Review

Surgery in space

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Background: **There has been renewed public interest in manned space exploration owing to novel initiatives by private and governmental bodies. Long-term goals include manned missions to, and potential colonization of, nearby planets. Travel distances and mission length required for these would render Earth-based treatment and telemedical solutions unfeasible. These issues present an anticipatory challenge to planners, and novel or adaptive medical technologies must therefore be devised to diagnose and treat the range of medical issues that future space travellers will encounter.**

Methods: **The aim was to conduct a search of the literature pertaining to human physiology, pathology, trauma and surgery in space.**

Results: **Known physiological alterations include fluid redistribution, cardiovascular changes, bone and muscle atrophy, and effects of ionizing radiation. Potential pathological mechanisms identified include trauma, cancer and common surgical conditions, such as appendicitis.**

Conclusion: **Potential surgical treatment modalities must consist of self-sufficient and adaptive technology, especially in the face of uncertain pathophysiological mechanisms and logistical concerns.**

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Introduction

Spaceflight is flight exceeding 100 km altitude above sea level[1]. It subjects humans to a variety of adverse physical conditions including microgravity, radiation, temperature extremes and ionospheric plasma[2,3]. Interest in manned spaceflight has been rekindled by novel private and government initiatives. Proposed goals of deep space exploration and extraterrestrial colonization by humans will likely entail participants' sustained exposure to non-terrestrial environments for durations exceeding current records. Existing insights into the effects of spaceflight on human physiology are limited by a small subject set, and the comparatively short duration of current and previous missions[2,4]. Future long-haul missions will have the task of studying long-term exposure to non-terrestrial conditions on participant physiology[4]. Future astronauts or colonists will inevitably encounter a range of common pathologies during long-haul space travel[4]. Novel pathologies may arise from prolonged weightlessness[5,6], exposure to cosmic radiation[7,8] and trauma[9,10].

Aside from the relative paucity of knowledge regarding prolonged human exposure to extraterrestrial conditions, the logistics of both study and treatment of human disease in space are a hurdle facing planners. Because of rigorous training requirements, a limited number of physicians have experienced space travel first hand[11,12]. Furthermore, owing to the limited space aboard existing craft, there is little room for medical equipment. The current protocol for serious medical and surgical emergencies on board the International Space Station (ISS) involves emergency repatriation of the crew member to Earth for treatment[13]. As distances increase beyond low-Earth orbit, it is clear that dedicated solutions for on-board medical treatment are required[14–16]. This paper aims to provide a narrative view of the published knowledge regarding human pathophysiology in space travel, and a conceptual overview of surgical modalities that may be employed during long-haul space exploration.

Methods

Search strategy

Data for this review were identified by searches of MEDLINE, PubMed, Google Scholar and references from relevant articles. Search criteria included 'physiological changes during spaceflight', 'surgery and spaceflight', 'medicine and spaceflight', 'pathology and spaceflight', 'telemedicine and spaceflight', 'regenerative medicine and spaceflight', 'surgical robotics and spaceflight', 'autonomous surgical robots', without parentheses and with dates between 1960 and 2018. Only articles published in English were selected. References cited in selected publications were identified and used where appropriate.

Results

Effects of spaceflight on human physiology

Fluid shifts and cardiovascular compensation

On exposure to microgravity, body fluids are redistributed towards the head[3,17]. Compensating for volume redistribution are the cardiac, autonomic and vascular systems[18,19]. With greater fluid volume in the head and chest vessels, and resulting activation of central baroreceptors[20,21], the renin–angiotensin–aldosterone axis is suppressed and atrial natriuretic peptide is released from cardiac tissues. Salt and water are excreted, with net reduction in plasma volume. Reduced plasma volume causes a transient increase in haematocrit, and a decrease in both erythropoietin secretion and red cell mass. Combined, there is a net reduction in blood volume[22]. Compensatory decreases in BP and heart rate generally stay constant over the course of 6 months of prolonged microgravitational exposure and may lead to orthostatic intolerance on return to Earth[23]. The reduction in cardiac workload caused by prolonged spaceflight may reduce overall myocardial mass[23–25]. Despite loss of contractile mass, ejection fraction and arterial pulse wave velocities are preserved. Regular cardiovascular conditioning may provide a countermeasure against cardiac remodelling[25]. Other cardiac and vascular factors that remain to be studied in detail include the potential for cardiac dysrhythmias[26,27], and the effect of cosmic radiation on cardiac tissues and vasculature[25].

Musculoskeletal changes

In space, atrophy of the supportive bones and musculature occurs owing to absence of the gravitational forces that they conventionally resist[28]. Other causes of musculoskeletal atrophy are suboptimal nutrition and psychosocial stresses associated with spaceflight[29]. Postural muscles atrophy, assuming a new equilibrium of increased protein degradation and decreased protein synthesis[30,31]. Microgravitational muscular atrophy affects type 2 (slow twitch) fibres to a greater extent than type 1 (fast twitch) fibres[5]. These changes may be mitigated by resistance training and conditioning while in space[29,32]. Bony structures also undergo atrophy in the absence of normal gravitational loading[6]. The loss of trophic gravitational stimulus causes significant bone demineralization[6,29]. Other causes of bone demineralization are lower vitamin D3 levels from reduced ambient light levels, and increased carbon dioxide concentrations causing bicarbonate-mediated demineralization[29]. Bone density is lost primarily from bones with weight-bearing function (lumbar vertebrae, pelvis, femoral neck, tibia, calcaneus)[29,31,33]. Urinary/faecal markers of bone resorption increase, and blood levels of parathyroid hormone and 1,25-dihydroxyvitamin D are reduced[34]. It is predicted that the 2·5-year probable duration of a manned Mars mission will reduce bone density to osteoporotic levels without countermeasures[3]. As a result, astronauts are at increased risk of pathological fractures during physical activity (such as spacewalks) or on return to normal gravity[35,36]. In cases of bony fracture, callus formation[37] and angiogenesis[38] are impaired in space. Increased calcium excretion may also precipitate renal calculi[39,40], which may present as a surgical emergency.

Immune dysregulation

Leucocytosis has been observed during and after spaceflight. Changes include a doubled neutrophil count and alterations in monocyte, CD3+, CD4+, CD8+, B cell and natural killer cell counts and ratios[41]. Combined with increased virulence and number of microbes[42,43] within the confined cabin environment, immune dysregulation is significant enough to produce increased susceptibility to both bacterial and viral infections[44]. These factors are compounded by decreased mitogen sensitivity and alterations in the phenotypic expression of leucocyte adhesion factors[45,46]. Other consequences arising from spaceflight-mediated immune dysregulation include hypersensitivity, autoimmunity, allergy, latent viral reactivation and malignancies[3]. Psychosocial stressors may exacerbate physiological immune changes, as evidenced by increased levels of glucocorticoids and catecholamines[47]. This immune dysregulation may affect wound healing, which is of potential surgical consequence.

Neurovestibular system

Motion sickness describes symptoms precipitated by a discrepancy between visual and neurovestibular motion inputs. In space, loss of normal gravitational forces results in an altered perception of axial movement (space motion sickness). Fluid shifts within the vestibular canals underpin this phenomenon. Space motion sickness is generally benign and resolves after 1–2 days of acclimatization, although it may be persistent or severe enough to incapacitate[48–51]. Neurovestibular phenomena may be identified and managed by adequate preflight training, or standard antiemetic medications[52]. In theory, neurovestibular dysfunction may affect the ability to conduct fine motor tasks (like surgery); however, tests in artificial microgravity have demonstrated otherwise[53,54].

Potential pathologies encountered during spaceflight

Trauma

Trauma is of highest concern owing to its incapacitating and mission-compromising potential[9,55]. It may incapacitate any crew member, despite optimal physical health. Common aetiologies seen terrestrially include airway obstruction, haemopneumothorax, bony fractures, head injuries and bleeding[56,57]. Relevant to planetary exploration or spacewalks is the potential for crush-type and penetrating injuries, both of which may compromise protective-suit integrity[9,58]. Loss of protection conferred by the space suit may cause catastrophic flash fire or decompression into the space vacuum[59]. Even though objects in microgravity may be weightless, their mass is still retained, including their ability to produce traumatic injury upon acceleration[60]. These risks may be mitigated by use of armoured body protection. Nevertheless, modifications of existing Advanced Trauma Life Support (ATLS®) protocols[9,10,61] and contingency evacuation plans must be considered for all crewed spaceflights.

Non-traumatic surgical emergencies

Terrestrially, appendicitis and cholecystitis are common surgical emergencies[62,63]. Although no confirmed case of appendicitis has been documented in space travellers, there are at least two reports of suspected appendicitis in Russian cosmonauts, one of which resulted in emergency repatriation to Earth. In each patient, referred symptoms of urolithiasis and prostatitis mimicked those of appendicitis[64]. It is unclear, however, whether the physiological alterations occurring during spaceflight increase susceptibility to appendicitis[65]. As the risk of appendicitis decreases with increasing age[62], the age of prospective candidates might be a selection consideration. Unlike appendicitis, gallstone cholecystitis has several modifiable and non-modifiable risk factors[63], which can be minimized by adequate screening. Nevertheless, it is unknown whether altered immunity and physiology[44] during spaceflight increase susceptibility to both appendicitis or cholecystitis, rendering even healthy individuals prone to acute surgical pathologies. Prophylactic appendicectomy and cholecystectomy have been proposed for spaceflight candidates[65], as has conservative treatment of appendicitis[64] in the absence of adequately trained crew or hardware for surgical management. These potentially life-threatening conditions highlight the need for on-board diagnostic and treatment solutions.

Head injury and intracranial pathologies

There have been no documented head injuries in space. It has been suggested that intracranial pressure increases proportionally with fluid shifts induced by microgravity[66,67]. Consequently, the severity of traumatic or spontaneous intracranial haemorrhage may be increased in space[10]. Rigorous preflight screening, including cerebral angiography to exclude aneurysmal pathology, may decrease the likelihood of haemorrhagic events. In the event of intracranial haemorrhage, ability to perform burr holes or craniotomies in microgravity has been explored in animal subjects[68,69].

Radiation-induced pathology

Radiation sources in space consist of high-energy particles and galactic cosmic rays[8]. Chromosomal and DNA damage from high-energy particles differs from that produced by terrestrial sources, such as γ rays. High-energy particles are thought to produce cancers of both higher grade and increased metastatic potential[7]. Consequently, epidemiological data from terrestrial studies cannot easily be extrapolated to the unique situation of space travel, although predictive models exist[7,70]. The National Aeronautics and Space Administration (NASA) predicts the risk of death from spaceflight-induced cancers to be 3 per cent[71]. This figure has been disputed; alternative models place the risk of death from both solid and hollow-organ cancers, and leukaemias as being substantially higher, based on duration and total number of missions[7,70–72]. If verified, these models indicate high potential for malignancy in those who take the 2·5-year long round trip to Mars.

Infections

Dysregulation of the immune system and microbial flora, along with close-quarters co-habitation, heightened microbial virulence, pathogen resistance and impaired clearance of aerosols in microgravity all increase the risk of infection. Candidates for NASA-sponsored missions require both standardized and specialist vaccinations, in addition to rigorous medical and dental screening to exclude tuberculosis, methicillin-resistant *Staphylococcus aureus* and human immunodeficiency virus. Despite these thorough measures, recommendations include broader-spectrum screening and vaccination coverage, improved-efficiency particulate air filtration systems and reverse-osmosis water purifiers[73,74]. Environmental contagion control is of particular importance if dedicated surgical suites aboard spacecraft are to be realized.

Diagnosis of surgical disease in space

Clinical ultrasound imaging has been tested successfully aboard the ISS by non-medical crew members according to focused assessment with sonography for trauma (FAST) protocols[75–79]. Ultrasonography has been used successfully in space for musculoskeletal[76,78], ocular (as a surrogate for intracranial pressure changes)[75], thoracic[77], abdominal and pelvic[79] imaging. It can reliably diagnose haemoperitoneum, haemothorax and pneumothorax[77,80,81]. Although clinical ultrasound equipment is compact and ultrasonography is easy to perform in trauma situations, its accuracy as a diagnostic tool is user-dependent[82,83]. In a zero-gravity environment, fluid may assume a diffuse distribution within anatomical planes (such as pleura), potentially complicating interpretation. Three-dimensional (3D) ultrasound imaging has been suggested as an alternative with, or without contrast to diagnose and monitor internal bleeding[9]. It is obvious that a compact device, permitting imaging of acute and chronic pathologies throughout the bony and soft tissue systems of the body, is required.

Advanced Trauma Life Support in space

In space, ATLS® protocols must be adapted to incorporate unique pathophysiological mechanisms[9,60,84]. Airway support, including intubation, is a viable prospect, although potentially complicated by facial oedema[85]. Regarding breathing, both tension pneumothorax and haemothorax can be diagnosed by ultrasonography. It is not known how a severe bleed or cardiac failure would affect the haemodynamic state assumed secondary to microgravitational fluid shifts[86]. Consequently, the risks of bleeding may be amplified. Prolonged fluid infusion may drain limited supplies, adversely affect clotting profile or induce hypothermia[9]. For limb and extremity trauma, tourniquets or haemostatic dressings may be adequate[87,88]. For life-threatening intra-abdominal or intrathoracic bleeding, application of external pressure is inadequate for control[9]. On Earth, access to necessary diagnostic and interventional facilities may permit expectant management of haemodynamically stable patients with truncal trauma, saving intervention for the event of deterioration[89–91]. In space, late haemodynamic deterioration following trauma may prove difficult to address owing to homeostatic decompensation, limited access to facilities and equipment, or lack of trained staff[9,92]. Because of these concerns, the concept of damage control surgery in space has been introduced[93,94]. For a surgical abdomen, this includes an exploratory laparotomy to achieve, at a minimum, haemostasis or irrigation of endogenous bacterial contamination.

Open surgery

For situations in which observation, simple haemostasis or conservative treatment is inadequate, and assuming that the relevant expertise is available, surgical intervention is required. Surgery in space carries additional risks and logistical concerns. Experimental research into space surgery has been conducted in both simulated microgravity and aboard spacecraft[9,68,84,92,94,95]. In microgravity, the patient will need to be restrained for positioning. Restraint may also be required for operating personnel and equipment to ensure adequate line of sight, access and freedom of movement[10,96,97]. These considerations have led to the concept of a traumapod, which is an enclosed suite providing all necessary facilities and equipment for surgery in adverse environments[98–101]. Proposed adaptation of this concept to space includes a dedicated medical module incorporated within the construction of the spacecraft[101] (*Fig. 1*).

Conventional skin preparation has proven adequate owing to the inherent surface tension of antiseptic liquids and adhesive drapes[60,97,102]. A notable concern for open surgery is the effect of exposure to microgravity on exposed internal surfaces or bleeding sites. Because of the surface tension of blood, it tends to pool and form domes that can fragment on disruption by instruments. These fragments may float off the surface and disperse throughout the cabin, potentially creating a biohazard[10]. The tendency of organs to eviscerate has also been reported. In addition, the tendency of floating bowel to abut the abdominal wall causes a theoretical risk of instrumental perforation[10,96]. A proposed solution to the effect of microgravity on exposed body surfaces and fluids is to have a hermetically sealed enclosure placed over the surgical site. Designs incorporate either pressurized air or sterile fluid as a differential between the anatomical site and the cabin atmosphere, preventing evisceration and containing floating debris. Although these systems have been tested with some success, remaining issues include: size and versatility for different procedures, visual windows, light refraction in gases or fluids, mixing of blood with a fluid medium, pressure loss and fogging[10,97,102–104].

Minimally invasive surgery

Modern endoscopic equipment includes a fibre-optic camera and light source to visualize the operating field, and a variety of surgical tools to hold, manipulate, cauterize, cut or suture tissue. In space, laparoscopic surgery is the obvious solution to contain the organs and reduce biological contamination[10]. In contrast to open surgery, laparoscopic surgery carries an additional learning curve[105,106],

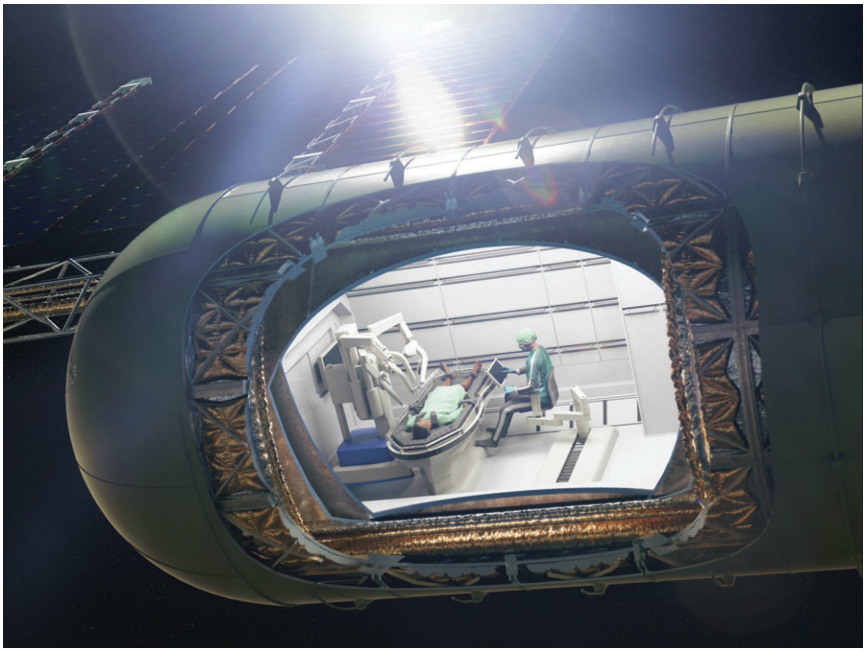

Fig. 1 Virtually rendered cutaway view of a postulated traumapod surgical module. Multiple layers of thermal and radiation shielding are visible. A four-armed surgical robot is situated within the module. The patient is tethered to the operating table, while the assistant, using a touchscreen console, is tethered to the module structure via a movable chair. Illustration by T. Trapp (https://www.planvis.co.uk)

but is commonly employed by modern surgeons. The microgravity environment may confuse orientation, because of subjective loss of up-and-down perception, although in simulated trials this was not an issue[107,108]. Insufflation of carbon dioxide within a body cavity, however, may compromise a patient who has already experienced physiological deconditioning and pathology[9,10]. Finally, if the damage control philosophy is to be applied, endoscopic surgery may be of less benefit than a more definitive laparotomy[9,10].

Robotic surgery

Surgical robots were initially devised for military use in combat zones[109,110]. Modern surgical robots are controlled by a surgeon situated at a console, located at a distance from the robot and operating table, yet with a stereoscopic view of the operating field[95,109]. Advantages of robotic surgery include optimization of traditional endoscopy, superior axial mobility compared with the human hand, minimization of fatigue, and enhanced ergonomics[111,112]. Disadvantages include cost, power requirements, loss of haptic feedback and requirement for an assistant or scope operator[113]. Although their benefit over routine open or endoscopic surgery is disputed, surgical robots permit long-distance telesurgery[95,109,110]. Their employment could therefore negate the requirement for an on-board surgeon; they have been used for procedures conducted intercontinentally[114], underwater[110] and in simulated microgravity[95]. Their use, however, would be limited to craft whose distance would not confer significant radio signal delay[15,95].

Discussion

Conditions requiring surgery in space will be rare, but offer huge logistical challenges for optimal management. Particular to surgery, telemedicine can permit consultation and instruction during surgical procedures[115,116]. This may allow guidance on conducting simple surgical procedures for non-medical crew members. For more significant interventions in the absence of a trained crew member, the use of teleoperated surgical robots has been suggested[14,95,96,117]. This distance may be expanded to allow telesurgery between a surgeon on Earth and a robot aboard a spacecraft. Although Earth-to-space telesurgery is yet to be achieved, NASA has successfully accomplished several basic procedures at an underwater facility designed as an analogue for the space environment[110]. A potential issue regarding telemedicine and telesurgery on board spacecraft is the communication delay between the craft and Earth. The distance between Earth and Mars is 48 600 000 miles, meaning a communication delay of anywhere between 4 and 22 min for radio signals[15]. Current telesurgical capabilities are not feasible for a Mars mission. A fully autonomous surgical robot[14,98,118] could solve this issue by dispensing with the need for a distance operator or crew surgeon.

Looking further ahead, facilitated endogenous repair[119] involves the regeneration of native tissues by using a molecular stimulus to initiate reparative processes. These principles may be applied to mitigate microgravity-induced bony demineralization. One potential approach involves use of absorbable nanoparticulate scaffolds that simultaneously provide temporary structural support while eluting drugs that stimulate differentiation of endogenous mesenchymal stem cells, precursors to osteoblasts. Another approach involves the extrinsic delivery of mesenchymal stem cells to desired sites directly via nanoparticulate delivery systems[120]. The use of nanoparticulate delivery systems provides the ability to tune drug delivery via either extrinsic signals or endogenous homeostatic cues.

A potential solution to the extremely limited space aboard spacecraft is the inclusion of a 3D printer[121]. 3D printing permits fabrication of complex objects from a computer-aided design template. As surgical instrumentation is highly specialized and often unique to a subspecialty, it would be impossible to carry all the equipment necessary to treat every anticipated space pathology. A digital database of surgical tool templates for fabrication as needed[122,123] would effectively solve the issue of limited stowage. Further, 3D-printed instruments may be disposable, meaning no requirement for space-occupying sterilization equipment. Other potential uses for stereolithography are fabrication of dressings[124], splints[125], prostheses[126] and even pharmaceuticals[127].

Although the concept of surgery in space may seem esoteric, it is important to start planning early if new frontiers in space travel are to be achieved. Successful implementation will rely on adaptation of core principles already familiar to the surgeon. The extreme environment of space, however, produces several unique changes in human physiology that future practitioners of space surgery must take into consideration. Resourcefulness and innovation will inevitably be required to meet these challenges.

Disclosure

The authors declare no conflict of interest.

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