Fiscal Year:	FY 2011	**Task Last Updated:**	FY 07/05/2011
PI Name:	Anbar, Ariel Ph.D.		
Project Title:	Rapid measurements of bone loss using tracer-less calcium isotope analysis of blood and urine		
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 (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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Zip Code:	85287	**Congressional District:**	9
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2007 Crew Health NNJ07ZSA002N
Start Date:	05/20/2008	**End Date:**	03/19/2013
No. of Post Docs:		**No. of PhD Degrees:**	1
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
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Flight Program:			
Flight Assignment:	NOTE: Received extension to 3/19/2013 per NSSC (Ed., 5/8/2012) NOTE: Received extension to 5/19/2012 per C. Guidry/JSC and NSSC [Ed. 3/2/2011]		
Key Personnel Changes/Previous PI:	None		
COI Name (Institution):	Skulan, Jospeh (University of Wisconsin-Madison Geology Museum) Smith, Scott (Human Adaptation and Countermeasures Division) Bullen, Thomas (USGS)		
Grant/Contract No.:	NNX08AQ36G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	We propose to develop a method to rapidly detect changes in bone mineral balance by measuring the natural (i.e., tracer-less) isotope composition of calcium in blood and/or urine. This method would provide a way to detect incipient bone loss before changes in bone density are detectable by conventional X-Ray methods. The resorption of bone when astronauts are exposed to microgravity is a major challenge for NASA's plans for human exploration of the Moon and Mars. Our proposed technique would be immediately valuable in ground-based studies of countermeasure strategies, accelerating the pace of discovery of countermeasures to bone loss. In the long run, flight-qualified versions of mass spectrometric or other systems for Ca isotope characterization could accompany astronauts on long-duration missions. Precise measurements of the calcium isotope composition in blood or urine provide information about bone mineral balance because the isotopic composition of calcium in human soft tissues is naturally affected by the relative rates of bone formation and resorption. Specifically, lighter calcium isotopes are preferentially incorporated into bone during formation. Because of the short residence time of calcium in soft tissues, calcium isotope ratios should change rapidly in response to changes bone gain or loss. These changes, while small, can be measured by multiple collector inductively coupled plasma mass spectrometry (MC-ICP-MS) or thermal ionization mass spectrometry (TIMS). The proposal team recently demonstrated the promise of this method in a published pilot study in which we measured calcium isotopes in a small suite of urine samples from a bed rest study. Here, we propose an expanded examination of bed rest samples, involving a larger number of subjects, measurements of blood and dietary samples as well as urine, and daily or even sub-daily sampling. This research would address critical questions unresolved by the pilot study.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	We are developing a technique that uses analyses of natural variations in the calcium isotope composition of urine, blood and other biological materials to measure changes in bone mineral balance. The focus of this research is detecting bone loss resulting from skeletal unloading in the microgravity of space, but our technique is equally applicable wherever disruptions in bone mineral balance are an issue. Ca isotope analysis may provide a way of detecting incipient bone loss before it has produced any measurable change in bone mineral density, and long before it has progressed to osteopenia or osteoporosis. Because soft tissue Ca isotope composition changes very rapidly in response to changes in bone mineral balance, our technique also may be used to rapidly assess the effectiveness of treatments designed to alter bone mineral balance, greatly accelerating the pace of discovery of new treatments for metabolic bone diseases such as osteoporosis.
Task Progress:	During the past year our efforts have progressed from methods development to the isotopic analysis of urine, blood and food samples from a 12 subject, 30 day bed rest study conducted between October, 2009 and May 2010 at the General Clinical Research Center (GCRC) at the University of Texas Medical Branch in Galveston. Although the bulk of blood and urine samples have not yet been analyzed, Ca isotopic measurements have been made of a full 44 day (30 days of bed rest plus one week preceding and following bed rest) time series of urine samples from all 12 subjects. These data confirm the central premise of our research, that Ca isotope ratios in urine change in response to changes in bone mineral balance (BMB). More specifically, we conclude that 1. Urine Ca becomes isotopically lighter 5 to 7 days after the start of bed rest. This change in Ca isotope composition is highly statistically significant, and probably reflects the initiation of negative BMB in response to bed rest. N-telepeptide (NTx), a biochemical marker of bone resorption, also increases sharply at 5 to 7 days; bone specific alkaline phosphatase (BSAP), a marker of bone formation, does not change. 2. Background variation, as measured by day-to-day changes in urinary Ca isotope composition of 24 hour urine pools for each subject, in subjects prior to the start of bed rest, is only about half as large as the change that that we attribute to the onset of bone loss. This demonstrates that under conditions of bed rest the Ca isotopic signal of bone loss is not swamped by background ‘noise’ from factors other than bone loss that might affect the Ca isotope composition of urine. 3. Void-by-void urine sampling was conducted on all subjects before or after the bed rest period. This high density sampling was used to detect possible diurnal changes in urinary Ca isotope composition, and to document the magnitude of intra-subject background variation in isotope composition. Only a fraction of these samples have been analyzed, but initial data show no evidence of a diurnal cycle, and indicate that variation in urinary Ca isotope composition over the course of a day is no greater than the day to day variation between 24 hour pooled urine samples. 4. Using published estimates of the magnitude of change in Ca isotope composition occurring during bone mineral formation we estimate that the change in urinary Ca isotope composition observed during bed rest reflects a bone mineral loss rate of about 6%/year. This estimate agrees well with radiometric measurements of bone loss in bed rest. On the basis of the preceding we conclude bone loss typically observed in spaceflight should be easily resolvable using the Ca isotope technique. The success of countermeasures to bone loss also should be reflected in urinary Ca isotope composition. Over the next year we will complete the analysis of samples from the 30 day bed rest study. These additional analyses will allow us to determine how well urine tracks changes in Ca isotope composition, to measure the effect of changes in dietary Ca isotope composition on that of urine and blood, and to better constrain the magnitude of background variation in the Ca isotope compositions of urine and blood.
Bibliography Type:	Description: (Last Updated: 10/09/2019)
Abstracts for Journals and Proceedings	Morgan JLL, Abbott DH, Anbar AD, Gordon G, Skulan JL, Colman RJ. "Rapid Changes in Bone Mineral Balance in Response to Estrogen Depletion in Rhesus Monkeys Detected Using Tracer-less Calcium Stable Isotope Technique." Presented at the 92nd meeting of The Endocrine Society, San Diego, California, June 19-22, 2010. Endocrine Reviews, 2010 Jun;31(3 Suppl 1):S1071. , Jun-2010