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| **Fiscal Year:** | FY 2012 | **Task Last Updated:** | FY 03/27/2013 |
| **PI Name:** | Clarke, Mark Ph.D. | | |
| **Project Title:** | Monitoring of Bone Loss Biomarkers in Human Sweat: A Non-Invasive, Time Efficient Means of Monitoring Bone Resorption Markers under Micro and Partial Gravity Loading Conditions | | |
| **Division Name:** | Human Research | | |
| **Program/Discipline:** | HUMAN RESEARCH | | |
| **Program/Discipline--Element/Subdiscipline:** | HUMAN RESEARCH--Biomedical countermeasures | | |
| **Joint Agency Name:** | | **TechPort:** | Yes |
| **Human Research Program Elements:** | (1) **HHC**:Human Health Countermeasures | | |
| **Human Research Program Risks:** | (1) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone<br>(2) **Osteo**:Risk Of Early Onset Osteoporosis Due To Spaceflight | | |
| **Space Biology Element:** | None | | |
| **Space Biology Cross-Element Discipline:** | None | | |
| **Space Biology Special Category:** | None | | |
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| **City:** | Houston | **State:** | TX |
| **Zip Code:** | 77204 | **Congressional District:** | 18 |
| **Comments:** | | | |
| **Project Type:** | Ground | **Solicitation / Funding Source:** | 2007 Crew Health NNJ07ZSA002N |
| **Start Date:** | 05/20/2008 | **End Date:** | 05/20/2012 |
| **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:** | 1 | **No. of Bachelor's Degrees:** | 0 |
| **No. of Bachelor's Candidates:** | 0 | **Monitoring Center:** | NASA JSC |
| **Contact Monitor:** | Maher, Jacilyn | **Contact Phone:** | |
| **Contact Email:** | jacilyn.maher56@nasa.gov | | |
| **Flight Program:** | | | |
| **Flight Assignment:** | NOTE: End date is now 5/20/2012 (Ed., 11/14/2011)<br>NOTE: New end date is 11/20/2011 per NSSC information (Ed., 5/31/2011) | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | O'Connor, Dan ( University of Houston ) | | |
| **Grant/Contract No.:** | NNX08AQ37G | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |

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| **Task Description:** | We propose to validate that the rate and extent of unloading-induced bone loss in humans can be assessed by monitoring the levels of two bone resorption markers in sweat, namely ionized calcium and collagen break-down products. Initial testing will be carried out in a young healthy population (at rest and during activity) and then in a clinical population undergoing active bone loss, namely spinal cord injury patients. All groups will include both male and female participants. Biomarker concentration will be determined in contemporaneous samples of sweat, blood, and urine collected during both short (24 hr) and long-term studies (multiple sessions over a period of months) to define the relationship between biomarker levels in the respective biological samples. Several different sweat collection techniques will be investigated to determine the most appropriate and efficient means of sample collection suitable for deployment during a space flight mission. These experiments will also include investigation of the most appropriate biomarker analysis techniques that allow for future deployment in micro- or partial gravity environments. This near-real-time monitoring approach may also provide the information required to justify modifying an ineffective bone loss countermeasure prescription during a mission. One of the approaches tested will be a novel, micro-fabricated fluid collection capillary array, known as the micro-fabricated sweat patch (MSP) device, specifically developed for use in microgravity. The MSP technology was initially developed because of its potential to become an autonomous, solid-state collection/analysis device worn on the skin of an astronaut requiring little or no crew interaction to perform its monitoring function. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | Loss of bone mass, density, and structural integrity is a significant health risk in a variety of populations such as the elderly, post-menopausal women, young female athletes, and astronauts. Such changes in overall bone quality lead to a greater risk of bone fracture and potentially a reduced rate of bone healing after injury. The ability to monitor biomarkers of bone remodeling (e.g., ionized calcium, collagen cross links) using sweat as an analytical sample provides an attractive alternative to the more invasive and costly measures presently employed such as a bone density scans by dual-energy X-ray absorptiometry (DXA), 24 hour urine collection protocols, or whole blood analyses. The development of a non-invasive, skin-mounted monitoring device which allows the quantitation of ionized calcium and/or collagen cross links in sweat will allow bone loss to be monitored in a wide variety of terrestrial populations that to date have not easily been monitored outside of a clinical setting. This particular project focuses on validating the concept that sweat analysis can be used as a non-invasive means of monitoring bone loss in crew members during periods of mechanical unloading under altered gravitational conditions. In addition, this project is also investigating the best technical approach to collecting a sweat sample which is specifically applicable to the space flight environment while utilizing well-accepted, clinically validated analytical methods. Development of a technology capable of real-time monitoring of biomarkers of bone loss that satisfies the criteria required for use in the space flight environment (i.e., non-invasive/non-intrusive, passive, small, light-weight, low power) has many direct applications in various populations here on Earth. |
| **Task Progress:** | The overall goal of this project was to validate the concept that the rate and extent of unloading-induced bone loss in humans can be assessed by monitoring the levels of two bone resorption markers in sweat, namely ionized calcium ($Ca^{2+}$) and total collagen cross-links (T-CCL) (i.e., the pyridinium cross-links PYD & DPD) The original funded project plan called for a phased approach consisting of three phases; the first phase focused on selection of the most appropriate and efficient means of collecting a sweat sample from an individual compatible with the microgravity environment of space flight coupled with biochemical validation that these sweat samples contained bone resorption markers at levels capable of being detected using standard laboratory analysis techniques; the second phase focused on validation of the concept that bone resorption marker levels detected in sweat samples accurately and consistently reflected circulating levels and/or urine levels of these biomarkers; and the third phase focused on longitudinal assessment of bone resorption marker level in sweat, blood, and urine in young and old populations undergoing active bone formation or bone loss, respectively.<br>After successful completion of Phase I, preliminary data generated during Phase II indicated that the NASA criterion measure for bone loss during space flight (i.e., 24 hr urinary ionized calcium excretion), while related to calcium and T-CCL levels in sweat samples actively produced during defined exercise, were not predictive of 24 hr urine calcium excretion rates. After consultation and review of the preliminary Phase II results by representatives of the NASA-Johsnon Space Center-Human Research Program (JSC-HRP), the focus of Phase II was redirected to explore collection of a 24 hr sweat sample, rather than collection of a discrete, exercise-induced “active” sweat sample, to determine if a 24 hr integrated sweat sample was predictive of biomarker concentrations found in 24 hr urine samples. This redirection of effort required the identification and validation of additional commercially available absorbant materials which did not contain endogenous biomarker signal as well as a means of extracting the biomarkers from the absorbant material compatible with fluid handling limitations in the space flight environment. After identifying and developing such a collection method, this approach was then utilized to answer the question of whether or not biomarker levels in an integrated 24 hr sweat sample was predictive of those found in a concurrent 24 hr urine sample in a convenience of healthy individuals.<br><br>After successful completion of Phase II, the NASA-JSC-HRP program indicated that they wished to deploy the sweat monitoring technology in a NASA bed-rest campaigns being performed at the GCRC at University of Texas Medical Branch (UTMB) instead of in young and old subject populations as originally planned. Unfortunately however, during the last 9 months of the project NASA had to postpone bed-rest operations resulting in a joint decision by NASA-HRP and the Principal Investigator to utilize spinal-injured patients recruited from the Texas Medical Center (rather than NASA bed rest subjects) in which to test the 24 hr sweat monitoring technology as means of assessing bone loss. The resulting time delay surrounding availability of bed rest subjects and the subsequent decision to utilize spinal chord injury (SCI) patients, coupled with the additional requirement to seek Committee for the Protection of Human Subjects (CPHS) approval for testing in a new subject population resulted in NASA granting a one year no-cost extension to the project. Limited data gathered in the final year of the project provides evidence that biomarker levels in a 24 hr integrated sweat sample are predictive of those levels found in 24 hr urine samples in SCI patients. These data indicate that 24 hr sweat sample collection (using a collection and analysis scheme compatible with space flight operations) in a terrestrial human population undergoing active bone loss in a similar fashion to crew members during space flight is a non-invasive, time-efficient alternative to on-orbit 24 hr urine void collection as means of assessing biomarkers of bone loss. In addition, the ability to perform this type of sample collection using a microgravity compatible approach to liquid sample handling and the use of simple colorimetric based analysis techniques is of notable operational relevancy. Our data and validated methodologies suggest that sweat biomarker analysis (as an operationally compatible means of assessing and/or monitoring bone loss in crew members during space flight) should be considered for further |

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| | development as a “real-time” analytical method for assessment of space flight-induced bone loss and a valid means of monitoring the efficacy of “in-flight” bone loss countermeasures.<br><br>[Editor's note 3/27/2013: No Task Book report received. Progress section and Bibliography compiled from PI's Final Technical Report submitted January 2013] |
| **Bibliography Type:** | Description: (Last Updated: 03/08/2018) |
| **Abstracts for Journals and Proceedings** | Clarke MS, Babcock LW, Diak D, O'Connor DP. "Sweat Analysis for Assessment of Bone Loss Biomarkers." 2012 NASA Human Research Program Investigators’ Workshop, Houston, TX, February 14-16, 2012.<br>2012 NASA Human Research Program Investigators’ Workshop, Houston, TX, February 14-16, 2012. , Feb-2012 |
| **Abstracts for Journals and Proceedings** | Clarke MS, Knoblauch MA, O'Connor DP. "Monitoring Biomarkers of Bone Loss in Human Sweat." 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011.<br>18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011. , Apr-2011 |
| **Abstracts for Journals and Proceedings** | Clarke MS, Knoblauch MA, O'Connor DL. "Sweat and Biomarkers --can sweat be used to monitor biomarkers of bone loss?" 2010 NASA Human Research Program Investigators’ Workshop, Houston, TX, February 3-5, 2010.<br>2010 NASA Human Research Program Investigators’ Workshop, Houston, TX, February 3-5, 2010. , Feb-2010 |
| **Abstracts for Journals and Proceedings** | Clarke MS, Knoblauch MA, O'Connor DL. "Monitoring of biomarkers of bone loss in human sweat - a non-invasive, time efficient means of monitoring bone resorption markers under micro- and partial gravity loading conditions." 2009 NASA Human Research Program Investigators’ Workshop, League City, TX, February 2-4, 2009.<br>2009 NASA Human Research Program Investigators’ Workshop, League City, TX, February 2-4, 2009. , Feb-2009 |
| **NASA Technical Documents** | Clarke MS, Feeback DL. "Microgravity-Compatible Sweat Collection and Analysis Device." MSC-23625-1 NASA Tech Briefs. , Jul-2011 |