Fiscal Year:	FY 2017	**Task Last Updated:**	FY 08/24/2016
PI Name:	LeBlanc, Adrian Ph.D.		
Project Title:	Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss: SMO-021		
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		
PI Email:	adleblanc2@gmail.com	**Fax:**	FY
PI Organization Type:	NON-PROFIT	**Phone:**	281-244-2012
Organization Name:	Universities Space Research Association		
PI Address 1:	Division of Space Life Sciences		
PI Address 2:	3600 Bay Area Blvd		
PI Web Page:			
City:	Houston	**State:**	TX
Zip Code:	77058	**Congressional District:**	22
Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	Directed Research
Start Date:	10/01/2006	**End Date:**	03/31/2017
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
Contact Monitor:	Maher, Jacilyn	**Contact Phone:**	
Contact Email:	jacilyn.maher56@nasa.gov		
Flight Program:	ISS		
Flight Assignment:	ISS NOTE: End date changed to 3/31/2017 due to PI's retirement (Ed., 8/2/17) NOTE: End date changed to 2/03/2018 per HRP technology information (Ed., 9/2/14) NOTE: End date is 8/31/2015 per HRP Master Task List dtd 7/12/11 (Ed., 8/4/11) NOTE: Extended to 9/30/2013 per PI (Ed., 11/5/2010)		
Key Personnel Changes/Previous PI:	August 2016 Report: Drs. Takahura Yasui, M.D., Ph.D. and Atsushi Okada, M.D., Ph.D. (both from Nagoya City University) have been added as Co-Investigators to provide expertise in the analysis and interpretation of renal stone-related data. August 2013 Report: Dr. Joyce Keyak (University of California at Irvine) has been added as a Co-Investigator. Dr. Keyak provides expertise in the area of Finite Element Modeling using hip QCT scans, and she is a co-author of presentations and publications resulting from this flight study. Toshio Matsumoto, M.D., Ph.D., is the Japanese Co-Principal Investigator of this study, a joint project between NASA and JAXA. Dr. Matsumoto is affiliated with the Department of Medicine and Regulatory Sciences, University of Tokushima Graduate School of Medicine. His contact information is: Phone 81-88-633-7119/Fax 81-88-633-7407; Toshimat@clin.med.tokkushima-u.ac.jp .		

COI Name (Institution):	Jones, Jeffrey M.D. (Baylor College of Medicine) Shapiro, Jay M.D. (Kennedy Krieger Institute) Lang, Tom Ph.D. (University of California at San Francisco) Shackelford, Linda M.D. (NASA Johnson Space Center) Smith, Scott Ph.D. (NASA-Johnson Space Center) Evans, Harlan Ph.D. (Wyle Laboratories) Spector, Elisabeth (Wyle Laboratories) Sibonga, Jean Ph.D. (NASA Johnson Space Center) Nakamura, Toshitaka M.D., Ph.D. (University of Occupational and Environmental Health) Kohri, Kenjiro M.D., Ph.D. (Nagoya City University) Ohshima, Hiroshi M.D., Ph.D. (Japan Aerospace Exploration Agency (JAXA)) Keyak, Joyce Ph.D. (University of California, Irvine) Yasui, Takahura M.D., Ph.D. (Nagoya City University) Okada, Atsushi M.D., Ph.D. (Nagoya City University) Matsumoto, Toshio M.D., Ph.D. (Co-PI : University of Tokushima Graduate School of Medicine, Japan)
Grant/Contract No.:	Directed Research
Performance Goal No.:	
Performance Goal Text:	
Task Description:	The purpose of this Supplementary Medical Objective is to determine whether bisphosphonates, in conjunction with the routine in-flight exercise program, will protect International Space Station (ISS) crewmembers from the regional decreases in bone mineral density documented on previous ISS flights. Two dosing regimens will be tested: (1) an oral dose of 70 mg alendronate taken weekly during flight and (2) and I.V. dose of zoledronic acid 4 mg, administered just once approximately 45 days before flight. Our rationale for including both alendronate and zoledronic acid is that two dosing options will: maximize crew participation, increase the countermeasure options available to flight surgeons, increase scientific opportunities, and minimize the effects of operational and logistical constraints. Use of both oral and I.V. options can accommodate both crew and flight surgeon preferences (e.g., based on individual drug sensitivity, relevant health conditions, or other considerations). Operational and logistical constraints may favor one option versus the other. For example, stowage limits may limit use of alendronate on certain flights, while the ability to titrate the in-flight dose in response to on-orbit measurements of bone resorption would favor the weekly dosing regimen. Long-duration (e.g., 2+ year) missions would require in-flight re-dosing of I.V. zoledronic acid. The purpose of this study is not to test one dosing option versus the other. Rather, we intend to show that bisphosphonates-plus-exercise will have a measurable effect versus exercise alone in preventing space flight induced bone loss. Secondary goals will be to document the return to normal bone remodeling post-flight in crewmembers who took bisphosphonates. See also https://
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	While the primary purpose of this research is to develop a countermeasure to protect crewmembers against bone loss during long duration space flight, this research may provide insight into the mechanisms and prevention of bone atrophy in other disuse conditions.
Task Progress:	The original intent of this study was to test 10 long-duration crewmembers taking one of two bisphosphonate regimens: either 70 mg per week alendronate or a single infusion of 4 mg of Zoledronic acid. After the study began testing in 2009, the Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS) determined that only alendronate would be offered to U.S. crewmembers, while both dosing options could be offered to International Partners. It was further stipulated that only 10 alendronate subjects would be allowed. Of these, 2 dropped out prior to flight for various reasons and one crewmember reported GI symptoms very early inflight and therefore the investigators terminated the inflight dosing of this subject. We have now completed testing on the remainder 7 crewmembers taking alendronate during flight. All scheduled testing sessions for the 7 treated subjects—pre-flight, in-flight and post-flight--have been completed. DXA, pQCT, QCT, and blood and urine data have been collated and analyses of the major parameters of interest have been performed through R+30, including statistical analyses. These results were published in June 2013 in the journal Osteoporosis International (LeBlanc A, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford L, Smith SM, Evans H, Spector E, Ploutz-Snyder R, et al. (2013). Bisphosphonates as a supplement to exercise to protect bone during long-duration space flight. Osteoporosis International 24(7): 2105-2114). The results of R+12-month testing (DXA and QCT) on this group were presented at the 2014 Meeting of the American Society for Bone and Mineral Research in Houston, TX, (September 2014) and at the NASA Human Research Program Investigators' Workshop in Galveston, TX, (February 2015). Additional updates were presented at the 2016 NASA Human Research Program Investigator's Workshop in Galveston, TX, (February 2016) and the 2017 NASA Human Research Program Investigator's Workshop in Galveston, TX, in January 2017. In 2011, the study obtained approval to add a new control group, consisting of approximately 10 ISS crewmembers not taking bisphosphonates, but otherwise participating in essentially the same pre-, in-, and post-flight testing as the 7 treated subjects. The new control group should allow us to distinguish the relative effects of bisphosphonates vs. the confounder of Advanced Resistive Exercise Device (ARED) exercise, particularly at the level of trabecular vs. cortical bone. All treated subjects in this study have used the ARED device, whereas our previous control group used the older IRED or other resistive exercise device, capable of much lower loads than ARED. Testing on this new control group began in 2012, and, to date, 10 crewmembers have consented to participate. Of these, 9 crewmembers have returned from ISS flights. Eight of these have completed all post-flight testing through R+1 year, one has completed all post flight testing except one year return, and the remaining test subject has completed preflight testing. Immediate post-flight testing on this subject is expected in late 2016. It is anticipated that the control group will complete testing in ~late 2017. Preliminary results (DXA and QCT) for the first 9 of these control subjects will be presented at the 2016 Meeting of the American Society for Bone and Mineral Research in Atlanta GA, (September 2016).

	All testing to date for the first 8 control subjects, including QCT, DXA, pQCT, abdominal ultrasound, and blood and urine testing, has been completed on schedule and without incident. ISS sample return is complete for the first 6 control subjects. In Summary (as of March 2017) Exercise + Alendronate 7 crewmembers completed ISS mission (mean 5.5mo). All crewmembers took 70mg/wk oral alendronate starting 3 weeks prior to and during flight. Results are: reduced bone loss, eliminated elevated resorption and uncoupling, reduced urinary Ca and calculated bone strength was maintained. Results published in 2013 ARED exercise alone Ten subjects completed flight using newer exercise protocol and device (ARED) Results-reduced bone loss by about 50% compared to early ISS crewmembers using IRED, systemic resorption remains elevated, uncoupling appears to remain elevated for most of flight based on systemic markers, urinary Ca remains elevated and bone strength appears to be maintained
Bibliography Type:	Description: (Last Updated: 06/29/2023)
Abstracts for Journals and Proceedings	LeBlanc A, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford LC, Smith SM, Evans HJ, Spector ER, Ploutz-Snyder R, Sibonga J, Nakamura T, Kohri K, Ohshima H, Moralez G. "Update of Bisphosphonate Flight Experiment." Presented at the 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. , Jan-2015
Abstracts for Journals and Proceedings	LeBlanc A, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford LC, Smith SM, Evans HJ, Spector ER, Ploutz-Snyder R, Sibonga J, Nakamura T, Kohri K, Ohshima H, Moralez G. "Spaceflight Bone Atrophy: Problem Solved? " 37th Annual Meeting of the American Society for Bone and Mineral Research, Seattle, Washington, October 9-12, 2015. Journal of Bone and Mineral Research. 2015;30 (Suppl 1). , Oct-2015
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Abstracts for Journals and Proceedings	Spector ER, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford LC, Smith SM, Evans HJ, Spector ER, Ploutz-Snyder R, Sibonga J, Nakamura T, Kohri K, Ohshima H, Moralez G, LeBlanc A. "Bone Loss Countermeasures for Long Duration Space Flight." ASBMR 2016 (American Society for Bone and Mineral Research), Atlanta, Georgia, September 16-19, 2016. ASBMR 2016 (American Society for Bone and Mineral Research), Atlanta, Georgia, September 16-19, 2016. , Sep-2016
Abstracts for Journals and Proceedings	LeBlanc A. "Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss: SMO-21." 2017 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 23-26, 2017. 2017 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 23-26, 2017. , Jan-2017
Articles in Peer-reviewed Journals	Sibonga J, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford L, Smith SM, Young M, Keyak J, Kohri K, Ohshima H, Spector E, LeBlanc A. "Resistive exercise in astronauts on prolonged spaceflights provides partial protection against spaceflight-induced bone loss." Bone. 2019 Nov;128:112037. [2019 Aug 7 Epub] https://doi.org/10.1016/j.bone.2019.07.013 ; PubMed PMID: 31400472 , Nov-2019
Articles in Peer-reviewed Journals	Okada A, Matsumoto T, Ohshima H, Isomura T, Koga T, Yasui T, Kohri K, LeBlanc A, Spector E, Jones J, Shackelford L, Sibonga J. "Bisphosphonate use may reduce the risk of urolithiasis in astronauts on long-term spaceflights." JBMR Plus. 2022 Jan;6(1):e10550. https://doi.org/10.1002/jbm4.10550 ; PMID: 35079672; PMCID: PMC8770998 , Jan-2022
Articles in Peer-reviewed Journals	Shelhamer M, Bloomberg J, LeBlanc A, Prisk GK, Sibonga J, Smith SM, Zwart SR, Norsk P. "Selected discoveries from human research in space that are relevant to human health on Earth." npj Microgravity. 2020 Feb 12;6(1):5. https://www.nature.com/articles/s41526-020-0095-y ; PMID: 32128361; PMCID: PMC7016134 , Feb-2020
Books/Book Chapters	Schneider VS, Ploutz-Snyder L, LeBlanc AD, Sibonga J. "Musculoskeletal adaptation to space flight." in "Space physiology and medicine: From evidence to practice. " Ed. A.E. Nicogossian et al. New York: Springer, 2016. p. 347-365. https://doi.org/10.1007/978-1-4939-6652-3_13 , Dec-2016