Update on Bioprinting and Biofabrication in Support of Aerospace Missions and the Human Condition

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This column is coordinated and edited by Valerie E. Martindale, Ph.D. These articles are not peer-reviewed. The AsMA Science and Technology Committee provides the Watch as a forum to introduce and discuss a variety of topics involving all aspects of civil and military aerospace medicine. Please send your submissions and comments via email to: vemartindale@hotmail.com. Watch columns are available at www.asma.org through the "Read the Journal" link.

Extended duration missions in space are a reality. We are in a crucial preparatory phase in aerospace medicine and human performance as we prepare for human missions to Mars, intermediate duration missions, and a return to the Earth's Moon projected for 2024.[1,4] Artemis, achieving lunar landing on the South Pole by 2024, will use complementary government and commercial equipment to achieve a sustainable architecture and crew delivery. However, enhanced knowledge of physiology, psychology, human factors, and adaptive processes, and specific tools are required to allow full crew functionality in space. Systems engineering is an essential element of space design, involving considerations of restrictions on mass, volume, and power consumption.

What may be an essential element of the human-enabling toolkit in space is 3-D printing, also known as additive manufacturing, which has been evolving since the 1980s. Known for its product adaptability and multiuse capabilities, this technique may be modified for medical technology and other crew support applications.[2,5]

Magnetic bioprinters are evolving in parallel with the advancement of additive manufacturing and nanotechnology. Magnetic bioprinting goes beyond the management of living cells, tissue spheroids, and synthetic microscaffolds by using magnetic fields in microgravity.

When developing 3-D printed prototypes, imagery of all types, most commonly X-ray, CT, MRI, and ultrasound, may be expeditiously transformed from digital information to n-dimensional physical models. These models are scalable, from nanoscale to full scale replicas of hardware or liveware (i.e., a bioprinted or n-dimensional model using living tissue or organs). Economic forecasts predict the field of medical 3D printing will grow to approximately $3.5 billion USD by 2025, an estimated compound annual growth of 17.7% since 2017.[2,3]

Limitations to traditional 3-D printing in microgravity environments have necessitated the transition to magnetic 3-D bioprinting. The development of this technique has enabled biofabrication in space and has enabled the next phase of transformative technology to programmable self-assembly of tissue and organ spheroids, independent of gravitational orientation and synthetic solid micro- and nano-scaffolding. Complementary bioprinting technologies such as acoustic or magnetic methodologies employing 'raster-scannable' patterned physical (versus 'virtual' computer) fields are evolving to enable printing of more complex and adaptive geometrics.

We know that aging and disease processes are accelerated in space [Campbell M., International Space Medicine Summit, Houston, October 2019; personal communication].[1] If we consider the living laboratory of the International Space Station, we may further our knowledge and understanding of these conditions and subsequent countermeasure development.

'In-situ' space health care has evolved rapidly to take advantage of rapidly advancing technologies such as bioprinting and biofabrication to address challenging space medicine problems, such as ensuring effective microbial therapeutics in space to accommodate immunologic dysfunction and treatment of musculoskeletal injuries. Specifically, biofabrication of new drug delivery techniques[5] is under development to enable gravity-independent therapeutics. Biofabrication of musculoskeletal adjunctive therapies for acute rehabilitation and injury recovery are now also possible.

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NASA has funded a number of biofabrication initiatives in space according to Liz Warren, Associate Program Scientist for CASIS (Center for the Advancement of Science in Space). Microgravity may even be used as a cofactor of bioprinting technology. In contrast to traditional bioprinting, this approach employs a scaffold-free, nozzle-free, and label-free (i.e., without using magnetic nanoparticles) approach called formative biofabrication. This approach is superior to traditional biofabrication and may be used for space radiation studies to provide support for long-term crewed spaceflights, including the Moon and Mars programs.

3D Bioprinting Solutions® developed a novel space 3-D bioprinter which will enable rapid, label-free 3-D biofabrication of 3-D tissue and organ constructs in microgravity by using magnetic fields on the International Space Station. Evolution of this shared international infrastructure is essential for cooperative engagement and mission success. Subsequently, bioprinted constructs may be transported back to Earth employing a holistic cuvette system designed to hold multiple samples and enable subsequent shared data analysis and results.

Exemplary models of applied biofabrication include bioprinted intestinal chips for testing and evaluating astronaut response to menu options and personalized nutrition for extended duration missions. Tissue spheroids are being rapidly constructed to model thyroid and cartilage function (i.e., thyrospheres and chondrospheres) in microgravity conditions and histology is then performed on Earth to determine internal structure and architecture. Blood-brain barrier and kidney biofabrication are also underway. Kidney tissue fabrication, including organoids, may lead to further understanding of preventive measures for kidney stones. Calcium oxalate stones have long been recognized as more prevalent in microgravity conditions, with contributing factors of stasis, dehydration, and bone demineralization. In addition, current therapies for neuro-ocular syndrome may be contributory.[5,6]

In addition to the advanced knowledge and understanding of structural and functional remodeling and adaptation in space, an understanding of pharmacokinetics in space may accelerate our understanding of drug function and untoward side-effects on Earth. Our understanding of human aging and brain function and structure may also be advanced through work in microgravity, given the known acceleration of these human conditions in space [Campbell M., International Space Medicine Summit, Houston, October 2019; personal communication].[1]

Biofabrication is not intended to be a stand-alone technology. For example, co-development of artificial intelligence, nanotechnologies, robotics, and material science are enabling technologies for space missions. Training and mission rehearsal platforms currently employ all these technological areas, thus further integrating medical missions into a holistic space mission.

In consideration of the challenge of space health maintenance, the application of biofabrication and enabling technologies is realistic and likely to rapidly advance the field and effective therapeutic interventions. Surgical experts support these synergistic uses of technology [Campbell M., International Space Medicine Summit, Houston, October 2019; personal communication].[6]

As increasingly sophisticated space missions are planned and deployed, mission success requires technology to evolve with the spacecraft and crew, and as a component of its architecture. Human sustainability in space requires a systems engineering approach; ideally one that considers the human-in-the-loop as an essential component of the machine and vice versa. This is not to imply that either human or machine are independent or superior, but rather, an integrated system under co-development and adaptation. Mission to the Moon, Moon to Mars, and beyond are evolutionary steps punctuated by leaps in technology and human understanding in the international environment of space.

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