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Project Title:	Validation of On-Orbit Methodology for the Assessment of Cardiac Function and Changes in the Circulating Volume Using Ultrasound and Braslet-M Occlusion Cuffs, SDTO 17011 U/R (Braslet)		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Operational and clinical research		
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Space Biology Special Category:	None		
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Key Personnel Changes/Previous PI:	V.V. Bogomolov is the Russian Co-PI for this investigation		
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Task Description:

Validation of On-Orbit Methodology for the Assessment of Cardiac Function and Changes in the Circulating Volume Using Ultrasound and Braslet-M Occlusion Cuffs (Braslet) is Station Development Test Objective (SDTO) 17011 sponsored by NASA and Russian Federal Space Agency (FSA). Braslet is testing the ability of ultrasound to detect cardiovascular changes in response to volume distribution changes that are induced by the Braslet occlusion cuffs. Understanding the effects of this countermeasure on cardiovascular function in a microgravity environment will be useful for both medical operations and future research.
See also https://

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

Space Applications
This SDTO will provide refinements in remote guidance techniques which will allow detailed ultrasound exams to be performed in space with remote guidance by technicians and physicians on the ground. This will enhance the diagnostic and research capabilities of the International Space Station (ISS) ultrasound. Data will also be collected regarding the utility and potentially expanded uses of the Braslet-M device for both ISS and exploration class missions. A more detailed understanding of the cardiovascular response to microgravity-induced fluid shifts will also be gained from this work.

Earth Applications

Refinements in remote guidance techniques provided by Braslet will similarly allow detailed ultrasound exams to be performed in terrestrial locations remote from experienced ultrasound technicians and physicians. Examples include rural clinics, disaster areas, and military applications. Additionally, during this SDTO data will be collected regarding the physiological responses to altered circulatory volume distribution which may lend insight to the diagnosis and treatment of terrestrial conditions (such as cardiovascular disease) which result in altered fluid status.

The Braslet SDTO was a limited in-flight investigation pursuing the development, testing, and validation of novel non-invasive methodologies for cardiovascular system evaluation in conditions of space flight with an emphasis on using Braslet-M device for hemodynamic modification. The objectives of this study were fully met:
• Non-invasive ultrasound measurement techniques for comprehensive cardiac and vascular evaluation were establish and validated

• A methodology was developed and validated to assess the circulating volume changes and cardiac function in space flight conditions, through short-term hemodynamic modification using Braslet-M occlusion cuffs

• The utility of Valsalva and Mueller respiratory maneuvers as means of modifying preload and afterload was verified as a technique to obtain additional functional information regarding the effect of Braslet and its clinical and scientific significance

• The tissue Doppler capability of the Human Research Facility (HRF) Ultrasound was activated and tested

The human body experiences significant volume shifts and reduction in venous reserve during extended exposure to microgravity. The cardiovascular system preserves effective circulating volume through standard homeostatic physiological response to reduced gravity. Therefore even though astronauts and cosmonauts are hypovolemic by terrestrial standards, they are euvolemic by space standards. This effect can be partially and acutely reverted towards terrestrial fluid distribution and overall hypovolemia through the use of Braslet.

The Braslet-M device, when used per the current calibration and directions, consistently causes fluid sequestration in the vascular bed of the lower extremities. This was demonstrated through the significant distention of venous reservoirs of lower extremities as detected by consistent increases in femoral vein cross-sectional area. This SDTO also demonstrated the effectiveness of the Braslet in temporarily reducing the effective circulating volume during space flight, as demonstrated by cardiac parameters which indicate a reduction in preload. Modified Valsalva and Mueller maneuvers resulted in measureable changes in hemodynamic distribution. Although many of these changes did not reach statistical significance, the trends were clear. Since breathing maneuvers were not tightly regulated or monitored, it is likely that the pressures created by these maneuvers varied from subject to subject, and even between individual data points within the same session. These variations in pressures may have resulted in a broader distribution of data points, precluding statistical conclusions in this relatively low n study. However, due to clear trends and several significant indicators in the data, a healthy individual’s volume status can be estimated by observing specific effects of the Braslet-M device on the effective circulating volume when respiratory maneuvers are performed.

Initially the team expected the internal jugular vein (IJV) to be a simple and reliable indicator of fluid status. While this is the case in most subjects, the variability in this data was large, perhaps due to the extreme compliance of this vessel. For example, simple actions such as speaking during scanning sessions resulted in large changes in the IJV area. The IJV is near maximal distention in chronic microgravity environments. The trends in the data indicate that Braslet relieved much of the excess cephalic fluid load and allowed a broader range of venous areas. While not achieving statistical significance, this is an excellent example of the synergy of fluid sequestration by Braslet superimposed with breathing maneuvers to broaden the range of sensitivity.

This SDTO demonstrated that minimal crew training, combined with just-in-time on-orbit training and remote expert guidance, can be successfully used to complete complex medical diagnostic tasks such as advanced ultrasound examinations. Ultrasound was rapidly and accurately performed by all crewmember operators in a number of specific applications which have direct operational relevance to current and future missions and would provide direct, important medical information to impact the diagnosis and treatment of in-flight medical conditions. The expanded ultrasound applications described and performed for this SDTO are also relevant to space medical and physiologic research. Minimal resources, training, and crew time were required to complete these complex tasks; this should serve as a successful model for future space flight operations and experiments. Elements of general telemedicine, training, and scanning techniques developed and refined during this SDTO are already being incorporated into routine medical operations. Specific elements of vascular scanning and fluid shift alterations may be used in the near future to address pressing crew health questions related to intracranial hypertension.

Task Progress:	The Braslet device has potential medical application due to its mechanism of action. Pulmonary edema secondary to left ventricular failure is caused by increased pulmonary venous pressure and ensuing interstitial edema. Nitroglycerin acts through the release of nitrous oxide and its effect is modulated by vascular endothelial superoxide levels, to relax vascular smooth muscle. The principal benefit of these changes is to decrease systemic vascular resistance, increase venous compliance, decrease pulmonary capillary wedge pressure and mean arterial pressure, which should relieve cardiac-induced pulmonary edema. Given the microgravity-induced cephalad fluid shifts and the changes in lower-extremity intravascular volume, the use of common venodilators such as nitroglycerin may not be as efficacious in the immediate treatment of pulmonary edema. It is known that rotating tourniquets or thigh cuffs induce lower extremity venous pooling and reduce the circulating blood volume, which reduces left ventricular end-diastolic pressure. This investigation showed that the Braslet thigh cuffs impede lower-extremity venous return but not arterial flow. A device like the Braslet can be used to treat congestive heart failure and orthopnea in many parts of the world as well as in reduced gravity environments. While Braslet imparts a physical effect as opposed to a pharmaceutical effect, the effective dose can still be estimated by measuring the constraining effect with the resultant fluid sequestration and cardiovascular effect. This relationship is not well understood for Braslet, and is being currently being researched under the “Braslet Investigation Grant” (NSBRI--National Space Biomedical Research Institute--PI Scott Dulchavsky). Load-dependent echo measurements such as spectral flow Doppler through the mitral valve measure blood flow into the left ventricle during early and late diastole. This mitral valve inflow also reflects changes to the load on the left ventricle. Mitral inflow Doppler is a load-dependent parameter and decreases in response to reduced preload. By manipulating preload with Braslet and Mueller respiratory maneuvers, a reduction in preload can be measured as lower velocities and extended relaxation slopes in the mitral valve waveform. This inflow pattern demonstrates the effect of the Braslet. Tissue Doppler (TD), unlike the spectral inflow Doppler, is a relatively independent loading parameter used in echocardiography. The myocardial performance index (sometimes referred to as Tei index) is calculated using diastolic and systolic time intervals as a combined measure of myocardial performance (IVCT+IVRT/ET). The Tei index is a simple and feasible indicator of overall ventricular function. In this study Tei was calculated from the time indices of both the right ventricular (RV) TD and left ventricular TD. Normal terrestrial Tei indices in the RV are < 0.3, while the data collected in microgravity during this SDTO show that all but one subject are consistently above this level. It is hypothesized that this is a result of chronic exposure to microgravity resulting in transiently increased right ventricle pressure or left atrial pressures. However it is not yet clear what this finding means, as the Tei index has been traditionally considered a relatively load-independent parameter. It is interesting to note that application of Braslet does reduce the RV Tei index, indicating a shift toward terrestrial fluid distribution and cardiac performance presumably as a result of reduction to the effective circulating volume. In a microgravity-adapted crewmember, reduction in circulating volume brings central and cephalic fluid status closer to that seen terrestrially. LV E’ (left ventricular velocity) was significantly reduced during all maneuvers when Braslet was applied. The data therefore suggest that this is a repeatable and reliable means to assess volume status change on the order of that induced by Braslet. This measure is, however, less sensitive to the smaller and more acute changes induced by the breathing maneuvers. Mueller maneuver with Braslet on caused a profound decrease in RV IVRT which may be due to significantly reduced preload secondary to a reduced effective circulating volume. This is further seen in the trend of reduced Tei index during Mueller maneuvers, even with Braslet off. These findings are consistent with a supine patient on Earth who is hypovolemic. This indicates that Braslet causes the expected fluid sequestration in the lower extremities, which is clearly reflected in echocardiographic parameters. Previously, the effect of acute volume change to the RV was unknown in any group of long duration astronauts. Hemodynamic manipulation with the Braslet-M as a tool for assessing RV physiology in space proved to be a useful non-invasive evaluation of RV function using the on-board ISS ultrasound. Further understanding of RV function could be significant to long duration crewmember cardiac health and requires additional review. This study revealed a small but useful reference data set for future clinical and research studies in echocardiography. In Conclusion: • Remotely guided ultrasound is an effective and objective means of measuring fluid status changes, including the physiological effects of Braslet. • The Braslet device reduces the effective circulating volume. • Valsalva and Mueller respiratory maneuvers augment the physiologic responses to fluid sequestration. • Tissue Doppler is a reliable and sensitive tool for assessing fluid status changes, particularly the LV E’ parameter.
Bibliography Type:	Description: (Last Updated: 08/30/2018)
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