

## Bisphosphonate ISS Flight Experiment

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The bisphosphonate study is a collaborative effort between the NASA and JAXA space agencies to investigate the potential for antiresorptive drugs to mitigate bone changes associated with long-duration spaceflight. Elevated bone resorption is a hallmark of human spaceflight and bed rest (common zero-G analog). We tested whether an antiresorptive drug in combination with in-flight exercise would ameliorate bone loss and hypercalcuria during long-duration spaceflight. Measurements include DXA, QCT, pQCT, and urine and blood biomarkers. We have completed analysis of 7 crewmembers treated with alendronate during flight and the immediate postflight (R+<2 week) data collection in 5 of 10 controls without treatment. Both groups used the advanced resistive exercise device (ARED) during their missions.

We previously reported the pre/postflight results of crew taking alendronate during flight (Osteoporosis Int. 24:2105–2114, 2013). The purpose of this report is to present the 12-month follow-up data in the treated astronauts and to compare these results with preliminary data from untreated crewmembers exercising with ARED (ARED control) or without ARED (Pre-ARED control). Results: the table presents DXA and QCT BMD expressed as percentage change from preflight in the control astronauts (18 Pre-ARED and the current 5 ARED-1-year data not yet available) and the 7 treated subjects. As shown previously the combination of exercise plus antiresorptive is effective in preventing bone loss during flight. Bone measures for treated subjects, 1 year after return from space remain at or near baseline values. Except in one region, the treated group maintained or gained bone 1 year after flight. Biomarker data are not currently available for either control group and therefore not presented. However, data from other studies with or without ARED show elevated bone resorption and urinary Ca excretion while bisphosphonate treated subjects show decreases during flight. Comparing the two control groups suggests significant but incomplete improvement in maintaining BMD using the newer exercise protocols compared to earlier resistive exercise protocols. Quantitative characterization of this improvement requires additional measurements in the ARED control group that we are currently collecting. In conclusion, these results indicate that an antiresorptive may be an effective adjunct to exercise during long-duration spaceflight.

% Change from Preflight (Mean  $\pm$  SD)

	<i>Pre-ARED Control</i>	<i>ARED Control</i>	<i>Alendronate Treated</i>	
	<i>(n=18)</i>	<i>(n=5)</i>	<i>(n=7)</i>	
	<b>R+&lt;2 week</b>	<b>R+&lt;2 week</b>	<b>R+&lt;2 week</b>	<b>R+1 year</b>
<b>DXA BMD</b>				
Total Hip	-6.2 $\pm$ 2.8	-2.7 $\pm$ 3.2	-0.2 $\pm$ 1.5	0.8 $\pm$ 1.4
Trochanter	-6.8 $\pm$ 4.8	-3.8 $\pm$ 2.9	0.02 $\pm$ 2.3	2.1 $\pm$ 1.2
Femur Neck	-6.6 $\pm$ 3.0	0.8 $\pm$ 4.6	-0.7 $\pm$ 1.2	1.5 $\pm$ 1.7
Lumbar Spine	-3.9 $\pm$ 3.2	-3.7 $\pm$ 2.3	2.8 $\pm$ 4.0	3.9 $\pm$ 3.8
<b>QCT BMD</b>				
Trabecular Total Hip	-13.6 $\pm$ 6.4	-6.9 $\pm$ 8.0	-1.1 $\pm$ 9.8	-1.1 $\pm$ 12.1
Cortical Total Hip	-3.2 $\pm$ 3.5	-3.6 $\pm$ 0.4	-0.6 $\pm$ 4.7	-2.9 $\pm$ 3.7
Trabecular Trochanter	-13.5 $\pm$ 6.5	-5.6 $\pm$ 7.8	-1.9 $\pm$ 9.9	-1.2 $\pm$ 12.4
Cortical Trochanter	-3.2 $\pm$ 3.3	-4.6 $\pm$ 1.4	-0.5 $\pm$ 5.0	-3.2 $\pm$ 4.3
Trabecular Femur Neck	-15.0 $\pm$ 9.8	-15.8 $\pm$ 15.8	6.5 $\pm$ 14.8	2.8 $\pm$ 7.2
Cortical Femur Neck	-4.0 $\pm$ 5.5	-3.2 $\pm$ 2.6	-1.0 $\pm$ 4.8	-3.9 $\pm$ 3.1