Fiscal Year:	FY 2006	**Task Last Updated:**	FY 01/08/2007
PI Name:	Buckey, Jay C. M.D.		
Project Title:	Improved Bubble Detection for EVA		
Division Name:	Human Research		
Program/Discipline:	NSBRI Teams		
Program/Discipline--Element/Subdiscipline:	NSBRI Teams--Technology Development Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **DCS**:Risk of Mission Impacts and Long-Term Health Issues due to Decompression Sickness		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	jay.buckey@dartmouth.edu	**Fax:**	FY 603-650-6013
PI Organization Type:	UNIVERSITY	**Phone:**	603-650-6012
Organization Name:	Dartmouth College		
PI Address 1:	Department of Medicine		
PI Address 2:	1 Medical Center Drive		
PI Web Page:			
City:	Lebanon	**State:**	NH
Zip Code:	03756-0001	**Congressional District:**	2
Comments:	Address updated 9/2008		
Project Type:	Ground	**Solicitation / Funding Source:**	2003 Biomedical Research & Countermeasures 03-OBPR-04
Start Date:	07/01/2004	**End Date:**	06/30/2008
No. of Post Docs:	0	**No. of PhD Degrees:**	1
No. of PhD Candidates:	1	**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:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Magari, Patrick (Creare, Inc.) Knaus, Darin (Creare, Inc.) MacKenzie, Todd (Dartmouth College)		
Grant/Contract No.:	NCC 9-58-TD00402		
Performance Goal No.:			
Performance Goal Text:			

Task Description:

Assembly of the International Space Station (ISS) and lunar exploration require extensive and unprecedented extra-vehicular activity. Current spacecraft and suit designs force astronauts to move between different pressure environments, making decompression sickness (DCS) a potential risk. DCS risk mitigation strategies reduce operational efficiency. The objective of this effort is to improve EVA efficiency and safety by developing and validating new bubble detection technology using dual-frequency ultrasound. The Creare dual-frequency instrument (CDFI) can detect and size bubbles through the chest wall as they move through the heart. Also, signals consistent with bubbles can be detected in tissue. Potentially, this technology could be used to: (a) characterize bubble dynamics during decompression sickness (DCS), (b) detect the earliest stages of DCS, (c) develop and evaluate non-compressive countermeasures for DCS, (d) diagnose DCS in tissue or joints, and (4) mitigate DCS risk by improving preventive strategies such as oxygen pre-breathing and limiting activity at particular times.
Detecting and sizing bubbles intravascularly (a new and unique capability) allows for bubble size histograms to be constructed during the development and treatment of DCS. The change of bubble size distribution during decompression stress may indicate DCS severity. Before using the device either for quantitative research or operations, the sizing ability needs to be quantified in optimal in-vitro conditions. The calibration system developed for this project can create monodisperse distributions of microbubbles at the sizes likely to occur during decompression stress. Work in the past year has focused on improving the optical sizing capability (used for comparison to the ultrasonically determined size), developing tissue equivalent phantoms, and reducing standing waves in the in-vitro test setup. A full calibration is currently underway.

Tissue bubble detection is also a unique capability. The CDFI potentially can detect very small bubbles (the possible precursors of larger bubbles in tissue or blood) and identify larger bubbles in areas with symptoms of pain or discomfort consistent with DCS. Interpreting tissue bubble signals, however, requires knowledge of other potential sources of false bubble signals in tissue. Work in this past year has identified the mechanisms for false positive signals and methods to minimize them have been developed. A significant accomplishment was the demonstration of the ability to detect contrast bubbles (Definity®) injected into tissue (in anesthetized swine). Bubble signals were returned only from the area where Definity® had been injected and not from other areas, including tissues like bone, which strongly reflects ultrasound. False bubble signals were not detected. This demonstrated the ability of the system to detect stationary bubbles in tissue.

In the past year the first human tissue bubble studies were performed. Additionally, a new technique to measure gas saturation in tissue is being explored. In-vitro work has shown that the point at which bubbles are created by cavitation varies with gas saturation. This offers a potential new way to determine gas saturation in tissue, which could potentially lead to a new way to assess DCS risk.

For the coming year, the plan is to: (a) complete the in-vitro calibration, (b) track bubble sizes during decompression stress in anesthetized swine, (c) determine if signals consistent with bubbles can be detected in human muscle and assess if these signals change after exercise or immobilization and (d) develop the cavitation threshold as a method to measure gas saturation in tissue or blood.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

The results from this study are also applicable for divers, aviators, high-altitude parachutists and others who are exposed to the risk of decompression sickness.
Another application for this technology is bubble monitoring during coronary artery bypass surgery or valve replacement surgery. Patients who have coronary artery bypass surgery are at risk for having solid and gaseous emboli reach the brain when they are on the "pump" (the cardiopulmonary bypass circuit). The Creare dual-frequency ultrasound unit could be used to monitor for bubbles in the bypass circuit and could distinguish between solid and gaseous emboli. A collaboration with Dr. Donny Likosky is underway to advance this work.

The cavitation approach can be used to determine to assess the gas saturation in fluids such as hydraulic fluid, which is important for industrial and aviation applications. Creare is currently developing an instrument based on this concept for the U.S. Air Force.

The bubble generator that has been developed for this project is currently being supplied to a large industrial manufacturer in the pharmaceuticals industry to calibrate a Doppler-based detector, which monitors a manufacturing process.

Creare is also applying the knowledge gained on the bubble acoustics knowledge and expertise gained in this effort to a Department of Energy project to mitigate cavitation damage in the Spallation Neutron Source (SNS) being developed at Oak Ridge National Laboratory. In this facility, a large acoustic wave is produced in the mercury spallation target when proton pulses very rapidly and repeatedly enter the mercury. The acoustic wave reflects off the vessel walls and causes the mercury to cavitate which results in severe damage to the vessel when the SNS is operated at the desired full power level. Creare is characterizing the ability of various stabilized bubbles to dampen the large acoustic wave and, thereby, mitigate the resulting cavitation damage.

Tissue Bubble Detection
The detection of frequent, unexplained false bubble signals had been complicating bubble detection. Work in the past year successfully identified the mechanism underlying a major source of false bubble signals. These signals originated from previously undetected electrical interference. After solving this problem an in-vivo test of tissue bubble detection was performed using Definity® ultrasonic contrast agent. Experiments in a water tank showed that a small amount of Definity® produced bubble signals, while water did not. Subsequently, Definity® was injected into thigh tissue in an anesthetized swine. Measurements were taken at several points on the thigh and bubble signals were only returned from the area where Definity® had been injected. False bubble signals were not detected, even from strong ultrasound reflectors like bone.

Calibration

Previous in-vivo studies have shown that bubbles can be detected and sized transthoracically during decompression stress. Before the information from in-vivo studies can be used scientifically, however, a calibration of the device against bubbles of known size is essential. This calibration, however, is technically challenging since it requires (1)

Task Progress:	streams of small bubbles of known size, (2) phantoms that match tissue attenuation characteristics and (3) the elimination of standing ultrasonic waves from the test setup, which can confound the results. This past year, tissue-like phantoms were built using special polyurethane formulations that mimic the attenuation properties of tissue. Measurements were taken to determine the presence and magnitude of standing ultrasonic waves created in the phantom and test setup during calibration. Once this was characterized, countermeasures were employed to minimize standing waves. Currently, an initial set of calibration data is under review to ascertain whether all the technical factors involved in calibration have been solved. Cavitation The amount of dissolved inert gas within a tissue strongly influences whether bubbles will form in the tissue during decompression stress. At present, however, no method exists to assess gas saturation within tissue. As the amount of ultrasonic energy sent into the tissue increases, it reaches a point where bubbles form spontaneously. This bubble formation process is called cavitation. When the bubbles cavitate, ultrasonic signals at multiple harmonics can be detected indicating that cavitation has occurred. Work in the past year has explored whether the point at which bubbles cavitate within a fluid could be used to assess gas saturation. We have shown that the bubble cavitation threshold (as measured by the returned ultrasonic signals) decreases with increasing gas saturation in the liquid. Further work is underway to determine if this method could be useful to measure gas saturation in tissue and hence as a measure for DCS risk.
Bibliography Type:	Description: (Last Updated: 05/20/2025)
Articles in Peer-reviewed Journals	Buckey JC, Knaus DA, Alvarenga DL, Kenton MA, Magari PJ. "Dual-frequency ultrasound for detecting and sizing bubbles." Acta Astronaut. 2005 May-Jun;56(9-12):1041-7. PMID: 15835064 , May-2005