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Application of Microgravity Experiments in Plastic Surgery: A Literature Review

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Background: Interest in microgravity is growing in the medical and surgical fields. This literature review aims to synthesize existing evidence on microgravity applications in plastic surgery, focusing on experimental methods, outcomes, and prospects.

Methods: All reported articles up to October 2023, including publications and news reports, were screened for inclusion using Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. The PubMed keywords and Boolean operators were "plastic surgery AND microgravity," "plastic surgery AND spaceflight," "wound healing AND microgravity," "skin aging AND microgravity," "skin cancer AND microgravity," and "melanoma AND microgravity."

Results: A total of 201 articles were identified, and 14 studies were included. Plastic surgery procedures can be performed under microgravity, resulting in a delayed wound healing process. Four studies demonstrated that microgravity could reduce skin thickness and modify cell metabolism. In 2 studies, neoplastic melanoma cells have shown behavioral modifications under microgravity with induced apoptosis but increased potential for metastasis.

Conclusions: Microgravity represents a unique environment with potential implications in plastic surgery, although further rigorous studies need to be conducted in humans. The anticipated rise and development of spaceflights render the study of biological changes in space an impactful and significant topic. *(Plast Reconstr Surg Glob Open 2025;13:e6802; doi: 10.1097/GOX.0000000000006802; Published online 27 May 2025.)*

INTRODUCTION

Microgravity has been of high interest in the last decades in medical and surgical research.[1] It also represents opportunities to explore novel surgical techniques and assess their feasibility and effectiveness under extreme conditions.[2] Multiple studies have already shown the effect of microgravity on cells and tissues, including increased cell adhesions and aggregation in organoids and spheroids, apoptosis signaling in endothelial cells, and proliferation of keratinocytes, among others. Real microgravity can be obtained by spaceflights, using a spacecraft in orbit or linked to a shuttle.[3] These techniques allow full immersion but are poorly accessible, which explains the development of alternative models, such as parabolic flights[4] performed by dedicated planes reaching true 0*g* (free fall) but only for short periods (seconds). As for microgravity simulation, head-down bed rest (HDBR)[5] in humans has demonstrated some similarities with microgravity, such as fluid redistribution to the upper body. Similarly, hindlimb unloading (HUL)[6] in rodents, which is based on discharging a limb, represents a cheap and easy method to emulate microgravity. For cell studies, random position machines, 3-dimensional (3D) clinostats, or rotating wall vessels developed by National Aeronautics and Space Administration (NASA)[7] can induce a random modulable rotation of multiple frames in different axes, creating low-shear mixing.

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To date, NASA and the European Space Agency (ESA) have conducted multiple studies exploring surgery in space,[1,8] including the management of bleeding.[9] Access to space has also been facilitated through the contribution of SpaceX,[10] whose technology is increasingly used in the field.[11] In the field of plastic surgery, which involves multiple physiological processes and is currently experiencing significant advancements, comprehensive literature reviews that gather all relevant evidence are lacking. Studies have shown that malignancies, severe burns, and lacerations figure among the conditions most likely to occur in space, along with minor traumatic injuries to the skin and mucus membranes.[12] Thus, with the development of the space industry and tourism,[13] an augmentation of space journeys could be expected, as well as these injuries that would require specialized care supported by evidence-based medicine.[2] This review seeks to compile current evidence on the applications of microgravity in plastic surgery and to propose potential future directions for expanding and strengthening research in this area.

Takeaways

Question: What is the current understanding of microgravity's impact on plastic surgery?

Findings: Early studies demonstrate the feasibility of microsurgery and lipoma removal in microgravity. Microgravity seems to delay wound healing, reduce skin thickness, and influence cell metabolism. Melanoma cells also show altered apoptosis and metastasis behavior in this environment.

Meanings: Microgravity significantly affects key biological processes relevant to plastic surgery. As space travel becomes more common, understanding these effects is vital to adapt surgical practices for extraterrestrial settings.

MATERIALS AND METHODS

Research Strategy

A literature review was performed on PubMed and TRIP Database sources. This review was conducted according to the Cochrane Handbook for Intervention Reviews guidelines,[14] version 5.1.0. The study complied with the AMSTAR checklist (Assessing the Methodological Quality of Systematic Reviews) and is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.[15] A protocol was developed, published, and made available in the National Institute of Health Research Prospective Register of Systematic Reviews (PROSPERO) database, accessible at https://www.crd.york.ac.uk/PROSPERO, registration number CRD42023487358.

All reported articles and news reports up to October 2023 were screened before inclusion for analysis. The keywords and Boolean operators used on PubMed were “Plastic surgery AND microgravity,” “wound healing AND microgravity,” “skin aging AND microgravity,” and “melanoma AND microgravity.” Additionally, reference lists of selected articles were also manually examined to identify additional potentially eligible articles.

Article Selection and Inclusion and Exclusion Criteria

Original research articles were selected based on the title and abstract. All clinical trials related to plastic surgery procedures under microgravity conditions were included. Articles focusing on the impact of microgravity on longevity without mention of the skin or soft tissues were excluded. Reviews and in vitro studies without ex vivo or in vivo experiments were excluded from the analysis. Articles written in languages other than English were excluded.

Data Collection

For each publication, we recorded whether the experiments were conducted under simulated or real microgravity, the experimental models, the number of individuals, and the main outcomes of reported experiments. The study type and the duration of the experiments were also listed.

RESULTS

Included Articles

Out of 201 initially screened articles, 14 publications were included in this review (Fig. 1). Accordingly, 187 articles were not retained because they were considered off-topic (n = 151), nonoriginal (n = 29), duplicates (n = 6), or inaccessible (n = 1).

These articles were reported in 4 categories: plastic surgery procedures (n = 2), wound healing (n = 4), skin aging (n = 6), and skin cancer (n = 2) and included 8 noncomparative and 6 comparative studies.

The feature simulated (n = 5) or real gravity (n = 9) was studied in all articles. The most represented model was the rat (n = 6) among other in vivo models, and the number of subjects greatly varied depending on it (ie, 60–455 rats; 3 mice; unmentioned for leeches; 1–6 humans). Follow-up periods across studies ranged from 1 day[16,17] to 14 months[18] (Table 1).

Plastic Surgery Procedures Under Microgravity

The first attempt to perform microsurgery under microgravity was described in 2003 by Pinsolle et al[16] to identify the limits of precise surgical gestures. The procedure consisted of a section/reparation of the sciatic nerve and the tail artery in 4 rats during parabolic flights in 2 ESA centers. The operator, stabilized by a harness and using magnetized instruments on the operating table, performed 4 and 7 microstitches on the nerve and the artery, respectively (10/0 nonabsorbable monofilament). The outcomes were successful anastomoses and coaptations with a positive patency test for the artery and a 20% delay compared with similar procedures on the ground, with minor to no technical limitations.

This was followed in 2008 by reports from Martin et al,[17] who aimed at adapting an air filtration device to allow asepsis of space operating units and to develop specific equipment for the first human surgical procedure under microgravity. They described the removal of a superficial

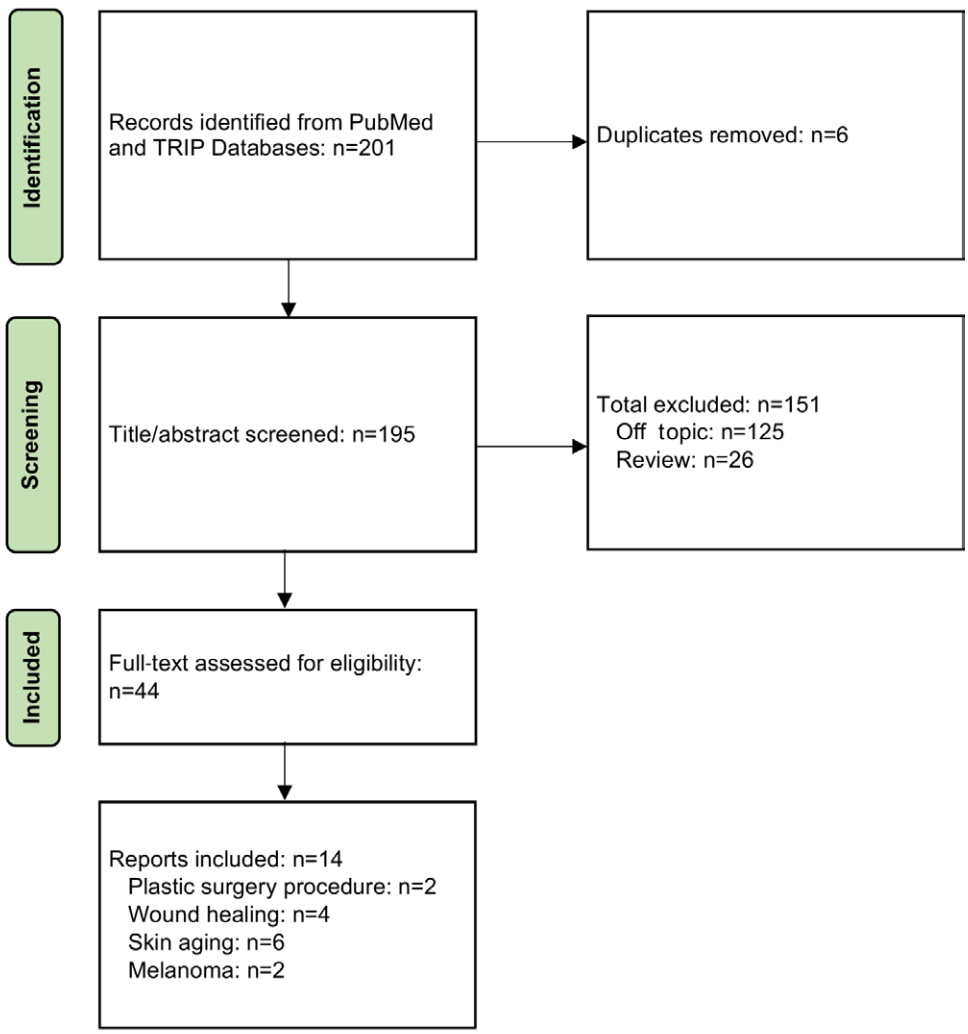

Fig. 1. Flowchart or the review.

lipoma, performed in a 47-year-old man's forearm[17] in a specifically designed 8 × 4 m^2 operating room. The local anesthesia and the sterilization of the surgeon's arms were performed on the ground. The surgery lasted 21 parabolas (7 min 40 s). The main inconvenience, according to the authors, was not the weightlessness but the delay (around 20%) caused by the parabolic flight. The air quality (qualified as ISO 6 or 7) was considered acceptable.

Wound Healing

In 1999, Davidson et al[19] compared the granulation tissue and collagen content in real microgravity conditions (space shuttle for 10 d) versus control (on the ground) in 344 rats undergoing superficial wounds. A subcutaneous abdominal polyvinyl acetal sponge was implanted in each animal through a midline incision as a model for fine wound healing analysis. The animals then received growth factors or a placebo. After 10 days in space, the sponge analysis revealed a significant reduction of granulation tissue cellularity and a 62% reduction in collagen content in the microgravity group, independently from the addition of growth factors.

Radek et al[20] performed a study involving 6 punch wounds on the back of 60 rats undergoing either HUL or normal conditions for 35 days (Fig. 2). The rats were killed at different time points (days 3, 7, 10, 14, and 21) to proceed with skin histological analyses, assessing re-epithelialization, angiogenesis, and collagen formation in a blinded design. A significantly diminished keratinocyte migration and a reduction of vascularity were found on the first days in the HUL group, but this delay was caught up by day 10. Moreover, their analyses did not objectify a decrease in total wound collagen content.

As an in vivo model, leeches have been investigated[21] in simulated microgravity versus control with and without the addition of platelet-rich plasma (PRP). A 2-mm surgical wound was created and sutured on the animals' dorsal skin. Animals were then separated into experimental groups (controls [ground]; microgravity; control+PRP; and microgravity+PRP). Simultaneously, an in vitro comparison was performed using a scratch fibroblast monolayer assay. After 72 hours, histology revealed a significant delay in the wound healing process in vitro (reduced cell migration) in the microgravity group as well as in

Table 1. Descriptions of the Studies and Outcomes

Reference	Experiment	Simulated/ Real Microgravity	Domain	Type	Exposure Duration	Field of Observation	Outcomes
Martin et al[17]	First plastic surgery procedure in man in microgravity	Real microgravity (parabolic flight)	4 rats and 1 human	Noncomparative	7 min 40 s (removal procedure)	Feasibility of plastic surgery in space	Feasible microsurgery; stable setup; successful lipoma removal; air quality acceptable
Pinsolle et al[16]	Microsurgery in microgravity	Real microgravity (parabolic flight)	4 rats	Noncomparative	11 min 20 s: artery procedure; 5 min 40 s mean: nerve procedure	Feasibility of plastic surgery in space	Successful stitches of artery and nerve under a microscope
Davidson et al[19]	Intrinsic wound healing and growth factor responses in microgravity	Real microgravity (orbit)	344 rats	Comparative	10 d	Wound healing	Delayed angiogenesis; reduction of collagen content
Radek et al[20]	Mechanical unloading on keratinocyte migration and angiogenesis during cutaneous wound healing	Simulated (HLU)	60 rats	Comparative	21 d	Wound healing	Delayed angiogenesis; no significant difference in collagen content
Cialdai et al[21]	Microgravity on healing process and effectiveness of PRP as a countermeasure study in vivo and in vitro	Simulated microgravity (RPM)	Leeches	Comparative	3 d	Wound healing	Delayed scarring (no statistic); reduced collagen density; improving healing and collagen density after PRP
Rai et al[22]	Mucosal wound healing	Real microgravity (orbit)	3 humans	Noncomparative	Around 16 + 21 d	Wound healing	Delayed scarring of the mucosal wound
Karlin et al[23]	Effect of microgravity on eyelid and brow position	Real microgravity (spaceflight)	18 humans	Noncomparative	<5 y	Skin aging	Augmentation of the pupil–eyebrow distance; no augmentation of the pupil–eyelid distance
Neutelings et al[24]	Skin physiology in microgravity	Real microgravity (orbit)	6 rats	Comparative	3 mo	Skin aging	Reduced thickness of the skin; increasement of hair follicles
Tronnier et al[25]	Change in skin physiological parameters in space	Real microgravity (spaceflight)	1 human	Noncomparative	160 d	Skin aging	Reduced thickness of the skin; reduced elasticity; coarser skin aspect
König et al[18]	Multiphoton tomography of astronauts	Real microgravity (spaceflight)	2 humans	Noncomparative	6 mo	Skin aging	No sign of accelerated skin aging; thinning of the epidermis; slower metabolism
Braun et al[26]	Effects of long-term missions on the International Space Station on skin physiological parameters	Real microgravity (spaceflight)	6 humans	Noncomparative	Mean flight time: 167 d	Skin aging	No loss of skin hydration; thickness/ density and elasticity unchanged
Wang et al[27]	Imaging assessment of human stress	Simulated microgravity (HDBR)	6 humans	Noncomparative	10 d	Skin aging	Induced oxidative stress in skin
Taga et al[28]	Melanoma growth and tumorigenicity in microgravity models	Simulated microgravity (RVW)	Murine B16-L10 melanoma cells and mice	Comparative	48 h and 14 d	Skin cancer	In vitro: induction of apoptosis, and melanin production and reduced growth; in vivo: increasement of the tumor size
Tan et al[29]	Microgravity on tumoral cell apoptosis	Simulated microgravity (RPM)	Murine BL6 melanoma cells	Comparative	24 h and 21 d	Skin cancer	In vitro: induction of apoptosis in melanoma cells; in vivo: reduced invasiveness and metastasis activity

RPM, random position machine; RVW, rotating wall vessel.

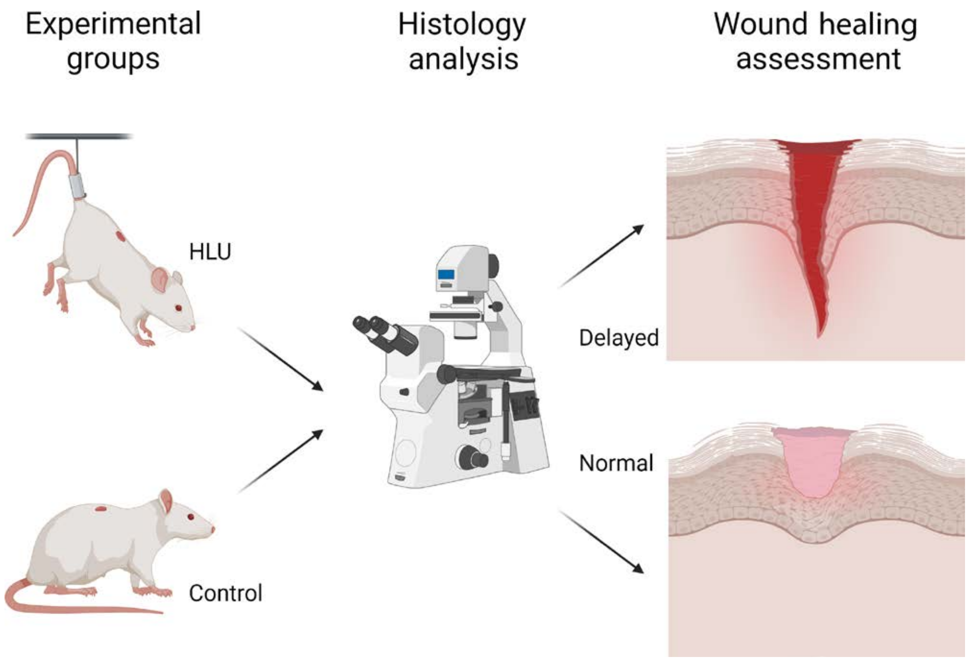

Fig. 2. Schematic of the experimental design of wound healing assessment in rats undergoing HLU condition.

vivo (with no explored statistical significance). In addition, a significant reduction of collagen fiber density was observed at 96 hours. With the PRP treatment, no differences in delays were observed between the ground and microgravity groups, but the healing was considered better (with a significantly higher collagen density) in the microgravity group.

In 2012, Rai et al[22] conducted experiments on mucosal wound healing in 2 human subjects. They compared 2 palatine wounds created 20 and 2 days before the mission in each astronaut. The cortisol levels were also measured in daily salivary samples, and the participants were asked to fill out a 10-item perceived stress scale up to day 14. A mean wound healing delay of 5 days (21 versus 16) was observed in 2-day-old wounds when compared with 20-day-old wounds. The cortisol levels showed a significant increase between vacation and mission time in both subjects, which showed a significant correlation with wound healing ($r = 67$).

Aging

In 2008, the first study on human skin physiology was coordinated by the ESA[25] in an International Space Station astronaut. The forearm epidermis, skin surface, and cutis were observed without treatment, whereas the contralateral side received skin care emulsion. The measures were done preflight (day −332), in-flight (159 d), and after landing (day +62). A thinning with a decrement of elasticity (via ultrasound analysis) and a coarser aspect of the skin (with photographs) were mentioned at the end of the spaceflight (no statistical significance explored).

In 2014, the first experiment using an animal model was conducted with 3 mice sent to the International Space Station for 3 months[24] compared with 3 animals on the ground. At the end of the experiment, the histological analysis displayed a significantly reduced thickness (15%; $P = 0.05$) with a 42% increase in newly synthesized procollagen ($P = 0.03$) in the space mice skin, but skin collagen density and hydration were not significantly different. Transcriptomic analysis revealed a significant upregulation of proteins controlling collagen turnover, aligning with the authors' hypothesis of early degradation of defective procollagen.

Continuing the SkinCare project, a collaboration between NASA and ESA initiated the Skin-B project in 2013[30] to evaluate the impact of real gravity (spaceflight) on astronauts' skin aging. The objective involved comparing parameters such as skin hydration, transepidermal water loss, surface profile, elasticity, density/thickness, and microcirculation before, during, and after the spaceflight. As a result, a team from Germany[18] published initial data from 2 astronauts undergoing this experiment. Multiphoton tomography was utilized to provide "in vivo histology" through fluorescence measurement (indicative of metabolism and thickness of the skin), along with second harmonic generation to autofluorescence to determine the aging index of the dermis (SAAID) with 6 measures on astronauts' volar forearms. In comparison, there was no decrease in the SAAID index between pre- and postflight evaluation, but a decrease in autofluorescence suggested lower metabolism associated with epidermal thinning. These findings were completed by a subsequent publication in 2019,[26] where each astronaut underwent 2 preflight, around 5 in-flight, and 3 postflight sessions. The average flight duration was 167 days. No significant variations were observed between the average values among the parameters measured both on the ground and in flight (skin hydration, transepidermal water loss, and skin surface profile). Other parameters, including skin elasticity and thickness/density (unchanged) and skin microcirculation (initial decrease followed by return to comparative values), were measured only on the ground due to feasibility considerations.

In a study conducted in 2021, the effects of microgravity on the brows and eyelids[23] were examined using 112 photographs from 18 astronauts on Earth (n = 55) and in space (n = 57), gathered over 5 years, from a NASA image library. Digital measurements from the center of the pupil to the upper eyelid margin remained unchanged in microgravity, but the mean distance between the pupil and the brow significantly increased by 3.7 mm ($P < 0.01$). These results suggest that spaceflight impacts the brow and eyelid in distinct ways, emphasizing the physiological differences in the regulation of these anatomical structures; eyelid height seems to remain highly regulated under various conditions, whereas brow height shows vulnerability to gravity-induced changes.

In 2022, a team from China also investigated the effects of microgravity on skin aging using a −6 degree HDBR position in 6 volunteers for 35 days.[27] The authors conducted 5 imaging sessions of the left volar forearm, front chest, and forehead (on days 1, 3, 8, 15, and +7) using a handheld 2-photon microscope to measure skin autofluorescence, focusing on oxidative state markers such as SAAID. Concurrently, they measured serum levels of oxidative markers. The results did not indicate a decrease in basal cell SAAID during the HDBR period but a significant increase in serum markers.

Skin Cancer

Taga et al[28] observed murine melanoma cells for tumorigenicity characteristics in vitro and in vivo. After 48 hours of culture under simulated microgravity through rotating wall vessel, significant growth limitation was observed along with increased melanin production and apoptosis rate compared with control conditions (culture flasks on the ground). Subsequently, when incubated subcutaneously in mice, these cells exhibited a significant increase in tumor size.

In 2018, Tan et al[29] investigated BL6-10 melanoma cells under simulated microgravity, focusing on adhesion, progression, metastasis, and markers of cell adhesion to the extracellular environment. After 24 hours in a clinostat, melanoma cells under microgravity exhibited typical noninvasive, epithelial-like cell behavior under microscopy but showed inhibition of adhesion cell markers compared with control 1 g cells, suggesting more favorable outcomes. However, invasiveness (assessed with a Boyden chamber) and metastatic activity (observed in lung colony 21 days after injecting cells in mice) were significantly reduced compared with controls.

DISCUSSION

With the advent of space exploration, there is an increased need for the implementation of medical and surgical techniques in this rapidly evolving field. Although our understanding of the effects of gravity on human physiology has advanced over recent decades, the feasibility of surgical approaches under microgravity remains elusive. In this review, we evaluated the practical aspects of such procedures in the field of plastic surgery and demonstrated the need for further research on wound healing, skin aging, and skin cancer studies.

Among all included reports, only 2 studies (with 1 involving humans) addressed procedural aspects of plastic surgery under microgravity. Despite the growing interest in space exploration, no further studies have been conducted since 2008. Nonetheless, these pioneering reports have paved the way for exploring low-risk procedures under microgravity, such as stitches and minor skin excisions, as well as for refining techniques and facilities.

Interestingly, a consistent finding across all studies on wound healing is a delay in the healing process.[31] However, the only clinical study[22] had several limitations, including a short follow-up, limited sample size, and confounding factors such as uncontrolled dietary and sleep routines among participants.

In the analyzed studies, microgravity seems to induce skin thinning, although the SkinCare project[25] could not validate this observation due to various incidents, nor could the Skin-B study.[32] In contrast, some authors have suggested that conditions during space missions may have improved for astronauts, indicating that certain contributing factors might not have been fully accounted for. The study by Neutelings et al[24] seems to be more rigorous, although it involved only 6 mice. The main outcomes were reduced skin thickness and an increase in hair follicles. Additionally, a 2016 study reported that astronauts often cited skin rashes as a primary symptom during spaceflight.[33] A survey involving 8 astronauts in the Skin-B project[32] echoed similar concerns, with peeling, rash, and dryness being common complaints among the 23 reported skin symptoms. These findings were also replicated in vitro in a 3D clinostat study.[34] In the eyebrow study,[23] the use of photographs alone is a significant limitation, as there was no information on the timing, duration, or persistence of microgravity effects. The observed eyebrow lift could be attributed to the relative predominance of the brow elevator muscles in the absence of gravity, as well as fluid shifts in the upper half of the body, potentially approximating the aesthetic outcomes of a brow lift. Furthermore, other stress factors, such as ionizing radiation and psychological stress, may also contribute to skin damage.[35] Although studies solely focusing on these effects were excluded, it would be relevant to consider these stress factors when analyzing skin physiology in space.

Another major field in plastic and reconstructive surgery is melanoma excision, currently the primary treatment for most tumors. Research suggests that microgravity could potentially influence the aggressiveness and apoptosis of melanoma cells in vitro. However, findings on cell behavior under these conditions are contradictory. A review of intracellular signaling molecule modulation (cyclic GMP) in melanoma cells[36] indicated a tendency

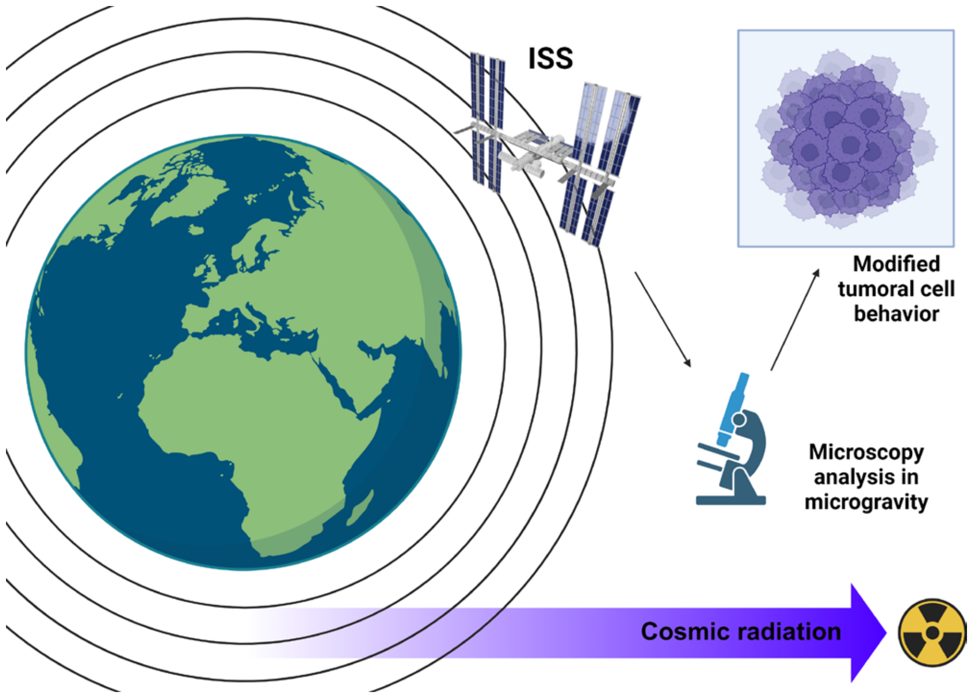

Fig. 3. Schematic of the remote monitoring of CSC behavior in a lab-on-chip subjected to real microgravity. Cosmic radiation increases with distance from the Earth, in contrast to gravity, as represented by the black lines. CSC, cancer stem cells; ISS, International Space Station.

for transformation from nonmetastatic to metastatic phenotypes under microgravity conditions. Conversely, the same review suggested that this pathway might reduce aggressiveness in metastatic tumors. These findings illustrate the variability of gravitational effects on cellular processes, with no clear consensus on their beneficial or harmful nature. As interest in this area grows, new technologies such as lab-on-chip[37] (Fig. 3) emerge as valuable tools, enabling laboratory-scale experiments in space aboard nanosatellites for remote research. These all-glass lab-on-chips have shown biocompatibility with melanoma stem cell cultures under simulated microgravity,[38] yielding promising results. Such advancements open up a range of research possibilities with potentially significant clinical implications by investigating unexplored conditions and unique environmental factors.

In this review, studies reliant on in vitro assays[39,40] were excluded, as they lack the biological complexity and interactions among cells and systems (endocrine, neural, immune, etc.). Reports on bone fracture and muscle healing,[41,42] although relevant, were excluded as they fall within orthopedic surgery. Recent studies have suggested using skin culture[43] or ex vivo models[44] with potential applications in wound healing and drug development. Additional models could be developed through 3D bioprinting, as proposed in a recent review.[45] This innovative approach may eliminate the need for native tissue and offers flexibility in skin graft shape (eg, thickness and size), potentially enabling extended skin defect coverage.

The strength of this review lies in its comprehensive coverage of multiple aspects of plastic surgery, compiled for the first time. However, the primary limitation is the scarcity of available studies, highlighting the novelty and emerging nature of this field.

Overall, microgravity-related plastic surgery can be explored in 2 contexts. First, performing plastic surgery in a microgravity environment. The skin may require increased care due to potential structural changes noted in the literature, which could be addressed through cosmetic and aesthetic procedures. Demand for aesthetic treatments has grown significantly,[46] aiming to counter early signs of aging such as reduced hydration, thickness, and elasticity.[47] Delayed wound healing may necessitate specialized plastic surgery techniques and ongoing monitoring. However, if healing delays are too severe, some procedures might be contraindicated.

Second, microgravity provides a platform for plastic surgery research with potential Earth applications. Lab-on-chip technology, for instance, could be instrumental in studying melanoma cancer stem cell mechanisms in microgravity, possibly paving the way for more effective treatments.[48] Furthermore, microgravity as a simulated environment, such as in the Karlin et al[23] study, offers intriguing possibilities. However, the associated high costs and logistical challenges may limit its use for modest outcomes. As interest in this field expands and technology advances, significant discoveries are likely.

CONCLUSIONS

This literature review gives an early overview of plastic surgery applications under microgravity and paves the way for new studies to address specific challenges presented by this environment. We highlighted that microgravity can potentially delay wound healing and reduce skin thickness and elasticity, as important cellular pathways and cellular characteristics in melanoma cells seem to vary under microgravity conditions. However, further studies involving human subjects and more advanced wound models are necessary to validate these preliminary observations.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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