

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.