



EUROPEAN COLORECTAL CONGRESS

Spotlight on the colon

1 – 5 December 2019, St.Gallen, Switzerland

MASTERCLASS

When the appendix plays nasty: intraoperative surprises, immediate solutions and long-term treatment options
Justin Davies, Cambridge, UK

All you need to know about stomas but never dared to ask
Willem Bemelman, Amsterdam, NL

The colorectal anastomosis: time-proven wisdom, innovative configurations, and salvage techniques
André d'Hoore, Leuven, BE

Extended lymph node dissection: indications, surgical anatomy and technical approaches
Peter Sagar, Leeds, UK

taTME in 2020 – when the dust settles: current and innovative indications, implementation and practical advices
Roel Hompes, Amsterdam, NL

To ostomize or to fear a leak – purpose and function of a diversion and clinical experience with virtual ileostomy
Gabriela Möslein, Wuppertal, DE

Is the longer the new better – how to safely extend the interval after neoadjuvant chemotherapy prior to surgery for locally advanced rectal cancer
Ronan O'Connell, Dublin, IE

Complete mesocolic excision: indications, surgical approaches, pitfalls and an appraisal of the literature
Paris Tekkis, London, UK

All the secrets of the pelvic floor – common disorders and proven solutions
Julie Cornish, Cardiff, UK

The views of an Editor and the wisdom of an Expert: contemporary publications with the potential and improve practice
Neil Mortensen, Oxford, UK

The EBSQ Coloproctology Examination
Michel Adamina, Winterthur, CH

SCIENTIFIC PROGRAMME

Pathophysiology and non-operative management of symptomatic uncomplicated diverticular disease
Robin Spiller, Nottingham, UK

Surgery of acute diverticulitis – evidence, eminence and real life
Willem Bemelman, Amsterdam, NL

Management of atypical diverticulitis
Dieter Hahnloser, Lausanne, CH

Hartmann reversal: open, laparoscopic or transanal?
Roel Hompes, Amsterdam, NL

The surgeon personality – influence on decision making, risk-taking and outcomes
Desmond Winter, Dublin, IE

Clinical applications of image-guided cancer surgery
Cornelis van de Velde, Leiden, NL

Volvulus of the colon – a treatment algorithm
Peter Sagar, Leeds, UK

Hereditary colorectal cancer syndromes: tailored surgical treatment
Gabriela Möslein, Wuppertal, DE

Lars Pählman and Herand Abcarian (2015)
Herand Abcarian, Chicago, US



Lars Pählman Lecture
Steven Wexner
Weston, US

Iterative cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases
Vic Verwaal, Aarhus, DK

Is anastomotic leak an infectious disease
Ronan O'Connell, Dublin, IE

Neoadjuvant chemotherapy for advanced colon cancer: clinical and pathological Results
Dion Morton, Birmingham, UK
Philip Quirke, Leeds, UK

Mechanical bowel obstruction: rush to the OR or stent and dine
Neil Mortensen, Oxford, UK

Controversies in IBD surgery
André d'Hoore, Leuven, BE

How to deal with IBD and dysplasia
Janindra Warusavitarné
London, UK

Perianal Crohn – avoiding delay and best surgical practice
Justin Davies, Cambridge, UK

Perianal Crohn – stem cells therapy and current medical approach
Gerhard Rogler, Zürich, CH

Is it time to invest in robotic surgery?
Antonino Spinelli, Milan, IT

New developments in robotic systems
Alberto Arezzo, Torino, IT

Robotic multivisceral resection
Paris Tekkis, London, UK

Posterior component separation for abdominal wall reconstruction: evolution from open to minimal invasive using the robotic platform
Filip Muysoms, Gent, BE

Coloproctology 4.0 – the networked surgeon
Richard Brady
Newcastle upon Tyne, UK

The elderly colorectal patient – functional outcomes and patient reported outcomes
Isacco Montroni, Faenza, IT

The microbiome and colorectal cancer
Philip Quirke, Leeds, UK

Surgical management of rectal endometriosis
Eric Rullier, Bordeaux, FR



EAES Presidential Lecture 3D printing for the general surgeon
Andrea Pietrabissa, Pavia, IT

ROUNDTABLE

Herand Abcarian, Chicago, US
Bill Heald, Basingstoke, UK

Management of locoregionally advanced colon cancer
Torbjörn Holm, Stockholm, SE

Artificial intelligence in colorectal surgery
Michele Diana, Strasbourg, FR

The mesentery in colonic diseases
Calvin Coffey, Luimneach, IE

Technical pearls and typical mistakes in minimal invasive colectomy
Antonio Lacy, Barcelona, ES

Choosing the right anastomotic technique in colon surgery
Roberto Persiani, Rom, IT

Precision surgery: past, present and future
Brendan Moran, Basingstoke, UK

Poster award
Michel Adamina, Winterthur, CH

Information & Registration

www.colorectalsurgery.eu

The publication of this advertisement does not constitute endorsement by the society, publisher, or Editors, and is unrelated to the content that follows



Surgery in space

S. S. Panesar¹  and K. Ashkan²

¹Department of Neurological Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, and ²Department of Neurosurgery, King's College Hospital NHS Foundation Trust, London, UK

Correspondence to: Dr S. S. Panesar, Department of Neurological Surgery, University of Pittsburgh, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, USA (e-mail: ssp29@pitt.edu)

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.

Paper accepted 11 May 2018

Published online 20 June 2018 in Wiley Online Library (www.bjs.co.uk). DOI: 10.1002/bjs.10908

Introduction

Spaceflight is flight exceeding 100 km altitude above sea level¹. 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 physiology⁴. Future astronauts or colonists will inevitably encounter a range of common pathologies during long-haul space travel⁴. 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 treatment¹³. 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 volume²². 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 Earth²³. 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 remodelling²⁵. 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 vasculature²⁵.

Musculoskeletal changes

In space, atrophy of the supportive bones and musculature occurs owing to absence of the gravitational forces that they conventionally resist²⁸. Other causes of musculoskeletal atrophy are suboptimal nutrition and psychosocial stresses associated with spaceflight²⁹. 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) fibres⁵. 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 loading⁶. 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 demineralization²⁹. 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 reduced³⁴. It is predicted that the 2.5-year probable duration of a manned Mars mission will reduce bone density to osteoporotic levels without countermeasures³. 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 formation³⁷ and angiogenesis³⁸ 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 ratios⁴¹. 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 infections⁴⁴. 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 malignancies³. Psychosocial stressors may exacerbate physiological immune changes, as evidenced by increased levels of glucocorticoids and catecholamines⁴⁷. 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 medications⁵². 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 vacuum⁵⁹. Even though objects in microgravity may be weightless, their mass is still retained, including their ability to produce traumatic injury upon acceleration⁶⁰. 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 appendicitis⁶⁴. It is unclear, however, whether the physiological alterations occurring during spaceflight increase susceptibility to appendicitis⁶⁵. As the risk of appendicitis decreases with increasing age⁶², the age of prospective candidates might be a selection consideration. Unlike appendicitis, gallstone cholecystitis has several modifiable and non-modifiable risk factors⁶³, which can be minimized by adequate screening. Nevertheless, it is unknown whether altered immunity and physiology⁴⁴ during spaceflight increase susceptibility to both appendicitis or cholecystitis, rendering even healthy individuals prone to acute surgical pathologies. Prophylactic appendectomy and cholecystectomy have been proposed for spaceflight candidates⁶⁵, as has conservative treatment of appendicitis⁶⁴ 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 space¹⁰. 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 rays⁸. 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 potential⁷. 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 cent⁷¹. 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, thoracic⁷⁷, abdominal and pelvic⁷⁹ 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 bleeding⁹. 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 oedema⁸⁵. 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 shifts⁸⁶. Consequently, the risks of bleeding may be amplified. Prolonged fluid infusion may drain limited supplies, adversely affect clotting profile or induce hypothermia⁹. 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 control⁹. 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 spacecraft¹⁰¹ (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 biohazard¹⁰. 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 contamination¹⁰. In contrast to open surgery, laparoscopic surgery carries an additional learning curve^{105,106},

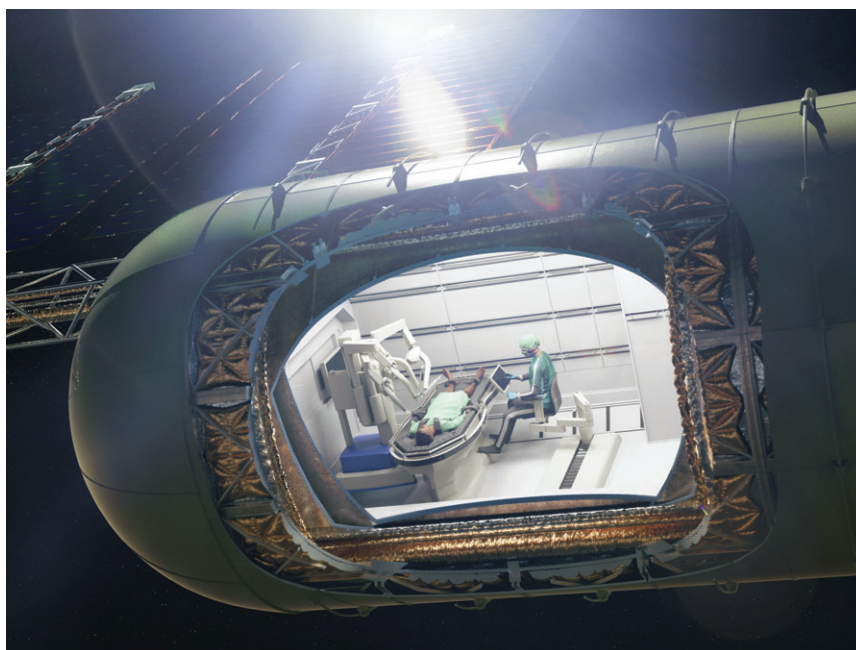


Fig. 1 Virtually rendered cutaway view of a postulated traumapod surgical module. Multiple layers of thermal and radiation shielding are visible. A four-armed surgical robot is situated within the module. The patient is tethered to the operating table, while the assistant, using a touchscreen console, 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 operator¹¹³. 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 intercontinentally¹¹⁴, underwater¹¹⁰ and in simulated microgravity⁹⁵. 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 environment¹¹⁰. 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 signals¹⁵. 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 repair¹¹⁹ 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 systems¹²⁰. 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 printer¹²¹. 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 dressings¹²⁴, splints¹²⁵, prostheses¹²⁶ and even pharmaceuticals¹²⁷.

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.

References

- 1 Fernandez de Córdoba S. *Presentation of the Karman Separation Line, Used as the Boundary Separating Aeronautics and Astronautics*. <https://www.fai.org/page/icare-boundary> [accessed 26 March 2011].
- 2 Thirsk R, Kuipers A, Mukai C, Williams D. The space-flight environment: the International Space Station and beyond. *CMAJ* 2009; **180**: 1216–1220.
- 3 Williams D, Kuipers A, Mukai C, Thirsk R. Acclimation during space flight: effects on human physiology. *CMAJ* 2009; **180**: 1317–1323.
- 4 White RJ, Averner M. Humans in space. *Nature* 2001; **409**: 1115–1118.
- 5 Fitts RH, Riley DR, Widrick JJ. Physiology of a microgravity environment invited review: microgravity and skeletal muscle. *J Appl Physiol (1985)* 2000; **89**: 823–839.
- 6 Vico L, Collet P, Guignandon A, Lafage-Proust MH, Thomas T, Rehaillia M *et al*. Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts. *Lancet* 2000; **355**: 1607–1611.
- 7 Cucinotta FA, Schimmerling W, Wilson JW, Peterson LE, Badhwar GD, Saganti PB *et al*. Space radiation cancer risks and uncertainties for Mars missions. *Radiat Res* 2001; **156**: 682–688.
- 8 Hellweg CE, Baumstark-Khan C. Getting ready for the manned mission to Mars: the astronauts' risk from space radiation. *Naturwissenschaften* 2007; **94**: 517–526.
- 9 Kirkpatrick AW, Ball CG, Campbell M, Williams DR, Parazynski SE, Mattox KL *et al*. Severe traumatic injury during long duration spaceflight: light years beyond ATLS. *J Trauma Manag Outcomes* 2009; **3**: 4.
- 10 Campbell MR. A review of surgical care in space. *J Am Coll Surg* 2002; **194**: 802–812.
- 11 Thirsk R. Physicians as astronauts. *McGill J Med* 2011; **13**: 69.
- 12 Jackson JS, Pedersen FT. *Redefining the (Emergency) Physician–Astronaut*. <https://www.emra.org/emresident/article/redefining-the-emergency-physician-astronaut/> [accessed 1 January 2018].
- 13 Bacal K, Beck G, McSwain NE Jr. A concept of operations for contingency medical care on the International Space Station. *Mil Med* 2004; **169**: 631–641.
- 14 Hamilton D, Smart K, Melton S, Polk JD, Johnson-Throop K. Autonomous medical care for exploration class space missions. *J Trauma* 2008; **64**(Suppl): S354–S363.
- 15 Nicogossian AE, Pober DF, Roy SA. Evolution of telemedicine in the space program and earth applications. *Telemed J E Health* 2001; **7**: 1–15.
- 16 Davis JR. Medical issues for a mission to Mars. *Aviat Space Environ Med* 1999; **70**: 162–168.
- 17 Hargens AR, Richardson S. Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight. *Respir Physiol Neurobiol* 2009; **169**(Suppl 1): S30–S33.
- 18 Levine BD, Zuckerman JH, Pawelczyk JA. Cardiac atrophy after bed-rest deconditioning: a nonneural mechanism for orthostatic intolerance. *Circulation* 1997; **96**: 517–525.
- 19 Levine BD, Pawelczyk JA, Ertl AC, Cox JF, Zuckerman JH, Diedrich A *et al*. Human muscle sympathetic neural and haemodynamic responses to tilt following spaceflight. *J Physiol* 2002; **538**: 331–340.

- 20 Convertino VA, Doerr DF, Ludwig DA, Vernikos J. Effect of simulated microgravity on cardiopulmonary baroreflex control of forearm vascular resistance. *Am J Physiol* 1994; **266**: R1962–R1969.
- 21 Di Rienzo M, Castiglioni P, Iellamo F, Volterrani M, Pagani M, Mancina G *et al.* Dynamic adaptation of cardiac baroreflex sensitivity to prolonged exposure to microgravity: data from a 16-day spaceflight. *J Appl Physiol* (1985) 2008; **105**: 1569–1575.
- 22 Guell A. Countermeasures: extending manned spaceflight. *Acta Astronaut* 1995; **35**: 271–280.
- 23 Verheyden B, Liu J, Beckers F, Aubert AE. Adaptation of heart rate and blood pressure to short and long duration space missions. *Respir Physiol Neurobiol* 2009; **169**(Suppl 1): S13–S16.
- 24 Convertino VA, Cooke WH. Evaluation of cardiovascular risks of spaceflight does not support the NASA bioastronautics critical path roadmap. *Aviat Space Environ Med* 2005; **76**: 869–876.
- 25 Convertino VA. Status of cardiovascular issues related to space flight: implications for future research directions. *Respir Physiol Neurobiol* 2009; **169**(Suppl 1): S34–S37.
- 26 Fritsch-Yelle JM, Leuenberger UA, D'Aunno DS, Rossum AC, Brown TE, Wood ML *et al.* An episode of ventricular tachycardia during long-duration spaceflight. *Am J Cardiol* 1998; **81**: 1391–1392.
- 27 D'Aunno DS, Dougherty AH, DeBlock HF, Meck JV. Effect of short- and long-duration spaceflight on QTc intervals in healthy astronauts. *Am J Cardiol* 2003; **91**: 494–497.
- 28 Shackelford LC. Musculoskeletal response to space flight. In *Principles of Clinical Medicine for Space Flight*, Barratt MR, Pool SL (eds). Springer: New York, 2008; 293–306.
- 29 Buckley JC Jr. *Space Physiology* (1st edn). Oxford University Press: New York, 2006.
- 30 Clément G. *Fundamentals of Space Medicine* (2nd edn). Springer: New York, 2011.
- 31 García-Ruiz JM, Drenth J, Riès-Kautt M, Tardieu A. Physical sciences and applications. In *A World Without Gravity: Research in Space for Health and Industrial Processes*, Fittin B, Battrick B (eds). European Space Agency: Noordwijk, 2001; 159–171.
- 32 Gopalakrishnan R, Genc KO, Rice AJ, Lee SM, Evans HJ, Maender CC *et al.* Muscle volume, strength, endurance, and exercise loads during 6-month missions in space. *Aviat Space Environ Med* 2010; **81**: 91–104.
- 33 Lang T, LeBlanc A, Evans H, Lu Y, Genant H, Yu A. Cortical and trabecular bone mineral loss from the spine and hip in long-duration spaceflight. *J Bone Miner Res* 2004; **19**: 1006–1012.
- 34 Holick MF. Microgravity-induced bone loss – will it limit human space exploration? *Lancet* 2000; **355**: 1569–1570.
- 35 Cavanagh PR, Licata AA, Rice AJ. Exercise and pharmacological countermeasures for bone loss during long-duration space flight. *Gravitational Space Res* 2007; **18**: 39–58.
- 36 Keyak JH, Koyama AK, LeBlanc A, Lu Y, Lang TF. Reduction in proximal femoral strength due to long-duration spaceflight. *Bone* 2009; **44**: 449–453.
- 37 Sweeney JR, Gruber HE, Kirchen ME, Marshall GJ. Effects of non weight bearing on callus formation. *Physiologist* 1985; **28**(Suppl): S63–S64.
- 38 Hausman MR, Schaffler MB, Majeska RJ. Prevention of fracture healing in rats by an inhibitor of angiogenesis. *Bone* 2001; **29**: 560–564.
- 39 Pietrzyk RA, Jones JA, Sams CF, Whitson PA. Renal stone formation among astronauts. *Aviat Space Environ Med* 2007; **78**(Suppl): A9–A13.
- 40 Whitson PA, Pietrzyk RA, Sams CF. Urine volume and its effects on renal stone risk in astronauts. *Aviat Space Environ Med* 2001; **72**: 368–372.
- 41 Borchers AT, Keen CL, Gershwin ME. Microgravity and immune responsiveness: implications for space travel. *Nutrition* 2002; **18**: 889–898.
- 42 Klaus DM, Howard HN. Antibiotic efficacy and microbial virulence during space flight. *Trends Biotechnol* 2006; **24**: 131–136.
- 43 Chopra V, Fadl AA, Sha J, Chopra S, Galindo CL, Chopra AK. Alterations in the virulence potential of enteric pathogens and bacterial–host cell interactions under simulated microgravity conditions. *J Toxicol Environ Health A* 2006; **69**: 1345–1370.
- 44 Ott CM, Crabbé A, Wilson JW, Barrila J, Castro SL, Nickerson CA. Microbial stress: spaceflight-induced alterations in microbial virulence and infectious disease risks for the crew. In *Stress Challenges and Immunity in Space*, Chouker A (ed). Springer: Heidelberg, 2012; 203–225.
- 45 Cogoli A, Tschopp A. Lymphocyte reactivity during spaceflight. *Immunol Today* 1985; **6**: 1–4.
- 46 Gridley DS, Slater JM, Luo-Owen X, Rizvi A, Chapes SK, Stodieck LS *et al.* Spaceflight effects on T lymphocyte distribution, function and gene expression. *J Appl Physiol* (1985) 2009; **106**: 194–202.
- 47 Grigoriev AI, Popova IA, Ushakov AS. Metabolic and hormonal status of crewmembers in short-term spaceflights. *Aviat Space Environ Med* 1987; **58**: A121–A125.
- 48 Gorgiladze GI, Brianov II. [Space motion sickness.] *Kosm Biol Aviakosm Med* 1989; **23**: 4–14.
- 49 Homick JL. Space motion sickness. *Acta Astronaut* 1979; **6**: 1259–1272.
- 50 Lackner JR, Dizio P. Space motion sickness. *Exp Brain Res* 2006; **175**: 377–399.
- 51 Vanderploeg JM, Stewart DF, Davis JR. Space motion sickness. *ESA Proceedings of 2nd International Conference on Space Physiology*, Houston, 1986. <https://ntrs.nasa.gov/search.jsp?R=19870001260> [accessed 25 May 2018].
- 52 Jennings RT. Managing space motion sickness. *J Vestib Res* 1998; **8**: 67–70.
- 53 Ross HE. Motor skills under varied gravitoinertial force in parabolic flight. *Acta Astronaut* 1991; **23**: 85–95.
- 54 Rafiq A, Hummel R, Lavrentyev V, Derry W, Williams D, Merrell RC. Microgravity effects on fine motor skills: tying

- surgical knots during parabolic flight. *Aviat Space Environ Med* 2006; **77**: 852–856.
- 55 Billica RD, Pool SL, Nicogossian AE. Crew health care programs. In *Space Physiology and Medicine: From Evidence to Practice*, Nicogossian AE, Williams RS, Huntoon CL, Doarn CR, Polk JD, Schneider VS (eds). Springer: New York, 1994; 402–423.
- 56 DiMaggio C, Ayoung-Chee P, Shinseki M, Wilson C, Marshall G, Lee DC *et al.* Traumatic injury in the United States: in-patient epidemiology 2000–2011. *Injury* 2016; **47**: 1393–1403.
- 57 DiMaggio CJ, Avraham JB, Lee DC, Frangos SG, Wall SP. The epidemiology of emergency department trauma discharges in the United States. *Acad Emerg Med* 2017; **24**: 1244–1256.
- 58 Kirkpatrick AW, Campbell MR, Novinkov OL, Goncharov IB, Kovachevich IV. Blunt trauma and operative care in microgravity: a review of microgravity physiology and surgical investigations with implications for critical care and operative treatment in space. *J Am Coll Surg* 1997; **184**: 441–453.
- 59 Roth EM. *Rapid (Explosive) Decompression Emergencies in Pressure-suited Subjects*. National Aeronautics and Space Agency: Washington, 1968. <https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/19690004637.pdf> [accessed 25 May 2018].
- 60 McCuaig KE, Houtchens BA. Management of trauma and emergency surgery in space. *J Trauma* 1992; **33**: 610–625.
- 61 Pressley W, Thangavelu M. Addressing the space-based medical facility capability gap with Project SOLACE: Space Orbiting Lifeboat And medical Care during Evacuation. *AIAA SPACE and Astronautics Forum and Exposition*, Orlando, 2017. <https://arc.aiaa.org/doi/10.2514/6.2017-5207> [accessed 25 May 2018].
- 62 Buckius MT, McGrath B, Monk J, Grim R, Bell T, Ahuja V. Changing epidemiology of acute appendicitis in the United States: study period 1993–2008. *J Surg Res* 2012; **175**: 185–190.
- 63 Kimura Y, Takada T, Strasberg SM, Pitt HA, Gouma DJ, Garden OJ *et al.* TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci* 2013; **20**: 8–23.
- 64 Campbell MR, Johnston SL III, Marshburn T, Kane J, Lugg D. Nonoperative treatment of suspected appendicitis in remote medical care environments: implications for future spaceflight medical care. *J Am Coll Surg* 2004; **198**: 822–830.
- 65 Ball CG, Kirkpatrick AW, Williams DR, Jones JA, Polk JD, Vanderploeg JM *et al.* Prophylactic surgery prior to extended-duration space flight: is the benefit worth the risk? *Can J Surg* 2012; **55**: 125–131.
- 66 Hoshide R, Jandial R. Gravity of intracranial pressure shifts in outer space. *World Neurosurg* 2017; **102**: 659–660.
- 67 Taylor CR, Hanna M, Behnke BJ, Stabley JN, McCullough DJ, Davis RT III *et al.* Spaceflight-induced alterations in cerebral artery vasoconstrictor, mechanical, and structural properties: implications for elevated cerebral perfusion and intracranial pressure. *FASEB J* 2013; **27**: 2282–2292.
- 68 Campbell MR, Williams DR, Buckley JC Jr, Kirkpatrick AW. Animal surgery during spaceflight on the Neurolab Shuttle mission. *Aviat Space Environ Med* 2005; **76**: 589–593.
- 69 Billica RD, Doarn CR. A health maintenance facility for space station freedom. *Cutis* 1991; **48**: 315–318.
- 70 Cucinotta FA, To K, Cacao E. Predictions of space radiation fatality risk for exploration missions. *Life Sci Space Res (Amst)* 2017; **13**: 1–11.
- 71 Cucinotta FA. Review of NASA approach to space radiation risk assessments for Mars exploration. *Health Phys* 2015; **108**: 131–142.
- 72 Cucinotta FA. Space radiation risks for astronauts on multiple International Space Station missions. *PLoS One* 2014; **9**: e96099.
- 73 Mermel LA. Infection prevention and control during prolonged human space travel. *Clin Infect Dis* 2013; **56**: 123–130.
- 74 Sonnenfeld G, Butel JS, Shearer WT. Effects of the space flight environment on the immune system. *Rev Environ Health* 2003; **18**: 1–18.
- 75 Chiao L, Sharipov S, Sargsyan AE, Melton S, Hamilton DR, McFarlin K *et al.* Ocular examination for trauma; clinical ultrasound aboard the International Space Station. *J Trauma* 2005; **58**: 885–889.
- 76 Fincke EM, Padalka G, Lee D, van Holsbeeck M, Sargsyan AE, Hamilton DR *et al.* Evaluation of shoulder integrity in space: first report of musculoskeletal US on the International Space Station. *Radiology* 2005; **234**: 319–322.
- 77 Dulchavsky SA, Schwarz KL, Kirkpatrick AW, Billica RD, Williams DR, Diebel LN *et al.* Prospective evaluation of thoracic ultrasound in the detection of pneumothorax. *J Trauma* 2001; **50**: 201–205.
- 78 Marshburn TH, Hadfield CA, Sargsyan AE, Garcia K, Ebert D, Dulchavsky SA. New heights in ultrasound: first report of spinal ultrasound from the International Space Station. *J Emerg Med* 2014; **46**: 61–70.
- 79 Sargsyan AE, Hamilton DR, Jones JA, Melton S, Whitson PA, Kirkpatrick AW *et al.* FAST at MACH 20: clinical ultrasound aboard the International Space Station. *J Trauma* 2005; **58**: 35–39.
- 80 Kwon D, Bouffard JA, van Holsbeeck M, Sargsyan AE, Hamilton DR, Melton SL *et al.* Battling fire and ice: remote guidance ultrasound to diagnose injury on the International Space Station and the ice rink. *Am J Surg* 2007; **193**: 417–420.
- 81 Scalea TM, Rodriguez A, Chiu WC, Brennehan FD, Fallon WF Jr, Kato K *et al.* Focused assessment with sonography for trauma (FAST): results from an international consensus conference. *J Trauma* 1999; **46**: 466–472.
- 82 Dente CJ, Ustin J, Feliciano DV, Rozycki GS, Wyrzykowski AD, Nicholas JM *et al.* The accuracy of thoracic ultrasound

- for detection of pneumothorax is not sustained over time: a preliminary study. *J Trauma* 2007; **62**: 1384–1389.
- 83 Rippey JC, Royse AG. Ultrasound in trauma. *Best Pract Res Clin Anaesthesiol* 2009; **23**: 343–362.
 - 84 Kirkpatrick AW, Campbell MR, Jones JA, Broderick TJ, Ball CG, McBeth PB *et al.* Extraterrestrial hemorrhage control: terrestrial developments in technique, technology, and philosophy with applicability to traumatic hemorrhage control in long-duration spaceflight. *J Am Coll Surg* 2005; **200**: 64–76.
 - 85 Komorowski M, Fleming S. Intubation after rapid sequence induction performed by non-medical personnel during space exploration missions: a simulation pilot study in a Mars analogue environment. *Extrem Physiol Med* 2015; **4**: 19.
 - 86 Komorowski M, Fleming S, Kirkpatrick AW. Fundamentals of anesthesiology for spaceflight. *J Cardiothorac Vasc Anesth* 2016; **30**: 781–790.
 - 87 Committee on National Association of Emergency Medical Technicians (US) P-HTLS. Trauma of the American College of Surgeons. *PHTLS: Basic and Advanced Prehospital Trauma Life Support*. Mosby: Maryland Heights, 2004.
 - 88 Gordy SD, Rhee P, Schreiber MA. Military applications of novel hemostatic devices. *Expert Rev Med Devices* 2011; **8**: 41–47.
 - 89 Biffi WL, Moore EE. Management guidelines for penetrating abdominal trauma. *Curr Opin Crit Care* 2010; **16**: 609–617.
 - 90 Como JJ, Bokhari F, Chiu WC, Duane TM, Holevar MR, Tandoh MA *et al.* Practice management guidelines for selective nonoperative management of penetrating abdominal trauma. *J Trauma* 2010; **68**: 721–733.
 - 91 Petrowsky H, Raeder S, Zuercher L, Platz A, Simmen HP, Puhon MA *et al.* A quarter century experience in liver trauma: a plea for early computed tomography and conservative management for all hemodynamically stable patients. *World J Surg* 2012; **36**: 247–254.
 - 92 Alexander DJ. Trauma and surgical capabilities for space exploration. In *Trauma Team Dynamics*. Springer: Cham, 2016; 253–266.
 - 93 Kirkpatrick AW, Tien H, LaPorta AT, Lavell K, Keillor J, Wright Beatty HE *et al.* The marriage of surgical simulation and telementoring for damage-control surgical training of operational first responders: a pilot study. *J Trauma Acute Care Surg* 2015; **79**: 741–747.
 - 94 Kirkpatrick AW, McKee JL, Tien H, LaPorta AJ, Lavell K, Leslie T *et al.* Damage control surgery in weightlessness: a comparative study of simulated torso hemorrhage control comparing terrestrial and weightless conditions. *J Trauma Acute Care Surg* 2017; **82**: 392–399.
 - 95 Haidegger T, Sándor J, Benyó Z. Surgery in space: the future of robotic telesurgery. *Surg Endosc* 2011; **25**: 681–690.
 - 96 Campbell MR, Billica RD. Surgical capabilities. In *Principles of Clinical Medicine for Space Flight*, Barratt MR, Pool SL (eds). Springer: New York, 2008; 123–137.
 - 97 Campbell MR, Billica RD, Johnston SL III. Animal surgery in microgravity. *Aviat Space Environ Med* 1993; **64**: 58–62.
 - 98 Friedman DC, Doshier J, Kowalewski T, Rosen J, Hannaford B. Automated tool handling for the trauma pod surgical robot. *2007 IEEE International Conference on Robotics and Automation*, Rome, 2007; 1936–1941.
 - 99 Garcia P, Rosen J, Kapoor C, Noakes M, Elbert G, Treat M *et al.* Trauma Pod: a semi-automated telerobotic surgical system. *Int J Med Robot* 2009; **5**: 136–146.
 - 100 Tesar D, Kapoor C, Pholsiri C, Jung E, Giem G, Knoll J. *Trauma Pod/Operating Room of the Future*. Texas University at Austin: Austin, 2006.
 - 101 McBeth PB, Keaney M, Ball CG, Saary J, Broderick TJ, Kock MV *et al.* Aeromobile modular critical care, resuscitation, and surgical suites for operational medicine. *J Trauma* 2011; **71**(Suppl 1): S494–S500.
 - 102 Markham SM, Rock JA. Microgravity testing a surgical isolation containment system for space station use. *Aviat Space Environ Med* 1991; **62**: 691–693.
 - 103 Hayden JA, Pantalos GM, Burgess JE, Antaki JF. A hermetically sealed, fluid-filled surgical enclosure for microgravity. *Aviat Space Environ Med* 2013; **84**: 1298–1303.
 - 104 Mutke HG. Equipment for surgical interventions and childbirth in weightlessness. *Acta Astronaut* 1981; **8**: 399–403.
 - 105 Tekkis PP, Senagore AJ, Delaney CP, Fazio VW. Evaluation of the learning curve in laparoscopic colorectal surgery: comparison of right-sided and left-sided resections. *Ann Surg* 2005; **242**: 83–91.
 - 106 Vickers AJ, Savage CJ, Hruza M, Tuerk I, Koenig P, Martínez-Piñeiro L *et al.* The surgical learning curve for laparoscopic radical prostatectomy: a retrospective cohort study. *Lancet Oncol* 2009; **10**: 475–480.
 - 107 Panait L, Broderick T, Rafiq A, Speich J, Doarn CR, Merrell RC. Measurement of laparoscopic skills in microgravity anticipates the space surgeon. *Am J Surg* 2004; **188**: 549–552.
 - 108 Campbell MR, Kirkpatrick AW, Billica RD, Johnston SL, Jennings R, Short D *et al.* Endoscopic surgery in weightlessness: the investigation of basic principles for surgery in space. *Surg Endosc* 2001; **15**: 1413–1418.
 - 109 Marohn MR, Hanly EJ. Twenty-first century surgery using twenty-first century technology: surgical robotics. *Curr Surg* 2004; **61**: 466–473.
 - 110 Doarn CR, Anvari M, Low T, Broderick TJ. Evaluation of teleoperated surgical robots in an enclosed undersea environment. *Telemed J E Health* 2009; **15**: 325–335.
 - 111 Moorthy K, Munz Y, Dosis A, Hernandez J, Martin S, Bello F *et al.* Dexterity enhancement with robotic surgery. *Surg Endosc* 2004; **18**: 790–795.

- 112 Berguer R, Smith W. An ergonomic comparison of robotic and laparoscopic technique: the influence of surgeon experience and task complexity. *J Surg Res* 2006; **134**: 87–92.
- 113 Herron DM, Marohn M; SAGES-MIRA Robotic Surgery Consensus Group. A consensus document on robotic surgery. *Surg Endosc* 2008; **22**: 313–325.
- 114 Marescaux J, Leroy J, Gagner M, Rubino F, Mutter D, Vix M *et al.* Transatlantic robot-assisted telesurgery. *Nature* 2001; **413**: 379–380.
- 115 Eadie LH, Seifalian AM, Davidson BR. Telemedicine in surgery. *Br J Surg* 2003; **90**: 647–658.
- 116 Merrell RC. Telemedicine in surgery. *Eur Surg* 2005; **37**: 270–273.
- 117 Rentschler ME, Dumpert J, Lehman A, Berg K, Platt SR, Oleynikov D *et al.* *In vivo* robots for tele-surgery during long-term space flight. *Space 2006 Conference*, San Jose, 2006.
- 118 Moustiris GP, Hiridis SC, Deliparaschos KM, Konstantinidis KM. Evolution of autonomous and semi-autonomous robotic surgical systems: a review of the literature. *Int J Med Robot* 2011; **7**: 375–392.
- 119 Evans CH, Palmer GD, Pascher A, Porter R, Kwong FN, Gouze E *et al.* Facilitated endogenous repair: making tissue engineering simple, practical, and economical. *Tissue Eng* 2007; **13**: 1987–1993.
- 120 Grattoni A, Tasciotti E, Fine D, Fernandez-Moure JS, Sakamoto J, Hu Y *et al.* Nanotechnologies and regenerative medical approaches for space and terrestrial medicine. *Aviat Space Environ Med* 2012; **83**: 1025–1036.
- 121 Leach N. 3D printing in space. *Architect Des* 2014; **84**: 108–113.
- 122 Rankin TM, Giovinco NA, Cucher DJ, Watts G, Hurwitz B, Armstrong DG. Three-dimensional printing surgical instruments: are we there yet? *J Surg Res* 2014; **189**: 193–197.
- 123 Wong JY, Pfahnl AC. 3D printing of surgical instruments for long-duration space missions. *Aviat Space Environ Med* 2014; **85**: 758–763.
- 124 Murphy SV, Skardal A, Atala A. Evaluation of hydrogels for bio-printing applications. *J Biomed Mater Res A* 2013; **101**: 272–284.
- 125 Chae MP, Rozen WM, McMenamin PG, Findlay MW, Spychal RT, Hunter-Smith DJ. Emerging applications of bedside 3D printing in plastic surgery. *Front Surg* 2015; **2**: 25.
- 126 Ventola CL. Medical applications for 3D printing: current and projected uses. *P T* 2014; **39**: 704–711.
- 127 Ursan ID, Chiu L, Pierce A. Three-dimensional drug printing: a structured review. *J Am Pharm Assoc (2003)* 2013; **53**: 136–144.



Have your say...

If you wish to comment on this, or any other article published in the *BJS*, you can:



Comment on the website www.bjs.co.uk



Follow & Tweet on Twitter @BJSurgery