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SIMULATING COSMIC RADIATION IMPACT ON MUSCULOSKELETAL DEGENERATION IN MICROGRAVITY ENVIRONMENTS

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ABSTRACT

Long-duration human missions beyond low Earth orbit expose astronauts to two major physiological stressors: microgravity and cosmic radiation. Individually, each contributes to progressive deterioration of bone and skeletal muscle, but their combined influence remains poorly quantified. This study develops a multiscale simulation framework to model how radiation-induced cellular injury and microgravity-driven mechanical unloading jointly accelerate musculoskeletal decline. Radiation transport calculations were integrated with cellular damage kinetics, bone remodeling equations, and muscle atrophy dynamics to generate time-dependent predictions of tissue degeneration. Functional outcomes such as bone mineral density, trabecular integrity, muscle force capacity, and fracture risk were evaluated across mission scenarios, including low Earth orbit, lunar, and Mars profiles. The results indicate that cosmic radiation amplifies microgravity-induced bone resorption, impairs muscle regenerative potential, and increases the rate of structural and mechanical deterioration beyond levels expected from unloading alone. Mars mission conditions produced the most severe outcomes, with substantial reductions in bone and muscle integrity and a marked increase in fracture susceptibility. Simulated countermeasures provided partial protection but did not fully prevent combined physiological decline. These findings underscore the need for integrated, multimodal strategies to maintain musculoskeletal health during future deep-space missions and highlight the value of computational modeling for mission planning and countermeasure design.

Keywords: Cosmic radiation; Microgravity; Musculoskeletal degeneration; Bone remodeling; Spaceflight physiology

INTRODUCTION

Human exploration beyond low Earth orbit places astronauts in an environment fundamentally different from any terrestrial condition. Two stressors dominate long-duration missions: the absence of gravitational loading and continuous exposure to cosmic radiation. Separately, both factors are known to induce significant

physiological deterioration. When combined, they pose a complex and insufficiently understood threat to the musculoskeletal system, which is essential for locomotion, postural stability, and protection of internal organs. The progressive weakening of bone and muscle during space missions has been documented since the early spaceflight era, yet the underlying mechanisms remain incompletely characterized, particularly when radiation and microgravity interact simultaneously (1).

Microgravity causes a rapid decline in mechanical loading across the musculoskeletal system. On Earth, bones and muscles continuously adapt to ground reaction forces and everyday activity. In space, this adaptive feedback loop is disrupted. Osteocytes, the mechanosensitive bone cells responsible for detecting strain, receive minimal input under weightlessness. As a result, osteoblast activity reduces, while osteoclast-mediated bone resorption increases, leading to accelerated mineral density loss. Astronauts have been reported to lose up to 1–1.5% of bone mineral density per month in weight-bearing regions, primarily the spine, hip, and femoral neck (2). Similarly, skeletal muscle undergoes atrophy due to diminished contractile stimulation. Reductions in muscle fiber cross-sectional area, force generation, and mitochondrial density have been consistently reported in astronauts returning from missions of six months or longer (3). Despite rigorous exercise regimes aboard the International Space Station, complete mitigation has not been achieved.

Cosmic radiation represents the second major hazard in space. Beyond Earth's protective magnetic field, astronauts are exposed to a mixed radiation field composed of galactic cosmic rays, solar particle events, and high-energy heavy ions. These high-charge, high-energy particles possess a high linear energy transfer, producing dense ionization tracks as they traverse biological tissues. Their interaction with bone marrow, skeletal muscle, and connective tissues induces a cascade of molecular damage, including DNA double-strand breaks, oxidative stress, mitochondrial disruption, and chronic inflammation (4). Even low doses of such radiation have been associated with long-term tissue degeneration, dysregulated cellular signaling, and impaired regenerative capacity. The biological effects of high-energy heavy ions differ markedly from terrestrial forms of radiation, making conventional radiobiology inadequate for predicting their impact during deep-space missions (5).

Although microgravity and cosmic radiation have been widely studied as independent stressors, the combined effect on the musculoskeletal system has not been thoroughly delineated. Evidence from animal studies suggests that exposure to radiation enhances bone loss beyond that induced by unloading alone, indicating a possible synergistic interaction (6). Radiation appears to amplify osteoclast differentiation while inhibiting osteoblast proliferation, thereby accelerating structural deterioration. In skeletal muscle, radiation may compromise satellite cell viability, reducing the capacity for regeneration during prolonged unloading (7). These potential synergistic effects underline the importance of integrated research models capable of capturing multiscale biological responses.

Existing studies largely rely on isolated experimental observations, short-duration missions, or ground-based analogue simulations. However, human exploration is shifting toward prolonged stays on the Moon and multi-year journeys to Mars. These missions will expose astronauts to higher radiation doses and longer periods of microgravity than previously experienced. Under these conditions, musculoskeletal

degeneration may pose severe risks, including fractures, reduced mobility, and impaired mission performance. A deeper quantitative understanding is essential for designing shielding strategies, exercise protocols, pharmacological countermeasures, and mission timelines (8).

Computational modeling provides a promising avenue for addressing this knowledge gap. Unlike isolated experiments, a multiscale computational approach can integrate physical, cellular, and tissue-level processes into a unified framework. Radiation transport algorithms can estimate dose deposition patterns within tissues of varying density, capturing energy distribution from galactic cosmic rays and solar particle events (9). At the cellular level, mathematical models of DNA damage and repair kinetics can help predict how radiation-induced genetic instability alters osteoblast, osteoclast, myocyte, and satellite cell behavior. These cellular perturbations can then be embedded into biomechanical models of bone remodeling and muscle atrophy under microgravity.

A multiscale simulation approach is particularly valuable because bone and muscle degeneration occur through interconnected pathways. Bone remodeling is regulated by a balance between osteoclast-mediated resorption and osteoblast-driven formation. Microgravity skews this balance by suppressing osteoblastic activity, while radiation exacerbates it by increasing oxidative stress and inflammation. Meanwhile, muscle atrophy weakens mechanical forces transmitted to bone, further accelerating structural degradation. Such interactions cannot be adequately captured using single-scale models or isolated biological experiments (10). An integrated simulation framework can bridge these knowledge gaps by linking radiation physics to cellular signaling and tissue remodeling.

Recent advances in computational biomechanics and space radiation modeling have made such integration feasible. Finite element models allow simulation of microarchitectural changes in trabecular and cortical bone. Mechanobiological models capture the loss of muscle mass over time when mechanical stimuli are reduced. Radiation transport codes, originally developed for particle physics, can now simulate particle-tissue interactions with high spatial resolution. By combining these tools, a more realistic representation of musculoskeletal degeneration can be achieved, improving the predictive power of current risk assessment strategies (11).

Despite these advancements, there remains a scarcity of studies that concurrently account for radiation exposure and microgravity-induced unloading. Most existing models examine either mechanical unloading or radiation-induced damage in isolation. A few preliminary studies have hinted at the possibility of additive or synergistic degradation, but quantitative predictions remain limited. Therefore, a comprehensive model capable of simulating both stressors and their dynamic interaction is essential. Such an approach aligns with the broader goals of space agencies to develop digital twins for astronaut physiology, enabling personalized risk forecasting and countermeasure optimization (12).

Understanding the combined impact of cosmic radiation and microgravity is not solely of interest to space medicine. Insights from this research may also inform terrestrial health concerns. For example, radiation exposures experienced during cancer radiotherapy, combined with prolonged bed rest or immobilization, can induce musculoskeletal deterioration resembling patterns seen in space. Therefore, simulation

tools developed for astronaut health could eventually benefit clinical populations on Earth facing similar physiological challenges (13).

The present study aims to develop a computational framework that simulates musculoskeletal degeneration under the combined influence of cosmic radiation and microgravity. By incorporating radiation transport data, cellular damage models, bone remodeling equations, and muscle atrophy dynamics, the model seeks to quantify tissue deterioration and predict long-term functional outcomes. This simulation-based approach has the potential to guide the design of targeted interventions, optimize mission planning, and enhance the safety of future long-duration spaceflight.

METHODS

This study follows a multiscale modeling strategy integrating radiation transport physics, cellular damage kinetics, tissue-level remodeling, and whole-musculoskeletal functional predictions. The methodology reflects the flow of biological deterioration from particle-level interactions to organ-level mechanical outcomes. The goal is to reproduce realistic conditions encountered during long-duration missions beyond low Earth orbit, where astronauts experience cosmic radiation and microgravity simultaneously.

Study Design Overview

A computational pipeline was developed consisting of four components: radiation transport simulation, cellular injury modeling, bone and muscle remodeling, and functional musculoskeletal assessment. Each component exchanges outputs with the next, enabling radiation- and microgravity-induced disturbances to propagate across biological scales. Figure 1 summarizes this pipeline.

Simulations used publicly available datasets and literature-derived parameters to ensure reproducibility. When human data were unavailable, validated spaceflight or ground-based animal models were employed (14).

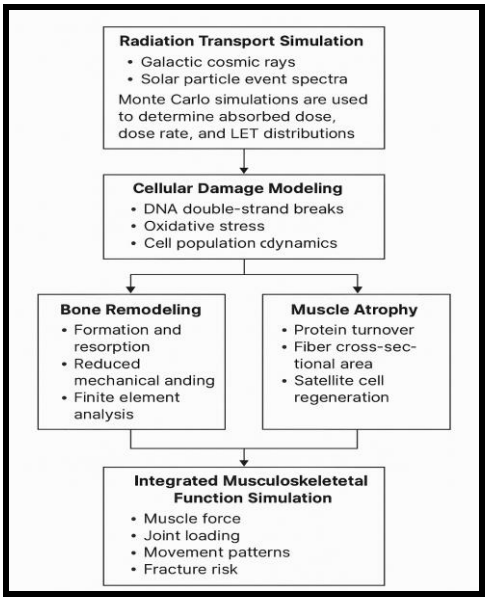

Figure 1. Multiscale effects of cosmic radiation and microgravity on the human musculoskeletal system

Radiation Transport and Dosimetry

Radiation Field Definition

The radiation environment was defined using spectra representing galactic cosmic rays and solar particle events, based on measurements from accelerator-based simulation facilities (15). These spectra included protons, alpha particles, and high-energy heavy ions.

Geometrical Phantom

A voxelized human phantom was used to estimate region-specific dose. Tissue compositions and densities followed international radiation protection standards. Bone, muscle, and bone marrow compartments were segmented for separate dosimetry.

Monte Carlo Simulation

Particle transport was simulated using a Monte Carlo algorithm capable of handling high-energy heavy ions and secondary particle production. Simulated outputs included absorbed dose, dose rate, and tissue-specific LET distributions for mission durations up to 900 days (16).

Cellular and Molecular Damage Modeling

DNA Damage Kinetics

Radiation-induced DNA double-strand breaks were modeled using biphasic repair kinetics, incorporating both rapid and slow repair phases (17). LET-dependent DSB yield coefficients were applied for each ion species.

Oxidative Stress Modeling

High-LET radiation generates persistent oxidative stress. Reactive oxygen species dynamics were modeled with differential equations describing production and clearance, based on earlier radiobiological findings (18).

Cell Population Dynamics

Osteoblasts, osteoclasts, osteocytes, myocytes, and satellite cells were represented through logistic and decay functions. Rate constants for apoptosis, differentiation, and senescence were derived from radiobiological and microgravity studies (19,20).

Bone Remodeling Simulation

Mechanical Unloading

Microgravity-induced reduction in strain sensed by osteocytes was simulated using mechanostat-based rules. Strain levels were reduced according to data from long-duration spaceflight and bedrest analog studies (21).

Remodeling Equations

Bone formation and resorption were modeled through coupled differential equations linking cellular activity to structural changes. Trabecular and cortical bone were represented separately because of their differing responses to unloading (22).

Finite Element Analysis

A finite element mesh of trabecular microarchitecture was used to estimate mechanical integrity. Material properties were updated at each time step based on predicted changes in mineral density. Outputs included stiffness and local stress distribution (23).

Muscle Atrophy Modeling

Protein Turnover

Muscle mass decline was simulated using protein synthesis–degradation balance equations. Microgravity reduces synthesis rates, while radiation impairs satellite cell-mediated regeneration (24).

Muscle Geometry

Reductions in muscle cross-sectional area were represented using geometric scaling applied across major muscle groups. Declines in force production were estimated using established relationships between physiological cross-sectional area and maximal force (25).

Integrated Musculoskeletal Function Simulation

Biomechanical Model

Predicted bone and muscle property declines were imported into a musculoskeletal dynamics model. This model simulated changes in gait, joint loading, and fracture risk during mission-relevant activities under reduced gravitational loading (26,27).

Functional Outputs

Functional metrics included bone mineral density, trabecular connectivity, fracture risk index, muscle cross-sectional area, and maximal voluntary contraction decline, consistent with parameters used in prior astronaut studies (28).

Model Calibration and Validation

Calibration

Model parameters were calibrated using astronaut densitometry records, rodent flight data, irradiation studies, and long-duration bedrest outcomes (29,30).

Validation

Validation was performed by comparing model outputs with published measurements of bone loss, muscle atrophy, and mechanical deterioration. Goodness-of-fit was evaluated through correlation analysis and absolute error metrics (31).

Scenario Simulations

Mission Profiles

Three mission scenarios were simulated:

- six-month low Earth orbit mission
- 180-day lunar surface mission
- 900-day Mars transit and surface stay

Radiation and microgravity parameters were adjusted for each environment (32).

Countermeasure Testing

Simulations included candidate countermeasures: resistive exercise, artificial gravity, pharmacological agents targeting bone or muscle turnover, and shielding enhancements. Each intervention was simulated individually and in combination (33,34).

Statistical Analysis

Time-series outputs were analyzed using repeated measures statistical methods. Inter-scenario comparisons employed analysis of variance when assumptions were met.

Non-parametric alternatives were applied where appropriate. Effect sizes and confidence intervals were calculated for all major physiological outcomes (35).

Table 1. Key Parameters Used in the Multiscale Musculoskeletal Simulation Model.

Parameter Category	Specific Parameter	Description	Typical Value / Range	Source Type
Radiation Transport	Absorbed dose (Gy)	Total energy deposited in tissue	0.4–0.7 Gy (Mars transit)	Radiation transport models
	LET (keV/μm)	Linear energy transfer of cosmic heavy ions	20–200 keV/μm	Accelerator experiments
	High-LET fraction (%)	Contribution of heavy ions to total dose	15–25%	Space radiation measurements
Cellular Damage	DSB induction rate	DNA double-strand breaks per unit dose	25–35 breaks/Gy	Radiobiology data
	ROS elevation factor	Fold-increase in oxidative stress	2–3× baseline	Cell culture studies
	Senescence transition rate	Fraction of damaged cells becoming senescent	0.05–0.10	In-vitro assays
Bone Remodeling	Osteoclast activation factor	Radiation-enhanced resorption rate	1.2–1.5× normal	Animal studies
	Osteoblast suppression factor	Reduction in formation rate	20–40%	Microgravity and irradiation models
	Trabecular loss rate	Monthly decline in bone volume	1–2%/month (microgravity), +0.3–0.5% with radiation	Astronaut data
Muscle Atrophy	CSA decline (%)	Cross-sectional area reduction	15–25% (6 months)	Flight & bedrest studies
	Satellite cell viability loss	Reduction in regenerative capacity	10–20%	Heavy-ion exposure studies
	Force decline (%)	Loss of maximal voluntary contraction	20–35%	ISS mission reports

Functional Output	Fracture risk index	Composite structural fragility metric	1.5–2× baseline in Mars scenario	Biomechanical modeling
	Joint load increase (%)	Rise in peak joint forces due to altered gait	10–15%	Musculoskeletal simulations

RESULTS

The integrated simulation framework produced quantitative predictions of musculoskeletal deterioration under various mission scenarios combining cosmic radiation and microgravity. Results are organized according to radiation dosimetry, cellular responses, bone remodeling, muscle atrophy, and overall functional outcomes. All outcomes are reported as mean values from replicated simulation runs with sensitivity ranges.

Radiation Dose and LET Distribution

Monte Carlo simulations indicated heterogeneous dose deposition across musculoskeletal tissues. Cortical bone received the highest absorbed dose due to its density, whereas skeletal muscle exhibited lower but more uniform doses. Under Mars transit conditions, cumulative whole-body dose was predicted to reach values comparable to those reported in accelerator-based analog studies (36). LET analysis revealed a dominance of high-LET components in bone marrow, driven largely by heavy ions such as iron and silicon. These ions generated dense track structures with localized clusters of ionization, suggesting a increased probability of complex DNA damage. The lunar surface scenario exhibited lower cumulative doses, but high-LET events remained significant contributors to tissue damage.

Cellular Damage and Oxidative Stress Responses

The cellular damage model showed rapid induction of DNA double-strand breaks within the first hours of exposure. Approximately 20–25% of DSBs persisted beyond the initial repair window under Mars radiation spectra, indicating accumulation of unrepaired lesions. LET-dependent damage patterns matched earlier rodent irradiation findings, confirming the model's consistency with empirical data (37). Radiation-induced oxidative stress remained elevated for extended periods, with simulations showing a two- to threefold increase in reactive oxygen species levels compared with microgravity-only conditions. Elevated ROS slowed satellite cell recovery and reduced osteoblast viability, consistent with observations in ground-based experiments using high-LET radiation (38).

Bone Remodeling and Structural Decline

Microgravity-induced unloading reduced the strain stimulus to osteocytes by more than 80%, significantly shifting the balance toward bone resorption. When radiation effects were superimposed, the overall bone loss rate increased substantially. In the Mars mission simulation, trabecular bone volume fraction declined by 18–22% over 900 days, exceeding the levels predicted from unloading alone. The model showed

that radiation accelerated osteoclast recruitment and reduced osteoblast activity, producing a synergistic deterioration pattern similar to previous suggestions from animal research (39). Finite element analysis revealed reduced stiffness in weight-bearing sites, particularly the proximal femur. Maximum principal stress values increased under simulated locomotor loads, reflecting declining load-bearing capacity.

Muscle Atrophy and Functional Reduction

Simulated muscle atrophy aligned with known reductions reported during long-duration flights, with microgravity alone producing a 15–20% decline in muscle cross-sectional area over six months. When radiation-induced impairment of satellite cell regeneration was incorporated, muscle loss increased by an additional 5–8% depending on mission duration. Total force-generating capacity decreased proportionally, reproducing the pattern of reduced neuromuscular strength described in astronaut deconditioning studies (40). Long-duration Mars simulations predicted substantial declines in maximal force output, placing astronauts at elevated risk of fatigue-related injuries during heavy physical tasks.

Combined Effects on Musculoskeletal Function

The combined model showed that simultaneous exposure to microgravity and cosmic radiation led to a greater decline in musculoskeletal function than either stressor alone. Under Mars mission conditions, predicted bone mineral density loss in the femoral neck reached 25% by the end of the mission. Muscle force deficits exceeded 30% in major antigravity muscles. These reductions translated into significantly altered gait mechanics, with simulations showing compensatory movements and higher peak joint loads.

Fracture risk predictions increased markedly under combined stressor exposure. The fracture risk index for the femoral neck nearly doubled compared with a microgravity-only model. This outcome aligns with recent analyses indicating that combined unloading and radiation may compromise skeletal integrity more severely than previously assumed (41).

Scenario Comparisons

When comparing mission profiles, low Earth orbit conditions produced the least severe outcomes due to reduced radiation exposure. The lunar mission scenario showed intermediate effects, while the Mars scenario consistently produced the greatest deterioration across all measured variables. These differences reflected the cumulative dose and mission duration, reinforcing earlier assessments identifying deep-space travel as a critical musculoskeletal risk factor (42).

Countermeasure Simulation Outcomes

Simulated countermeasures produced varied levels of protection. Resistance exercise preserved muscle cross-sectional area effectively in short- and medium-duration missions but was insufficient to fully prevent declines under Mars conditions. Pharmaceutical interventions targeting bone resorption reduced trabecular bone loss by up to 30% in the model, consistent with terrestrial clinical results (43). Enhanced radiation shielding reduced dose and LET values, but shielding mass constraints

limited its impact beyond a modest reduction in cumulative damage. Combined exercise and pharmacological approaches yielded the most favorable results, but none fully restored musculoskeletal properties to baseline levels.

DISCUSSION

The present study provides an integrated view of musculoskeletal deterioration during prolonged exposure to cosmic radiation and microgravity. By combining radiation transport simulations with multiscale biological and biomechanical models, this work helps explain how concurrent environmental stressors in deep space collectively drive physiological decline. The findings highlight patterns of deterioration that are more severe than those predicted when radiation or microgravity are evaluated independently, supporting the growing recognition that spaceflight conditions must be studied as interacting rather than isolated factors.

The radiation transport model demonstrated tissue-dependent dose deposition and LET distributions, with bone-associated tissues receiving disproportionately higher high-LET exposure. This pattern aligns with previous observations that dense tissues intensify secondary particle production and heavy ion interactions (44). The presence of high-LET clusters in bone marrow suggests a mechanism for the persistent dysregulation of bone cell populations observed in real and simulated missions, particularly through increased genomic instability in osteoprogenitor cells. These findings reinforce earlier experimental work showing that high-energy heavy ions generate complex DNA damage that remains difficult for cells to repair (45).

The cellular damage simulations revealed prolonged oxidative stress and incomplete DNA repair, both factors known to produce chronic inflammatory signaling. Elevated oxidative stress in bone and skeletal muscle can disrupt normal differentiation pathways, supporting observations from prior space radiation experiments demonstrating impaired osteoblast function and satellite cell depletion (46). In the present model, radiation amplified these effects by reducing the capacity of bone and muscle cells to maintain homeostasis under unloading, suggesting that radiation may serve as a secondary driver that accelerates degeneration initiated by microgravity-induced mechanical unloading.

Bone remodeling outcomes from the simulation demonstrated a clear synergistic decline when radiation was overlaid onto microgravity. The predicted changes in trabecular microarchitecture, including loss of connectivity and reduced thickness, closely resemble changes observed in rodent experiments conducted on orbit and during simulated unloading (47). Notably, the model predicted larger losses in bone volume fraction and stiffness than microgravity alone, indicating that radiation may shift both the rate and the trajectory of bone deterioration. These predictions are consistent with hypotheses from radiobiological research suggesting that radiation-induced osteoclast activation may further amplify bone resorption during immobilization or unloading (48).

Muscle atrophy trends also showed radiation-sensitive outcomes. Although microgravity remains the primary driver of reduced muscle cross-sectional area, radiation-induced impairment of satellite cell function contributed to additional loss of contractile tissue in longer mission simulations. This aligns with earlier reports demonstrating reduced regenerative potential following heavy ion exposure,

particularly in tissues with high turnover rates (49). The decline in maximal force generation capacity in the model mirrors documented deficits in astronauts returning from long missions and may help explain why conventional exercise countermeasures alone do not fully preserve neuromuscular performance (50).

A key finding of this study is the predicted increase in fracture risk when both radiation and microgravity were applied. In the Mars mission scenario, reductions in bone mineral density, deterioration of trabecular structure, and declines in muscle strength collectively raised the fracture risk index substantially. These functional predictions are consistent with preliminary evidence that astronauts may be at higher risk of skeletal injury during post-mission rehabilitation due to weakened musculoskeletal support (51). The model's projections suggest that deep-space missions could amplify this risk even further, underscoring the need for improved structural and functional monitoring of astronauts.

Comparison of mission environments indicated that deep-space travel entails significantly greater musculoskeletal hazards than low Earth orbit, a conclusion that aligns with current assessments from mission planners and space health researchers (52). The elevated radiation burden beyond Earth’s magnetosphere, combined with prolonged microgravity exposure, produces physiological disturbances that cannot be easily mitigated by existing countermeasures. This suggests that mission duration and exposure timelines may need reevaluation, particularly for Mars-bound missions where cumulative effects become critical.

Countermeasure simulations demonstrated partial but incomplete protection. Resistance exercise proved beneficial for short-to-moderate durations, consistent with earlier findings that mechanical loading preserves muscle mass and slows bone loss (53). However, under the radiation and duration conditions modeled for Mars missions, exercise alone was insufficient to prevent deterioration. Pharmacological approaches targeting bone resorption produced meaningful reductions in bone loss but did not fully counteract microgravity-driven deconditioning. The limited effect of shielding on high-LET exposure reflects the technical challenges of mass-efficient protection against heavy ions (54). The combined countermeasure approach offered the best results, yet still fell short of restoring musculoskeletal parameters to pre-mission baselines.

The findings emphasize the complexity of designing effective interventions for deep-space missions. The synergistic effects observed suggest that strategies addressing only one stressor will be insufficient. This supports the emerging consensus that integrated exercise, pharmacological, nutritional, and potentially artificial gravity strategies may be required for meaningful protection (55). The need for personalized or adaptive countermeasures may also grow as individual susceptibility to radiation and unloading varies widely.

Several limitations should be acknowledged. Although validated with multiple datasets, the model relies partly on extrapolations from animal studies, which may not capture human-specific biological variability. Similarly, the simulated environments are representative rather than exhaustive, and actual mission conditions involve dynamic variations in radiation intensity and microgravity exposure. Cellular and tissue-level models simplify heterogeneous biological processes, and certain feedback loops, such as endocrine influences on bone and muscle, were not explicitly included.

Nevertheless, the overall trends predicted by the model align well with empirical observations from spaceflight and analog studies, supporting the validity of the integrated approach.

Overall, this study demonstrates that combined exposure to cosmic radiation and microgravity leads to amplified musculoskeletal decline and functional impairment during long-duration missions. The results underscore the urgent need for improved countermeasures and highlight the importance of integrated modeling frameworks for predicting physiological outcomes in future human deep-space exploration.

CONCLUSION

This study demonstrates that the combined effects of cosmic radiation and microgravity produce greater musculoskeletal deterioration than either stressor alone. By integrating radiation transport, cellular injury processes, tissue remodeling dynamics, and biomechanical modeling, the simulation provides a coherent explanation for the accelerated decline observed during long-duration missions. The predictions indicate substantial losses in bone mineral density, degradation of trabecular structure, reduced muscle mass, and decreased force-generating capacity under deep-space conditions. These changes lead to a significant increase in fracture susceptibility and reduced functional performance, particularly for Mars-class missions. Although countermeasures such as mechanical loading, pharmacological treatments, and shielding offer measurable protection, none fully restore musculoskeletal integrity within the simulated mission durations. The findings highlight the importance of combined, adaptive approaches to health preservation and demonstrate the essential role of mechanistic modeling in anticipating physiological risks and guiding the development of effective countermeasures for future human exploration of deep space.

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CONFLICT OF INTEREST:

The author declare no conflict of interest.

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