Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2026.66.010339

Renal Adaptations to Microgravity: Clinical Implications for Long-Duration Space Missions

Ramona Nicotera[1]*, Giovanni Mazzitello[2] and Walter Gianluca Mastroianni[3]

[1]*Department of Nephrology and Dialysis, ASP Catanzaro, Catanzaro, Italy*

[2]*Head of Nephrology and Dialysis Unit, ASP Catanzaro, Catanzaro, Italy*

[3]*Engineer, Catanzaro, Italy*

***Corresponding author:** Ramona Nicotera, Department of Nephrology and Dialysis, ASP Catanzaro, Catanzaro, Italy

ARTICLE INFO

Received: August 07, 2026

Published: August 13, 2026

Citation: Ramona Nicotera, Giovanni Mazzitello and Walter Gianluca Mastroianni. Renal Adaptations to Microgravity: Clinical Implications for Long-Duration Space Missions. Biomed J Sci & Tech Res 66(3)-2026. BJSTR. MS.ID.010339.

ABSTRACT

Human spaceflight has evolved from short orbital missions to long-duration stays aboard the International Space Station, with future exploration programs targeting the Moon and Mars. These advances have intensified interest in understanding the physiological adaptations induced by prolonged exposure to microgravity and the space environment. Among the organ systems involved, the kidney plays a central role in maintaining fluid, electrolyte, and acid–base homeostasis and is therefore particularly susceptible to the hemodynamic and metabolic changes associated with spaceflight. Microgravity induces an immediate cephalad fluid shift, triggering neuroendocrine adaptations that promote diuresis, natriuresis, and plasma volume contraction. Although these responses are largely reversible, prolonged exposure contributes to a new homeostatic equilibrium that may impair cardiovascular adaptation upon return to Earth's gravity. Simultaneously, skeletal unloading promotes bone resorption, hypercalciuria, and urinary supersaturation, substantially increasing the risk of nephrolithiasis, one of the most clinically relevant renal complications during long-duration missions. In addition, growing experimental evidence suggests that exposure to galactic cosmic radiation may induce oxidative stress. Endothelial dysfunction, DNA damage, and renal fibrosis, although direct evidence in astronauts remains limited. Current countermeasures combine resistive exercise, nutritional optimization.

Hydration protocols and selected pharmacological interventions, including bisphosphonates. Vitamin D supplementation, and urinary alkalinization strategies. Nevertheless, the effectiveness of these approaches during future deep-space missions remains to be fully established. This review summarizes the current understanding of renal physiological adaptations to microgravity, the mechanisms underlying spaceflight-associated kidney injury, and the preventive and therapeutic strategies currently under investigation. Furthermore, it highlights existing knowledge gaps and discusses how advances in space nephrology may improve not only astronaut health but also our understanding of kidney physiology and disease on Earth.

Keywords: Microgravity; Space Flight; Kidney Diseases; Renal Function; Fluid Balance; Nephrolithiasis; Bone Resorption; Calcium Metabolism; Radiation Exposure; Astronauts

Introduction

Spaceflight exposes the human body to environmental conditions for which it is not evolutionarily adapted, requiring complex physiological responses involving multiple organ systems. Space medicine has consequently developed as an interdisciplinary field aimed at understanding, preventing, and managing the health risks associated with human space exploration. Since the first orbital missions and, more recently, long-duration stays aboard the International Space Station (ISS), research has progressively shifted from the characterization of acute physiological changes to the investigation of chronic adaptations relevant to future deep-space missions. The space environment is primarily characterized by microgravity and increased exposure to ionizing radiation. Microgravity, resulting from continuous free fall rather than the absence of gravity, induces profound physiological changes, including cephalad fluid redistribution, reduced mechanical loading of bone and muscle, and neuroendocrine adaptations. In parallel, radiation exposure beyond Earth's magnetosphere increases the risk of DNA damage, oxidative stress, and long-term tissue injury. These physical stressors, combined with isolation, confinement, circadian disruption, and limited medical resources. Generate

complex multisystem responses that pose major challenges for prolonged exploration missions. Among the organs affected, the kidney is particularly vulnerable because of its fundamental role in fluid and electrolyte homeostasis, acid–base balance, and mineral metabolism.

Renal adaptation reflects the interaction between cardiovascular, endocrine, skeletal, and environmental changes induced by spaceflight. This review summarizes current evidence on renal adaptation during spaceflight, with particular emphasis on microgravity-induced fluid redistribution, nephrolithiasis risk, radiation-associated renal injury, and emerging strategies to preserve kidney function during long-duration missions.

Renal Physiology and Fluid Redistribution During Microgravity

The kidney plays a pivotal role in maintaining fluid, electrolyte, acid–base, and blood pressure homeostasis during spaceflight. In microgravity, the loss of the normal hydrostatic gradient causes a cephalad redistribution of approximately 1–2 L of body fluids ("fluid shift"), increasing central blood volume and triggering cardiovascular and neuroendocrine responses that mimic volume expansion despite unchanged total body water. This adaptation is characterized by suppression of the renin–angiotensin–aldosterone system and vasopressin secretion, together with increased atrial natriuretic peptide release, promoting natriuresis and diuresis. Consequently, plasma volume progressively decreases until a new steady state ("volume resetting") is established, an adaptation that supports cardiovascular function in microgravity but contributes to orthostatic intolerance after return to Earth's gravity. Renal adaptation involves dynamic modulation of glomerular filtration, tubular sodium transport, and water reabsorption in response to altered hemodynamic and hormonal conditions. Evidence from spaceflight and ground-based analogues indicates that these changes are largely functional and reversible after short- and medium-duration missions, with no persistent structural renal injury.

However, the long-term effects of prolonged or repeated microgravity exposure remain uncertain and may become increasingly relevant during future deep-space missions. Understanding these mechanisms is essential for interpreting subsequent alterations in mineral metabolism, urinary composition, and nephrolithiasis risk during spaceflight.

Renal Function During Microgravity: Adaptation Versus Injury

Microgravity induces significant hemodynamic and neuroendocrine changes that influence renal physiology. The cephalad fluid shift initially increases renal perfusion and modifies intrarenal hemodynamics, producing transient changes in glomerular filtration rate (GFR), while overall renal filtration capacity appears to remain preserved. Current evidence indicates that these alterations reflect physiological adaptation rather than progressive renal dysfunction or structural kidney injury during short- and medium-duration missions [1-3]. Renal adaptation is mediated by coordinated hormonal responses, including suppression of the renin–angiotensin–aldosterone system (RAAS), reduced vasopressin secretion, and increased natriuretic peptide activity, which regulate tubular sodium and water handling to maintain fluid and electrolyte homeostasis under microgravity conditions [1,2,4,5]. Ground-based analogues, particularly head-down bed rest studies, have confirmed many of these adaptive mechanisms, reproducing central fluid redistribution, cardiovascular deconditioning, and increased urinary calcium excretion observed during spaceflight [6,7]. Although astronauts participating in long-duration ISS missions have not shown persistent reductions in renal function or an increased incidence of chronic kidney disease attributable to microgravity alone, current evidence remains limited by the small number of studied individuals and the duration of available missions [1,8].

Future exploration missions may pose greater challenges, as prolonged exposure to microgravity together with ionizing radiation, altered nutrition, reduced physical activity, and limited medical support could impair renal adaptive capacity and promote subtle tubular, microvascular, or oxidative damage [9-15]. Overall, the available evidence supports the concept that renal responses to microgravity are predominantly adaptive. However, because kidney function is closely integrated with cardiovascular regulation, skeletal metabolism, and mineral homeostasis, long-duration spaceflight may increase susceptibility to renal complications through multiple interacting mechanisms, highlighting the need for continuous renal monitoring and the identification of sensitive biomarkers of early renal stress [9-14,16-19].

Spaceflight-Associated Nephrolithiasis: The Bone–Kidney Axis

Nephrolithiasis is one of the most clinically significant renal complications of spaceflight, particularly during long-duration missions. Although renal function remains largely adaptive, microgravity-induced alterations in mineral metabolism, urinary composition, and fluid balance create a lithogenic environment that increases the risk of kidney stone formation [16-19]. The primary mechanism underlying this risk is skeletal unloading. In the absence of mechanical loading, bone remodeling shifts toward increased osteoclastic resorption, leading to progressive loss of bone mineral, particularly in weight-bearing regions [20-23]. The resulting release of calcium and phosphate increases urinary calcium excretion (hypercalciuria), a major metabolic risk factor for calcium-based nephrolithiasis. Both spaceflight and ground-based analogue studies have consistently demonstrated increased bone turnover and urinary calcium excretion during microgravity exposure [16,24]. Additional urinary changes further promote lithogenesis. Reduced urine volume, resulting from altered fluid regulation and hydration, together with decreased urinary citrate—an important inhibitor of calcium crystal formation—increases urinary supersaturation. Favoring calcium oxalate and calcium phosphate crystal nucleation, aggregation, and stone growth

[16-19,25-27]. These metabolic alterations may persist beyond the mission, extending the period of increased stone risk after return to Earth [18,19,25].

Nephrolithiasis represents a potentially serious hazard during deep-space missions, where diagnostic capabilities. Urological interventions, and medical evacuation are severely limited. Consequently, even a single obstructive stone could compromise astronaut health and mission success [19]. Evidence from prolonged bed-rest studies has reproduced many of the mechanisms observed during spaceflight, including skeletal unloading, hypercalciuria, and changes in urinary chemistry, providing valuable insights despite the limitations of terrestrial analogues [6,7,24]. Overall, current evidence indicates that spaceflight-associated nephrolithiasis is a systemic consequence of microgravity-induced alterations in the bone–kidney axis rather than an isolated renal disorder. Preventive strategies should therefore integrate preservation of bone mass, adequate hydration, nutritional optimization, and monitoring of urinary lithogenic risk factors to reduce stone formation during future long-duration missions [16,17].

Space Radiation and Potential Renal Consequences

In addition to microgravity, ionizing radiation represents one of the major hazards of long-duration space exploration. While astronauts aboard the International Space Station (ISS) remain partially protected by Earth's magnetosphere, future lunar and Mars missions will involve substantially greater exposure to galactic cosmic rays (GCRs) and solar particle events (SPEs), increasing concerns about long-term health effects [9-12]. Space radiation is composed of highly energetic charged particles capable of penetrating biological tissues and inducing direct DNA damage as well as indirect injury through reactive oxygen species (ROS) generation. Oxidative stress, mitochondrial dysfunction, persistent DNA damage, and endothelial injury have been identified as key mechanisms that may contribute to inflammation, microvascular dysfunction, and progressive renal tissue remodeling, particularly in metabolically active tubular epithelial cells [12-14,27-31].Current evidence for radiation-induced renal injury is derived primarily from experimental models and ground-based simulations, which have provided important mechanistic insights but cannot fully replicate the complex conditions of human spaceflight [11,15,32]. To date, no clear increase in chronic kidney disease has been demonstrated in astronauts. However, most available data originate from relatively short missions in low-Earth orbit, where radiation exposure is partially attenuated by Earth's magnetic field [9-11].

Recent multi-omics studies, including the NASA Twins Study, have revealed molecular adaptations associated with long-duration spaceflight, involving oxidative stress, inflammation, DNA repair, and mitochondrial pathways. Although renal-specific signatures remain poorly defined, these approaches may facilitate the identification of early biomarkers of radiation-induced kidney stress [32-36]. Consequently, radiation-related renal injury should currently be regarded as a potential rather than established clinical consequence of spaceflight, highlighting the need for continued biological monitoring and the development of effective countermeasures for future deep-space missions [9-15,28-40].

Exercise and Mechanical Countermeasures for Bone Preservation

The prevention of skeletal deterioration represents one of the central challenges in long-duration human spaceflight. Because microgravity removes the mechanical stimulus required for normal bone remodeling, astronauts experience a progressive reduction in bone mineral density, particularly in weight-bearing skeletal regions. This process is clinically relevant not only because of fracture risk but also because of its direct relationship with renal physiology through increased calcium mobilization and urinary calcium excretion, contributing to nephrolithiasis risk [16,17,20-24]. The primary countermeasure currently used to limit spaceflight-induced bone loss is structured physical exercise. On Earth, mechanical loading generated by body weight and muscle contraction provides essential signals regulating osteoblast and osteocyte activity. In microgravity, these stimuli are markedly reduced, resulting in increased osteoclastic bone resorption and an imbalance between bone formation and degradation [22,23]. The development of advanced exercise devices aboard the International Space Station has therefore represented a major achievement in space medicine. The Advanced Resistive Exercise Device (ARED) allows astronauts to perform high-intensity resistive training. Designed to reproduce mechanical forces similar to those experienced during terrestrial weight-bearing exercise.

Studies conducted during long-duration ISS missions have demonstrated that combined resistance exercise and nutritional optimization can substantially reduce, although not completely eliminate, bone loss associated with microgravity exposure [41,42]. Resistance exercise also has potential indirect renal benefits. By attenuating skeletal calcium release, physical training may reduce hypercalciuria and decrease urinary supersaturation for calcium-containing salts. Therefore, exercise should be considered not only a musculoskeletal countermeasure but also an important component of nephrolithiasis prevention strategies during spaceflight [16,17,24]. Despite these advances, exercise alone is insufficient to completely prevent skeletal demineralization during prolonged missions. The magnitude of bone loss varies considerably among astronauts and depends on mission duration, individual susceptibility, baseline skeletal characteristics, nutritional status, and adherence to exercise protocols [20-23]. For this reason, current approaches emphasize integrated countermeasure programs combining mechanical stimulation and nutritional support. Pharmacological interventions, and continuous physiological monitoring. Future exploration missions, particularly those lasting several years, will likely require personalized countermeasure strategies based on individual risk profiles and real-time biological monitoring [43,44]. In addition to traditional exercise approaches, alternative strategies are being investigated, including artificial gravity, vibration-based stimulation, and optimized mechanical loading protocols.

Artificial gravity represents a particularly attractive theoretical approach because it could simultaneously address multiple consequences of microgravity, including bone loss, cardiovascular deconditioning, and fluid redistribution. However, technological limitations currently prevent its routine implementation during human space missions [45]. Overall, exercise remains the cornerstone of skeletal preservation during spaceflight. By maintaining bone integrity and limiting excessive mineral release, physical countermeasures also play a fundamental role in protecting renal health and reducing the risk of spaceflight-associated nephrolithiasis.

Pharmacological Prevention of Bone Loss: Bisphosphonates and Vitamin D

Although exercise remains the primary countermeasure against microgravity-induced bone loss, pharmacological interventions may provide additional protection during long-duration missions by limiting osteoclastic bone resorption, preserving bone mineral density, and reducing hypercalciuria [44,46-48]. Bisphosphonates are the most extensively investigated agents. By inhibiting osteoclast activity, they reduce skeletal calcium release and have shown efficacy in attenuating bone loss when combined with resistance exercise [47,48]. Among these, alendronate and zoledronic acid appear particularly promising. Zoledronic acid may offer practical advantages for spaceflight because of its high potency and prolonged duration of action, allowing administration as a single intravenous dose. However, its use requires careful evaluation of potential adverse effects, including excessive suppression of bone remodeling and disturbances in calcium and phosphate homeostasis [47-50]. From a nephrological perspective, reducing bone resorption may lower hypercalciuria and nephrolithiasis risk, although treatment should be individualized rather than routinely administered to all astronauts. Vitamin D supplementation is another important component of skeletal preservation, as limited ultraviolet exposure during spaceflight may predispose astronauts to vitamin D insufficiency [43,51,52]. Adequate supplementation supports bone health, but excessive intake may increase intestinal calcium absorption and urinary calcium excretion, potentially enhancing stone risk in susceptible individuals [16,51].

Current evidence therefore supports individualized vitamin D replacement based on biochemical monitoring, including serum vitamin D, calcium levels, urinary calcium excretion, and markers of bone turnover [16,43]. Overall, future pharmacological strategies are expected to integrate exercise, nutrition, targeted drug therapy, and biomarker-guided monitoring to preserve both skeletal and renal health during prolonged exploration missions beyond low-Earth orbit [16,43-52].

Prevention and Management of Nephrolithiasis During Spaceflight

Preventing nephrolithiasis is a major priority in space medicine, as the limited diagnostic and therapeutic resources available during long-duration missions make the management of acute stone events particularly challenging [18,19,25]. The cornerstone of prevention is adequate hydration, which increases urinary volume, reduces urinary supersaturation, and lowers the risk of calcium-based stone formation [15-18]. Nutritional management also plays a key role. Appropriate sodium restriction may reduce urinary calcium excretion, whereas adequate dietary calcium intake should be maintained to avoid increased intestinal oxalate absorption and paradoxical calcium oxalate stone formation [16,17,26]. Individual risk assessment should include monitoring of urinary volume, calcium, citrate, oxalate, phosphate, and urinary supersaturation, with emerging portable diagnostic technologies offering potential applications for in-flight metabolic surveillance [19]. Among pharmacological strategies, potassium citrate is the most extensively studied agent because it increases urinary citrate levels and inhibits calcium crystal formation. Although widely used for calcium nephrolithiasis on Earth, its use during spaceflight requires careful monitoring of renal function and electrolyte balance [53-55]. Likewise, interventions aimed at limiting bone resorption, including exercise and antiresorptive therapies, may indirectly reduce hypercalciuria and stone risk by preserving skeletal mineral homeostasis [16,17,24,47]. Overall, effective prevention of spaceflight associated, nephrolithiasis requires an integrated approach combining hydration, nutritional optimization, and preservation of bone health. Pharmacological interventions when appropriate, and individualized metabolic monitoring. Such strategies will be essential for reducing renal complications during future long-duration exploration missions [16-19,24-26,47,53-55].

Cardiovascular and Renal Monitoring During Long-Duration Missions

Cardiovascular stability is essential for preserving renal function during spaceflight because systemic hemodynamics directly influence renal perfusion, glomerular filtration, and fluid homeostasis [10-13]. Microgravity-induced fluid redistribution and the subsequent reduction in plasma volume contribute to cardiovascular adaptation during flight but predispose astronauts to orthostatic intolerance upon return to Earth's gravity, owing to impaired venous return, altered baroreflex function, autonomic dysregulation, and vascular deconditioning [4,5,56-58].Current countermeasures are primarily non-pharmacological and include aerobic and resistance exercise, adequate fluid and salt loading before re-entry, and structured post-flight rehabilitation to restore cardiovascular function [41,57,58]. Pharmacological interventions, such as the α-adrenergic agonist midodrine, may be considered in selected individuals with persistent orthostatic intolerance but are not routinely recommended because of their potential effects on systemic and renal hemodynamics [57]. Future long-duration missions will require integrated cardio-renal monitoring to detect early physiological maladaptation. Continuous assessment of blood pressure, hydration status, renal function, urinary biochemical parameters, and metabolic markers, supported by wearable sensors, miniaturized diagnostic devices. Emerging molecular biomarkers, may enable personalized interventions before clinically significant cardiovascular or renal complications develop [1,2,32-36].

Discussion and Future Perspectives

Human spaceflight represents a unique physiological challenge requiring coordinated adaptation across multiple organ systems. The kidney plays a central role in maintaining fluid, electrolyte, and mineral homeostasis, and most renal changes observed during spaceflight appear to represent functional adaptations aimed at preserving internal equilibrium rather than isolated pathological processes [1,2,8]. Current evidence suggests that renal adaptation to short- and medium-duration missions is largely reversible, involving changes in filtration, tubular transport, and hormonal regulation without clear evidence of permanent structural injury. However, the limits of renal adaptability during prolonged exposure remain uncertain, particularly for future exploration missions extending beyond low-Earth orbit [1-3]. Spaceflight-associated nephrolithiasis represents one of the major challenges in space nephrology and exemplifies the complex interaction between organ systems. Microgravity-induced skeletal unloading promotes bone resorption, calcium mobilization, and hypercalciuria, linking musculoskeletal deterioration to increased kidney stone risk through the bone–kidney axis. Preventive strategies combining exercise, hydration, nutritional optimization. Pharmacological interventions, and individualized metabolic monitoring will be essential, although their effectiveness during multi-year missions remains to be fully established [16-19,24,44]. Radiation exposure remains another unresolved concern.

Experimental evidence indicates that cosmic radiation may induce oxidative stress, DNA damage, endothelial dysfunction, and inflammatory responses, but the long-term renal consequences in astronauts are still unclear. Future deep-space missions will be critical for defining the interaction between radiation exposure, microgravity, aging, and renal vulnerability [9-14]. Advances in molecular and systems biology, including transcriptomic, proteomic, metabolomic, and epigenetic approaches, may provide new opportunities to identify early biomarkers of renal stress and guide preventive interventions before clinically significant damage occurs [32-36]. Similarly, integrated cardio-renal monitoring platforms combining hemodynamic parameters, urinary biomarkers, bone metabolism indicators, and molecular signatures may enable personalized countermeasures tailored to individual physiological responses [1,2]. Beyond space exploration, research in space nephrology offers valuable insights into terrestrial conditions characterized by immobilization. Osteoporosis, and sarcopenia. Cardiovascular deconditioning and altered mineral metabolism. Microgravity therefore represents a unique model for investigating fundamental mechanisms of human disease and developing novel therapeutic approaches [6,7,43]. Future exploration missions will require a transition from reactive treatment strategies toward proactive prevention based on personalized, multidisciplinary approaches. In this context, nephrology will play a central role in preserving astronaut health by maintaining fluid balance, metabolic stability, and physiological resilience during prolonged exposure to extraterrestrial environments [59-80].

Conclusion

Human adaptation to spaceflight represents a remarkable example of physiological plasticity, with multiple organ systems undergoing coordinated modifications to preserve homeostasis in an environment characterized by microgravity, radiation exposure, and isolation. Among these adaptations, renal responses are of particular importance because the kidney plays a central role in regulating fluid balance, electrolyte homeostasis, acid–base equilibrium, and mineral metabolism. Current evidence suggests that microgravity does not cause irreversible renal injury in healthy astronauts during short- and medium-duration missions. Instead, the kidney undergoes complex functional adaptations involving fluid redistribution, neurohormonal regulation, and modulation of tubular electrolyte handling. However, the long-term consequences of prolonged exposure remain uncertain, as future deep-space missions may challenge renal resilience through the combined effects of altered hemodynamics, skeletal calcium mobilization, increased urinary lithogenic risk, and radiation-induced cellular stress. Nephrolithiasis remains the most established renal complication associated with spaceflight. The interaction between skeletal unloading, enhanced bone resorption, hypercalciuria, and altered urinary composition creates a favorable environment for calcium-based stone formation. Effective prevention will therefore require integrated strategies combining exercise, hydration, nutritional optimization, pharmacological interventions when appropriate, and individualized metabolic surveillance.

Future developments in space nephrology will rely on personalized countermeasures supported by molecular biomarkers, continuous physiological monitoring, and multidisciplinary approaches. As human exploration extends beyond low-Earth orbit, preservation of renal health will become an essential component of astronaut safety and mission success. Beyond space exploration, the study of renal adaptation to microgravity provides a unique model for investigating fundamental mechanisms of fluid regulation, bone metabolism, oxidative stress, and nephrolithiasis. Space medicine may therefore contribute not only to future human exploration but also to advancing our understanding of renal and systemic diseases on Earth.

Conflict of Interest

The authors declare that they have no conflicts of interest related to this manuscript.

References

1. Norsk P, Christensen NJ (2000) The renal system in space: fluid regulation and adaptation to microgravity. Acta Physiol Scand 168(1): 101-107.
2. Drummer C, Norsk P, Heer M (2001) Water and electrolyte metabolism in space. Am J Nephrol 21(2): 95-102.
3. Friberg P, Karlsen FM, Norsk P (1998) Renal function during weightlessness. Acta Physiol Scand Suppl 643: 11-16.
4. Norsk P (2020) Adaptation of the cardiovascular system to weightlessness: surprises, paradoxes and implications for deep space missions. Acta Physiol (Oxf) 228(3): e13434.

5. Norsk P, Asmar A, Damgaard M, Christensen NJ (2015) Fluid shifts, vasodilatation and ambulatory blood pressure reduction during long duration spaceflight. J Physiol 593(3): 573-584.
6. Hargens AR, Vico L (2016) Long-duration bed rest as an analog to microgravity. J Appl Physiol 120(8): 891-903.
7. Morey-Holton ER, Globus RK (2002) Hindlimb unloading rodent model: technical aspects. J Appl Physiol 92(4): 1367-1377.
8. Williams DR, Kuipers A, Mukai C, Thirsk R (2009) Acclimation during space flight: effects on human physiology. CMAJ 180(13): 1317-1323.
9. Cucinotta FA, Durante M (2006) Cancer risk from exposure to galactic cosmic rays: implications for space exploration by human beings. Lancet Oncol 7(5): 431-435.
10. Durante M, Cucinotta FA (2011) Physical basis of radiation protection in space travel. Rev Mod Phys 83(4): 1245-1281.
11. Chancellor JC, Scott GB, Sutton JP (2014) Space radiation: the number one risk to astronaut health beyond low Earth orbit. Life (Basel) 4(3): 491-510.
12. Kennedy AR (2015) Biological effects of space radiation and development of effective countermeasures. Life Sci Space Res 1: 10-43.
13. Hellweg CE, Baumstark-Khan C (2007) Getting ready for the Moon: the importance of research on cellular responses to radiation exposure. Mutat Res 613(2-3): 105-118.
14. Moreno-Villanueva M, Wong M, Lu T, Zhang Y, Wu H, et al. (2017) Interplay of space radiation and microgravity in cellular damage. Life Sci Space Res 13: 1-10.
15. Simonsen LC, Slaba TC, Guida P, Rusek A (2020) NASA's first ground-based Galactic Cosmic Ray Simulator: enabling a new era in space radiobiology research. PLoS Biol 18(5): e3000669.
16. Smith SM, Heer MA, Shackelford LC, Sibonga JD, Ploutz-Snyder L, et al. (2012) Bone metabolism and renal stone risk during spaceflight. Nutrients 4(9): 1194-1212.
17. Zwart SR, Heer M, Smith SM (2012) The role of nutrition in spaceflight-induced bone loss and renal stone risk. Nutrition 28(8): 820-826.
18. Whitson PA, Pietrzyk RA, Pak CY, Cintron NM (1993) Alterations in renal stone risk factors after spaceflight. J Urol 150(3): 803-807.
19. Pietrzyk RA, Jones JA, Sams CF, Whitson PA (2007) Renal stone formation in spaceflight: mechanisms and countermeasures. Am J Kidney Dis 49(6): 822-831.
20. LeBlanc A, Lin C, Shackelford L, Sinitsyn V, Evans H, et al. (2000) Muscle and bone changes during long-duration spaceflight. Eur J Appl Physiol 81(1-2): 1-7.
21. Lang T, LeBlanc A, Evans H, Lu Y, Genant H, et al. (2004) Cortical and trabecular bone mineral loss from the spine and hip in long-duration spaceflight. J Bone Miner Res 19(6): 1006-1012
22. Sibonga JD (2013) Spaceflight-induced bone loss: data from humans, animals, and cellular models. J Musculoskelet Neuronal Interact 13(1): 1-9.
23. Vico L, Collet P, Guignandon A, Lafage-Proust MH, Thomas T, et al. (2000) Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts. Lancet 355(9215).
24. Smith SM, Wastney ME, Morukov BV, Larina IM, Nyquist LE, et al. (1998) Calcium metabolism before, during, and after a 90-day bed rest: urinary calcium loss and bone turnover. J Bone Miner Res 13(12): 1819-1827.
25. Whitson PA, Pietrzyk RA, Morukov BV, Sams CF (2001) The risk of renal stone formation during and after long duration space flight. Nephron 89(3): 350-355.
26. Pak CY, Poindexter JR, Adams-Huet B, Pearle MS (2003) Predictive value of urinary calcium and citrate in nephrolithiasis. Kidney Int 64(3): 1047-1055.
27. Worcester EM, Coe FL (2010) Calcium kidney stones. N Engl J Med 363(10): 954-963.
28. Wang Y, Boerma M, Zhou D (2016) Ionizing radiation-induced endothelial responses and vascular injury. Radiat Res 186(5): 407-414.
29. Little MP (2000) Radiation carcinogenesis. Carcinogenesis 21(3): 397-404.
30. Morgan WF, Sowa MB (2015) Non-targeted effects of ionizing radiation: implications for risk assessment and radiation protection. Mutat Res 751: 31-41.
31. Durante M, Kronenberg A (2005) Ground-based research with energetic heavy ions for space radiation protection. Radiat Res. 164(5): 711-718.
32. Garrett-Bakelman FE, Mandeville V, Darshi M (2019) The NASA Twins Study: molecular and physiological adaptations to long-duration spaceflight. Science 364(6436): eaau8650.
33. Beheshti A, McDonald JT, Miller J, Grabham P, Costes SV, et al. (2019) Gene expression changes in the human body during spaceflight: implications for radiation and microgravity response. NPJ Microgravity 5: 26.
34. Overbey EG, da Silveira WA, Stanbouly S (2021) NASA GeneLab RNA sequencing datasets reveal molecular responses to spaceflight. Cell Rep 33(13): 108376.
35. Da Silveira WA, Fazelinia H, Rosenthal SB (2020) Comprehensive multi-omics analysis reveals molecular adaptations to spaceflight. Cell 183(5): 1185-1201.e20.
36. Afshinnekoo E, Scott RT, MacKay MJ (2020) Fundamental biological features of spaceflight: advancing the field of space health. Cell 183(5): 1162-1184.
37. Prasad KN, Cole WC, Haase GM (2009) Radiation protection in humans: extending the concept of as low as reasonably achievable (ALARA). J Cancer Res Ther 5(1): 1-7.
38. Riley PA (1994) Free radicals in biology: oxidative stress and the effects of ionizing radiation. Int J Radiat Biol 65(1): 27-33.
39. Halliwell B, Gutteridge JMC (2015) Free radicals in biology and medicine. 5th ed. Oxford: Oxford University Press.
40. Durante M, Pugliese M, James N, Cucinotta FA (2013) High-energy particle radiation therapy and space radiation protection. Br J Radiol 86(1025): 20120699.
41. Shackelford LC, LeBlanc AD, Driscoll TB, Evans HJ, Rianon NJ, et al. (2004) Resistance exercise as a countermeasure to disuse-induced bone loss. J Bone Miner Res 19(1): 108-118.
42. Cavanagh PR, Licata AA, Rice AJ (2005) Exercise and pharmacological countermeasures for bone loss during long-duration space flight. Gravit Space Biol Bull 18(2): 39-58.
43. Smith SM, Davis-Street JE, Rice BL, Nillen JL, Gillman PL, et al. (2001) Nutritional considerations for long-duration space flight: nutrition and bone health. Nutrition 17(6): S46-S49.
44. Smith SM, Heer MA, Wang Z, Huntoon CL, Zwart SR, et al. (2014) Nutritional biochemistry of spaceflight and countermeasures. Annu Rev Nutr 34: 1-25.
45. Clément G, Bukley AP (2007) Artificial Gravity. Springer
46. Zwart SR, Kloeris VL, Perchonok MH, Braby LA, Smith SM, et al. (2009) Assessment of nutrient stability in the International Space Station food system. J Food Sci 74(7): H209-H217.

47. LeBlanc A, Matsumoto T, Jones J, Shapiro J, Lang T, et al. (2013) Bisphosphonates as a countermeasure to spaceflight-induced bone loss. Bone 52(2): 470-476.

48. Leblanc AD, Driscoll TB, Shackelford LC, Evans HJ, Rianon NJ, et al. (2013) Alendronate as an effective countermeasure against spaceflight-induced bone loss. J Bone Miner Res 28(9): 2117-2125.

49. Tanaka H, Chui SC, Aoki M, Nagai T, Inoue S, et al. (2000) Effects of bisphosphonates on bone remodeling under unloading conditions. Bone 27(3): 417-424.

50. Iwamoto J, Takeda T, Sato Y (2005) Effects of bisphosphonates on bone loss induced by immobilization and unloading. J Bone Miner Metab 23(3): 243-249.

51. Camozzi V, Frigo AC, Zaninotto M (2017) Vitamin D status and supplementation in extreme environments and spaceflight conditions. Nutrients 9(7): 676.

52. Smith SM, Zwart SR, Heer M (2006) Human adaptation to spaceflight: role of nutrition in bone and renal physiology. Nutrition 22(9): 934-938.

53. Pak CY (1997) Medical management of urinary stone disease. Nephrol Dial Transplant 12(5): 925-928.

54. Ettinger B, Pak CY, Citron JT, Thomas C, Adams-Huet B, et al. (1997) Potassium-magnesium citrate is an effective preventive therapy against recurrent calcium oxalate nephrolithiasis. J Urol 158(6): 2069-2073.

55. Barcelo P, Wuhl O, Servitge E, Rousaud A, Pak CY, et al. (1993) Randomized double-blind study of potassium citrate in idiopathic hypocitraturic calcium nephrolithiasis. J Urol 150(6): 1761-1764.

56. Buckey JC Jr, Lane LD, Levine BD, Watenpaugh DE, Wright SJ, et al. (1996) Orthostatic intolerance after spaceflight. J Appl Physiol 81(1): 7-18.

57. Fu Q, Witkowski S, Levine BD (2006) Vasoconstrictor responsiveness and orthostatic intolerance after spaceflight. J Appl Physiol 101(4): 1065-1070.

58. Platts SH, Tuxhorn JA, Ribeiro LC, Stenger MB, Almeida FA, et al. (2009) Development of countermeasures to prevent orthostatic intolerance after spaceflight. Aviat Space Environ Med 80(3): A54-A59

59. Nicogossian AE, Huntoon CL, Pool SL (2016) Space Physiology and Medicine. (4th Edn.)., Philadelphia: Lea & Febiger.

60. Buckey JC Jr (2006) Space Physiology. New York: Oxford University Press.

61. Demontis GC, Germani MM, Caiani EG, Barravecchio IA, Passino C, et al. (2023) Human spaceflight and the physiological effects of microgravity. Nat Rev Physiol 5: 167-183.

62. Garrett-Bakelman FE, Darshi M, Green SJ, Gur RC, Lin L, et al. (2019) The NASA Twins Study: a multidimensional analysis of a year-long human spaceflight. Science 364(6436): eaau8650.

63. Demontis GC, Germani MM, Caiani EG, Barravecchio IA, Passino C, et al. (2023) Human spaceflight and the physiological effects of microgravity. Nat Rev Physiol 5: 167-183.

64. Leach CS, Alfrey CP, Suki WN, Leonard JI, Rambaut PC, et al. (1985) Regulation of body fluid compartments during short-term spaceflight. J Appl Physiol Respir Environ Exerc Physiol.

65. Leach CS, Rambaut PC, Johnson PC (1983) Regulation of body fluid volume during spaceflight. Physiologist 26(6 Suppl): S11-S14.

66. Perhonen MA, Franco F, Lane LD, Buckey JC, Blomqvist CG, et al. (2001) Cardiac atrophy after bed rest and spaceflight. J Appl Physiol 91(2): 645-653.

67. Watenpaugh DE, Hargens AR (1996) The cardiovascular system in microgravity. In: Fregly MJ, Blatteis CM, editors. Handbook of Physiology: Environmental Physiology. Bethesda (MD): American Physiological Society.

68. Hargens AR, Richardson S (2009) Cardiovascular adaptations, fluid shifts, and orthostatic intolerance in spaceflight. Acta Astronaut 64(7-8): 657-663.

69. Norsk P, Damgaard M, Petersen L, González-Alonso J (2006) Vasodilatation in humans during microgravity. J Physiol 575(Pt 2): 605-616.

70. Hughson RL, Helm A, Durante M (2018) Heart in space: effect of the extraterrestrial environment on the cardiovascular system. Nat Rev Cardiol 15(3): 167-180.

71. Crucian BE, Chouker A, Simpson RJ, Mehta S, Marshall G, et al. (2018) Immune system dysregulation during spaceflight: potential countermeasures. Front Immunol 9: 1435.

72. LeBlanc AD, Schneider VS, Evans HJ, Pientok C, Rowe R, et al. (1990) Bone mineral loss and recovery after 17 weeks of bed rest. J Bone Miner Res 5(8): 843-850.

73. LeBlanc AD, Schneider VS, Evans HJ, Engelbretson DA, Krebs JM, et al. (1990) Bone mineral loss and recovery after 17 weeks of bed rest. J Bone Miner Res 5(8): 843-850.

74. Vico L, Chappard D, Alexandre C, Palle S, Minaire P, et al. (1987) Effects of a 120 day period of bed-rest on bone mass and bone cell activity in man: attempts at countermeasure. Bone 8(5): 283-290.

75. Globus RK, Morey-Holton E (2016) Hindlimb unloading: rodent analog for microgravity. J Appl Physiol 120(10): 1196-1206.

76. Taylor EN, Stampfer MJ, Curhan GC (2004) Dietary factors and the risk of incident kidney stones in men. N Engl J Med 351(11): 112-120.

77. Zerwekh JE (2008) Bone calcium mobilization and renal stone risk during spaceflight and immobilization. Am J Physiol Renal Physiol 295(1): F1-F7.

78. Mader TH, Gibson CR, Pass AF, Kramer PD, Lee SM, et al. (2011) Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts after long-duration space flight. JAMA 306(10): 1185-1191.

79. Hargens AR, Bhattacharya R, Schneider SM (2013) Space physiology VI: exercise, bone loss, and cardiovascular adaptation. Eur J Appl Physiol 113(5): 1001-1012.

80. White RJ, Averner M (2001) Humans in space: the challenge of maintaining health. Science 293(5539): 2048-2051.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2026.66.010339

Ramona Nicotera . Biomed J Sci & Tech Res

Submission Link: https://biomedres.us/submit-manuscript.php