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Perspective Article

Hylonome

What do we know about fracture risk in long-duration spaceflight?

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Introduction

Skeletal fracture represents a serious medical scenario, which must be taken into account in the design of exploration class space missions, such as those proposed for Mars. The risk of skeletal fracture represents the probability of encountering a condition in which the applied load to bone exceeds its strength. Ideally, to understand the risk of skeletal fracture incurred by crew members in these missions, we must understand the variety of potential loading conditions applied to the skeleton during the mission and the strength of the skeleton with respect to those loads. Our knowledge in this area is incomplete and requires much study in terms of modeling the range of mechanical loads associated with excursions onto planetary surfaces, how those loads are modified by spacesuit designs, and which skeletal sites are placed most at risk by those loading conditions. While we are far at present from having such an integrated picture of skeletal fracture risk, considerable effort has been made to understand the effect of spaceflight on some of the elements of bone fracture risk and we will summarize that knowledge here.

Effect of long-duration spaceflight on skeletal integrity

Bone loss is one of the primary medical complications associated with the prolonged skeletal unloading in long-duration spaceflight. Studies of the Skylab and Salyut crew members in the 1970s using calcium balance measurements and early bone mass measurements by single photon absorptiometry showed calcium loss and reduced bone mass in the calcaneus, a load bearing site, but not the radius[1-3]. A study of the Russian MIR spacecraft in the 1990s characterized the magnitude and regional extent of bone loss. Leblanc et al. carried out a systematic study using dual X-ray absorptiometry (DXA) (Hologic QDR-1000) on a cohort of 18 cosmonauts undergoing MIR missions lasting 4-6 months on the average[4]. Measurements in the spine, hip, tibia and total body were performed pre- and post-flight and showed considerable variability between individuals and within individuals as a function of skeletal site. The results showed that measurement sites in the load-bearing lower skeleton showed higher losses than the spine and arms, with a maximum average loss of 1.5% per month in the trochanter. The loss of bone mass in the lower skeleton appears to comprise distinct rates of loss in the cortical and trabecular compartments. A study by Vico et al. used computed tomography (CT) to examine changes of cortical and trabecular bone in the tibia, finding significant declines in both cortical and trabecular BMD (1% and 5%, respectively)[5]. A 2004 study in which 14 crew members of the International Space Station (ISS) were studied pre-flight and post-flight showed that the loss of bone in the hip showed large variations as a function of compartment and of anatomic sub-region. Hip measurements included measures of trabecular, cortical and integral BMD, BMC and volume for the femoral neck, trochanteric and total femur regions approximately matched to DXA. It was found that rates of integral bone loss ranged 0.9-1%/month in the spine and 1.2-1.5% in the hip, which were comparable to previous pre-postflight DXA studies on the MIR crews. In measures of proximal femoral compartmental bone, they found high rates of trabecular BMD loss (2.5-2.7%/month, $p<0.001$). In all hip regions of interest, cortical bone volume declined significantly (1.1-1.3%/month, $p<0.05$). However, the volumes of the integral regions (representing the total periosteal volume) did not change, indicating that the cortical bone was lost from the endosteal margin. When calculated in terms of bone mass, over 90% of

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the bone mass loss resulted from endocortical thinning. The study also estimated indices of bending/torsional and axial compressive strength of the femoral neck. These strength indices showed a monthly decline which was similar to that of trabecular bone, indicating that the loss of trabecular and cortical bone translated into a sizeable loss of estimated bone strength (2.5%/month).

Patient-specific finite element modeling (FEM)

NASA-funded research is currently underway to explore the effect of spaceflight on hip strength using FEM, a mathematical technique used by engineers to evaluate the strength of complex structures such as engine parts, bridges and, more recently, bones[6-9]. The structure is divided into "finite elements" (discrete pieces of the structure) to form an "FE mesh" so that it can be analyzed. The advantage of using FE modeling in this study is that this method can account for the material heterogeneity and irregular geometry of the femur, factors that cannot be considered using other approaches. Dr. Joyce Keyak developed an automated, CT scan-based method of generating patient-specific FE models of bone[10,11]. This method takes advantage of the voxel-based nature of quantitative CT scan data to achieve fully automated mesh generation and, more significantly, to allow heterogeneous material properties to be specified. The FE models can be analyzed using a loading condition simulating a load on the femur in a single-legged gait or a fall backwards and to the side with an impact on the greater trochanter. This procedure has been extensively tested *in vitro*, with high correlations to measured failure load for both loading conditions (r=0.95 and 0.96 for fall and stance loading conditions, respectively)[7,12]. In addition to their close correlation with fracture load, the FE models depict areas of high strain, which occur at the sites where the bones fracture *in vitro*, and where fractures occur *in vivo*. In both loading conditions, the FE model produces 3-D image data depicting the spatial distribution of element factor of safety (FOS), a quantity which represents the propensity of a given element to fail when subjected to a specific loading condition. The goal of the research is to characterize the loss of bone strength (based on pre-flight and post-flight CT measurements taken in the crew of the ISS) with respect to single-legged gait and stance loading, providing an estimate of the loads required to cause mechanical failure of the hip in these conditions. Initial data from this study indicate that bone strength with respect to simulated single-legged gait and fall loading conditions declines at a rate similar to that shown for the cross-sectional bone strength indices described above, resulting in a sizeable potential decrease over a six-month flight in the load required to fracture the hip. The likelihood that the failure loads calculated for the hip may be experienced during exploration missions will require further study involving modeling of the forces exerted in routine gait and falls during excursions onto the moon and Mars surfaces.

Fall risk

Studies of aging and physical disability indicate that loss of muscle strength and indices of balance are associated with risk of falling[13], and that falls are one of the most serious risk factors for bone fractures in the elderly[14,15]. If muscle atrophy associated with prolonged skeletal unloading in spaceflight has similar effects in crews of Mars missions, for example, the fracture risk associated with increased skeletal fragility may be compounded by an increased risk of falling. Declines of muscle mass and muscle strength are associated with spaceflight, and a recent study of 4 subjects undergoing 90 days bed rest showed declines in indices of postural stability averaging 68%-82% (J. Muir, H. Evans, S. Judex, Y. Qin, T. Lang, C.T. Rubin, "Extended bed-rest, like spaceflight, causes rapid and significant loss of Bone Mineral Density and Postural Control", 28th Meeting of the American Society of Bone and Mineral Research, Philadelphia, PA, September 2006).

Summary

The preponderance of evidence shows that, on average, crews of long-duration spaceflight appear to experience severe loss of bone mass, particularly in the lower skeleton. In the proximal femur, a recent study has shown that the loss of trabecular and cortical bone, taken together, may result in losses of proximal femoral strength in the order of 15% for a six-month flight. These findings, taken together with data on muscle loss and decreased postural stability in bed rest, indicate that the risk of fracture may increase due to both decreased bone strength and an increased risk of falling. A better understanding of whether the observed changes in bone strength and postural stability translate to increased fracture risk will benefit from modeling of the loads associated with physical activities and potential falls on the surface of the Moon and Mars.

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