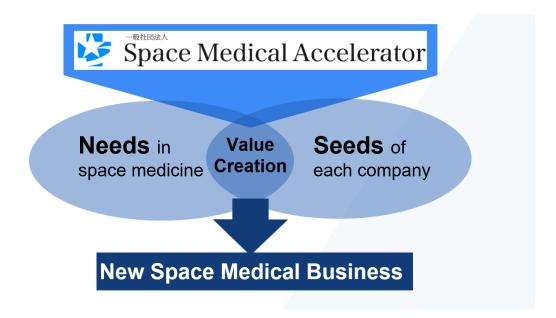
Medical Care in Space - The Challenge of the Space Medical Accelerator

Masayuki Goto, Hiroki Fukushima, Hiroyuki Konno, Shungo Kuromatsu, Satoshi T Ito, Hitoshi Tange

I. Introduction.

The importance of health care in space is increasing with the acceleration of human spaceflight, including civilian spaceflight. The Space Medical Accelerator is a general incorporated association established in 2022 with the aim of creating new technologies and services related to medicine, which will be indispensable for the advancement of many people into space in the near future. Its members include the founder, Dr Goto, a surgeon and space medicine researcher, as well as doctors, researchers and engineers with expertise in space medicine. The team analyses research papers and business news in this field on a daily basis and provides customers, such as companies aiming for new space projects in the medical and life science fields, with the knowledge of a specialist team, including on-site needs, future issues and medical evidence (Figure 1). Medical treatment in space is often considered to be a special kind of medical treatment far removed from that on the ground, but it faces issues similar to those in the current medical field on the ground, such as limited medical resources and telemedicine, including medical treatment in remote areas and online medical treatment. In addition, many scientific results have been produced in space experiments utilizing the microgravity environment of the ISS, such as drug discovery research using protein crystal formation, and in fields such as ageing medicine and regenerative medicine, which will bring a quantum leap to medical care on Earth. The Space Medical Accelerator has the vision of 'New medicine from space for all', and is working to create a new fusion between industry, government and academia in this field, and to develop medical care in space. The Space Medical Accelerator has a vision of 'new medicine from space, for all' and aims to create a new fusion between industry, government and academia in this field and to develop the medical industry in space. The current position and future challenges in space medicine will be introduced based on the expertise of each member of the company.

Figure 1 SMA provides customers such as companies aiming for new space projects in the medical and life science fields with the medical knowledge to create new space business



II. Specific issues related to medical care in space

1. Study of the application of production strategies to on-orbit platforms

The International Space Station (ISS) currently plays a major role as an experimental facility, but in the near future, during the phase of expanded use of the Earth orbiting platform by the private sector, it is expected that the 'factory' aspect of the ISS will increase, where medical and bio-themed services will be continuously performed. In the

near future, the 'factory' aspect is expected to grow in the phase of expanded use of Earth orbital platforms by private companies, where medical and bio-themed services will be continuously performed. The scale of the market for space manufacturing is already being studied, particularly in the USA ^{1), 2)}, and Redwire has begun selling engineering crystals manufactured in space ³⁾. This chapter examines the logic ^{4), 5), 6)} and of a 'production strategy' to increase the competitiveness of a factory by applying it to the services of a future on-orbit platform, and examines what an on-orbit 'factory' might look like. Although production strategies usually take into account a composite of diverse factors, in this case the focus is on two aspects: profit and invested capital (Table 1).

[Profit growth]

- One direction for increasing profits is to maximise the factory's capacity to perform as much work as possible.

- Factory capacity corresponds to the capacity of the rate-limiting process in the production process. The identification of the rate-limiting process in orbital services requires a detailed study, but qualitatively speaking, 'rocket launches' are a good

candidate.

- The aim is to constantly fill the capacity allocated for on-orbit services at each launch, i.e. the payload, and to have the other processes be able to handle this capacity on a regular basis.

[Compression of invested capital]

- In the direction of minimizing invested capital, time is a major factor in orbital services.

- One approach is to minimize crew time, i.e. the time spent occupying astronauts, whose hourly rate is extremely high. The main approach is automation, which includes not only the production work itself but also simulation technology that eliminates the time required for preparation and confirmation meetings.

- Another is the minimization of the time spent occupying the on-orbit platform, i.e. lead time. In order to continue production in a very limited space on orbit, it is necessary to thoroughly implement the 'one-piece flow' concept, whereby production lots are kept small and intermediate inventories are reduced.

	Profit growth
Direction	Maximise the capacity of the factory to do more work than it possesses
Rate controlling process	Plant capacity corresponds to the capacity of the rate-limiting process in the production process Rate-limiting processes in on-orbit services need to be identified
Sufficiency	Satisfy the allocated payload for each launch Other processes aim to have the capacity to handle it routinely

 Table 1
 Profit growth and compression of invested capital on orbital platforms

	Compression of invested capital
Direction	Minimising time (crew time and lead time)
Crew time	Minimising astronaut-dependent time
	Use of automation and simulation technology

	Minimising platform occupation time
Lead time	
	Implementing a one-piece sink strategy

In view of these factors, 'just-in-time production that handles the maximum launch payload with the minimum crew time and lead time' can be considered as a production mode to be aimed for in on-orbit services. On the other hand, there are several issues to be addressed in realizing such production, including upstream business processes, such as responding to various customer needs with a combination of standard and optional menus (so-called modular design), rather than a one-size-fits-all response to customer needs. We will continue to consider what form the 'factory-isation' of on-orbit platforms should take in the future.

2. Mental health in the age of space travel

The time is approaching when space travel will be available to everyone: according to an article in Forbes on 26 September 2023, the number of space travelers will already reach 68 in the 18 months from 2021, and there is already a waiting list of 800 people for a \$66.6m space tour offered by Virgin Galactic ⁷. Currently, space travel is generally a short tour that takes you on a ballistic flight into space and lets you experience a few

minutes of weightlessness. In the future, however, long-duration tours, such as the one by private citizen Yusaku Maezawa to the International Space Station in 2021, will become a reality. Many people may have an elegant image of a 'stay in space', but the reality is that space is an extreme environment where death is the only possibility. When one calmly considers that there is no physical escape, it is natural to feel fear in space due to a psychological sense of entrapment and pressure. In addition, space rockets and space stations are completely artificial environments and are not places where one can relax as in nature. A variety of stimuli such as noise, vibration, light, smells, toxins, radiation and communication with other people from different cultures can cause stress, and the mental effects of these factors should be taken into account. Even astronauts who have undergone rigorous selection and training receive a variety of mental care during their stay in space⁸⁾. Solutions to mental health problems in space could be widely applied to modern society, where people are exposed to both tangible and intangible stresses. Enabling the general public to spend time in space without mental illness is a major challenge in the future era of space travel, and requires approaches from a variety of fields.

3. The rise of space medicine in academia and challenges for the next generation

Most research in space medicine has been published mainly by the Japanese Society of Aerospace and Environmental Medicine. In 2022, at the 122nd Annual Scientific Meeting of the Japanese Surgical Society, a symposium entitled 'Moonshots for Medicine in 2050' will be held, with the theme of 'Space Medicine in the Space Century'. In 2023, 'Space Medicine x Cardiology' was held at the 87th Annual Meeting of the Japanese Society of Cardiology as a symposium organized by the President. In this context, young people are also making their presence felt in the field of space medicine, and many students, mainly from the Space Medicine Japan Youth Community (SMJYC), a student community interested in space medicine, and the International University of Health and Welfare's Space Medicine Research Society, participated in the 69th Congress of the Japanese Society of Aerospace and Environmental Medicine in 2023. The students participated in the 69th Congress of the Japanese Society of Aerospace and Environmental Medicine in 2023. In fact, 11 student abstracts were presented and a separate student session was organized. For a long time, basic research has been the mainstream in the field of space medicine in Japan, but the clinical aspect of space medicine has been attracting increasing attention among students, and a 'Society for Clinical Medicine in Space' is being organized by volunteers at SMJYC. However, there are few experts in the clinical field of space medicine in Japan, and it is

not easy to tackle the clinical field of space medicine in Japan. However, we believe that it is essential for the sustainable development of space medicine in Japan to support the participation of more people and companies in space medicine, rather than monopolizing the knowledge of the current experts. We would like to play a part in this and actively contribute to the progress of space medicine.

4. Space mouse experiments and the future of ageing research

Ageing is a risk factor for diseases such as cancer and diabetes, and it is known that when DNA damage occurs, DNA modification changes and signaling occur during the repair process, leading to cellular senescence, a state in which cells irreversibly fail to divide ⁹⁾. It has been suggested that the accumulation of cellular senescent cells in an individual leads to individual ageing, such as organ dysfunction and reduced immunity ¹⁰⁾. The ageing mechanism is being elucidated through experiments using genetically modified mice conducted on Earth. The unique environment of outer space is attracting attention for elucidating the ageing mechanism¹¹⁾. In the 1970s, astronauts who had flown in space for long periods of time reported symptoms observed in the elderly, such as reduced bone density, muscle atrophy, blood changes and metabolic abnormalities¹²⁾. On the ISS, research on mammalian ageing has been conducted using mice as model organisms. In 2018, it was found that Nrf2, a gene related to oxidative stress, is activated in space ¹³⁾. This gene is highly expressed in old mice, providing experimental evidence of accelerated ageing. In addition, an experiment conducted in 2020 showed that the expression of p21 (Cdkn1a), one of the marker genes for cellular senescence, increased in mouse bone marrow stem cells under microgravity conditions¹⁴. Furthermore, as of February 2024, an experiment on metabolic abnormalities in the liver under microgravity conditions is underway on the mission with the participation of astronaut Satoshi Furukawa¹⁵⁾. In the future, lunar exploration by the Artemis mission is planned, and mouse experiments in deep space are also expected. Insights gained from space mouse experiments provide knowledge and technology essential for human survival and health for future exploration and migration to the Moon and Mars. In addition, it will pave the way for humans to live healthier and longer lives on Earth.

5. Muscle and bone atrophy in microgravity

In a microgravity environment, the loss of the load on muscles and bones due to gravity causes muscle and bone atrophy, similar to disuse. Muscle and bone atrophy can lead to

problems such as increased risk of fractures and reduced mobility after return to Earth. It takes about six weeks for the muscles to return to their original volume and several years for the bones¹⁶⁾, so this is an important issue for astronauts to maintain their health during their stay in space and after their return. The current solution to this problem is two hours of daily exercise. On the ISS, astronauts exercise for a total of two hours daily, one hour for strength training and one hour for aerobic exercise, to prevent muscle and bone atrophy. Muscle mass is reduced by 10-20% during long stays in space, but the current exercise programme has reduced this to around 5%¹⁷⁾. However, the time commitment is high, requiring up to two hours of exercise per day to maintain muscle and bone mass. At present, there is potential for pharmaceutical measures to combat bone atrophy. It has been reported that bisphosphonates, which are used to treat osteoporosis, are effective in preventing bone atrophy in space ¹⁸⁾. On the other hand, drugs to reduce muscle atrophy are still in the research phase. Research on genes involved in the regulation of muscle synthesis and degradation, and proteins such as Cbl-b¹⁹ involved in their expression pathways is ongoing, and the development of drugs that enable the maintenance of muscle mass without exercise is expected. The development of such drugs to prevent muscle atrophy is desirable not only for long-term space stays but also for maintaining the health of the elderly. There are currently no

reports of fractures in space due to bone loss, but the risk of fractures in space will increase with the exploration of planets such as the Moon and Mars. The Moon has onesixth the Earth's gravity and Mars one-third the Earth's gravity, but in cases such as Mars, where it takes longer to arrive and muscle atrophy is expected upon landing, a rehabilitation plan for readaptation to the local gravity environment should be considered. Furthermore, if space travelers are able to stay in space for longer periods of time in the future, muscle and bone atrophy will be a challenge to their health. The current solution of two hours of exercise per day is a considerable burden for nonastronaut travelers. Easy and time-saving ways to maintain bone and muscle mass are in great demand both in space and on the ground.

III. Conclusion

The above is an overview of some of the trends in space medicine based on the knowledge held by our Space Medical Accelerator. Although the medical field in space is still in its infancy as an industry, it is estimated that by 2035 the market size of 'on-orbit manufacturing and R&D', including life science fields such as regenerative medicine and bio-manufacturing, will be worth USD 2.5 billion, and that of space travel USD 3.3 billion20), and thus has great potential²⁰⁾. We will continue to raise public understanding and momentum in this field through educational activities such as symposium events, corporate lectures and seminars, while working daily to accumulate research trends and build a network with the aim of deploying many Japanese medical technologies in space in the coming manned space age.

Reference

- Nanoracks. (2019, January 14). Outpost: An In-Orbit Commercial Space Station Habitat Development Enabling Cost-Effective and Sustainable U.S. Presence in Low-Earth Orbit. <u>https://nanoracks.com/wp-content/uploads/NanoRacks-</u> LEOCOM-Study-RELEASE.pdf
- Kulu, E. (2023, October). In-Space Economy in 2023-Statistical Overview and Trends. In 74th International Astronautical Congress (IAC 2023).
- Redwire. (2022, June 23) Redwire Opens New Commercial Market for In Space Production with First Sale of Space-Manufactured Optical Crystal. https://redwirespace.com/newsroom/redwire-opens-new-commercial-market-forin-spaceproduction-with-first-sale-of-space-manufactured-optical-crystal/

4. エリヤフ・ゴールドラット. (2001). ザ・ゴール. ダイヤモンド社.

5. 大野耐一. (1978). トヨタ生産方式. ダイヤモンド社.

 6. 田中正知. (2004). 時間軸を入れた収益性評価法の一考察--J コスト論. IE レビュー:
 Official publication of the Japan Institute of Industrial Engineering/日本インダストリア ル・エンジニア リング協会 [編], 45(1), 85-92.

7. 鈴木喜生. (2023, September 26). 増え続ける宇宙旅行者、6660 万円のツアーに
 800 人待ち. Forbes Japan. https://forbesjapan.com/articles/detail/66215

8. JAXA 宇宙航空研究開発機構. (2016, June 15). 精神心理支援. https://iss.jaxa.jp/med/research/mental/

Rodier, F., Coppé, J. P., Patil, C. K., Hoeijmakers, W. A., Muñoz, D. P., Raza, S. R., ...
 & Campisi, J. (2009). Persistent DNA damage signalling triggers senescence-associated inflammatory cytokine secretion. Nature cell biology, 11(8), 973-979.

10. Baker, D. J., Childs, B. G., Durik, M., Wijers, M. E., Sieben, C. J., Zhong, J., ... & Van Deursen, J. M. (2016). Naturally occurring p16Ink4a-positive cells shorten healthy lifespan. Nature, 530(7589), 184-189.

11. Demontis, G. C., Germani, M. M., Caiani, E. G., Barravecchia, I., Passino, C., &

Angeloni, D. (2017). Human pathophysiological adaptations to the space environment. Frontiers in physiology, 8, 197834.

12. Dietlein, L. F. (1977). Skylab: a beginning. Biomedical results from Skylab, 377, 408.

13. Uruno, A., Saigusa, D., Suzuki, T., Yumoto, A., Nakamura, T., Matsukawa, N., ... & Yamamoto, M. (2021). Nrf2 plays a critical role in the metabolic response during and after spaceflight. Communications biology, 4(1), 1381.

14. Juran, C. M., Zvirblyte, J., Cheng-Campbell, M., Blaber, E. A., & Almeida, E. A.
(2021). Cdkn1a deletion or suppression by cyclic stretch enhance the osteogenic
potential of bone marrow mesenchymal stem cell-derived cultures. Stem cell research,
56, 102513.

15. Dominic Hart. (2023)., 'Space-Age' Research Looks to Provide New Human Health Insights. NASA. https://www.nasa.gov/ames/space-biosciences/space-age-researchlooks-to-provide-new-humanhealth-insights/

16. 藤田真敬(2019). 宇宙航空医学入門 再版. 鳳文書林出版販売.

17. Davis, J., Stepanak, J., Fogarty, J., & Blue, R. (2021). Fundamentals of Aerospace Medicine. Lippincott Williams & Wilkins. 18. Sibonga, J., Matsumoto, T., Jones, J., Shapiro, J., Lang, T., Shackelford, L., ... & LeBlanc, A. (2019). Resistive exercise in astronauts on prolonged spaceflights provides partial protection against spaceflight-induced bone loss. Bone, 128, 112037.

19. Ikeda, C., Abe, T., Sakai, A., Hirasaka, K., & Nikawa, T. (2012). Space flight/bedrest immobilization and bone. Space flight and bed rest-mediated muscle atrophy. Clinical Calcium, 22(12), 1813-1820.

20. Deloitte. (2022). The Commercialization of Low Earth Orbit.
https://www2.deloitte.com/content/dam/Deloitte/us/Documents/public-sector/usgps-thecommercialization-of-leo-vol-2-an-orbit-for-everyone.pd