Effects of Spaceflight on the Microarchitecture and Mechanics of the Lumbar Spine of Mice Flown on Space Shuttle Mission STS-118

Stefanie Gonzalez, BS1, Alicia Ortega, PhD1, Anthony Lau, PhD1, Eric Livingston, MS2, Elizabeth Marshall2, Ted Bateman, PhD2, Louis Stodieck, PhD1, Virginia Ferguson, PhD1.

1University of Colorado, Boulder, CO, USA, 2University of North Carolina, Chapel Hill, NC, USA.

Disclosures:

Introduction: Spaceflight provides an accelerated model of osteoporosis with approximately 0.5-2% loss of bone mass per month reported for astronauts, approximately ten times faster than post-menopausal women [1]. Annually over 8.9 million fractures occur worldwide [2] due to osteoporosis, thus research gleaned from countermeasures could address this public health concern. Bone quality is first compromised in the weight-bearing bones (hip, tibia, femur, and lumbar spine) thus inducing osteoporosis. In this study, the lumbar spine from mice flown on Space Shuttle Endeavor (STS-118) for ~13 days were used to evaluate the effects of microgravity on vertebral bone microarchitecture and mechanics and the intervertebral disc (IVD) height.

Methods: Twenty-four female (n=12/group), 9-week-old C57BL/6 mice were assigned to either ground control (GC) or spaceflight (SF) groups. Mice from each group were housed under identical conditions in NASA Animal Enclosure Modules (AEM). All mice were sacrificed within 3-6 hours following landing (SF) or the end of a matched study duration (GC). Mice were weighed and body composition was assessed using nuclear magnetic resonance (NMR) imaging (Bruker Minispec). Micro-CT (Scanco microCT 80; 10µm voxel size) was used to characterize the 3D trabecular bone microarchitecture in the L5 vertebrae via measures of bone volume fraction (BV/TV), connectivity density (Conn.D), trabecular number (Tb.N), trabecular thickness (Tb.Th), and trabecular spacing (Tb.Sp). MicroCT data of L5 vertebrae were meshed to produce subject specific finite element analysis (FEA) models where a 1.50 mm tall segment of the L5 vertebral body was isolated starting at the superior endplate and a downward displacement of 7.5 µm was applied to the superior face of the vertebral body to assess stiffness and structural efficiency (i.e., stiffness per amount of bone volume). Preliminary intervertebral disc (IVD) height measurements were obtained by performing a low-resolution micro-CT scan (25 µm voxel size) of the L4-5 segment of the lumbar spine (n = 3/group). Measurements were made from the resulting images at the vertebral midplane from the sagittal view using ImageJ software. Measurements were normalized by calculating the disc height index (DHI) to compare the intervertebral disc height across samples [3,4]. The DHI was calculated by averaging the anterior, posterior, and mid disc regions over the adjacent vertebral body height (Figure 1) [5]. A two-sample t-test assuming unequal variance was used to assess the statistical significance between the GC and SF groups, the mean ± SD are presented.

Results: Microgravity exposure over 13 days caused significantly reduced body weight, and body composition analysis by NMR revealed that these body weight differences were primarily due to reduced lean mass. Microarchitectural parameters of the trabecular bone at the L5 vertebrae showed significantly diminished measures of BV/TV (-13.9%, p<0.0001) and Tb.Th (-11.4%, p<0.0001), thus indicating that the trabecular bone microarchitecture in the L5 vertebrae was compromised following ~13 days of microgravity exposure (Table 1). FEA revealed that the diminished vertebral microarchitecture following SF was sufficient to result in statistically reduced measures of effective stiffness (-12.8%, p<0.0001) and normalized stiffness efficiency (-4.3%, p<0.0001) (Figure 2). The structural integrity of the lumbar vertebrae therefore diminished with SF. Additionally, IVD height is related to the degree of disc degeneration and it is one of the most important characteristic features of the IVD degeneration. With SF, preliminary measures (from an initial sample of n = 3/group) of the DHI tended to increase (+12.8%, N.S.) to indicate that lumbar disc expansion may occur in mice subjected to microgravity. These preliminary results compel analysis of statistically relevant sample numbers to assess lumbar disc height alterations in SF as well as further study of the etiology of lumbar disc changes and their potential influence on disc degeneration.

Discussion: While we have previously shown that the long bones from these same mice showed more pronounced changes with microgravity exposure [6], the same micro-CT measures in the lumbar vertebrae are comparably less affected. Also, unlike hindlimb long bones that are largely unloaded during SF, video footage collected during the STS-118 mission (on days 5 and 6 of the flight) showed that the SF mice were physically active and moved easily around the AEMs. It is likely that the vertebral bones are thus loaded to a greater extent, by forces produced when mice move around the AEM, than the hindlimbs and consequently experience less pronounced bone changes with microgravity exposure.

Significance: Collectively, the results presented herein suggest that the microstructure and mechanical properties of trabecular bone in the lumbar vertebrae are compromised with musculoskeletal unloading during spaceflight and that these bone changes may occur concomitant with IVD expansion.

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Table 1 – Microarchitecture parameters obtained via microCT for the ground control (GC) and spaceflight (SF) groups. *p < 0.0001.

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<th>BVTV (%)</th>
<th>Comp.D (mm³)</th>
<th>Tb.N (mm³)</th>
<th>Tb.Th (mm)</th>
<th>Tb.Sp (mm)</th>
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<tr>
<td>GC (n=12)</td>
<td>0.248 ± 0.059</td>
<td>201 ± 37.8</td>
<td>4.66 ± 0.217</td>
<td>0.049 ± 0.001</td>
<td>0.205 ± 0.010</td>
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<tr>
<td>SF (n=11)</td>
<td>0.210 ± 0.016*</td>
<td>211 ± 31.8</td>
<td>4.68 ± 0.135</td>
<td>0.044 ± 0.002*</td>
<td>0.209 ± 0.008</td>
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Figure 1 — MicroCT image of trabecular bone in the L4 and L5 region. DII was calculated as: DII = 2 * (d/e-f) * (A-B-C+D+H-I).

Figure 2 — Finite element analysis performed using microCT images for the GC (n=12) and SF (n=11) groups, *p<0.05. The effective stiffness values for the GC were 2882±133 and 2899±122 for SF in units of N/mm. The normalized stiffness efficiency was 3116±69.4 for GC and 2953±54.1 for SF in units of N/mm² / Bone Volume (mm³).

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