhD Candidates:</b>	0	<b>No. of Master' Degrees:</b>	0
<b>No. of Master's Candidates:</b>	0	<b>No. of Bachelor's Degrees:</b>	0
<b>No. of Bachelor's Candidates:</b>	5	<b>Monitoring Center:</b>	NSBRI
<b>Contact Monitor:</b>	<b>Contact Phone:</b>		
<b>Contact Email:</b>			
<b>Flight Program:</b>			
<b>Flight Assignment:</b>			
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Buckey, Jay ( MENTOR/ Dartmouth College )		
<b>Grant/Contract No.:</b>	NCC 9-58-PF04103		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>			

**POSTDOCTORAL FELLOWSHIP**

This project assessed distortion product otoacoustic emissions (DPOAE) as a non-invasive measure of intracranial pressure changes. The long-term interaction between intracranial pressure (ICP) and the ocular globe may cause visual acuity changes in spaceflight. Changes in DPOAE responses correlate with changes in ICP, making DPOAEs a useful proxy measure. The technique used here, DPOAE level/phase mapping (DPOAE L/P maps), collects data at multiple sites throughout the cochlea and provides a comprehensive picture of cochlear responses to ICP changes. This work was done in conjunction with an existing National Space Biomedical Research Institute (NSBRI)-funded set of experiments, Cranial Venous Modeling (CA03401). It also leveraged data from our Office of Naval Research and EPSCoR research grants. This study provides a novel way to make detailed DPOAE mapping measurements in association with multiple ocular and cranial vascular measurements.

**Task Description:**

Specific Aim 1: Create DPOAE level/phase maps to characterize changes as a result of the isolated effects of fluid shifts and alterations in hydrostatic gradients. In the first reporting year, DPOAE level/phase maps were collected in two experiments. Although there were visually apparent changes, we did not have a statistical basis by which to compare the data. Therefore, in conjunction with a project funded by the Office of Naval Research, a normative group of maps were collected on 29 subjects in 4 visits each. Data represented the normal range of variability that could be expected in the maps, and provides a statistical basis to compare the postural and fluid shift data to assess changes. Experimental data was collected--data in an experiment where 16 subjects underwent lower body negative and positive pressure (LBNP and LBPP) in both the supine and prone positions. DPOAE maps were collected on 13 subjects in 7 experimental conditions. In this way, the individual effects of time, gravitational direction, and fluid shifts on the DPOAE maps were isolated.

Specific Aim 2: Determine the DPOAE level/phase map response signature to fluid shifts and hydrostatic gradient changes. This research uses random field theory to calculate regional changes in maps across all subjects. The repeatability cohort described in Specific Aim 1 was used as the population's normal range of variation. Subjects in the experimental conditions were compared to the population averages at each distortion product data point. Regions within the cochlea most sensitive to DPOAE amplitude changes were found, and changes were most pronounced in the prone position under LBPP. These regions, in the  $2f_1 - f_2$  region of the map between 6-8 kHz are consistent with regions most sensitive to changes in stapes velocity and basilar membrane stiffness. DPOAE phase data is analyzed with two dimensional Fourier transforms. Due to its cyclical response, phase data may be broken down into characteristic parameters using two-dimensional Fourier transforms. Development of these methods is ongoing.

Specific Aim 3: Explore the relationship between ocular and cranial vascular measurements to changes seen in DPOAE level/phase maps. Tympanometry was measured for each subject to assess changes in middle ear state as an additional explanatory factor. The tympanometry results indicate that middle ear status, particularly the tympanic peak pressure, may be a relevant factor in explaining changes in DPOAE Level maps. Also, in conjunction with each experiment, additional ocular measures were taken, including intraocular pressure (IOP) and ocular geometry such as axial length and aqueous depth. These results indicate changes in fluid shift and in posture cause correlated alterations in the measured parameters. This emphasizes the need for numerical modeling to develop explanatory hypotheses for changes to these integrated physiological systems.

**Rationale for HRP Directed Research:****Research Impact/Earth Benefits:**

Noninvasive measures of ICP are critical for evaluating traumatic brain injury, concussions, and idiopathic intracranial hypertension. Clinical DPOAE measures focus on the input ratio of frequencies at  $F1/F2 = 1.2$ . This data set can be used to find the region of the cochlea most sensitive to changes in ICP, which may provide a more robust testing range by which to establish a noninvasive measure of ICP. Although this study can not transition from DPOAEs directly to ICP because no invasive measures are taken in conjunction with the map data, it provides the basis for future studies to improve this technique for clinical applications.

**Task Progress:**

Specific Aim 1: In the first reporting year, DPOAE level/phase maps were collected in two experiments. Although there were visually apparent changes, we did not have a statistical basis by which to compare the data. Therefore, in conjunction with a project funded by the Office of Naval Research, a normative group of maps were collected on 29 subjects. Data were taken 4 times, so repeatability could be assessed. That set of data represented the normal range of variability that could be expected in the maps, and provides a statistical basis to compare the postural and fluid shift data to assess changes. Experimental data was collected in an experiment where 16 subjects underwent lower body negative and positive pressure in both the supine and prone positions. DPOAE maps were collected on 13 subjects in 7 experimental conditions. In this way, the individual effects of time, gravitational direction, and fluid shifts on the DPOAE L/P maps were isolated.

Specific Aim 2: This research uses random field theory to calculate regional changes in maps across all subjects. The repeatability cohort described in Specific Aim 1 was used as the population's normal range of variation. Subjects in the experimental conditions were compared to the population averages at each distortion product data point. Regions within the cochlea most sensitive to DPOAE amplitude changes were found, and changes were most pronounced in the prone position under LBPP. These regions, in the  $2f_1 - f_2$  region of the map between 6-8 kHz are consistent with regions most sensitive to changes in stapes velocity and basilar membrane stiffness. Work is ongoing to define the decision criteria, the Euler Characteristic used in the random field theory methodology, to ensure that the DPOAE map's inherent smoothness is accurately accounted for. Several statistical strategies have been identified to analyze DPOAE phase data. Due to its cyclical response, phase data may be broken down into characteristic parameters using two-dimensional Fourier transforms. Development of these methods is ongoing.

Specific Aim 3: Tympanometry was measured for each subject to assess changes in middle ear state as an additional explanatory factor for potential changes in DPOAE maps. The tympanometry results from the repeatability cohort and fluid shift/posture subjects indicate that middle ear status, particularly the tympanic peak pressure, may be a relevant factor in explaining changes in DPOAE Level maps. Also, in conjunction with each experiment, additional ocular measures were taken, including intraocular pressure (IOP) and ocular geometry such as axial length and aqueous depth. These results indicate changes in fluid shift and in posture cause correlated alterations in the measured parameters. This emphasizes the need for numerical modeling to develop explanatory hypotheses for changes to these integrated physiological systems.

Bibliography Type:	Description: (Last Updated: 03/26/2025)
Abstracts for Journals and Proceedings	Anderson AP, Fellows AM, Buckey JC. "DPOAE Mapping as a Measure of Cochlear Sensitivity to Postural Changes." Association for Research in Otolaryngology 39th MidWinter Meeting, San Diego, CA, February 20-24, 2016. Association for Research in Otolaryngology 39th MidWinter Meeting, San Diego, CA, February 20-24, 2016. Abstracts. , Feb-2016
Articles in Peer-reviewed Journals	Anderson AP, Swan JG, Phillips SD, Knaus DA, Kattamis NT, Toutain-Kidd CM, Zegans ME, Fellows AM, Buckey JC. "Acute effects of changes to the gravitational vector on the eye." J Appl Physiol (1985). 2016 Apr 15;120(8):939-46. Epub 2015 Dec 10. <a href="http://dx.doi.org/10.1152/japplphysiol.00730.2015">http://dx.doi.org/10.1152/japplphysiol.00730.2015</a> ; PubMed <a href="#">PMID: 26662052</a> , Apr-2016
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