

Supplementary Tables

Supplementary Table 1. Bone densitometry data before and after spaceflight.

	<i>N</i>	Pre-flight	Post-flight
<i>Bone Densitometry</i>			
LS aBMD	17	1.072 (1.017, 1.143)	1.064 (0.971, 1.119)**
FN aBMD – Dom	15	0.839 (0.801, 0.929)	0.809 (0.749, 0.907)**
FN aBMD – ND	16	0.841 (0.798, 0.910)	0.806 (0.759, 0.901)**
TH aBMD – Dom	16	1.025 (0.974, 1.12)	0.986 (0.890, 1.071)**
TH aBMD – ND	17	1.009 (0.982, 1.095)	0.985 (0.908, 1.035)**
<i>Body mass and composition</i>			
Total mass (g)	17	79664 (75414, 86955)	78753 (74456, 89277)
Total lean mass (g) ^a	17	56544 (50907, 62329)	57385 (51606, 62795)
Total lean (%) ^a	17	70.3 (69.1, 73.3)	72.0 (70.3, 74.0)
Total fat mass (g)	17	20106 (17442, 24527)	19861 (17393, 23410)
Total fat (%)	17	25.9 (23.6, 27.5)	24.4 (22.7, 26.4)

Data are median (interquartile range). ^atotal lean mass less bone mineral content

** $p < 0.01$ for difference post- vs. pre-flight based on Wilcoxon signed rank test. Pairwise percent change data presented in text.

LS, lumbar spine; FN, femoral neck; TH, total hip; aBMD, areal bone mineral density; Dom, dominant limb; ND, non-dominant limb.

Supplementary Table 2. Relationship between pre-flight biochemical markers and change in HR-pQCT bone variables.

	Tt.vBMD		F.Load		Ct.vBMD		Tb.vBMD	
	Dom	ND	Dom	ND	Dom	ND	Dom	ND
<i>Tibia^a</i>								
CTx (ug/d)	-0.006 (-0.009, -0.002)	-0.005 (-0.008, -0.001)	-0.231 (-0.404, -0.057)	-0.248 (-0.521, 0.025)	-0.017 (-0.031, -0.002)	-0.021 (-0.040, -0.002)	-0.002 (-0.006, 0.002)	0.000 (-0.004, 0.003)
CTx (ug/mmol Cr)	-0.132 (-0.203, -0.060)	-0.123 (-0.182, -0.064)	-4.857 (-8.529, -1.184)	-6.169 (-10.472, -1.865)	-0.248 (-0.555, 0.059)	-0.303 (-0.708, 0.101)	-0.051 (-0.141, 0.04)	-0.027 (-0.097, 0.043)
NTx (nmol/d)	-0.012 (-0.034, 0.010)	-0.011 (-0.034, 0.011)	-0.664 (-1.549, 0.221)	-0.385 (-1.510, 0.740)	-0.035 (-0.102, 0.032)	-0.037 (-0.119, 0.045)	-0.004 (-0.024, 0.017)	0.002 (-0.017, 0.020)
NTx (nmol/mmol Cr)	-0.479 (-0.964, 0.005)	-0.432 (-0.923, 0.059)	-22.72 (-42.492, -2.948)	-18.553 (-42.702, 5.597)	-0.349 (-2.057, 1.358)	-0.462 (-2.493, 1.568)	-0.101 (-0.545, 0.342)	-0.053 (-0.507, 0.400)
OC (ng/mL)	-0.735 (-1.437, -0.033)	-0.525 (-1.229, 0.179)	-22.595 (-56.556, 11.365)	-21.712 (-55.959, 12.534)	-0.511 (-3.075, 2.053)	-0.268 (-3.262, 2.726)	-0.588 (-1.2, 0.024)	-0.294 (-0.941, 0.354)
P1NP (ug/L)	-0.354 (-0.588, -0.12)	-0.335 (-0.529, -0.140)	-13.624 (-23.415, -3.833)	-16.912 (-29.579, -4.245)	-0.281 (-1.259, 0.697)	-0.495 (-1.715, 0.726)	-0.263 (-0.468, -0.057)	-0.130 (-0.323, 0.062)
Sclerostin (pmol/L)	0.434 (0.046, 0.822)	0.289 (-0.105, 0.684)	18.600 (3.507, 33.693)	2.39 (-22.765, 27.544)	0.549 (-0.871, 1.969)	-0.066 (-1.939, 1.807)	0.247 (-0.125, 0.618)	-0.004 (-0.299, 0.292)
<i>Radius^b</i>								
CTx (ug/d)	-0.001 (-0.004, 0.001)	-0.002 (-0.007, 0.004)	0.060 (-0.113, 0.233)	-0.071 (-0.365, 0.222)	0.001 (-0.007, 0.009)	-0.002 (-0.015, 0.011)	0.000 (-0.002, 0.002)	-0.001 (-0.004, 0.002)
CTx (ug/mmol Cr)	-0.022 (-0.054, 0.01)	-0.021 (-0.099, 0.057)	0.601 (-1.668, 2.869)	0.061 (-4.079, 4.201)	-0.006 (-0.115, 0.104)	0.000 (-0.180, 0.181)	-0.007 (-0.034, 0.020)	-0.020 (-0.055, 0.016)
NTx (nmol/d)	0.003 (-0.007, 0.013)	0.005 (-0.014, 0.024)	0.504 (-0.057, 1.065)	-0.171 (-1.293, 0.95)	0.024 (-0.013, 0.061)	0.001 (-0.062, 0.064)	0.002 (-0.013, 0.018)	0.002 (-0.011, 0.016)
NTx (nmol/mmol Cr)	-0.016 (-0.191, 0.159)	-0.005 (-0.319, 0.308)	7.968 (-2.430, 18.365)	3.754 (-15.115, 22.623)	0.149 (-0.476, 0.774)	0.310 (-0.623, 1.243)	-0.082 (-0.332, 0.169)	-0.010 (-0.195, 0.174)
OC (ng/mL)	-0.140 (-0.334, 0.054)	0.036 (-0.36, 0.432)	3.082 (-10.505, 16.67)	11.649 (-10.678, 33.975)	-0.455 (-1.29, 0.381)	0.681 (-0.652, 2.014)	-0.170 (-0.498, 0.158)	0.013 (-0.325, 0.350)
P1NP (ug/L)	-0.066 (-0.158, 0.026)	0.016 (-0.209, 0.241)	1.119 (-5.883, 8.122)	4.53 (-5.737, 14.797)	0.065 (-0.283, 0.413)	0.128 (-0.374, 0.630)	-0.034 (-0.096, 0.028)	-0.067 (-0.212, 0.078)
Sclerostin (pmol/L)	0.042 (-0.097, 0.182)	-0.020 (-0.334, 0.294)	0.113 (-9.573, 9.799)	-11.291 (-17.612, 14.281)	-0.078 (-0.596, 0.441)	0.43 (-0.468, 1.328)	0.036 (-0.088, 0.159)	0.133 (-0.068, 0.334)

Data are coefficients (95% confidence interval) of the biomarker by time interaction, representing the change in bone variables per unit increase in biochemical marker. Mixed effects models included time (pre-, post-flight), mission duration, interaction between mission duration and time, biomarker and interaction between biomarker and time. Pre-flight biomarkers are mean of L-180 and L-45. **Bolded** values indicate a significant ($p < 0.05$) interaction with time in mixed effects model. CTx, type I collagen C-terminal cross-linked telopeptide; NTx, type I collagen N-terminal cross-linked telopeptide; OC, osteocalcin; P1NP, procollagen type I amino-terminal propeptide; Cr, creatinine.

Supplementary Table 3. Relationship between exercise and pre- to post-flight change in HR-pQCT trabecular bone variables

Tibia	Tb.vBMD (mg/cm ³)		Tb.BV/TV (%)		Tb.Th (µm)	
	Dom	ND	Dom	ND	Dom	ND
Pre-flight Run volume (hrs/wk)	5.3 (-8.4, -2.2)	-4.1 (-7.5, -0.7)	-0.65 (-1.03, -0.27)	-0.42 (-0.84, 0.00)	-4.71 (-7.91, -1.51)	-4.88 (-8.67, -1.09)
Change in Run volume (hrs/wk)	5.0 (-0.9, 11.0)	4.0 (-0.5, 8.6)	0.62 (-0.11, 1.36)	0.44 (-0.10, 0.98)	4.69 (-0.43, 9.80)	3.98 (-1.30, 9.25)
Pre-flight heel raise volume (reps/wk)	-0.023 (-0.092, 0.046)	-0.044 (-0.101, 0.014)	-0.004 (-0.012, 0.005)	-0.003 (-0.010, 0.004)	0.044 (-0.092, 0.003)	-0.067 (-0.117, -0.018)
Change in heel raise volume (reps/wk)	0.011 (-0.020, 0.043)	0.027 (0.001, 0.052)	0.002 (-0.002, 0.006)	0.003 (-0.001, 0.006)	0.013 (-0.015, 0.041)	0.030 (0.007, 0.058)
Change in deadlift volume (reps/wk)	0.022 (-0.009, 0.053)	0.029 (0.004, 0.055)	0.003 (-0.001, 0.007)	0.003 (-0.001, 0.006)	0.020 (-0.006, 0.045)	0.034 (0.008, 0.059)
In-flight deadlift volume (reps/wk)	0.023 (-0.005, 0.052)	0.029 (0.005, 0.053)	0.003 (-0.001, 0.006)	0.003 (-0.000, 0.006)	0.013 (-0.016, 0.042)	0.030 (0.001, 0.059)

Data are coefficients (95% confidence interval) of the exercise by time interaction, representing the change in bone variables per unit increase in exercise. Mixed effects models included time (pre-, post-flight), mission duration, interaction between mission duration and time, exercise and interaction between exercise and time. Tb.vBMD, trabecular volumetric bone mineral density; Tb.BV/TV, trabecular bone volume fraction; Tb.Th, trabecular thickness; Dom, dominant limb; ND, non-dominant limb. Note: A change of 4 mg/cm³, 0.5% and 5 µm for Tb.vBMD, Tb.BV/TV and Tb.Th, respectively, is equivalent to a relative change of approximately 2%. **Bolded** values indicate a significant ($p < 0.05$) interaction between exercise and time in mixed effects model.