Fiscal Year:	FY 2021	**Task Last Updated:**	FY 12/04/2021
PI Name:	Buckey, Jay C. M.D.		
Project Title:	Ultra-Compact Device for Monitoring Bone Loss and Kidney Stone Risk		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **ExMC**:Exploration Medical Capabilities		
Human Research Program Risks:	None		
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:**	2018 HERO 80JSC018N0001-Crew Health and Performance (FLAGSHIP, OMNIBUS). Appendix A-Flagship, Appendix B-Omnibus
Start Date:	09/01/2019	**End Date:**	08/31/2021
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Lemery, Jay	**Contact Phone:**	
Contact Email:	jay.lemery@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	Principal Investigator (PI) Jay Buckey, MD, became the main PI when the project started; original PI in the proposal was Aleksandra Stankovic, PhD.		
COI Name (Institution):	Phillips, Scott Ph.D. (Creare LLC) Knaus, Darin Ph.D. (Creare LLC)		
Grant/Contract No.:	80NSSC19K1632		
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Task Description:	Slowing bone loss and preventing kidney stone formation are critical for successful spaceflight. The capability to track bone loss and kidney stone risk while in space would provide the ability to track these risks directly and individualize the countermeasure program as needed. At present, post-flight measurements are used to establish the effectiveness of the in-flight bone loss/kidney stone prevention program. A preventive approach would be preferable, where ongoing in-flight measurements of countermeasure effectiveness allow for adjustments in the countermeasure program during the flight. Urinary calcium excretion is a reliable marker of bone loss and kidney stone formation risk. Urinary calcium excretion is often measured with a 24-hour urinary collection, but measuring just the calcium concentration in the first void of the day provides similar information to a 24-hour collection. Spot measurements of urinary calcium taken when an astronaut is voiding anyway, could provide key operational information with minimal impact on crew time, power, or stowage. The goal of this project is to provide an ultra-compact, robust, urinary calcium measurement system that could be used in space to assess whether urinary calcium levels are increasing inflight to a point where action is needed. We plan to measure urinary calcium concentration fluorimetrically using the fluorescent tracer calcein. The same robust assay was implemented in space during the Biosatellite 3 primate flight. Calcium binds with calcein to form a fluorescing complex and the magnitude of the fluorescence signal is proportional to calcium concentration for calcium-calcein mixtures. Urinary calcium is typically measured clinically using a clinical chemistry analyzer with colorimetric indicators. For spaceflight, fluorometry is preferred because the instrumentation can be extremely compact and simple. Laboratory chemical assays typically involve either significant disposables or washing of labware. In space, neither is desirable. We plan to develop an assay with an ultra-compact disposable based on a small capillary tube with the calcein reagent coated onto the interior wall of the capillary tube. Urine will be drawn into the tube using a sampling adapter on the urine funnel. The capillary tube, containing a fixed amount of urine and reagent, will then be inserted into a compact handheld fluorimeter to measure urinary calcium concentration. The proposed technology could provide a small, practical, in flight capability to monitor for bone loss and offer data on kidney stone risk.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Urinary calcium monitoring is important for kidney stone prevention and for tracking the effects of drugs for osteoporosis.
Task Progress:	At present, post-flight measurements are used to establish the effectiveness of the spaceflight bone loss and kidney stone prevention program. A preventive approach would be preferable, where ongoing in-flight measurements provide feedback on countermeasure effectiveness, allowing for adjustments in the countermeasure program during flight. Urinary calcium excretion is a reliable indicator of bone loss and kidney stone formation risk and is relatively easy to quantify. Urinary calcium levels increase profoundly in space. Recorded concentrations from the Skylab mission have shown 2-to-4-fold increases relative to preflight baselines. Urinary calcium excretion in clinical labs is often measured by collecting urine over a 24-hour period, but calcium concentration measurements taken from just the first void of the day provide similar information. Additionally, spot measurements of urinary calcium taken when an astronaut is voiding throughout the day provide key operational information with minimal impact on crew time, power, or stowage. We developed a device that measures urinary calcium concentration fluorimetrically using the marker calcein. Calcium binds with calcein to form a fluorescing complex, and the magnitude of the fluorescence signal is proportional to the calcium concentration of the sample. The assay we developed uses an ultra-compact disposable assay: a small capillary tube (an optrode) with a fixed amount of calcein reagent coated onto the interior wall. 20 uL of urine is drawn into the capillary tube which is then inserted into a compact handheld fluorimeter to measure urinary calcium concentration. The device reports the optical signal as a voltage on its LCD display, which can then be converted to the equivalent calcium concentration based on a calibration fit. In this study, the prototype fluorometer and optrode system were tested on urine samples to assess accuracy. 42 volunteers were recruited into the study and provided urine samples. Each urine sample was analyzed using a hospital clinical analyzer (Roche Cobas) for urinary calcium and urinary magnesium concentration and with the prototype for urinary calcium concentration. Using samples from the first 22 participants, we determined the correlation between the hospital analyzer and our prototype device to be R2=0.79 when excluding samples with high magnesium outliers (those greater than 120 mg/L magnesium concentration). Without excluding outliers, the correlation drops to 0.55. Magnesium reduces the accuracy of the prototype by interfering with the creation of calcein-calcium fluorescing complex. The intensity of the calcein-calcium fluorescence is the basis of the device reported urinary calcium concentration value. Magnesium interference can be suppressed by alkalizing the binding environment. With the remaining 20 samples, we carefully alkalized the urine samples to a pH of 13.5 before measuring with the prototype. With this adjusted method the correlation improved from 0.55 to 0.67 when including all samples. With high magnesium outliers removed, correlation was R2=0.78, a level similar to before implementing the careful alkalizing procedure. From our correlation analysis, we have noticed that the prototype device tends to read lower than the clinical analyzer. In a highly alkaline environment, calcium may precipitate out of the solution and can suppress the device reading. In the Biosatellite missions where a similar technology was used, potassium citrate was used to prevent precipitation of calcium. We studied the effect of potassium citrate and did not see a dramatic improvement with the addition of this reagent. Overall, the study showed a good correlation between the calcium measurements from the optrode and from the clinical analyzer (R2=0.79). The main issue is measurement range. Device accuracy improvements can be gained by extending the linear range of the device to minimize or remove the need to dilute the sample to within the current measurable range of the device. This can be accomplished by loading more reagent into the capillary tubes, or to manufacture different capillary tubes for different concentration ranges (e.g., tubes for the 0-30 mg/L range, tubes for the 30-60 mg/L range).
Bibliography Type:	Description: (Last Updated: 05/20/2025)
Abstracts for Journals and Proceedings	Lan L, Knaus DA, Devoy C, Phillips SD, Fellows AM, Buckey JC. "Ultra-Compact Device for Monitoring Bone Loss and Kidney Stone Risk." Presented at the 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021

Articles in Peer-reviewed Journals	Thamer S, Buckey JC Jr. "First void urinary calcium for tracking bone loss and kidney stone risk in space." Aerosp Med Hum Perform. 2022 Jul;93(7):546-50. https://doi.org/10.3357/AMHP.5979.2022 ; PMID: 35859310 , Jul-2022