Fiscal Year:	FY 2005	**Task Last Updated:**	FY 10/27/2005
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:**	1
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) Kenton, Marc (Creare) Knaus, Darin (Creare) 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 future space 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. Work in the past year has focused on performing a comprehensive calibration of the device. A major hurdle overcome in the present grant period was the ability to create monodisperse distributions of microbubbles at the sizes likely to occur during decompression sickness. This is achieved by shearing bubbles off the tip of a fine glass micropipette with a stream of water. The velocity of the shearing water stream is used to adjust the size of the bubble generated. Monodisperse bubbles as small as 40 microns have been generated in this manner. Smaller sizes can also be generated, but with a broader size distribution. Tissue bubble detection is also a unique capability. The CDFI can potentially 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 on other potential sources of false bubble signals in tissue. In the present grant period a major effort has been made to understand the sources of weakly nonlinear signals (potential false bubble signals). These efforts included the complete elimination of any potential nonlinear sources of mixing in the signal processing (e.g. amplifier clipping, impedance mismatches). Work this year has also lead to human use approval for the device. 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.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	If the bubble detection and sizing instrument proves to be effective for monitoring during cardiopulmonary bypass, this could be a significant benefit to patients. Currently, many patients experience decreases in cognitive function after cardiopulmonary bypass, and this is thought to be due to emboli reaching the brain. Improved monitoring could help reduce these emboli and their consequences. The results from this study are also applicable for divers, aviators 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 the 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 distinquish between solid and gaseous emboli. An application has been submitted to the NIH to advance this work. In addition to its NASA application, this technology could be used to improve the safety and efficiency of diving operations.
Task Progress:	Highly reflective targets -- strong versus weak mixers The Creare Dual Frequency Instrument (CDFI) exploits the fact that resonating bubbles are strong nonlinear mixers. Other objects and materials can be weak nonlinear mixers. In most cases weak mixers generate negligible mixing signals. If driven hard enough, however, a weak mixer can produce a detectable nonlinear mixing signal. Effort has been devoted over the last year to understanding weak sources of nonlinear signals to ensure that they do not affect either the calibration of the instrument or the bubble sizing measurements adversely. The CDFI electronics have been studied systematically to eliminate any potential electronic sources of mixing. In-vitro studies have examined the relationship of ultrasound power to non-linear mixing by weak mixers. Calibration bubbles Efforts have also been underway to calibrate the instrument by validating the mixing signals produced bubbles of known sizes. A major hurdle overcome in the present grant period was the ability to create monodisperse microbubble distributions at sizes likely to occur during decompression sickness (40 microns to 245 microns). This has been achieved by shearing bubbles off the tip of a fine glass micropipette with a stream of water. These bubble streams have been used to generate a calibration for the CDFI suitable for intravascular DCS studies. Further efforts will be undertaken to refine and expand this calibration for smaller bubble sizes. Human use approval A major advance during the present grant period was obtaining Dartmouth and Creare IRB approval for using the CDFI for extravascular human testing. The steps undertaken to obtain this approval included the full characterization of the transducers used in the CDFI to understand their power output, as well as a modification of the CDFI control software to calculate and display the mechanical and thermal indexes of the instrument’s output. The CDFI was designated as “non significant risk” by the Dartmouth IRB and thus did not require Investigational Device Exemption (IDE) from the FDA. Human use approval is especially important for the extravascular (tissue) bubble studies. For the initial studies, the conduct of extravascular bubble detection experiments is less complex with humans since the experiments will require voluntary exercise. In-vivo bubble sizes The CDFI has been used to show qualitative bubble size differences in in-vivo studies. Two separate bubble detection studies were used to compare the detected sizes of Definity™ contrast agent “bubbles” with DCS bubbles. In both studies, the right ventricular outflow track of an anesthetized swine was monitored. In one study, Definity™ ultrasound contrast bubbles were injected continuously, in the other, bubbles were monitored during DCS (grade 3-4). Bubble signals were detected at the small end of the bubble size scale during the Definity™ scan
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
Patents	US Patent 6,457,331 Patent Oct-2004 Kline-Schoder, R. and P. J. Magari "Bubble Measuring Instrument and Method"

Presentation	Bollinger, B. R., Buckey, JC., Alvarenga, D. L., Knaus, D. A., Kenton, M. A., and P. J. Magari "Improved bubble detection for EVA" N/A Jan-2005
Presentation	Buckey, JC., Knaus, D. A., Alvarenga, D. L., Kenton, M. A., Bollinger B., and P. J. Magari "Bubble detection and sizing using dual-frequency ultrasound" N/A May-2004