Fiscal Year:	FY 2014	**Task Last Updated:**	FY 01/27/2014
PI Name:	Sibonga, Jean Ph.D.		
Project Title:	Feasibility Study: QCT Modality for Risk Surveillance of Bone - Effects of In-flight Countermeasures on Sub-regions of the Hip Bone		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
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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Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	Directed Research
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No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
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Flight Program:	Pre/Post Flight		
Flight Assignment:	ISS NOTE: Gap changes per IRP Rev E (Ed., 1/27/14) NOTE: Title change per HRP and PI to "Feasibility Study: QCT Modality for Risk Surveillance of Bone - Effects of In-flight Countermeasures on Sub-regions of the Hip Bone"; previously "Occupational Risk Surveillance for Bone: Pilot Study - Effects of In-flight Countermeasures on Sub-regions of the Hip Bone" (Ed., 1/23/2013)		
Key Personnel Changes/Previous PI:	None		
COI Name (Institution):			
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Measurement of areal bone mineral density [aBMD, g/cm2] by dual-energy x-ray absorptiometry [DXA] is required by NASA for assessing skeletal integrity in astronauts. Advantages of DXA include the facts that aBMD is widely-applied predictor of fractures in the aging population and that there are aBMD-based guidelines for identifying persons at high risk for osteoporotic fractures. In contrast to the 2-d imaging by DXA, quantitative computed tomography [QCT] is a 3-d bone imaging technology that is used typically to scan the hip and spine. QCT is capable of measuring, volumetric BMD [BMD, mg/cm3] of separate cortical and trabecular sub-regions as well as of total (integral) bone. In contrast to the 2-d imaging by DXA, volumetric QCT at the hip is limited to research applications at this time because there is not enough medical evidence to determine how QCT data should be used in clinical practice. QCT however provides additional information on bone structure and increases the understanding of how bones respond to effectors of bone loss or gain. NASA recently convened a panel of clinical bone experts to review available medical and research information from astronauts who flew on long-duration space missions. As part of its charge, the panel identified a clinical trigger upon which the flight surgeon should have the astronaut evaluated further by an osteoporosis specialist. Specifically, the Panel recommended that if restoration to preflight BMD is not observed for the hip trabecular compartment at two years after return to earth, then that astronaut should be evaluated for possible therapeutic intervention to prevent premature osteoporotic fractures. This pilot study proposes to use preflight and postflight QCT scanning of the hips in ISS astronauts to evaluate the ability of in-flight countermeasures to prevent the occurrence of this clinical trigger. This study further hypothesizes that QCT scanning can distinguish the effects of different categories of in-flight countermeasures/activities on distinct sub-regions of the hip bone. For example, this pilot study will demonstrate that biochemically-based countermeasures (e.g., dietary manipulation of acidic to basic amino acid intake or bisphosphonates medication) will have a detectable prevention of BMD loss in hip trabecular compartment while biomechanically-based countermeasures (exercise regimens) will have detectable expansion of cortical bone apposition -- increasing both bone cross-sectional area and integral BMD as a consequence. These different effects on hip morphology will be subsequently translated to an effect on hip bone strength of the ISS astronaut. The combination of countermeasures that impact both compartments will more likely result in greater hip bone strength -- as estimated by analyzing QCT data by Finite Element Modeling (FEM) -- than of any singly applied countermeasure. This assertion will be approached in this pilot study by addressing the following Aims in each ISS astronaut: 1) Characterize the response of i) trabecular and cortical BMDs of the hip and ii) cross-sectional areas of cortical bone, trabecular bone and integral bone, to countermeasures that are either based upon biochemistry or mechanical-loading -- with QCT measures. 2) Translate the QCT-measured changes in hip bone morphology (Aim 1) to hip bone fracture loads (aka, "hip bone strength") using FEM. 3) Characterize QCT-measured changes in hip bone morphology (Aim 1) following a 12-month postflight period on earth and, in addition, translate these changes to the percentage recovery of preflight hip bone strength determined by FEM. By addressing these aims this pilot study, using a research tool, will provide preliminary data that are critical for clinical issues related to fracture risk: Are in-flight countermeasures and postflight activities sufficient to protect against incidence of a clinical trigger for medical intervention? Do countermeasures protect against a decline in bone strength? Can hip bone strength be sufficiently recovered? In addition, Trabecular Bone Score (TBS) analysis of DXA lumbar spine scans will be used to characterize bone microarchitecture of the lumbar spine and to determine if an effect of space flight can be detected in the retrospective ISS DXA data set. Like QCT, TBS may help fill a void with traditional DXA measurements, as it can differentiate between areas of bone that have the same areal BMD value but different 3-dimensional microsarchitecture in the trabecular bone compartment of the spine. This is achieved by retrospectively analyzing areal DXA scans and measuring the mean rate of variation of gray levels. Since QCT measurements in this study are being obtained only on the hip, TBS analyses will serve a similar purpose for the spine. In addition to the TBS analysis of ISS DXA scans, TBS analyses of retrospective precision study subjects will be used to determine measurement precision of this technique on a population similar to that of the astronauts.
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research, which requires focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal.
Research Impact/Earth Benefits:	Research Impact: This study will provide data in addition to the medically-required measurement of aBMD by DXA. There is a requirement in the osteoporosis field to expand evaluations beyond DXA aBMD (i.e., "Bone Quality") to evaluate fracture risk fully because aBMD does not account for 100% of bone strength. This requirement is particularly important for the subject with poorly defined bone loss, i.e., other than age-related bone loss. Moreover, a report of preflight and postflight QCT data from eleven ISS astronaut reveals that changes in hip bone strength by FEM do not correlate with changes in DXA aBMD. This absence of correlation suggests that DXA aBMD does not detect all of the changes in bone strength due to spaceflight that can be detected by QCT and FE modeling. Earth Benefits: This expanded assessment of skeletal integrity, being validated for spaceflight-induced bone loss in astronauts, would be relevant for the terrestrial, complicated patient (e.g., glucocorticoid-induced, alcohol-induced). Recently, FEM estimations of bone strength have been evaluated in population studies as predictors of incident hip fractures. These FE hip strengths are being evaluated for cut-points that would provide thresholds of acceptable bone health for active astronauts and aging retired astronauts. The development of these cut-points, as demonstrated for astronauts, would undergird the current discussions to use FE hip strength as a substitute for expensive and time-consuming prospective trials with fracture outcome -- the standard validation of hip fracture interventions.
	Since receiving Authorization-to-Proceed [ATP] in 12/1/2011, the Hip QCT study received IRB-approval on 3/21/2012 for consenting 10 ISS astronauts. Select-for-Flight decision was made on 7/9/2012. Astronaut consenting was initiated in 8/10/2012. In addition, there are six ISS astronauts who are participating in flight studies that are evaluating pharmaceutical and exercise as countermeasures, ["BP SMO" and "SPRINT," respectively]. Both of these flight studies are using QCT scans for measured hip outcomes. The Informed Consent Briefing [ICB] process for these six astronauts has also begun, with a request for hip QCT scans at the R+1 year and at R+2 year time points, if required. As of October 2013, 9 crewmembers have signed informed consents. Seven of these crewmembers have completed ISS flights as subjects for one or both of the countermeasure studies described above (3 active subjects and 4 controls); an eighth crewmember (control) will return from flight in November and a ninth crewmember (also a control) in the spring of

Task Progress:	2014. One of the 9 crewmembers has participated in R+1-year QCT testing specifically for the Hip QCT study, though these scans have not yet been analyzed. QCT data obtained to date for the various studies were reviewed in a closed-room session with a panel of clinical experts invited to the second Bone Summit, held at USRA and JSC on November 04 and 05, 2013. The panel recommended that QCT testing continue, with an emphasis on obtaining data on at least 10 control subject crewmembers (currently, only 6 of the Hip QCT consented crewmembers fall into this category). TBS analyses were completed for 51 ISS crewmembers' pre and post flight DXA lumbar spine scans. These data were summarized in an abstract that has been submitted to the International Society for Clinical Densitometry's 2014 annual meeting. Work is underway to complete TBS analyses of DXA precision study scans to determine reproducibility of the technique in a population similar to the astronaut corps.
Bibliography Type:	Description: (Last Updated: 05/24/2021)
Articles in Peer-reviewed Journals	Orwoll ES, Adler RA, Amin S, Binkley N, Lewiecki EM, Petak SM, Shapses SA, Sinaki M, Watts NB, Sibonga JD. "Skeletal health in long-duration astronauts: nature, assessment, and management recommendations from the NASA Bone Summit." J Bone Miner Res. 2013 Jun;28(6):1243-55. Review. http://dx.doi.org/10.1002/jbmr.1948 ; PubMed PMID: 23553962 , Jun-2013
Articles in Peer-reviewed Journals	Sibonga JD. "Spaceflight-induced bone loss: is there an osteoporosis risk?" Curr Osteoporos Rep. 2013 Jun;11(2):92-8. Review. http://dx.doi.org/10.1007/s11914-013-0136-5 ; PubMed PMID: 23564190 , Jun-2013