Recovery of Space-flight-induced Bone Loss: Bone Mineral Density After Long-duration Missions as Fitted with an Exponential Function

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Accelerated bone loss in crew members in space is a well-recognized effect of weightlessness on the skeletal system and a critical risk factor for the early onset of osteoporosis after return to Earth. Studies using calcium kinetics, site-specific bone densitometry, and bone turnover markers document atrophy in the gravitationally unloaded skeleton of crew members who had flown either on Skylab (28, 56, and 84 days) or on long-duration missions (>4 months) aboard the Russian Space Station *Mir* and the International Space Station (ISS). Although scientists have used calcium kinetics and bone biomarkers to characterize bone health during space flight, no reports have addressed the impact of space flight on long-term bone health after space flight; i.e., the recovery of skeletal integrity, its nature, and its time course.

Since the Skylab missions of the 1970s, scientists have used measurements of bone mineral and bone mineral density to evaluate the effects of space flight on the skeleton. More recently, researchers used quantitative computed tomography (QCT) scans of long-duration crew members to evaluate changes in volumetric bone mineral density and in hip structure after space flight. The report described herein expands on the QCT-measured changes in crew members (performed immediately and at 1 year after return from ISS mission) by evaluating the restoration of areal bone mineral density (BMD) in long-duration crew members who were periodically scanned by dual-energy x-ray absorptiometry (DXA) for almost as much as 5 years post-flight. We developed a method to analyze this repository of BMD data to describe the skeletal recovery of astronauts after their return to Earth. Through cooperative agreements with the Russian Space Agency, we obtained access to DXA data (pre- and post-flight BMD) of Russian cosmonauts who similarly served on long-duration missions to increase the value of this analysis. In our analysis, we attempted to provide an index that would reflect rate of BMD restoration after prolonged space habitation (typically between 4 and 6 months). This report is the first to characterize the recovery of space-flight-induced bone loss over multiple years on Earth in a crew member population of this size.

We applied an exponential mathematical function to a database of BMD measurements to describe the temporal, asymptotic recovery of BMD in crew members after return to Earth. The database contained BMD data from 45 different crew members serving over a total of 56 long-duration flights. From this mathematical fit of BMD changes during the post-flight period (representing both longitudinal and cross-sectional data), we assert that most crew members who flew on long-duration missions would return to a pre-flight BMD measure within 3 years – suggesting the period for recovery is greater than the duration of the mission. Our estimate of a longer recovery period is supported by similar, but limited, reports on recovery and is consistent with animal models of disuse. This estimation from our data is based on BMD changes in the trochanter, which is the skeletal site that consistently displays the greatest deficit in BMD in space flight and flight-analog studies and appears to take the longest (albeit, not statistically significant) time to recover. With our mathematical fit indicating an approximately 9-month 50% recovery time in the trochanter (figure 1), we estimate a substantial restoration (i.e., 15/16ths recovery at four times the half-life) to occur within 36 months of return. For each post-flight BMD scan, we plotted the percentage change between post- and pre-flight BMD against the number of days after landing when the scan was performed. The intercept of the fitted line represents the change in BMD as a direct consequence of space flight (at the time of landing). Dotted lines represent 95% confidence limits for the BMD data. Data points denoted by circles (vs. crosses) represent BMD changes measured in flyers who served on multiple long-duration missions. The intercept of the fitted line shows the space-flight-induced bone loss of 7.8% in the trochanter where 50% recovery time for loss would occur at 255 days, or about 8.5 months. We also generated similar plots and estimations from BMD scans of the femoral neck, lumbar spine, pelvis, and calcaneus (Table 1).

It is important, however, to note that skeletal recovery is highly variable among crew members. Some crew members recover within the first year after return while other crew members do not recover until much later. Factors

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continued

that contribute to this variability in recovery are likely to include nutrition, skeletal muscle reconditioning, and genetics. Some of these factors may delay the ability and motivation of crew members to become ambulatory and, thus, mechanically load their skeletons. It is interesting to note three outliers for BMD loss in the femoral neck (>15% deficit, data not shown) for which two were older than the average age of, or in space longer than the average duration for, long-duration crew members. The missions corresponding to these outliers also represent the outliers' first long-duration flight. Risk factors contributing to bone loss in crew members should also be considered to evaluate their influence on recovery. Collectively, future studies will not only need to evaluate how bone metabolism responds to changes in mechanical loading (at the molecular, cellular, and tissue level) but how changes in skeletal mass and structure correlate with changes in muscle forces, with expression of skeletally relevant genes, and with nutrient uptake in this crew member population.

This investigation addresses a fundamental issue of how bone mass responds to changes in skeletal loading. These results would have an additional relevance to patient populations subjected to prolonged periods of immobilization and to the skeleton's capacity to recover.

Skeletal Site	Loss at landing (%)	50% Recovery Time (days)
Femoral Neck	6.8 (5.7, 7.9)	211 (129, 346)
Trochanter	7.8 (6.8, 8.8)	255 (173, 377)
Pelvis	7.7 (6.5, 8.9)	97 (56, 168)
Lumbar Spine	4.9 (3.8, 6.0)	151 (72, 315)
Calcaneus	2.9 (2.0, 3.8)	163 (67, 395)

Table 1. *Summary of fitted data per skeletal site.*

The percentage of pre-flight BMD loss (L0) at the time of landing and the "50% recovery time" are listed per skeletal site. The 50% recovery time represents the number of days after landing at which half of the bone mineral lost during space flight is restored. We determined the L0 and recovery times from BMD data fitted to a two-parameter exponential function for recovery of skeletal BMD after landing: Lt = L0 *exp[ln(0.5)*t/HL]. Confidence limits (95%) for the fitted values are provided in parentheses. The intercept for the fitted data (L0) (figure 1) represents BMD loss as a direct consequence of space flight.

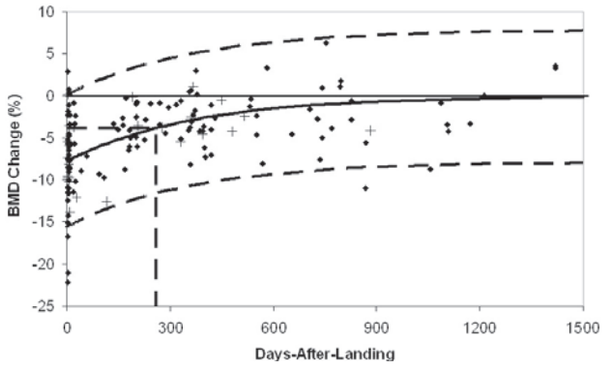

Fig. 1. *Changes in BMD at the trochanter after landing.*

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