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The Impact of Zero Gravity on Human Bone Density - A Literature Review of Spaceflight Data

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Abstract: Spending months in space without gravity takes a serious toll on the human skeleton because without the constant pull of gravity, bones especially in the spine, hips, and legs, lose strength fast, breaking down at a rate of 1–2% per month. This review looks at decades of spaceflight research, from Skylab and Mir to the International Space Station and NASA's Twins Study, to understand why this happens, how fast it occurs, and what can be done about it. The problem starts with the lack of mechanical loading, which signals bone cells to stop building new tissue while continuing to break down old bone. Changes in calcium balance, hormones, and other body systems make things worse, and recovery after returning to Earth is often incomplete. Astronauts currently rely on intense exercise, bone-protecting drugs, and carefully planned diets, but these are known to only slow down the losses. New ideas like creating artificial gravity, redesigning spacecraft for better loading, using personalized health plans, and monitoring bone health in real time could help protect future crews on missions to Mars or the Moon, and even space tourists. Ultimately, solving this problem is the key for space exploration and improving bone health here on Earth.

Table of Contents

1. Introduction 1
2. Bone Physiology in Earth's Gravity 3
3. Effects of Microgravity on Bone Density 5
4. Countermeasures and Mitigation Strategies 9
5. Data Sources and Methodological Considerations 12
6. Implications for Long-Duration Missions 14
7. Future Research Directions 15
8. Conclusion 16
9. References 17
10. Conflict of Interest 20
11. Funding 20

1. Introduction

1.1 Background

One of the most noticeable physiological challenges for an astronaut is the absence of gravitational force during long spaceflights, which negotiates with skeletal health, affecting bone density and structure. This long-term microgravity exposure disrupts the delicate balance between bone formation and resorption, which accelerates osteoporosis-like conditions, particularly in weight-bearing bones like the spine and femur, which also leads to a decrease in bone mineral density and increases both fracture risk during and after the missions, making post-flight rehabilitation much complicated. (Blaber et al., 2010). Zero gravity, or specifically microgravity, is a state where the gravitational force experienced by a body is very much minimized - it is not a lack of gravity but a state where its influence is negligible under conditions of free-fall. In orbital spaceflight, the spacecraft and all people in it are perpetually in free-fall about the Earth under constant acceleration, and as a result, the net force acting on the body appears to be zero, leading to a sensation of weightlessness (Blaber et al., 2010). Microgravity disturbs

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human physiology by altering its fluid dynamics, musculoskeletal loading, and cellular processes, which consequently presents a great number of challenges for spaceflight, especially on long-duration missions.

In a microgravity-environment, the lack of gravitational force on the human body results in an immediate cephalad fluid shift, with blood and interstitial fluid flowing from the lower extremities to the head and torso, which results in facial swelling and sinus congestion during the initial stages of space travel. Despite the elevated intracranial pressure, the heart experiences a reduction in cardiac volume, which has grave repercussions for overall cardiovascular performance - a principal cause of Spaceflight-Associated Neuro-ocular Syndrome (SANS), characterized by optic disc-edema and retinal alterations that impair vision. The mentioned fluid shift remains throughout the course of spaceflight and shows only partial recovery upon returning to Earth, where the astronauts further continue to exhibit changes in brain structure even a year after their mission, highlighting the long-term impact of microgravity on fluid dynamics and neurological function. (Man et al., 2022). The physiological impacts of human spaceflight, particularly the 'loss of bone density', were first documented during the Skylab missions in the early 1970s (Man et al., 2022). These observations indicated a high rate of bone mineral loss, averaging 1% to 1.5% per month - which is classified as "comparatively faster than normal osteoporotic individuals on Earth" (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023a).

Subsequent long-duration missions like the Soviet/Russian Mir and Salyut programs, as well as the International Space Station (ISS), consistently confirmed these early observations (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023a). Data from Mir and ISS showed that over 50% of crew members experienced at least a 10% loss in bone mineral density at specific skeletal sites, with some cosmonauts from Mir Mission recording losses as high as 15-20% (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023a). Therefore, bone loss, as observed across decades of missions, remains a major obstacle for human spaceflight.

1.2 Research Objectives

The key objectives of this paper are given as follows:

- To study the impact of zero gravity (microgravity) on human bone density, by collecting data from historical and contemporary space missions.
- To analyse the observations from various spaceflight programs, including Skylab, Mir, Salyut, the International Space Station (ISS) longitudinal studies, and the NASA Twin Study, to record the mechanisms, rates, and distribution of bone loss.
- To determine the effectiveness of contemporary countermeasures and mitigation strategies, such as exercises, pharmacological methods, and nutritional support, and explore the potential of future technologies, such as artificial gravity, narrowing down key directions for future research to ensure astronaut health during prolonged space exploration.

1.3 Scope and Limitations

This review is set to primarily focus on human studies and data derived from long-duration spaceflight missions, including those conducted on the ISS, Skylab, and Mir. The central emphasis remains on direct human physiological responses and adaptations to the space environment, while also studying the mechanistic results obtained from animal models, such as medaka fish and rodents (Chatani et al., 2015). A short note to keep in mind that 'short-duration spaceflights are not the central focus of this review as their bone loss consequences are considered minor (Carmeliet et al., 2001). There are several inherent limitations in spaceflight research studies that affect the interpretation of the data - the most important one being the low number of astronauts and cosmonauts available for such studies (Moosavi et al., 2021). Let's take a bone recovery study for instance, where data was gathered from a total of 45 individuals only, some of whom flew on multiple missions; the limited sample size impacts the statistical power of studies and the generalizability of findings to the wider population (Chatani et al., 2015).

Above this, the duration of studied space missions greatly varies, extending from 3.5 to 7 months on the ISS to 6 to 14 months on Salyut and Mir (Stavnichuk et al., 2020). This variability introduces factors that complicate direct comparisons, making it hard to isolate clear cause-and-effect relationships. Consequently, the specific exercise protocols and other countermeasures implemented also differ across such missions (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023b). Not every astronaut responds to microgravity the same way — there's a lot of individual differences in each, as in how their bodies adapt and how well the suggested countermeasures work for them. This inter-individual variability makes it hard to connect universal trends or to develop "one-size-fits-all" solutions (Sandal et al., 2020). Above these biological factors, human experimentation in space is subject to strict ethical guidelines, prioritizing astronaut safety along with logistical restraints such as limited crew time, specialized equipment availability, and that of sample collection and return, the scope of research is further

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restricted and limits its quality (Carmeliet et al., 2001). These restrictions must be recognized in order to preserve scientific integrity, frame the interpretation of the data that is currently available, and draw attention to the ongoing difficulties and requirements for further study in space physiology (Carmeliet et al., 2001).

2. Bone Physiology in Earth's Gravity

2.1 Bone Remodelling and Homeostasis

Bones are living tissues that are continuously restructured through a process known as bone remodelling, which acts as a fundamental for maintaining skeletal integrity in vertebrates, repairing micro-damage, and metabolically contributing to the body's calcium and phosphorus balance; usually by resorption of old or damaged bone, followed by the deposition of new bone material(Rowe et al., 2023). Osteoblasts and osteoclasts are the two main primary cell types that interact within each other to control this process (Rowe et al., 2023). Osteoblasts, also known as "bone-forming" cells or "builders," are responsible for synthesizing and secreting the bone matrix - composed of proteins, calcium, phosphate, and other minerals - which then solidifies into new bone tissue (Rowe et al., 2023). This primary cell is crucial for bone growth, reshaping bones as an individual ages, and repairing of damaged or broken bones (Chen et al., 2018).

On the other hand, osteoclasts function as the "demolition crew" (Kim et al., 2020). These are specialized cells that release enzymes and hydrogen ions to break down and resorb old or damaged bone tissue, which creates microscopic "scooped out" regions, known as Howship lacunae, making space for new, healthier bone to form (Rowe et al., 2023). Osteocytes, the most prevalent cell type within mature bone, reside within the bone matrix and act as mechanosensors which monitors mechanical stress and pressure changes and transmits signals to both osteoclasts and osteoblasts to orchestrate bone repair and adaptation (Rowe et al., 2023). The balance between osteoblast-mediated bone formation and osteoclast-mediated bone resorption is fundamental to bone homeostasis; with any disruption to this balance, as that which occurs in microgravity, leads to adverse changes in bone density and structure (Rowe et al., 2023).

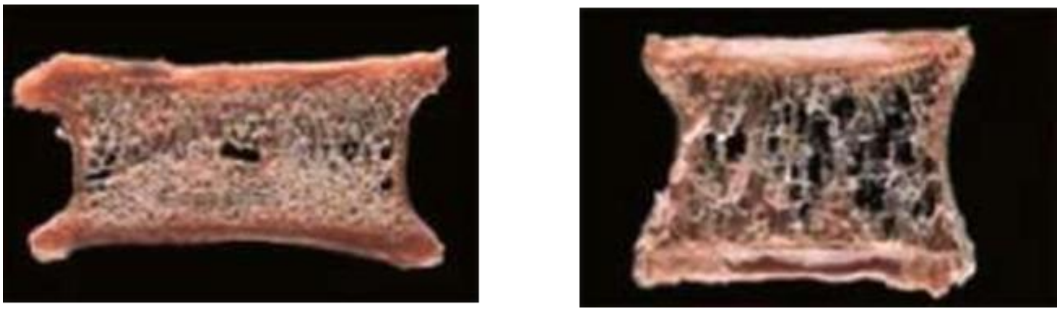

Fig. 1: A normal spinal bone (left) and a spinal bone with reduced bone density due to osteoporosis (right). (Courtesy: Tetsuro Inoue, professor emeritus, Hamamatsu University School of Medicine)

2.2 Mechanical Loading and Wolff's Law

On Earth, the skeletal system is constantly under mechanical loads due to gravity and other physical activities (Carmeliet et al., 2001). This induces continuous mechanical stress on the bone, which acts as the primary stimulus for maintaining bone density and strength (Loomer, 2001). The German anatomist and surgeon, Julius Wolff formalized this principle, now known as Wolff's Law, which states that bones adapt their architectural structure to the mechanical stresses placed upon it - which means that an increase in mechanical loading stimulates bone to strengthen its internal spongy (trabecular) and outer cortical layers while a decrease in stress leads to the weakening of these bone layers(Frost, 1994).

The characteristics of the applied forces such as their duration, magnitude, and rate are crucial factors of how bone integrity is altered. The cellular process by which mechanical forces are converted into biochemical signals that trigger bone remodelling is known as mechanotransduction.(Rowe et al., 2023) Wolff's Law provides the biomechanical framework for understanding and reasoning the spaceflight-induced bone loss - In the absence of gravitational loading, the body's adaptive response is to reduce bone mass, as the mechanical stimulus for maintenance is almost diminished. (Rowe et al., 2023).

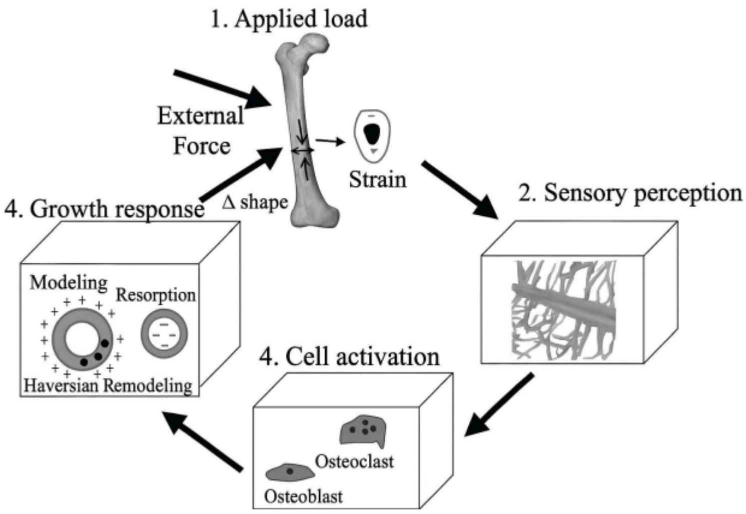

Fig. 2: Mechanobiological pathway of bone remodelling according to Wolff's Law, illustrating the sequence from mechanical loading to growth response. (Courtesy of Respire Physical Therapy, "Wolff's Law and Bone Fracture Recovery")

2.3 Bone Density Measurement Techniques

As discussed, accurate measurement of bone mineral density (BMD) is required for monitoring bone health on Earth and in space; for which, researchers typically rely on two main techniques: Dual-energy X-ray Absorptiometry (DEXA) and Quantitative Computed Tomography (QCT).

Dual-energy X-ray Absorptiometry (DEXA)

Dual-energy X-ray Absorptiometry (DEXA), also known as DXA, is an established clinical standard for measuring bone mineral density that provides accurate numbers for bone thickness and strength (Kohrt, 1998). The technique involves passing two low-dose X-ray beams of differing energy levels through the body, usually targeting the hip and lumbar (lower) spine (Kohrt, 1998). The differential absorption of these X-rays by the bone and soft tissue is used for the precise calculation of BMD (Haarbo et al., 1991). DEXA is predominantly used for the diagnosis of osteoporosis and for estimating an individual's fracture risk and the results are presented as a T-score, which compares an individual's BMD to that of a healthy young adult of the same sex, or a Z-score, which compares it to age-, sex-, and ethnicity-matched individuals(Kohrt, 1998). The radiation exposure associated with DEXA scans is very low to that of a standard X-ray (Kohrt, 1998). This method, hence, serves as a primary tool for monitoring changes in astronaut bone health before and after spaceflight, offering a quantitative and qualitative measure of overall bone mass alterations (Haarbo et al., 1991)

Quantitative Computed Tomography (QCT)

Quantitative Computed Tomography (QCT) is another advanced bone density test that focuses on the important weight-bearing regions of the skeletal system - lumbar spine and hip - and generates three-dimensional images using a CT scanner (Adams, 2009). An advantage of QCT over DEXA is its ability to differentiate and measure the BMD of the internal spongy (trabecular) bone independently from the dense outer cortical bone, and given that trabecular bone exhibits higher metabolic activity, it responds to changes (e.g., age, disease, therapy) earlier and to a greater extent than cortical bone, making detection of BMD alterations faster (Adams, 2009; Löffler et al., 2019). QCT is especially advantageous for patients with conditions such as scoliosis, arthritis, or obesity, where traditional DXA measurements are less accurate because of anatomical variations and artifacts (Engelke, 2017). This technique gives a more detailed perspective on bone microarchitecture, which is - first, the key for understanding the specific structural deterioration that occurs in microgravity and second, are not fully captured by areal BMD measurements from DEXA (Vico C Hargens, 2018a). This makes QCT a vital tool for advanced spaceflight bone research (Engelke, 2017).

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3. Effects of Microgravity on Bone Density

3.1 Mechanisms of Bone Loss in Microgravity

The abnormal environment of microgravity triggers a cascade of physiological changes in the human body that impacts the human bone density to a great level, which are driven by the absence of mechanical loading, which in turn alters calcium metabolism and leads to hormonal imbalances.

Absence of Mechanical Loading

As supported by Wolff's law, the primary driver of bone loss in microgravity (and of course, space) is the poorly present or absence of mechanical loading on the skeletal system (Carmeliet et al., 2001). What it means is that, in effect of the weightless environment of space, bones are not required to support the body against gravity, removing the constant mechanical stress that is essential for bone maintenance on Earth (Carmeliet et al., 2001). This lack of mechanical stress on bone structures signals a state of disuse to bone cells, thereby disrupting the normal bone remodelling process (Whalen et al., 1988).

This mentioned disruption in bone remodelling is a direct consequence of the bone's mechanosensing machinery, that involves osteocytes, receiving insufficient or altered signals in microgravity. On Earth, Wolff's Law dictates that bone adapts its structure to mechanical stresses; However, in microgravity, the activity of osteoblasts (bone-forming cells) considerably decreases so much, while osteoclasts (bone-resorbing cells) continue to operate at a normal pace, creating a detrimental imbalance where bone breakdown outpaces bone formation, which therefore inevitably results in a net loss of bone mass (Smith C Rice, n.d.). This continuous suppression of bone formation, prompted by the lack of adequate mechanical stimuli, illustrates why any effective countermeasure must be reintroduced to act up for sufficient and appropriate mechanical stimuli. Pharmacological or nutritional interventions, though supportive, cannot fully compensate for the lack of mechanical loading if the fundamental cellular signalling for bone formation is not adequately triggered (Smith C Rice, n.d.).

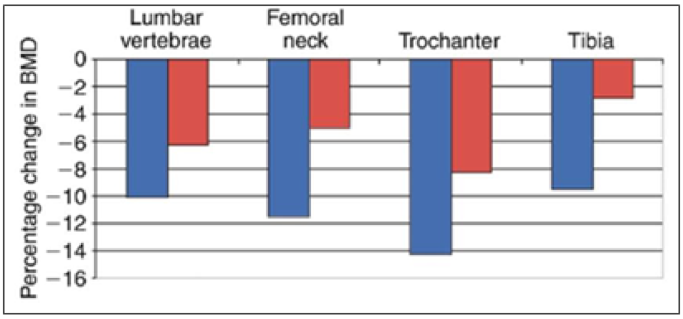

Fig. 3: Percentage change in femur region BMD for cosmonauts during space missions up to 180 days (blue and red are maximum and average gain/loss in BMD, respectively). (Charles et al., 2004)

Altered Calcium Metabolism

Exposure to microgravity also affects the systemic calcium and bone metabolism in the human physiology (Heer, 2002). It has been observed from several studies that there is an increased excretion of urinary calcium and a fair reduction in intestinal calcium absorption among astronauts, leading to an unfavourable calcium balance within the body (Smith C Rice, n.d.). To put it in numbers, estimates suggest that approximately 200-250 milligrams of calcium are lost from bone each day during spaceflight. (Reid C Bolland, 2020).

Apart from that, the breakdown of bone structure releases enough calcium into the bloodstream, that results in elevated calcium levels in the urine and decreased absorption from the gut, thereby increasing the risk of kidney stone formation. This phenomenon highlights the fact that spaceflight-induced bone loss is not only isolated to musculoskeletal issue but also to a systemic problem with high metabolic ripple effects. (Shackelford et al., 1999).

Hormonal Imbalances

Adding up to these, microgravity exposure brings a number of alterations in the hormonal regulations of the body such as reductions in parathyroid hormone (PTH) levels, which plays a crucial part in calcium regulation and bone remodelling (Heer, 2002; M. Heer et al., 1999). Estrogen deprivation is another factor in a few individuals that also contributes to increased urinary calcium loss and reduced intestinal calcium absorption (M. Heer et al., 1999).

The observed drop in PTH levels in space is a physiological feedback response by the body to the inclined ionized calcium levels resulting from the bone resorption, which suggests that the mentioned hormonal shift is a consequence of the altered bone metabolism and calcium dynamics, rather than the primary cause of bone loss, as the body attempts to compensate for elevated blood calcium(M. Heer et al., 1999). Understanding this mechanism is the base for developing pharmacological solutions because manipulating hormone levels directly without considering of the underlying mechanical unloading or calcium dysregulation is ineffective or leads to unintended systemic side effects (Heer, 2002).

3.2 Rate and Distribution of Bone Loss

Average Loss Rates per Month

Astronauts lose bone mineral density (BMD) at an average rate of 1% to 2% per month during spaceflight, which is very high compared to age-related bone loss on Earth, which typically averages about 1% per year for adults over 50 (Loomer, 2001; Stavnichuk et al., 2020). To put into picture - for a six- month mission, this rate of bone loss equates to a bone degradation situation typically seen over 20 years on Earth (Jean Sibonga et al., 2023).

Though bone loss is a minor concern for short-duration flights, it becomes a real setback for long-duration ones due to its cumulative effect. Moreover, few astronauts experience even higher rates of loss, with some showing up to a rate of 14% reduction in femoral neck BMD during 4.5 to 6-month missions (M. Heer et al., 1999). It is important to note that the nature of bone loss in space is qualitatively different from natural aging, i.e. bones age differently in space than they do on Earth - on Earth, the external part of the bone becomes fragile sooner than its interior part as a person ages, but in space, the internal part of the bone weakens faster than its exterior (Stavnichuk et al., 2020).This phenomenal difference in bone remodelling patterns (preferential internal versus external fragility) indicates that spaceflight-induced bone loss is not merely accelerated aging but a distinct pathological process in vertebrates(Rowe et al., 2023). Therefore, countermeasures and diagnostic criteria developed for age-related osteoporosis on Earth are not directly applicable or effective enough for astronauts, necessitating space-specific research that considers the unique microarchitectural changes (Harris et al., 1998).

Effects on Weight-Bearing Bones

Bone loss in microgravity is a highly region-specific effect- i.e. it predominantly affects the weight-bearing skeletal sites which include the spine (lumbar spine), hips (femur, femoral neck, trochanter, pelvis), and lower extremities (calcaneus, tibia); while non-weight-bearing bones, such as those in the arms show minimal to no changes (e.g., 0.1% loss per month) (Man et al., 2022). Thus, the distinct distribution of bone loss provides strong empirical support for Wolff's Law, demonstrating how bone adapts its structure in response to the local mechanical environment (Man et al., 2022). The localized nature of bone loss suggests that countermeasures too must be specifically made to provide targeted mechanical loading to the mostly affected weight-bearing regions. This too supports what we earlier discussed - that generalized exercise, or systemic pharmacological approaches do not fully address the regional heterogeneity of bone demineralization, requiring a more precise and focused strategy for preserving skeletal integrity during spaceflight.

3.3 Comparative Findings from Major Missions

Until now, studies from multiple space missions have given us various clues on how bone loss unfolds over time in microgravity and also revealed the underlying biological shifts that come with it.

Skylab Missions

The Skylab missions, as mentioned in section 1.1, marked the first organized effort to thoroughly collect musculoskeletal data on long-duration spaceflight as early as the 1970s; where it documented a considerable bone mineral loss and calcium excretion (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023b). Astronauts from Skylab 2, 3, and 4 have been observed to have experienced a decrease in their bone density of the calcaneus (heel bone) - up to 8%, with an average of 4% on the longest flights (59 and 84 days). The findings highlighted the rapid rate of bone demineralization in microgravity and its implications for skeletal health during long-duration space missions. (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023a, 2023b)

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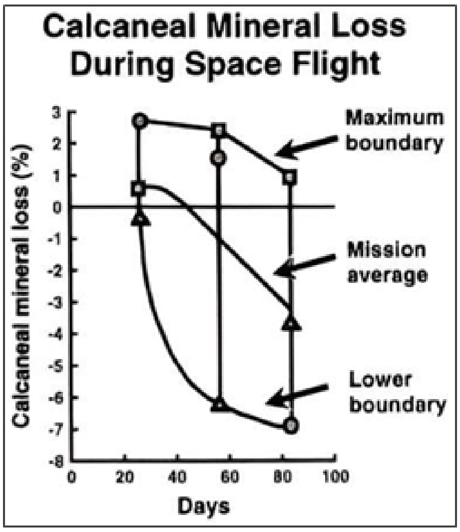

Fig. 4: Calcaneal bone mineral density loss in astronauts plotted against Skylab mission duration, showing increased loss with longer stays in microgravity. (Holick, 1998)

Mir and Salyut Programs

Observations recorded from cosmonauts on the Soviet/Russian Salyut and Mir programs further lined up along the Skylab findings, which reported losses in the calcaneus bone density as high as 19% after 140 days in microgravity (NASA Office of the Chief Health C Medical Officer (OCHMO), 2023b, 2023a). Multi-year observations in crewmembers of long-term Salyut and Mir missions (6 to 14 months) summarized that BMD losses were consistent in the trabecular bone of the lower skeleton (lumbar spine, femoral proximal epiphysis, pelvis) (Shackelford et al., 1999).

Over the course of multiple missions, post-flight BMD measurements generally remained within the thresholds defined by the World Health Organization (WHO); with several cases indicating localized reductions in BMD, consistent with osteopenia. (Shackelford et al., 1999) Data from 18 cosmonauts aboard the Mir space station between 1990 and 1995, obtained via dual-energy X-ray absorptiometry (DEXA), showed both the magnitude and anatomical distribution of bone loss (Shackelford et al., 1999). In individuals who participated in more than one mission, pre-flight assessments preceding subsequent flights suggested a delayed or incomplete recovery of BMD (Shackelford et al., 1999).

A follow-up study monitoring skeletal restoration over a three-year period post-flight reported that all 14 subjects experienced bone loss in at least one region of the spine or lower limbs during spaceflight, with only one astronaut achieving full recovery to baseline BMD values across all regions (Shackelford et al., 1999). These findings highlight the ongoing difficulty of restoring bone health after space missions and stress the urgent need for effective, well-targeted countermeasures.

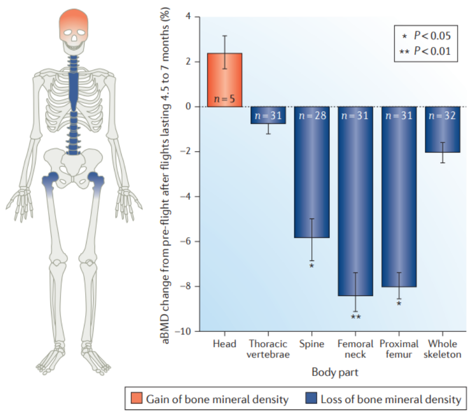

Fig. 5: Changes in Bone Mineral Density (BMD) in different body parts of cosmonauts after MIR Spaceflights (4.5–7 months). (Vico C Hargens, 2018b)

International Space Station (ISS) Studies

The ISS has been an important platform for extensive studies on bone density, monitoring crew members using dual-energy X-ray absorptiometry (DEXA) before and after long-duration missions (4-6 months), making it a necessary medical requirement at NASA Johnson Space Centre. The average losses of bone mineral after the long-duration spaceflights on the ISS ranged between 2% and 9% across all sites. (Sibonga et al., n.d.).

Studies using quantitative computed tomography (QCT) of the hip and spine along with high-resolution peripheral QCT (HR-pQCT) of the lower leg have shown loss of trabecular bone mineral density (Löffler et al., 2019). A steep drop in hip trabecular bone (an indicator of bone quality) and deficient, or delayed, bone recovery in some crewmembers have been documented from various 6-month spaceflight journeys (Sibonga et al., 2007). These trends also suggest that astronauts are at a great risk for premature or irreversible skeletal fragility because trabecular deterioration is directly linked with skeletal fragility and fractures in aging populations (Sibonga et al., n.d.).

Fig. 6: Comparative analysis of femur bone mineral density loss from multiple spaceflight studies aboard the International Space Station (ISS). (Image Courtesy: phys.org)

The TBone and TBone2 experiments on the ISS have further confirmed that rate and percentage of bone loss increase proportionally to the mission length. More than 50% of astronauts in the TBone study did not regain their pre-flight bone density even after a year on Earth, with those who spent less than six months in space recovering more bone than those on longer missions (Sibonga et al., n.d.). This indicates that bone lost during spaceflight journeys are not always completely regained, and rather opposite to what is expected, in some cases, it even continues to deteriorate after landing due to osteocyte death (Chen et al., 2018).

NASA Twin Study Findings

The NASA Twins Study provided many observations regarding the physiological, molecular, and cognitive changes in the human body due to exposure to spaceflight hazards, leveraging genetic similarity by comparing identical twin astronauts- Scott and Mark Kelly (Garrett-Bakelman et al., 2019). This study design provided only a few numbers of variables, with Scott Kelly spending 340 days on the ISS, while his brother Mark remaining on Earth as a control - making this study design very much validated for scientific investigation with high reliability and accurate results (Garrett-Bakelman et al., 2019).

The observations of the study stated that Scott's bone breakdown and bone reformation cycle occurred at a faster rate during the first six months of his mission but slowed down in the second half when his exercise volume was lower (Monica Edwards C Laurie Abadie, 2019). Although the study didn’t report the exact bone density measurements for Scott Kelly, it however revealed the fact that gene expression changes that are linked to bone formation were among the 7% of his genes that hadn’t returned to pre-flight levels even after six months from returning to Earth. This points to a lasting molecular imprint of spaceflight on bone-related biological pathways (Nathan Cranford, 2018).

The study also puts forth other interesting micro-physiological adaptations- one of such being the lengthening of Scott's telomeres (chromosome endcaps), which typically shorten with age (Colleen Walsh, 2019). Most of these telomeres, however, shortened back to near pre-flight levels within two days of his return to Earth. Thereby, the Twins Study gives a deep understanding on how genetic predispositions might influence individual responses to the space environment by comparing genetically identical individuals (identical twins) (Nathan Cranford, 2018).

This type of research is the bedrock for advancing personalized medicine approaches in spaceflight, identifying who is more prone to bone loss or other physiological changes and developing individualized countermeasures (Colleen Walsh, 2019). This design, therefore, develops an approach beyond the standardized type, optimizing astronauts' safety and their performances based on their individual biological profiles (Garrett-Bakelman et al., 2019).

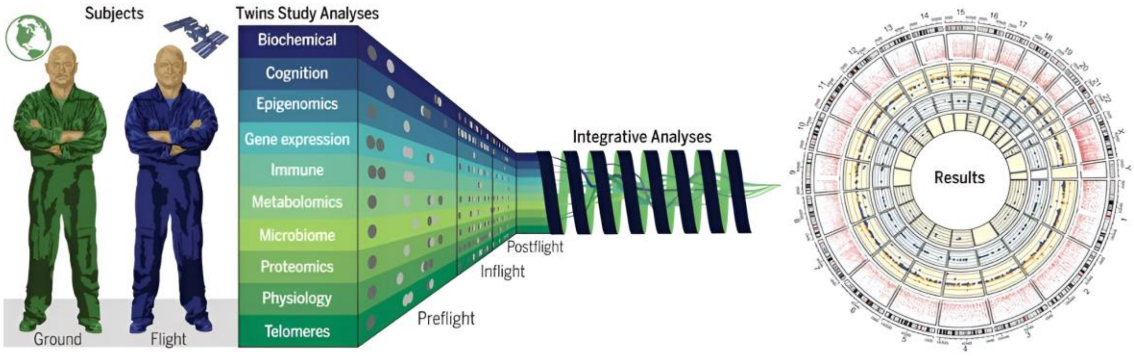

Fig. 7: (Left and middle) Genetically identical twin subjects (ground and flight) were characterized across 10 generalized biomedical modalities before (preflight), during (inflight), and after flight (postflight) for a total of 25 months (circles indicate time points at which data were collected). (Right) Data were integrated to guide biomedical metrics across various "-omes" for future missions (concentric circles indicate, from inner to outer, cytokines, proteome, transcriptome, and methylome).(Garrett-Bakelman et al., 2019)

4. Countermeasures and Mitigation Strategies

4.1 Exercise Regimens

Exercise acts as the base when dealing with muscle and bone loss in space, as it involves everything from the mechanical loading to the skeletal system. Three main and common exercise regimes practiced during medium to long duration spaceflight journeys are listed here.

Resistance Exercises (ARED – Advanced Resistive Exercise Device)

The Advanced Resistive Exercise Device (ARED) is basically a multi-exercise high-load resistive exercise device developed by NASA for the ISS program (Lamoreaux C Landeck, 2006). ARED works by using a system of vacuum cylinders and flywheel cables to simulate the process of free-weight exercises on Earth, providing a nearly constant resistance source (Lamoreaux C Landeck, 2006). It can deliver up to 600 pounds-force (2,700 N) for bar workouts (e.g., squats, deadlifts, heel raises) and 150 pounds-force (670 N) for cable workouts (Lamoreaux C Landeck, 2006).

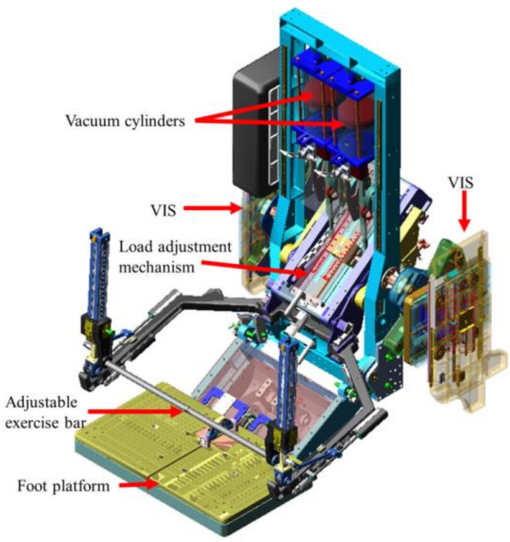

Fig. 8: Structural layout of the Advanced Resistive Exercise Device (ARED) showing vacuum cylinders, load adjustment mechanism, VIS, adjustable exercise bar, and foot platform. (Courtesy: NASA Digital Astronaut Project)

This high-load capability allows astronauts to perform a wider variety of exercises at higher loads, speeds, and longer strokes, which is crucial for effectively maintaining muscle strength and bone mass in microgravity

(Lamoreaux C Landeck, 2006).ARED is designed to target the lower extremity areas which are known to experience accelerated losses in muscle and bone during spaceflight (Jasen L. Raboin et al., 2005). Though ARED has shown a fair reduction of bone loss compared to other older devices, post-flight bone loss in the femur neck and hip have still been observed and remains to pose challenges (English et al., 2008).

Treadmills and Cycling with Harnesses

The Treadmill with Vibration Isolation and Stabilization (TVIS) and the Combined Operational Load Bearing External Resistance Treadmill (COLBERT) are specialized treadmills to provide cardiovascular and skeletal loading designed for use in microgravity (Bourdier et al., 2022; Korth C Reeves, 2015). Astronauts use harnesses and bungee cords to strap themselves to the treadmill to allow themselves to walk or run in a way that mimics Earth's gravity (Korth C Reeves, 2015). The load is set at 60% of the astronaut's body weight at the start of a mission and is gradually increased to 85%; This method, therefore, creates the necessarily required weight-bearing environment as that of Earth (Korth C Reeves, 2015).

Looking up for another form of Cardiovascular exercise, the Cycle Ergometer with Vibration Isolation and Stabilization (CEVIS) is a stationary bicycle which, unlike the bikes on Earth, does not require a seat or handlebars in microgravity - here, astronauts strap themselves to the pedals and use their legs to maintain position while cycling (Genc et al., 2010). These exercise countermeasures, though slow down the rate of bone loss, do not eliminate the problem entirely as studies show - i.e. despite following daily exercise programs strictly, astronauts still lose an average of 1% to 2% of their bone density per month (Genc et al., 2010)

Fig. 9: Astronauts using the COLBERT treadmill (left) and the CEVIS cycle ergometer (right) aboard the International Space Station (ISS). (Courtesy: The European Space Agency (left) and Danish Aerospace Company (right))

4.2 Pharmacological Interventions

Pharmacological agents are supplementary countermeasures to address the bone loss mechanisms that exercise alone cannot resolve.

Bisphosphonates

Bisphosphonates are a class of drugs used to treat osteoporosis on Earth that have been investigated for their potential to reduce spaceflight-induced bone loss that work by inhibiting osteoclastic bone resorption, thereby reducing the rate at which old bone tissue is broken down (LeBlanc et al., 2013a). Studies from various experiments show that the mixed combination of exercise (specifically with ARED) and bisphosphonate administration (e.g., 70 mg of alendronate weekly) can bring down the expected decrease in multiple measures of bone physiology affected by microgravity experienced during spaceflight - reducing the DXA-determined losses in bone mineral density of the spine, hip, and pelvis, as well as QCT-determined compartmental losses in trabecular and cortical bone mass in the hip (Rosenthal et al., 2024). The use of bisphosphonates has also been shown to help prevent the increase in urinary calcium excretion, which is associated with kidney stone formation (Rosenthal et al., 2024). Therefore, the combination of exercise plus an antiresorptive drug appears to be a useful strategy for protecting bone health during long-duration spaceflight (LeBlanc et al., 2013a)

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Vitamin D and Calcium Supplementation

Vitamin D and calcium are the pillars for bone health on Earth, and their deficiency increases the risk of bone loss (Smith C Rice, n.d.). Astronauts on long flights also experience low sunlight exposure, thereby leading to a decrease in vitamin D, which is essential for calcium absorption - calcium is the key component in growing and maintaining bones; however, experiments in space have shown that while an adequate calcium intake and vitamin D supplementation are mandatory, they do not efficiently counteract the development of space osteoporosis in contrast to terrestrial conditions (Reid C Bolland, 2020). This is partly because the absorption of calcium from the intestines decreases during spaceflight, meaning even extra calcium supplementation does not fully correct the bone loss (M. Heer et al., 1999). Though calcium supplements produce a fair 1% increase in bone density in the first year of terrestrial use, it is experimentally observed that this benefit does not increase further with continued supplementation (Reid C Bolland, 2020). Likewise, vitamin D supplements alone do not consistently improve bone density in clinical trials, except in specific subgroups with very low baseline levels (Tang et al., 2021). This indicates that while essential for overall health, these supplements are insufficient on their own to overcome the profound effects of microgravity on bone. (Tang et al., 2021).

4.3 Nutritional Support

Nutritional strategies play an important and complex role in maintaining astronauts' bone health during space missions, wherein intake of calcium, vitamin D, and other micro-nutrients are very important in microgravity. Carefully planned dietary regimens, combined with other countermeasures, are known to reduce the bone loss effects during long-duration spaceflight.

Caloric Intake and Bone Health

Adequate nutrition is one of the most important factors to be considered for astronauts during long-duration missions and reduced energy intake, which has been observed in spaceflight (e.g., Scott Kelly consumed 30% fewer calories than anticipated during the Twins Study) (Monica Edwards C Laurie Abadie, 2019) , enhances muscle catabolism, which in turn negatively impacts bone health due to the interdependence of the musculoskeletal system (Moosavi et al., 2021). As with calcium and vitamin D, adequate calorie and protein intake is essential for maintaining healthy bone structure; and providing an optimized diet with adequate amounts of these nutrients is also important to mitigate bone loss, with minimal to zero risk of side effects (Tang et al., 2021).

Micronutrient Balance

The balance of various micronutrients is also an important factor to keep in mind because space diets tend to have relatively higher amounts of sodium, averaging over 5000 mg/day for astronauts which is associated with increased amounts of calcium in the urine, which worsens bone loss and increases the risk of kidney stones (Smith C Rice, n.d.). The ratio of protein to potassium in the diet is also known to affect the bone metabolism (Smith C Rice, n.d.). Though increased protein intake (e.g., 1.5–2.0 g/kg/day) is beneficial for skeletal muscle, increased consumption of such sulfur-containing amino acids, often found in animal proteins, is associated with increased bone resorption which accelerates the bone loss during spaceflight (Hackney C English, 2014).

This puts on a compromising-dilemma for musculoskeletal countermeasures, where optimizing muscle parameters might directly worsen bone outcomes (Hackney C English, 2014). To protect both muscle and bone health, future studies are required which has to evaluate increased protein intake via non- sulfur-containing essential amino acids or leucine, in combination with exercise countermeasures, while also considering the influence of reduced energy intake (Hackney C English, 2014).

4.4 Future Technologies and Artificial Gravity

Centrifuge-based Solutions

Artificial gravity (AG), often produced by continuous rotation of a transit vehicle or intermittent use of a short-radius centrifuge within a habitat, is considered a highly promising countermeasure to deal with bone loss during spaceflight (Isasi et al., 2022). AG has the very potential to completely solve the bone loss experienced by astronauts, as it provides an omnipresent inertial loading that closely replicates the gravitational environment of Earth, which would provide an Earth-like loading to the musculoskeletal system, cardiovascular system, and graviceptors (Davis-Street C Paloski, 2005).

Studies have also shown and supported that the produced centrifugal force has a positive effect on bone; for instance, Biosatellite studies in rodents have shown that microgravity-induced osteoporosis and associated decreases in bone structural properties are minimizable by hyper-gravity produced by centrifugation (Smith et al., 2009). Ground-based bed rest studies in humans have also shown that intermittent exposure to 1G (by standing or walking) prevented the increase in urinary calcium excretion typically seen during simulated microgravity (Davis-Street C Paloski, 2005).

Though we know that 'continuous' AG provides the advantage of constant loading, even 'intermittent' centrifugation could be employed as a countermeasure to the topic of discussion (Davis-Street C Paloski, 2005). The biggest challenge for implementing this centrifuge-based artificial gravity is its large size and expense required to provide sufficient centrifugal force (Isasi et al., 2022). Further research is needed to identify several other parameters such as the minimum level, duration, and frequency of AG exposure required to maintain normal physiological functions (Clément et al., 2015).

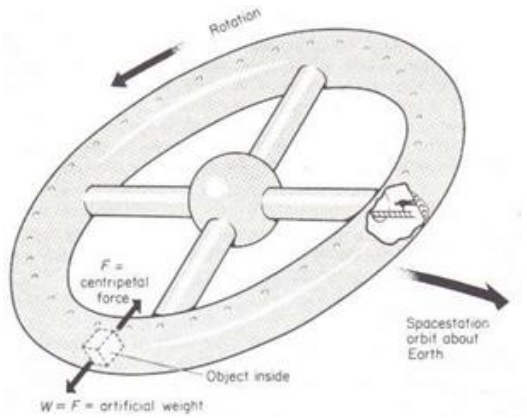

Fig. 10: Concept of artificial weight generation in a rotating space station, where centripetal force acts as artificial gravity for objects inside the station. (Courtesy: PhysicsMax - Artificial weight in a space station)

Habitat Design and In-flight Biomechanical Loading Systems

The design of future space habitats and the integration of in-flight biomechanical loading systems are another important aspect to look at while addressing musculoskeletal health. Understanding the combined effects on bone and muscle is paramount in this area, as these systems are anatomically and functionally interconnected (Moosavi et al., 2021). Bones are directly affected by muscle atrophy and changes in muscle strength, particularly at muscle attachments, thereby suggesting that most effective exercise countermeasures are to be robust, individualized, resistive exercise, primarily targeting muscle mass and strength (Moosavi et al., 2021).

A reductionist approach (a method of understanding complex systems by breaking them down into their individual, simpler components) focusing on only one part of the musculoskeletal system is insufficient for determining the most protective exercise protocols for astronauts (Moosavi et al., 2021). Future habitat designs are expected to bring systems that support more natural and consistent biomechanical loading, potentially through modified living spaces or integrated exercise equipment that better mimics Earth-like activities. This approach, considering the interplay between skeletal muscles, tendons, ligaments, and bones, is the essential key element for developing comprehensive countermeasures for long-duration spaceflight (Moosavi et al., 2021).

5. Data Sources and Methodological Considerations

The study of bone density in spaceflight depends on a variety of data sources and faces several methodological challenges; a brief information of the same is given herewith.

5.1 Spaceflight Data Repositories.

NASA's Life Sciences Data Archive (LSDA)

The Ames Life Sciences Data Archive (ALSDA), which is part of NASA's broader LSDA, is the official repository for non-human science data generated by NASA's Space Biology Program and Human Research Program, responsible for archiving, collecting, curating, and making available space-relevant higher-order phenotypic datasets, spanning biological levels from tissues and organs to whole organisms, physiology, and behaviour. The LSDA also acquires, stores, maintains, and distributes information from NASA-funded human life sciences investigations, enabling scientists to perform retrospective analyses across missions, experiments, disciplines, research subjects, and species, providing valuable data for understanding conditions like muscle atrophy and bone demineralization that are mimicked in space in healthy individuals. (Scott et al., 2020)

ESA and JAXA Mission Archives

The European Space Agency (ESA) and the Japan Aerospace Exploration Agency (JAXA) also keep their own archives of space mission data, helping build a shared global picture of how space affects the human body. ESA's Human Research Experiment Data Archive (HREDA) stores results from studies funded by its Directorate for Human and Robotic Exploration, going back as far as 1972, including both microgravity research and ground-based simulations (Vico et al., 2017). One example is the EDOS-1 project Early Detection of Osteoporosis in Space which contains detailed records of human bone density, changes in the microstructure of cortical and trabecular bone, and biochemical markers linked to bone breakdown (Vico et al., 2017). JAXA has contributed its own research, such as experiments with medaka fish aboard the ISS, which shed light on osteoclast activity and bone density changes in microgravity (Chatani et al., 2015). Through its AIREX repository, JAXA makes a wide range of aerospace-related academic papers available, including studies in life sciences (Life : Experiment - International Space Station - JAXA, 2007). Some of these come from joint projects with NASA, like research on bisphosphonates, further expanding the pool of international space health data (LeBlanc et al., 2013b).

NASA Twins Study and Bed Rest Studies

The NASA Twins Study (as discussed in Section 3.3.4) offered a rare opportunity to collect extensive physiological, molecular, and cognitive data from identical twin astronauts living in very different environments—one on Earth and one aboard the ISS (Garrett-Bakelman et al., 2019). The integrated dataset from this work has provided exceptional insights into the effects of long-duration spaceflight on the human body, including changes in bone formation networks (Nathan Cranford, 2018). On Earth, bed rest studies are often used as ground-based models to mimic some of the effects of microgravity on the body (Hargens C Vico, 2016). These experiments focus on systems such as bone, muscle, and the cardiovascular network.The most common method is the 6-degree head-down tilt (HDT) bed rest model, which helps researchers to study and test countermeasures for bone loss, muscle and heart atrophy, and orthostatic intolerance (Hargens C Vico, 2016). While bed rest cannot fully reproduce all aspects of spaceflight such as certain fluid shifts and body compression it provides a controlled setting to explore how the body responds to prolonged unloading and deconditioning (Hargens C Vico, 2016). This approach is fundamentally the base for understanding bone mineral loss and for assessing countermeasures before they are put into practice in actual missions.

5.2 Limitations in Data Interpretation

Small Sample Sizes

The primary challenge is the small sample size of astronaut cohorts who undertake long-duration space missions which restricts the statistical power of studies and the generalizability of the findings (Moosavi et al., 2021). While the data recorded is valuable, it still is a small number compared to terrestrial clinical trials. This constraint means that the observed changes, though attractively provides a base solution, are not representative or applicable to the entire astronaut population or future space travellers, and it further complicates the detection of subtle effects or rare individual responses (Sibonga et al., n.d.).

Variability in Duration and Intensity of Exposure

The duration of such studies with respect to space missions and the intensity of countermeasures implemented also vary considerably - that is, mission lengths can range from 3.5 to 7 months on the ISS (Gabel et al., 2022), with historical missions on Mir lasting up to 14 months (Stavnichuk et al., 2020), and the exercise regimens and other countermeasures have also evolved over time and differ among individuals (Man et al., 2022).

This variability introduces many complicating factors, making it very challenging to narrow down the precise impact of microgravity and the effectiveness of the specific countermeasures. Differences in individual cooperation to prescribed exercise protocols or dietary intake further increases the data variability, complicating direct comparisons and the identification of trends in the results so obtained (Loomer, 2001).

Ethical and Logistical Challenges of Human Experimentation in Space

Human experimentation in space is subject to strict ethical guidelines, prioritizing astronaut safety and well-being above everything, which obviously limits the interventions and experimental designs that can be implemented to obtain the desired data from result (Life : Experiment - International Space Station - JAXA, 2007). Logistical constraints, such as limited crew time for research activities, the specialized equipment required for in-flight measurements, and the complexities of collecting, preserving, and returning biological samples to Earth are some which restrict the scope and frequency of research (Steven T. Moore C Hamish G. MacDougall, 2010).

The lengthy process from data collection to analysis and eventual publication - which takes several months or even years - also gets in the way of putting research into action through effective countermeasures (Garrett-Bakelman et al., 2019). These practical difficulties necessitate reliance on ground-based analogues like bed rest studies, which, though being valuable and accurate enough, do not perfectly replicate the microgravity environment (Hargens C Vico, 2016).

6. Implications for Long-Duration Missions

The effects of zero gravity on human bone density carry important implications for planning and executing future long-duration space missions particularly to Mars and the Moon as well as for the growing field of space tourism.

6.1 Mars and Lunar Missions

Duration and Gravity Considerations

Future missions to Mars and the Moon will have astronauts in space for much longer stretches and keep them highly exposed to micro-gravity environments (Wagner, 2007). A round trip to Mars, for example, could take about three years, months spent in microgravity during transit, followed by time on the Martian surface (0.38g) or on the Moon (0.16g) (Carmeliet et al., 2001). The combined effects of prolonged microgravity and subsequent partial gravity are still poorly understood and very particularly, it’s unclear whether the physical deconditioning that occurs during flight can be reversed or even improved once astronauts are living in a 0.38g environment. These uncertainties raise important concerns for long-term astronaut health (Steven T. Moore C Hamish G. MacDougall, 2010).

Cumulative Risk of Bone Fragility and Fracture

In microgravity, bone mass declines rapidly on average 1–2% per month creating a substantial long-term risk of fragility and fracture for astronauts on extended missions (Man et al., 2022). Without strong countermeasures, a crew member could arrive on Mars with bones as fragile as those of an osteoporotic patient on Earth, making even everyday activities risky, let alone physically demanding mission tasks (Löffler et al., 2019). Research indicates that in just six months, trabecular and cortical bone loss in the proximal femur could translate to an estimated 15% reduction in bone strength (Sibonga et al., 2024). Muscle atrophy and reduced balance control add to this danger by increasing the likelihood of falls (Sibonga et al., 2024). The possibility of lasting skeletal damage and even an early onset of age-related issues like osteoporosis, after returning to Earth is a serious concern for missions lasting one to three years (Löffler et al., 2019).

6.2 Space Tourism and Commercial Spaceflight

The rise of space tourism and commercial spaceflight puts up a whole new set of questions about bone; because unlike professional astronauts, who are trained for years and are closely monitored by medical teams, the space tourists are everyday people- some older, some with health conditions, and most with only a short time to prepare (Carmeliet et al., 2001). Even a short trip to space, and hence being in microgravity, will start the cycle which weakens bones as they’re not exposed to the regular pressure and resistance, they need to stay strong, which also means a higher risk of injury once they’re back on Earth (Sibonga et al., 2024). Since, space travel is becoming something that people shall experience, there's a need to find better ways to protect their bones and their health in general before, during, and after their journey (Rowe et al., 2023).

Short-term Effects in Non-professional Astronauts

Though bone density loss does occur in shorter missions, the cumulative impact of the same is studied to be a little less severe than that for long-duration professional astronaut missions, making bone loss a fairly minor bone consequence in short-duration spaceflights (Orwoll et al., 2013). However, even short exposures to microgravity will initiate the discussed physiological adaptations, and the long-term effects of such exposures, especially on non- professional astronauts and those with pre-existing conditions, are less understood, making it very difficult to give space explorations and tourism a clear path (Baran et al., 2022).

Preparedness of Private Space Travelers

Unlike professional astronauts who take regular medical screening and continuous monitoring throughout their careers, commercial spaceflight participants have varying health profiles and are not subjected to the same medical requirements or countermeasure regimens (Robert E. Lewis, 2023). Medical evaluation and certification for commercial spaceflight participants, therefore, face many challenges due to limited guidance on the effects of microgravity on various medical conditions (Robert E. Lewis, 2023). Though a few professional astronaut corps have a well-established bone health program that includes pre- and post-flight DXA scans and biochemical analyses, such comprehensive protocols are standard for private travellers; and this directly pushes the development of appropriate medical standards and screening protocols stitched and tailored for commercial spaceflight participants so that their safety is ensured and their potential health risks, including bone fragility and fracture are medically taken care of (Jean Sibonga et al., 2023).

7. Future Research Directions

7.1 Longitudinal and Post-Flight Recovery Studies

One of the highlighted focuses of current research and studies is on how astronauts recover from bone loss after returning to Earth, and how long this recovery takes for each individual. It is now clear that although some bone mass is regained post-flight, both the speed and completeness of this process remain open questions (Man et al., 2022). In the TBone study, more than half of participating astronauts have still not recovered their pre-flight bone density even a year after returning, with those on shorter missions (less than six months) regaining more bones than those on longer missions (Loomer, 2001). Another investigation found that it could take up to three years for bone mass density to return to pre-flight levels; and even then, the recovered bone often had a different structure larger but more porous suggesting incomplete restoration of its original quality (Orwoll et al., 2013).

The discussed issue, which inherently leads to long-term risk of fractures for astronauts on Earth who have experienced substantial bone loss in space, is for a worse fact, not yet fully understood (Sibonga et al., 2024). Therefore, continued research is needed to monitor astronauts for many years after flight, to determine whether full recovery is possible and whether a plateau is reached, and whether there is an increased likelihood of early-onset osteoporosis or fractures later in life (Orwoll et al., 2013). Ongoing studies, such as TBone2, which began in 2023 and is scheduled to run until 2031, aim to explore the mechanisms behind bone loss and recovery in astronauts on missions lasting up to one year aboard the ISS (Korth C Reeves, 2015).

7.2 Integration with Other Physiological Systems

The human body functions as an interconnected system, and spaceflight-induced changes in one system often influence others. Therefore, future research must focus on the integration of bone health with other physiological systems.(Graebe et al., 2004) Bone loss is very much related to muscle atrophy, i.e. in microgravity, muscles weaken because they no longer need to work as hard, leading to a loss of mass and strength, particularly in postural muscles (Frost, 1994). This muscle unloading as stated earlier impacts bone health because bone structure and strength are affected by the changes in muscle strength, especially at muscle attachments (Moosavi et al., 2021).

Changes in cardiovascular activity also impact bone health due to the fluid shifts, reduced red blood cell mass, and cardiovascular deconditioning, such as reduced total blood volume and cardiac atrophy, occur as a result of microgravity (Graebe et al., 2004). These events will have repercussions on blood delivery to bones and total metabolic activity impacting functions involved in remodelling bones (Davis-Street C Paloski, 2005).

Neurometabolic changes are the next major concern, especially when it comes to balance and the risk of falling which is because many astronauts experience clumsiness, difficulty walking in a straight line, dizziness, and vertigo after returning to Earth with its effects linked to adaptations in the neurometabolic system during spaceflight. When these balance issues occur alongside weakened bones and muscles, the danger of falls and resulting fractures in a gravity environment rises sharply (Sibonga et al., 2024). These effects tell us how closely interconnected the body's physiological systems are and how addressing only one system in isolation is not enough to protect astronaut health (Graebe et al., 2004). Therefore, the countermeasures will need to be integrated and multi-spot repairing, targeting multiple systems at the same time to ensure that astronauts are able to safely carry out their regular and usual tasks upon returning to Earth and even while operating on other planetary surfaces (Hedge et al., 2022).

7.3 Development of Personalized Countermeasures

The observed variability in individual physiological responses to microgravity pulls upon itself the need for personalized countermeasures; advances in "Omics" methodologies (genomics, transcriptomics, proteomics, and metabolomics) are paving the way for a personalized medicine paradigm in spaceflight (Schmidt C Goodwin, 2013). This involves using information about an astronaut's genes, proteins, and metabolites, in the context of their diet, nutrition, lifestyle, and environment, to develop countermeasures customized for each individual and the specific mission (Schmidt C Goodwin, 2013). Research now aims to identify genomic markers that drive the various risk profiles or alter the effects of therapeutic drugs in space, making it the key pathway for identifying who is more susceptible to bone loss or other physiological changes, leading to individualized exercise and medication plans (Robert E. Lewis, 2023).

The development of wearable technology for bone health monitoring is also a promising avenue, where lightweight, flexible devices, embedded with biosensors, motion sensors, and even radiation detectors, provide real-time data on vital signs, activity levels, and potentially bone health indicators (Melissa L. Gaskill, 2024). Technologies like Radiofrequency Echographic Multi Spectrometry (REMS) are being explored by NASA for their portability, fast scan time, and radiation-free nature in these wearable devices which allows in-mission assessment of bone changes and real-time adjustments to the countermeasure strategies (Jaber et al., 2025).

AI-driven analytics and machine learning tools can process the large volumes of health data and provide real-time anomaly detection and predictive diagnostics, enabling astronauts to be aware of their potential health risks before the effects worsen during deep-space missions (Gupta C Ghosh, 2025). The continued advancement of adaptable wearable devices will be the prime driving factor to this effort for improving onboard health monitoring and supporting the broader progress of human space exploration (Melissa L. Gaskill, 2024).

8. Conclusion

The accumulated evidence from spaceflight studies, therefore, clearly shows that microgravity has a deep-rooted impact on human bone density, posing a major physiological challenge for long-duration missions. The underlying cause of the same is the loss or absence of mechanical loading, which disrupts the balance of bone remodelling, which in turn further results in a net decrease in bone mass. This process is additionally burdened by the changes recorded in calcium metabolism resulting in greater urinary calcium excretion and a higher risk of kidney stones and by hormonal adjustments that reflect the body's attempts to adapt. Summarizing the facts - astronauts lose an average of 1–2% of bone mineral density each month, with the most pronounced effects seen in weight-bearing bones such as the spine and hips, which is a far faster rate than age-related bone loss on Earth. Rather than being a simple acceleration of aging, spaceflight- induced bone loss represents a distinct pathological process which complicates the situation to the next level. Data from past missions such as Skylab and Mir along with those from the ongoing ISS research and the NASA Twins Study, clearly show that many astronauts struggle to fully recover the bone mass they lose during spaceflight.

Current countermeasures rely heavily on exercise, particularly the use of the ARED and treadmill or cycle ergometer systems with harnesses. Though these measures are known to slow down the rate of bone loss, they do not completely prevent it and pharmacological strategies most notably those using bisphosphonates have shown additional benefits when combined with these cardiovascular exercises. Nutritional approaches such as those including maintaining adequate calorie intake and carefully balancing micronutrients such as sodium and protein, also play a supportive role. Looking to the future and space, the success of extended missions to Mars or the Moon directly depends on more effective solutions such as artificial gravity, whether achieved through continuous rotation of a spacecraft or intermittent centrifuge use, offering a promising way to restore mechanical loading and thereby avoiding bone loss. The next big advancement lies in personalized medicine, where in genomic markers are used to predict risk, and wearable sensors for real-time health monitoring. Studying bone density loss in microgravity pushes forward the field of space medicine and also provides several details for tackling bone diseases on Earth like osteoporosis. Overcoming the challenges discussed in this paper will require continued teamwork across many fields bringing together experts in space medicine, engineering, nutrition, and genomics to create new solutions that protect astronauts' health and support humanity's long-term goals for exploring space.

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The author declares no competing conflict of interest.

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