Applications of antimicrobial 3D printing materials in space

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Commentary

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Applications of antimicrobial 3D printing materials in space

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Life in space can have many negative effects on the human body, from decreasing muscle mass, to weakening the immune system. Current flight experiment data indicate alterations in microbial virulence and astronaut immune function during spaceflight suggesting an increased risk of infectious disease during spaceflight missions [1]. Some crews members also experience chronic hypersensitivity reactions due to immune system dysregulation potentially limiting the longevity of space mission [1]. Previous findings from spaceflight experiments also suggest changes in microbial growth, including increased virulence and increased growth rate in microgravity. In combination with potential host susceptibility due to dysfunction in the immune system, the risk of infection may be much higher in the spaceflight environment than in a normal workplace environment [1].

NASA research

A recent study [1] found that 28 astronauts experienced an altered immune response during their 6-month mission aboard the International Space Station [2]. Unfortunately, the direct cause of this altered immune behavior has not been identified, but may be linked to radiation, microbes, stress, microgravity, altered sleep cycles and isolation [1]. In a prolonged space mission, these factors could cause increased susceptibility to illness and, in turn, limitations to human space exploration [1,2]. Scientists recently found that spaceflight can cause 'asymptomatic viral shedding' in astronauts [1]. Asymptomatic viral shedding refers to the presence of virus in the absence of clinical signs or symptoms. Furthermore, studies have demonstrated that the methicillin-resistant *S. aureus* strain demonstrated enhanced antibiotic resistance in microgravity-analog conditions suggesting potential alterations in antibiotic efficacy during spaceflights [3]. Given that medical conditions will occur during human spaceflight missions, there is a possibility of adverse health outcomes and decrements in performance during these missions and for long-term health. Thus, there is a critical need for preventive countermeasures to mitigate microbial risks during space flight missions.

NASA has a variety of methods at their disposal to control and reduce microbial contamination for planetary and crew protection during long space exploration missions [3]. Future long-duration exploration missions to Mars will bring new challenges to the health and wellbeing of astronauts. Additive manufacturing has been proposed as a suitable technology for manufacturing medical devices in zero gravity [4,5] to fulfill the orthopedic needs of crew members with promising applications in on-site emergency care, such as manufacturing of surgical instruments [4] and potentially wound care closures. NASA in collaboration with manufacturing partners Made In Space, Inc., launched the first 3D printer using Zero-G technology. The main objective of this project was to explore the potential use of fused deposition modeling for applications in microgravity [5]. The ability to manufacture medical devices in space provides a potential solution to current risks observed in human spaceflight [4–6]. Additive manufacturing in microgravity represents the first steps on the path toward sustainable and earth-independent exploration initiatives [4–6]. However, the reported immune dysfunction of astronauts in space and the potential virulence and viral antibiotic resistance during spaceflights suggests the critical need of developing preventive countermeasures for the manufacturing of medical devices associated to bacterial development [1–3]. The reported

Table 1. Bacterial analysis summary.

Laboratory	Inoculum (initial load, CFU/ml)	Log_{10} reduction at 24 h	Reduction (%)
1	Methicillin-resistant *S. aureus* (7.10×10^9)	1.65	98.95
	Escherichia coli (3.33×10^9)	1.32	95.03
2	*S. aureus* (6.3×10^5)	5.7	99.99
	E. coli (9.3×10^5)	4.6	99.99

CFU: Colony-forming unit.

immune dysfunction of astronauts in space and the potential virulence and viral antibiotic resistance during spaceflights limits dramatically the use of 3D printing technology, especially the development of medical devices. Thus, the use of antimicrobial 3D-printed filament has promising potential applications for manufacturing a wide range of medical devices associated to bacterial control, such as postoperative prostheses, wound dressing and surgical equipment [7].

A new standard for 3D printing materials

Previous findings [8,9] have found that copper composites can be used to development medical devices with potent antimicrobial properties. These antimicrobial properties and the environmental safety of copper make it an appealing replacement for silver and other antimicrobial compounds for the development of medical devices requiring microbial control [8]. Additionally, a study reported that compounds containing silver may cause irritation and staining of the skin [10]. Copper ions function by protein structural manipulation, inhibiting their biological activity and permeabilization of plasma membranes [11]. Copper also operates as a catalyst in the healing process of wounds as it plays a key role in the enhancement of angiogenesis (i.e., new formation of blood vessels) [12]. The incorporation of copper nanoparticles into a polymer matrix has resulted in an enhanced biocidal behavior [9]. This powerful biocidal action has promising applications for the development of medical devices associated to bacterial development [9]. The emerging 3D printing technology [13] and the development of new 'active' materials with biocidal properties [7] offer the exceptional opportunity to develop 'active' medical devices exhibiting antimicrobial behavior. PLACTIVE™ is an antibacterial 3D printing filament (PLACTIVE 1% Antibacterial Nanoparticles composite, Copper3D, Santiago, Chile), has shown to be up to 99.99% effective against *S. aureus* and *Escherichia coli* [7] (Table 1). The manufacturing process of antimicrobial medical devices (Figure 1) using a biocompatible antimicrobial 3D printing filament involves several processes, such as fermentation (corn to lactic acid), condensation (lactide) and polymerization (polylactic acid). The addition of copper antimicrobial nanocomposite additive to pellets at different concentrations allows the development of a multipurpose antimicrobial filament (PLACTIVE, Figure 1). The ecofriendly characteristics of this filament facilitate multiple recycling options including the production of new antimicrobial medical devices. The end cycle of this filament can classify as a renewable resource facilitated by semibiodegradation after the service life of the device and decreased antimicrobial properties (composting, Figure 1).

Previous investigation showed that antimicrobial 3D-printed filament could be used for the development of functional and effective antibacterial finger prostheses [7]. Hand injuries are the most common among astronauts in space [6]. Since hand injuries, such as mallet finger injuries, could adversely impact space missions [14,15]. Mallet fingers' injuries occur when the tip of the finger is compressed toward the hand. As the finger is compressed, the ligaments supporting the joints are stretched [6]. These injuries can lead to permanent deformities affecting the normal hand function of crew members [6]. Furthermore, surgical procedures are also predicted to occur in long-duration space missions, it is not possible to provide a full surgical capability because of mass, volume, skills, ancillary services and cost constraints and uncertainties regarding which surgical disorders may occur. Thus, 3D printing technology could prove useful for *in situ* manufacturing of surgical instruments for long-duration space missions (Figure 2). Previous investigations have demonstrated the ability to 3D print surgical effective instruments on Earth [16] with the intent of providing surgical capabilities for space missions [4,17]. However, the major issue with the implementation of these devices is the complexity of perform sterilization procedures required to minimize the risk of device contamination and development of infections [17]. It is possible that the development of antimicrobial materials with higher strength and stiffness would provide the opportunities to explore the development of durable antimicrobial surgical tools and prevent infections.

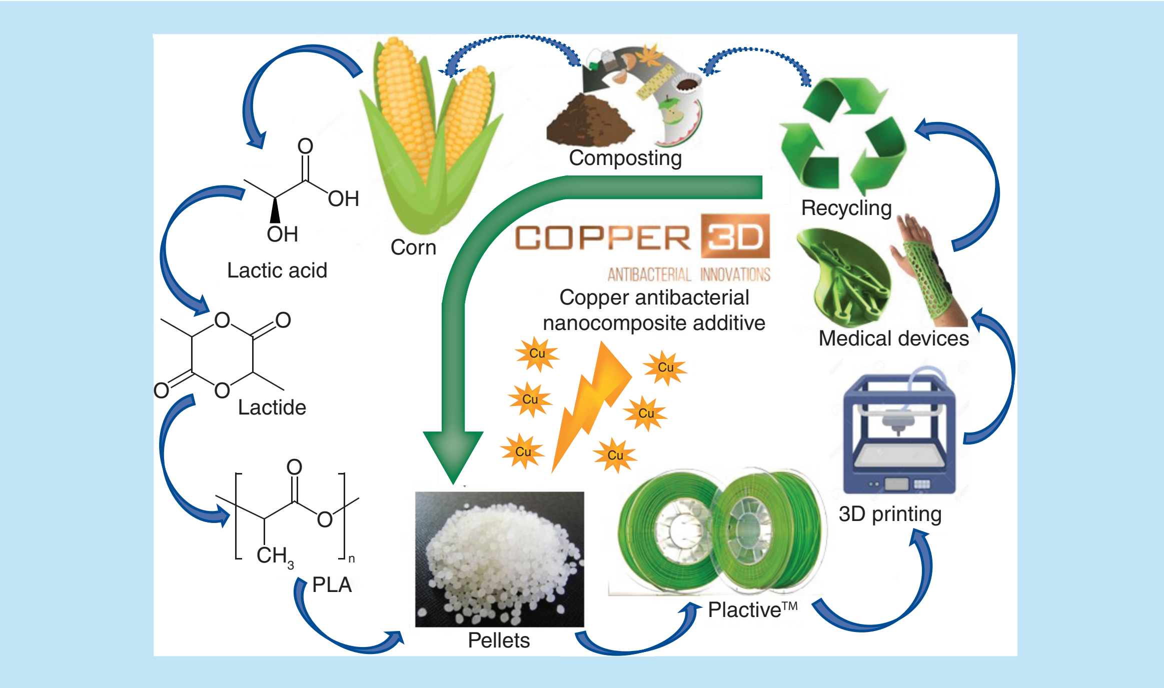

Figure 1. Manufacturing process of antimicrobial medical devices using a biodegradable antimicrobial 3D printing filament.

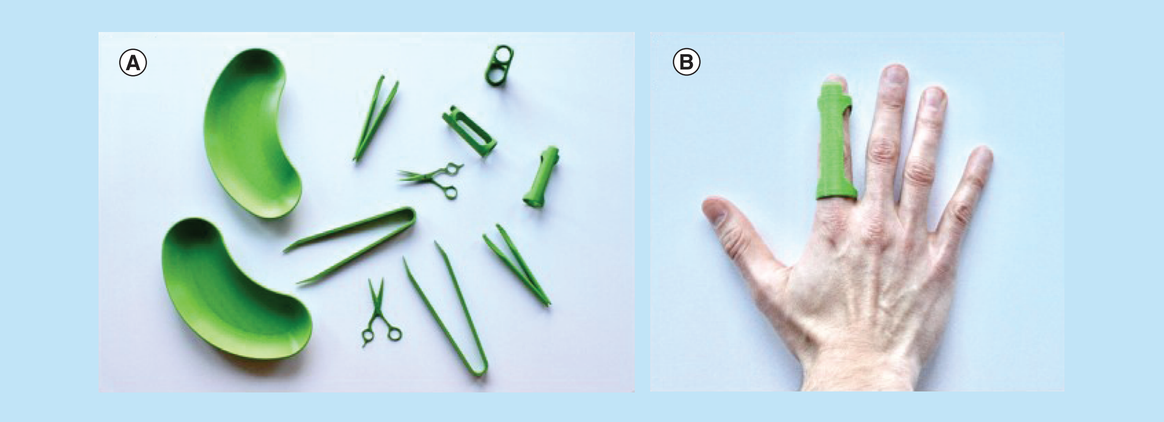

Figure 2. Examples of antimicrobial medical devices. (A) Antimicrobial 3D-printed surgical instruments. **(B)** Antimicrobial finger orthosis.

Conclusion

The development of antibacterial 3D printing filament with thermoforming capabilities have the potential of revolutionize patient care of crew members. Potential applications are not limited to only medical devices but any other nonmedical object critical to the crew members, such as sound protection panels. Medical devices containing bacteria eliminating properties will remove the need for sterilization techniques that require additional transportation space increasing the overall logistic burden to conserved space. The unprecedented accessibility of 3D printing technology and the implementation of antibacterial 3D printing filament to manufacture medical devices is not only critical during spaceflight missions but has a promising potential to a wide range of clinical applications on earth and on the civilian populations revolutionizing patient care.

Future perspective

The use of antimicrobial 3D printing materials, such as emerging thermoplastic polyurethane-based flexible materials, will play a major role in in the development of tissue-engineered scaffolds and other soft tissues including blood vessels and cardiac walls. Their applications will not be limited to astronauts in the International Space Station but can also be used for military personnel in the battlefield for prevention of infections associated with combat-related injuries. Sterilization and biocidal technology in combat support hospitals and emergency humanitarian relief settings must be capable of providing a wide range of 'on-demand' medical devices. Currently, the sterilization of medical devices depends on large-chamber stream sterilizers introducing a significant logistical burden. Treatment of battlefield trauma presents the unique logistical challenge of providing sterile medical devices to medical personnel. Transport and supply constraints limit the quantity and variety of medical devices available in the field and sterilization equipment is often not available to support the instruments required. There is a critical need to develop a raw material for the development of a variety of antimicrobial medical devices to address the current supply chain problems involving the medical care in austere medical environments. Antimicrobial 3D printing materials will provide an attractive solution to solve these real-world problems, especially in austere environments.

Financial & competing interests disclosure

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