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Project Title:	Monitoring Biomarkers for Muscular Atrophy Using Nanoelectronic Chip for Astronaut Health		
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Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	TRISH
Contact Monitor:		**Contact Phone:**	
Contact Email:			
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Task Description:	POSTDOCTORAL FELLOWSHIP Skeletal muscle atrophy is a serious health problem for astronauts in long-duration spaceflight under microgravity conditions. Current preventative measures and treatments against muscle atrophy require intense exercise and dietary regimens. Preemptive measurements during the onset of muscle atrophy have the potential to streamline these regimens, decreasing their daily footprint and increasing the quality of life for astronauts. The objective of our proposed project is to (1) develop a fully integrated disposable nanoelectrode array chip (with the size of a stamp) that can be interfaced with a handheld electronic system for simultaneous detection of the a panel of biomarkers to monitor the progression of skeletal muscle atrophy due to disuse under microgravity in long-duration spaceflights; and (2) use such quantitative information to guide the combined countermeasures of physical exercise and pharmaceuticals (i.e., specific protease inhibitors) so that the intensity, duration, and frequency of exercise can be reduced. The target biomarkers for this research is enzymatic proteases. These proteases have shown to be overexpressed for many illnesses including cancer, human immunodeficiency virus (HIV) and muscular atrophy, and operate by cleaving peptide sequences, effectively destroying critical biological proteins, such as muscle tissues. Monitoring protease biomarkers can serve as a critical early diagnostic tool for conditions specific to long term travel in microgravity. Several key factors currently limit similar healthcare diagnostics during long duration spaceflights. Instrumentation must have a small footprint, minimal power consumption and must be simple enough for untrained users to operate without accurately. Electrochemical sensors, such as the blood glucose monitor, have shown to be robust with a small instrumental footprint. To further decrease this footprint, we will use nanopatterned chips integrated to a microfluidic system to decrease the required amount of sample, minimizing the impact on the user. We will use this nanopatterned sensor to profile protease biomarkers known to be relevant to muscular atrophy and test the technique in analogs for human urine. To facilitate these measurements, we will use electrodes decorated with carbon nanofiber arrays, which have been previously shown to function in complex biological media. This approach to sample collection and measurement will allow for non-invasive sample collection and will remove the need for additional chemical reagents, further decreasing the footprint of the technique. Additionally, we will use this method to demonstrate the effectiveness of protease inhibitors, which may potentially serve as pharmaceutical treatments, further decreasing the need for extensive exercise regimes and dietary restrictions.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Skeletal muscle atrophy is among the most serious physiological concerns for long-term space travel and habitation. Countermeasures for muscle atrophy in microgravity conditions include exercise regimens, which can last up several hours per day. Daily monitoring of muscle atrophy progression has the potential to guide exercise regimens and pharmaceutical interventions to reduce the impact on daily life, potentially improving efficiency as well as crew morale. The atrophy process involves a decrease in the rate of muscle cell protein synthesis accompanied by an increase in the rate of protein degradation and apoptosis of various muscle components. Protease enzymes are key to the degradation of existing muscle tissue. Consequently, an early indicator of the onset of physiological muscle atrophy processes is increased activity of protease enzymes. A protease sensor will drastically improve capabilities for crew health monitoring by allowing real-time assessment of muscle atrophy progression and providing a framework for personalized countermeasures. Current techniques for monitoring proteases can only measure one protease at a time and require extensive sample processing in a laboratory environment. Most of these techniques detect the combined concentration of active and inactive proteases, which may not accurately represent physiological performance of the protease. This limitation can be addressed by measuring the activities of the protease enzymes, which accounts for reactivity and concentration of a specific protease. Keeping this goal in mind, we have developed a multiplexed gold microelectrode array sensor for quantifying protease activity. We have subsequently demonstrated this sensor’s applicability for multiplex detection of protease activity. We have developed hardware, fitting algorithms, and data processing scripts to demonstrate the multiplexing capabilities of this sensor array and the accompanying assay. Results and data processing can be obtained in less than one hour with minimal sample processing. This sensor can be used to establish a baseline for protease activity for an individual. Once the baseline has been established, continuous monitoring will be able to detect increases in protease activity prior to the molecular breakdown of muscle tissue. Furthermore, the resulting data can be used to guide preventative measures and treatments; thereby, reducing the risks to long term space habitation. We anticipate that the application of this technology will improve astronaut health, quality of life and, importantly, crew morale.
	The goal of this project is to conduct ground-based and International Space Station (ISS) in-flight evaluation of new ultrasound transducer ("ultrasound on a chip") technology coupled with artificial intelligence (AI) solutions to validate their operational usability in astronaut care, including flight, and their innovation potential for operational medical support across all phases of ISS missions. The novel ultra-portable imaging device prototype represents significant innovation for both short- and long-term needs of operational space medicine. The previously unavailable transducer technology allows using one probe for all imaging applications. Importantly, the device is based on the philosophy of continued development, expansion of "smart" features, novice operator-friendly features, and use of cloud-based resources with upgradeability through software and firmware evolution. The device is Digital Imaging and Communications in Medicine (DICOM)-compliant and Food and Drug Administration (FDA)-approved. Thus, the potential benefits identified by this proposal are: • Concept of operations with near-instantaneous availability of imaging technology, connectivity, and streamlined data handling; • Ultra-portability and small footprint (mass, power, volume) with single-probe solution for all imaging needs; • Deep learning-based tools with automatic target recognition and operator assistance; upgradeability of firmware and software; • Preset-based, intuitive operation supporting non-medical operators, yet offering multiple imaging applications pertinent to space medicine; • Resource savings. The investigation team is in the process of analyzing data. According to preliminary review of data, this device can serve as an excellent basis for further development and optimization. The approach entirely aligns with the concept of developing autonomous healthcare capabilities in conditions of exploration flight under conditions of multiple

Task Progress:	constraints, including absent real-time communications with Earth. In the original proposal the investigation team has proposed to: 1) Select a high-Technology Readiness Level (TRL), DICOM-compliant commercial off-the-shelf (COTS) ultrasound system, with a new single-probe imaging technology, advanced data management with upgradeable deep learning-based solutions, intuitive user interface, and connectivity. The Butterfly iQ (iQ) system (Butterfly Network Inc., N.Y., N.Y.), which has been FDA-cleared and available since 2018, is the only device on the market to meet the above criteria. Most of its features are not available in any single device in the market. 2) Acquire iQ (2 units), other necessary equipment, and supplies for ground-based evaluation (Phase 1). 3) Perform a ground-based evaluation of iQ (Phase 1). a. Review hardware and electronics, interfaces, and operating functionality through analysis of manufacturer-provided specifications and testing data; b. Test the iQ (all units) using an approved quality assurance phantom, in parallel with a full-featured device for comparison purposes (GE VividQ or similar, i.e., ISS Ultrasound 2), including assessment of: contrast resolution at multiple depths; axial, lateral, and elevational resolution; penetration depth; and others features. c. Perform standardized multi-target imaging tests in human subjects by two trained sonography specialists (Ultrasound subject matter experts/SMEs) in ten (10) human subjects (human-in-the-loop engineering evaluation with appropriate NASA Institutional Review Board/IRB approval). These tests will be duplicated with a full-featured system (similar to the current ISS Ultrasound 2) for comparison. Testing will be used to assess: • general usability and human factors; • image fidelity and limitations at three different depth ranges; • comparison of iQ with a full-featured system similar or identical to ISS Ultrasound 2. d. Perform standardized imaging tests and comparison with full-featured portable systems, by point-of-care ultrasound (POCUS) SME physician(s) using POCUS protocols (Focused Assessment with Sonography in Trauma/FAST exam and lung ultrasound protocol) in 5 (five) human subjects (human-in-the-loop engineering evaluation, with appropriate NASA approval), and ultrasound-guided vascular access using a COTS ultrasound-guided vascular access phantom. e. Assess effectiveness of remote guidance, using image streaming if available at the time of this evaluation. Non-Disclosure Agreement (NDA) and additional coordination with the Manufacturer for access to pre-release software may be required. If feasible, this will be performed by using novice operators in a limited scanning test in 5 (five) human subjects (human-in-the-loop engineering evaluation). f. Test effectiveness of AI solutions with novice operators using 10 human subjects (human-in-the-loop engineering evaluation) and observed by Ultrasound SMEs. 4) Develop the analysis framework and perform analysis of imagery, formalized ratings, comments, and observations from all assessments and imaging tests (#3: a-f, above) by ultrasound SMEs with determination of appropriateness of iQ as a prototype for NASA human health and performance capability. 5) Prepare a Ground-Based Evaluation (Phase 1) Report. Presentation of results to TRISH and appropriate NASA organizations/boards. In addition to the original goals and objectives, the team has initiated and advanced in the preparations for a technology demonstration of the iQ device using ISS as a technology development testbed. This activity is approved through a Supplement to the proposal, which sets a goal to demonstrate functionality and usability of an ultra-portable ultrasound system (Butterfly iQ, Butterfly Network, USA) aboard the ISS in a technology demonstration. At the time of this interim report, all data collection activities have been completed, and the team has started developing the data analysis framework and outlining the Final Report. Early findings of the investigation, which appear to be favorable, have been shared with the aerospace medicine community through interim reports to TRISH, as well as through presentations at appropriate NASA and public forums.
Bibliography Type:	Description: (Last Updated: 04/09/2022)
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