



A REVIEW OF 3D / 4D / 5D PRINTING APPLICATIONS FOR BIOMEDICAL SUPPLY CHAIN*

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ABSTRACT: The objective of this study is to critically review the applications of 3D, 4D and 5D printing technologies in the biomedical supply chain. The evolution of additive manufacturing has significant impacts on the healthcare sector in terms of supply chain optimization, cost reduction and developing customized medical solutions. 3D printing revolutionized the production of advanced biomedical devices, organs and tissues by making patient-specific strategies possible. 4D printing has demonstrated significant advantages especially in producing medical implants, prosthetics and regenerative tissue by providing dynamic structures that react to environmental stimuli. The new 5D printing improves accuracy and complexity by virtue of its multi-axis production feature. This research analyzes the effect of such technologies on the change they induce in biomedical product production and supply chain. Besides, the future directions and challenges of such technologies are analyzed and how they can reshape healthcare models are debated.

Keywords: Biomedical Supply Chain, 3D/4D/5D Printing, Healthcare Logistics, Additive Manufacturing, Personalized Medicine.

Jel Codes: I19, Y2, M11

BIYOMEDİKAL TEDARİK ZİNCİRİ İÇİN 3D / 4D / 5D BASKI UYGULAMALARININ İNCELENMESİ

ÖZ: Bu çalışmanın amacı, 3D, 4D ve 5D baskı teknolojilerinin biyomedikal tedarik zincirindeki uygulamalarını eleştirel bir şekilde incelemektir. Katmanlı üretimin evrimi, tedarik zinciri optimizasyonu, maliyet azaltma ve özelleştirilmiş tıbbi çözümler geliştirme açısından sağlık sektörü üzerinde önemli etkilere sahiptir. 3D baskı, hastaya özel stratejileri mümkün kılarak gelişmiş biyomedikal cihazların, organların ve dokuların üretiminde devrim yaratmıştır. 4D baskı, çevresel uyaranlara tepki veren dinamik yapılar sağlayarak özellikle tıbbi implant, protez ve rejeneratif doku üretiminde önemli avantajlar ortaya koymuştur. Yeni 5D baskı ise çok eksenli üretim özelliği sayesinde doğruluğu ve karmaşıklığı artırmaktadır. Bu araştırma, bu tür teknolojilerin biyomedikal ürün üretimi ve tedarik zincirinde neden oldukları değişim üzerindeki etkisini analiz etmektedir. Ayrıca, bu tür teknolojilerin gelecekteki yönleri ve zorlukları analiz edilmekte ve sağlık hizmetleri modellerini nasıl yeniden şekillendirebilecekleri tartışılmaktadır.

Anahtar Kelimeler: Biyomedikal Tedarik Zinciri, 3D/4D/5D Baskı, Sağlık Lojistiği, Katmanlı Üretim, Kişiselleştirilmiş Tıp.

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1. Introduction

Supply chain management is emerging as a strategic necessity for organizations attempting to maintain competitiveness and survivability. Supply chain management is particularly important for the healthcare sector because it is inherently complex with diverse sources of raw material, highly specialized services, and unstable internal processes (Yanamandra, 2018). Effective supply chain management in the healthcare industry not only enhances service quality but also plays a vital economic role in ensuring sustainability by maximizing the use of resources (Acar and Bozaykurt, 2017). Nevertheless, even though it could be beneficial, the health care industry has lagged behind in embracing superior supply chain management strategies relative to other industries (McKone-Sweet et al., 2005). The invention of additive manufacturing technologies, 3D printing, has brought groundbreaking developments in supply chain operations that streamline manufacturing, reduce delivery times, and cost savings (Çetinkaya and Boumaraf, 2020). In the medical field, 3D printing enables on-demand production of complex biomedical devices that are designed to match patient individual anatomical requirements, i.e., prosthetics, orthotics, scaffolds, and drug delivery devices (Chia and Wu, 2015). This capability has revolutionized the healthcare supply chain by lowering inventory requirements and lessening reliance on traditional manufacturing and distribution channels. From the development hubs of 3D technology, 4D printing introduces the element of time, which allows printed structures to change or alter their shape or function over time or in response to an environmental stimulus such as heat, humidity, or light (Erdoğan, 2019). This dynamic flexibility has vast potential for biomedical applications, such as designing prosthetics and implants that grow with the patient or medical devices that can adapt to changing physiological conditions. Furthermore, new 5D printing technology prints in several axes simultaneously, optimizing supply chain efficiency by minimizing material waste and speeding delivery time, with greater precision and structural integrity. These emerging manufacturing technologies are transforming the biomedical supply chain by enabling rapid, low-cost, and highly customized production processes. Not only are they shortening supply chain lead times, but they are also simplifying local production, reducing logistics complexity, and improving patient-specific healthcare solutions. As the application of 3D, 4D, and 5D printing technologies in biomedicine continues to grow, their impact on the healthcare supply chain is also bound to grow, driving greater innovation and efficiency. This study delves into these technological advancements, highlighting their transformative impact on healthcare logistics and their potential to redefine the future of biomedical supply chains.

2. Supply Chain Management and Healthcare Supply Chain

Supply chain management has been operationalized in numerous definitions in the literature. One of the most comprehensive definitions comes from the Council of Supply Chain Management Professionals (CSCMP), who define supply chain management as 'the planning and management of all activities related to sourcing and procurement, transformation and all logistics management activities.'. It also entails co-operation and co-ordination with channel partners, who may include suppliers, intermediaries, third-party service providers and customers.' This definition stresses the supply chain as a web of linked units that facilitate the flow of goods and services in the chain (Long, 2012). The supply chain is the whole chain of processes from procurement of raw materials to manufacturing, handling inventory, distribution and ultimate delivery of goods to retailers and end-consumers. Strategic management of this end-to-end process is known as supply chain management. According to Bowersox et al. (2012), supply chain management 'involves a network of organisations that work together to maximise strategic positioning and enhance operating effectiveness.'. This requires managerial practices that connect functional areas in one organisation and overcome trading partners and customers across organisational boundaries.'

The key aim of supply chain management is to optimize the coordination among manufacturers, suppliers, warehouses and distribution channels so that the product is delivered at the proper time, in the right place and in proper quantities, minimizing the overall cost of the system while fulfilling customer needs (Büyükoğlu and Vardaloğlu, 2008).

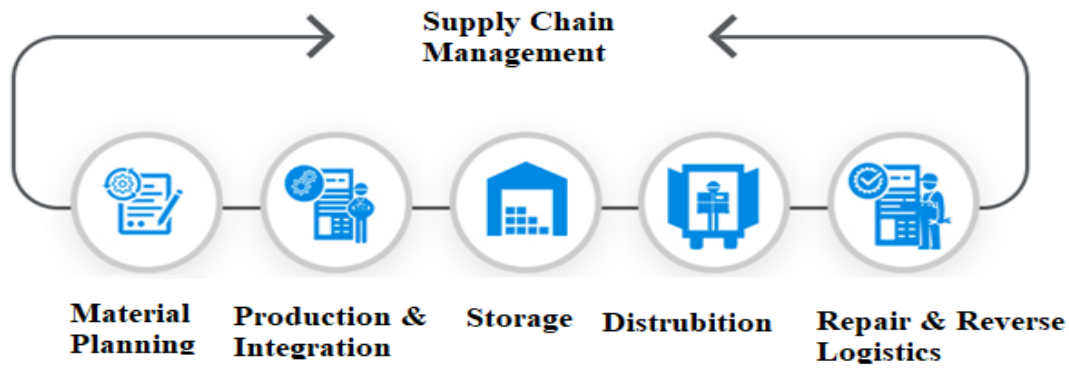


Figure 1: Supply Chain Management (Büyüközkan and Vardaloğlu., 2008).

Supply chains in all industries share the same characteristics. Medical supply chain systems are developed to serve a wide range of patients' needs that include orthotics, prosthetics, dental implants, artificial organs, bones, cartilage, muscles, blood vessels, nerves in the craniomaxillofacial complex, medical device components and other medical devices. Each of these categories requires a different supply chain process that is attuned to their specific needs.

Healthcare supply chain operations involve not only the distribution and management of physical products such as pharmaceuticals, medical devices and health aids, but also the coordination of patient flow in healthcare. Supply chain management in both cases is dependent on efficient coordination and integration of operational processes, which significantly improves the overall performance of healthcare supply chains (De Vries and Huijsman, 2011).

Principally, the objectives of the supply chain in the healthcare industry can be listed as follows (<https://www.zukunft-krankenhaus-einkauf.de/blog/einkaufsgemeinschaft/>, 2024) :

- To deliver medical products or supplies in the required quantities, at the location specified, under the optimal conditions and at the most cost-effective price,
- Reducing lead times and costs without sacrificing high levels of quality,
- Maximize space for patient care by minimizing inventory storage requirements,
- Improving the quality of health services provided to the patients,
- Reducing the carrying cost of inventories pertaining to medical supplies and
- Improving sustainable profitability and competitive advantage.

Figure 2 shows a typical supply chain for the healthcare industry.

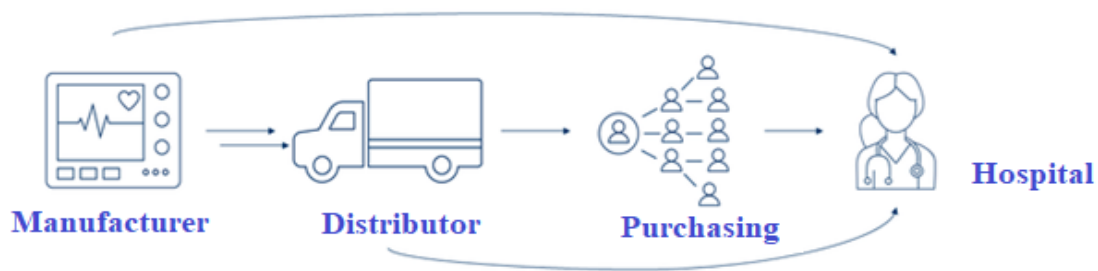


Figure 2: Health Industry Supply Chain (<https://www.zukunft-krankenhaus-einkauf.de>, 2024).

Human health is of the highest importance in the healthcare supply chain. Under such a circumstance, items such as orthoses, prostheses, dental implants, artificial organs, bones, cartilage, muscles, blood vessels and nerves of the craniomaxillofacial complex are special supply chain challenges. Such medical devices require fast, cost-effective and highly customized manufacturing solutions.

Application of 4D printing technology has fundamentally transformed healthcare supply chains by providing efficient and tailored production of such medical devices. The fact that 4D printed devices have the capacity to change over time and thus conform and adapt to the human body further improves patient comfort and compliance.

To effectively analyze the potential and ramifications of this technology, one must first learn the basic principles behind 3D and 4D printing.

3. 3D and 4D Printers

Once optimised, the speed and scale of conventional manufacturing are quintessential in achieving high manufacturing efficiency. By comparison, 3D printing possesses many intrinsic advantages, which include the ability to produce and supply small batches, the flexibility to produce highly customised geometries, and the potential for localised production and distribution of spare parts (Cetinkaya and Boumaraf, 2020). Integrated with CAD/CAM systems, 3D printing technology is an increasingly used computer-aided design and manufacturing tool. It is today a high-level solution that can be applied to all stages of the design and manufacturing process, for example, conceptual design, digital prototyping, production and final documentation (Oropello and Piegl, 2016). One of the greatest benefits of 3D printing is that it has the capability to produce complex geometries that are not possible through traditional manufacturing techniques like moulding or milling. A few other advantages of additive manufacturing include the capability to produce parts with hierarchical complexity, the integration of a number of diverse materials in a single part, and the fabrication of fully assembled functional mechanisms.

However, to fully exploit the unique advantages of 3D printing, conventional design methods must be redesigned and new tools developed that are suitable for the requirements of additive manufacturing (Oropello and Piegl, 2016).

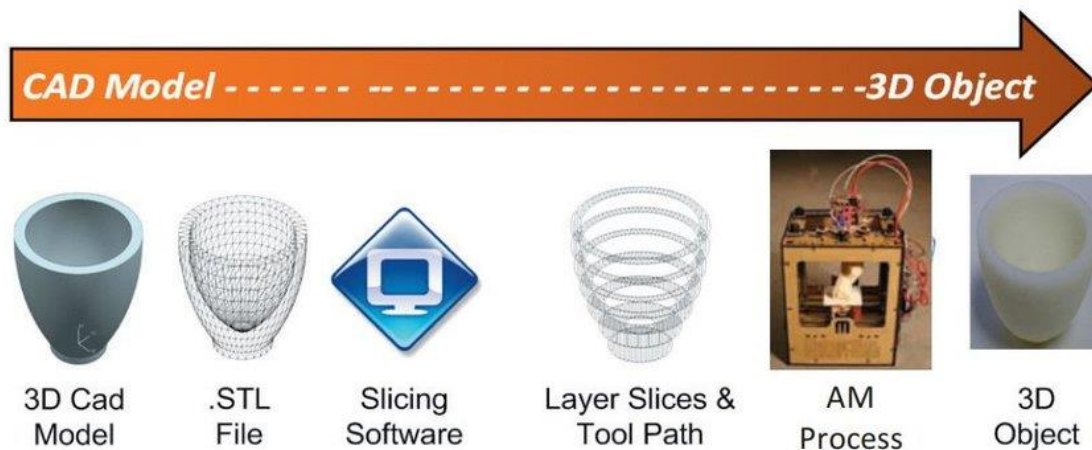


Figure 3: General 3D Printer Manufacturing Process (Campbell et al., 2011).

The 3D printing begins with the production of a 3D model using computer-aided design (CAD) software or by digitally scanning an object. The model is converted into sectional layers using specialized software that generates a digital file that is sent to a 3D printer. The printer builds the object layer by layer by precisely depositing or moulding the selected material (Campbell et al., 2011). In contrast, 4D printing introduces the time factor into 3D printing technology to allow printed objects to change in shape, function, or property over a period. This is possible through the use of intelligent materials to create dynamic structures with self-healing or self-assembly functions. This new approach promotes interdisciplinary collaboration, resulting in operational products through the integration of the time factor in their design (Erdoğan, 2019). Time, shape changing capacity, light, temperature and humidity are of great importance in 4D printing. Subjectively, objectively, goods manufactured with the assistance of 4D printing technology from intelligent and programmable materials can self-adjust to an environmental change without requiring any external stimulus (Kesayak, 2024).

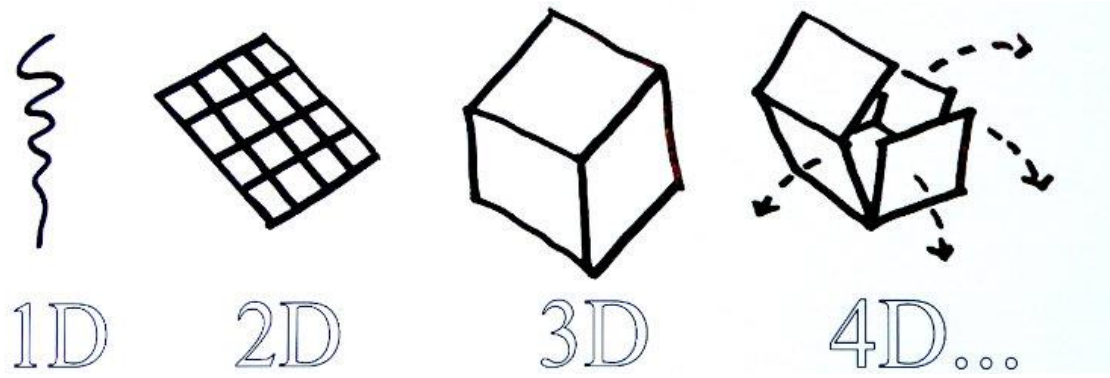


Figure 4: 4D object draft (Kesayak, 2024).

Shape memory materials or intelligent materials are new to the field of biomedicine but have gained important relevance in vital medical applications over the last few years. For example, materials manufactured using 4D printing technology can react to organ or tissue cells to enable implants to adapt, grow, and develop in the body. This function has facilitated advanced studies in critical healthcare applications (Erdoğan, 2019).

Figure 5 illustrates a standard 3D and 4D printer.

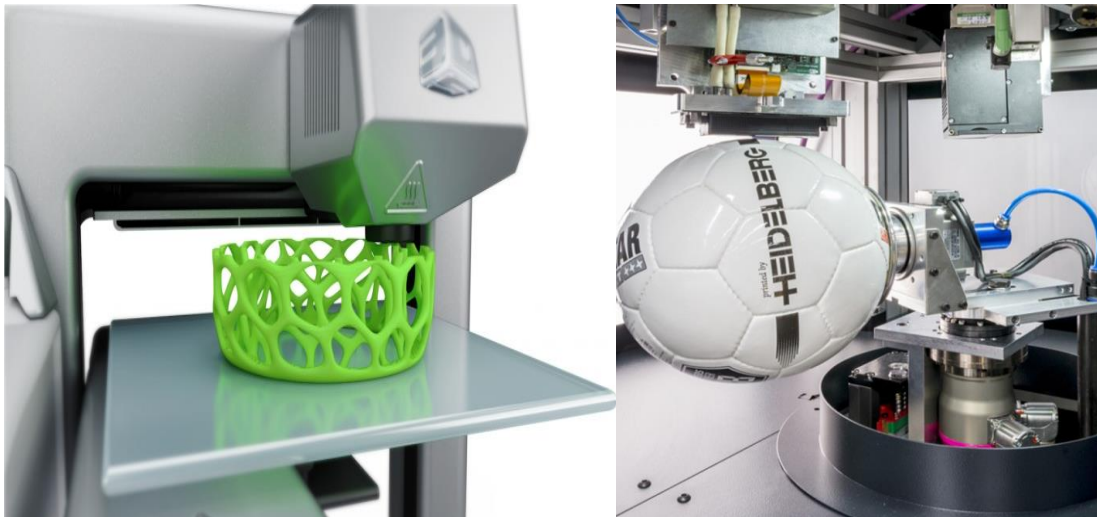




Figure 5: Standard 3D and 4D printers (Belleghem, 2024)

The biggest difference between 3D printing and 4D printing is the use of materials to be printed and the printing capability. The main differences between the two are summarized in Table 1 below.

Table 1: Differences between 3D printer and 4D printer, (<https://www.futurebridge.com>, 2024).

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Description	3D Printing	4D Printing
Dynamic Shape Change	<ul style="list-style-type: none"> No 	<ul style="list-style-type: none"> Changes in color, shape, function, etc.
Materials Used	<ul style="list-style-type: none"> Thermoplastics {Acrylonitrile butadiene styrene (ABS), etc.} Metals and alloys Biomaterials and gels Nanomaterials 	<ul style="list-style-type: none"> Smart materials – Shape Memory Alloys (SMA) and Shape Memory Polymers (SMP) Self-assembled materials Hydrophilic polymers, biomaterials, and plant oil
Printing Facility	<ul style="list-style-type: none"> 3D printer – Stereolithography (SLA) Fused Deposition Modeling (FDM) Selective Laser Sintering (SLS) 	<ul style="list-style-type: none"> 3D printer - Stereolithography (SLA) Multi-material 3D printers

Source: FutureBridge Analysis

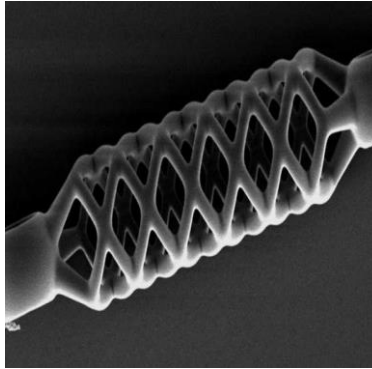
4D additive manufacturing is a novel technology that improves with the convergence of smart materials, sophisticated additive manufacturing system functions, and design strategies specific to this particular manufacturing technique (Khan et al., 2018). The most fascinating aspect of this technology is the use of shape memory materials (SMMs) in 3D printing (3DP), which have been of great interest since they respond sensitively to external stimuli, thus making 4D printing a new field of research (Biswas et al., 2021). Unlike traditional 3D printed objects, time as the fourth dimension causes these printed structures to change dynamically in their shape, size, or color upon exposure to exterior stimuli. 4D printing utilizes shape memory materials (SMMs), which consist of alloys and polymers, these can be prescribed to a temporary form and then move back to the natural form upon exposure to specific stimuli like changes in temperature, pH level changes, or the presence of water (Melocchi et al., 2024). This enables the production of complex three-dimensional structures that may change forms and shapes when exposed to stimuli. Although 4D printing is considered by some scientists as an evolution of 3D printing or additive manufacturing with the addition of temporal dynamics to it, the distinct deformation mechanism in 4D printing is characterized by the synergy between shape programming and strategic use of smart, active materials (mainly polymers) (Joshi et al., 2020).



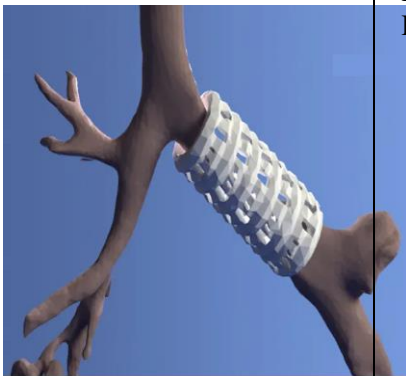
4. Production of Medical Materials, Artificial Tissues or Organs in the Health Sector with 4D Printers



Ever since additive manufacturing technologies emerged in the mid-1980s, numerous fields have benefited from high rates of manufacturing without the use of dedicated tools or molds. Such technologies have gained growing interest in biomedical devices, dentistry, and medicine (Bose et al., 2013). In the meantime, 3D printers have been a topic of great interest in surgery (Dawood et al., 2019). 3D printing technology plays an important role in resolving global health emergencies, especially during emergency times. 3D printing technology has managed to relieve shortages of medical supplies and personal protective equipment (Çetinkaya and Boumaraf, 2020). During COVID-19 pandemics, 3D printing technology has greatly assisted in the supply of protective items like face shields, masks, and ventilator parts. Bioprinting refers to the deposition of biomaterials with cells layer by layer to create functional tissues or organs in a pre-designed structural framework (Gopinathan and Noh, 2018). 3D printers play an important role in this process. 3D bioprinting, one of the latest technologies being utilized in tissue engineering and regenerative medicine, enables the fabrication of complex tissue structures with close similarity to natural tissues and organs (Gopinathan and Noh, 2018). It facilitates the artificial creation of organs and tissues through advanced 3D printing techniques by integrating cells, biomaterials, and growth factors (Akkuş et al., 2020). In addition to 3D printing, 4D printing technology is also an excellent innovation in this context. As opposed to traditional 3D printing, 4D printing adds the




element of time as the fourth dimension to build dynamic biological structures such as scaffolds, implants, and stents that can alter their shape in response to physiological environments. A good understanding of shape memory materials is necessary to realize the full potential of this manufacturing technique. These "smart" materials respond to environmental stimuli, thus eliminating the need for any external sensors or batteries (Kumar et al., 2008). 4D printed shape memory polymers and shape-shifting structures find a wide variety of applications in biomedical sciences, among others. By creating a revolution in personalized medicine, 4D printing technology is advancing a paradigm shift in the health sector (Li et al., 2020). It facilitates advancements in organ printing, tissue engineering, and self-assembly of biomaterials at the human scale. Moreover, 4D printing enables the production of biomedical splints, stents, bioprinting solutions, and orthodontic devices according to individual growth patterns (Javaid and Haleem, 2019). The novel method enables the production of smart medical implants and devices tailored to patient-specific needs. Using computed tomography (CT), magnetic resonance imaging (MRI), and other scanning technologies, the data of the patient can be obtained and converted to the 4D printing process according to layer-based manufacturing methods. As a result, implants that are created through 4D printing possess the capability to change their shape dynamically according to physiological change or natural growth of the human body. The functionality to change shape has tremendous advantages in biomedical applications, especially in creating personalized products for bone, ear tissue, and muscle reconstruction (Kumar et al., 2020). With the ability to personalize orthopedic implants and simplify surgery, 4D printing technology is developing rapidly. It is revolutionizing medicine by enabling the development of new, conformable internal splints, stents, and tissue and organ substitutes (Javaid and Haleem, 2019).


Table 2: 4D printing usage areas in the health sector, adapted from (Javaid, et al, 2018).

Medical Applications	Explanation	Examples	References
Smart stent	This type of technology in 4D printing is actually enabling the design of stents that can expand due to body heat and attain a desired shape over time. This ability, especially in complex surgical procedures, is advantageous for the rapid deployment of an intervention, potentially improving patient outcomes and working toward more efficient lifesaving interventions..		Zarek, et al., 2016; Bodaghi, et al., 2018; https://tectales.com/3d-printing/4d-printing-the-world-s-smallest-stent.html , 2021.

Organ production	<p>4D printing technology has great potential in the creation of complex three-dimensional organs. This method enables the creation of organs from the patient's own cellular material, enhancing biocompatibility and minimizing the risk of rejection.</p> <p>Therefore, 4D printing represents a very tangible hope for organ transplant, offering new possibilities to patients in need of life-saving procedures.</p>		<p>Miao et al., 2017; Saunders., 2017; Carlota., 2023</p>
Intelligent multi-material printing	<p>The layer-by-layer process in 4D printing enables the addition of smart polymers and increases the functionality and flexibility of printed structures.</p> <p>This approach enables a new practice of smart and customizable multi-material printing, especially in the development of medical implants.</p> <p>In addition, the technology supports the 3D printing of various body organs, and it offers great progress in personalized medical solutions along with regenerative medicine.</p>		<p>Ge, et al., 2016; Akbari, et al., 2018; https://www.mtaa.org.au/news/3d-printing-implantable-medical-devices., 2024</p>
Dyspnea (Breathing problem)	<p>4D printing technology can save the lives of infants who have respiratory distress. This new technique enables the rapid production of medical implants that adapt to an infant's growth and gradually change their shape over time to improve and facilitate respiratory function.</p> <p>This dynamic adaptability</p>		<p>Haq., 2023; Coi, 2024; Duhaime-Ross, 2024</p>

	offers a vital intervention, especially for young patients who are suffering from respiratory distress.		
Intelligent medical implants and tissue engineering	<p>4D printing technology enables the creation of materials that can transform their shape based on particular stimuli.</p> <p>This characteristic is particularly useful in biomedical implants and tissue engineering, where materials can shape and change form within the body.</p> <p>Also, 4D printing enables the regeneration of dynamic tissue like muscle, bone, and cardiovascular tissue by being able to modulate mechanical properties based on body movement and exercise.</p>		Hendrikson, et al., 2017; Mandon, et al., 2017; Durna., 2018.
Heart, kidney and liver printing	<p>In the coming developments, 4D printing integrated with smart materials can enable the printing of intricate organs like the heart, kidneys, and liver.</p> <p>The new technology has the potential to generate tissues and organs with superior flexibility, optimal biocompatibility, and exact genetic alignment.</p> <p>Such breakthroughs can revolutionize organ transplantation and significantly improve patient outcomes by minimizing the risks of rejection.</p>		Yi., 2017; Gosnell et al., 2016; Reddy, 2024

<p>Skin graft (skin patch)</p>	<p>4D printing technology has great potential to produce skin grafts that are near the natural color of the skin of a patient. The technique is particularly helpful for burn patients, as the printed grafts can readily merge with the body of the patient and even exhibit similar growth patterns to those of natural skin. This technology improves healing outcomes and improves aesthetic and functional recovery for patients.</p>		<p>Kahoo, et al., 2015; He, et al., 2018; Molitch-Hou, 2023</p>
<p>Manufacturing of smart medical devices</p>	<p>4D printing technology facilitates the production of complex, intelligent medical devices with complex functional attributes. The technology also enables the fabrication of time-critical surgery tools that have the ability to transform dynamically according to certain medical requirements, furthering surgical accuracy and patient results.</p>		<p>Kuang, et al., 2018; Pei and Loh, 2018; Castro et al, 2017; Zhao et al, 2018; Scott, 2023.</p>
<p>Complex surgeries</p>	<p>4D printing technology enables the production of haptic models that mirror body movements and anatomical appearances very closely. The technology can be utilized in very complex surgery in the future that is not possible with traditional manufacturing technology. With the integration of data from CT and MRI scans, 4D printing is able</p>		<p>Chae, et al, 2015; Lee, et al, 2017; Javaid, et al, 2018; Sanjeet and Albert, 2016; Tufnell, 2024.</p>

	<p>to replicate various limbs and anatomical models by utilizing smart materials and provide precise and detailed anatomical representation. This capability improves surgical planning and medical training by developing extremely accurate and realistic models.</p>		
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5. Conclusion and Discussion

3D, 4D and 5D printing technologies are revolutionizing the biomedical supply chain and making it efficient, cost-effective and enabling personalized healthcare solutions. While 3D printing enables the production of intricate biomedical devices such as patient-specific prostheses, implants and organs, 4D printing adds a time factor to these technologies and offers biocompatible and dynamic solutions. 5D printing, nonetheless, allows the manufacture of stronger and more precise medical devices with its multi-axis production. Such technologies reduce dependency on traditional supply chain processes, decouple logistics processes with localized manufacturing and promote sustainability.

Employing these new methods of production within the biomedical supply chain has various advantages such as rapid production, reduced cost, and increased compliance of patients. However, it also presents a few challenges:

Regulation and Standardization: Integration of 3D, 4D and 5D printing technologies into biomedical devices renders it a significant challenge to be in line with medical device regulations and quality standards. Compliance with international standards must be obtained at every step in the manufacture process.

Material Limitations: The development of biocompatible smart materials suitable for 4D and 5D printing is currently limited. This limits the scope of printable material available and inhibits proper solutions from being developed for application in the biomedical sector.

High Start-Up Costs: Since the acquisition of advanced printing technology and local manufacturing units requires huge capital investment, it is difficult for small and medium-sized healthcare organizations to obtain these technologies.

Technical Competence and Human Resource Development: Effective implementation of 3D, 4D and 5D printing technologies is a human resource with superior technical expertise. Therefore, it is an urgent requirement to develop education and training courses in medical printing and biomaterial sciences.

5.1. Recommendations

The following is suggested for widespread implementation and utilization of these technologies in the biomedical supply chain:

Acceleration of Regulatory Processes: Global regulatory guidelines decision for 3D, 4D and 5D printing technologies and acceleration of standardization processes will render the technologies safer and more efficient to implement.

Investment in Research on Materials: There needs to be coordination of private industry, research centers, and universities for the development of smart and biocompatible material. Providing greater alternatives for those materials that could be printed biomedical will expand their fields of usage.

Financial Incentives to Maximize Accessibility: Incentives, grants and government funding should be there to facilitate small- and medium-sized healthcare systems to invest in these technologies more easily.

Education and Workforce Development: Training courses in 3D, 4D and 5D printing should be expanded in medicine, engineering and material science. Highly skilled manpower should be trained by organizing courses and certification courses in this topic in universities and vocational training institutions.

Industry and Academic Cooperation: Improved cooperation should be ensured among biomedical producers, hospitals, and academic centers, thus accelerating the development of new printing technology and its exploitation in the industry.

Therefore, existing barriers need to be addressed in order to achieve the full potential of 3D, 4D and 5D printing technologies in the biomedical supply chain. Through strategic interventions in the domains of regulation, materials science, financial inclusion, and training of the workforce, these technologies will be utilized more widely in the healthcare sector and revolutionize personalized medicine practices even more.

Ethics Statement: *The authors declare that ethical rules were followed in all preparation processes of this study. In case of detection of a contrary situation, Turkish Journal of Social Sciences Research has no responsibility, all responsibility belongs to the author(s) of the study.*

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