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4D Printing in Healthcare: Technology Evaluation, Applications, and Market Size Forecasting

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Abstract: 4D printing (4-dimensional printing; also known as 4D bioprinting, shape-morphing systems or active origami) uses the same techniques of 3D printing through computer-programmed deposition of material in successive layers to create a three-dimensional object. The notion behind 4D printing is that it creates sophisticated three-dimensional structures that are capable of changing shape and form in response to environmental inputs. According to some academics, 4D printing is merely an extension of 3D printing or additive manufacturing with the added constraint of time as a fourth dimension. This paper presents a comprehensive overview of the basic mechanism of 4D printing technology and its application in addition to the use of this technology in healthcare fields. Finally, this paper presented a forecast for the 4D printing market size over the coming years.

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1. Introduction

The advent of 3D printing has revolutionized biomedical research. The development of complex, biologically relevant, and extremely accurate constructions that may be used for tissue engineering, drug delivery, and other biomedical applications has unquestionably considerably benefited modern healthcare [1].Despite the fact that 3D printing has eliminated certain industrial limits, such as reproducibility, accuracy, and precision, it has also created new challenges concerning the feasibility of building dynamic 3D structures. Fortunately, the combination of smart materials and 3D printing provided the answer to this dilemma, allowing printed objects to gain further biomimicry by responding to stimuli. Consequently, time has become the new dimension for 3D-printed objects, and 4D printing has been envisaged [2,3].

Using 3D printing, additive manufacturing creates a customized replica of the heart; nevertheless, its uses are limited. It aids in surgery planning, guiding, training, and analysis, and ultimately improves patient outcomes. However, it is necessary to create a 3D model of the heart or its part that may be implanted in the patient's body and functions and develops similarly to the real heart or its part. This type of 4D printing application could be regarded to satisfy a significant need of cardiologists [4].

2. Fundamentals of 4D printing

4D printing is the process by which a 3D-printed object morphs into another structure in response to external energy input, such as heat, light, or other environmental stimuli.

Typically, 3D printing begins with a computer-aided design (CAD) file that details the object's geometry and dimensions. The object is split into a succession of cross-sectional digital layers that are then created by the 3D printer. This technique is compatible with a wide variety of substances, including thermoplastic polymers, powders, metals, and ultraviolet (UV) curable resins. Four-dimensional (4D) printing is described as the printing of three-dimensional (3D) objects that can alter shape or function in response to external stimuli over time [5, 6]. The dimensions of printing are depicted in a schematic in Figure 1.

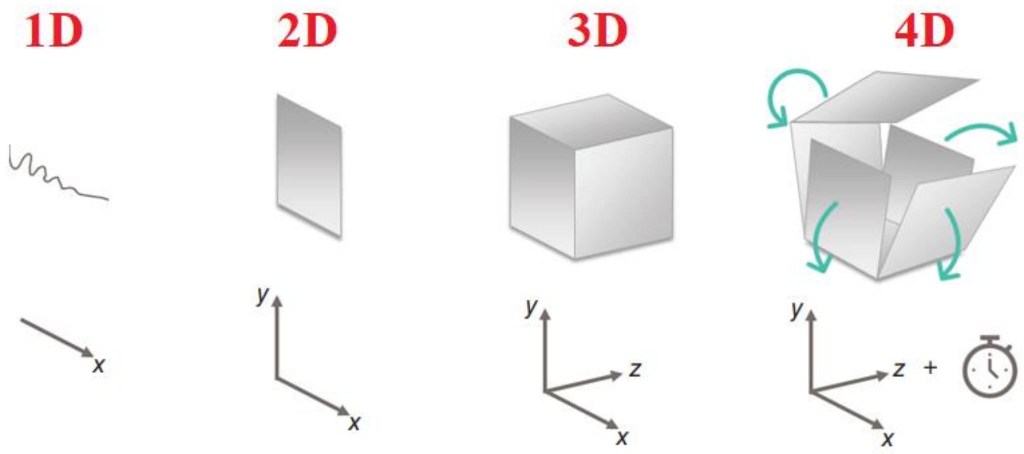

Figure 1 A diagram of 1D, 2D, 3D, and 4D printing dimensions.

The primary distinction between 4D printing and 3D printing is the use of intelligent design or responsive materials, which results in time-dependent object deformation. To accomplish this objective, the printed material must undergo a self-transformation in shape or function when exposed to an external stimulus such as osmotic pressure, heat, electricity, ultraviolet radiation, or another energy source [7].

Incorporating these extra capabilities creates significant design issues since 4D printed objects must be meticulously preprogrammed based on the mechanism of controlled smart materials that contain the desired material deformations. Because the majority of 3D printing materials are designed to produce only rigid, static things, the material selection for 4D printing is crucial.

In addition, using Figures 2 and 3, we can understand the comparison between 3D printing and 4D printing, where the use of materials to be printed and the printing facility. Exhibits 1 and 2 depicted below explain the major differences between 3D and 4D printing.

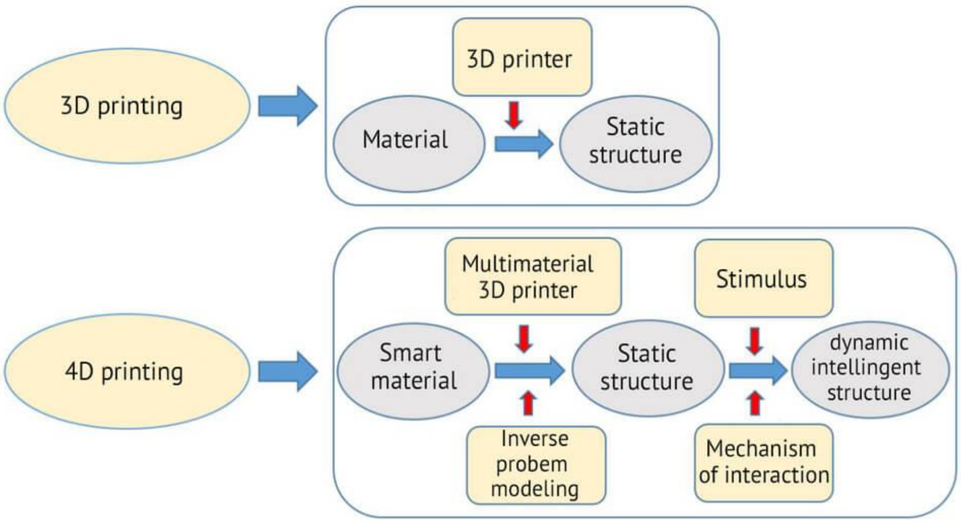

Figure 2 3D vs 4D printing process.

Description	3D Printing	4D Printing
Dynamic Shape Change	▪ No	▪ Changes in color, shape, function, etc.
Materials Used	▪ Thermoplastics {Acrylonitrile butadiene styrene (ABS), etc.} ▪ Metals and alloys ▪ Biomaterials and gels ▪ Nanomaterials	▪ Smart materials – Shape Memory Alloys (SMA) and Shape Memory Polymers (SMP) ▪ Self-assembled materials ▪ Hydrophilic polymers, biomaterials, and plant oil
Printing Facility	▪ 3D printer – Stereolithography (SLA) ▪ Fused Deposition Modeling (FDM) ▪ Selective Laser Sintering (SLS)	▪ 3D printer - Stereolithography (SLA) ▪ Multi-material 3D printers

Figure 3 The difference between 3D printing and 4D printing (Source: Future Bridge Analysis).

3. 4D printing and smart materials

Smart Material for 4D printing is one of the growing study disciplines in which different materials are synthesized for deformation mechanisms based on their responses to diverse external stimuli. The design of cutting-edge printers that can print on a variety of materials is the focus of equipment development. Currently, researchers are using 4D selective laser melting methods, direct inkjet cure, fused deposition modelling, stereography, laser-assisted bioprinting. In order to comprehend the functional architecture of 4D printed objects, it's necessary to first grasp what they're made of, research into mathematical modelling is essential [8,9,10]. There are various types of smart materials available, and these include Shape memory polymers, Electro-responsive polymers, Magnetic shape memory alloys, Smart inorganic polymers, Shape memory alloys, Temperature responsive polymers, Photoresponsive polymer, and electroactive polymers.

Materials for 4D printing are categorized according to their environment or how they react to external stimuli. This category includes materials that react when they come into touch with water or moisture. Researchers choose such materials because water is abundant and may be used in a variety of applications. Because of its strong response to water, hydrogel is one of the more intelligent materials in this category. These materials react with magnetic fields, light and current. For example, photographic chromophores swell with polymers at a specific location, and when they are exposed to natural light, they absorb light. When a current is passed through an ethanol-containing item, the volume expands and the overall matrix expands. Magnet nanoparticles are thus embedded in the printed item to provide magnetic control. [11,12,13].

4. 4D printing general applications

4D printing technology has the potential to revolutionize the current manufacturing process. This paper describes in full the opportunities that 4D printing presents.

4.1 Aerospace equipments

4D Printing refers to the use of traditional 3D printing to create objects with the incorporation of different materials, which are defined as smart materials and have the unique property of changing shape over time or other properties when triggered by an external energy source. Due to the new challenges, engineers are simultaneously required to have a deeper understanding of AM, advanced smart materials, and design (morphing structures in aerospace). Occasionally, these new requirements push these key cores to their individual limits; AM, for instance, must transition from producing nonfunctional parts to employing nanotechnologies. While analysis of the future aspects of the 4D printing technology market is already underway, specifically in the areas of programmable matter, end-user industry, and future scope, it is anticipated that the market will be widely commercialized by 2019. Although printing technology is still in its infancy, the global market is expected to expand by 42.5% annually between 2019 and 2025, reaching $537.8 million. The 4D printing industry is anticipated to have a similar future impact on industries such as aerospace as the 3D printing industry did in the past. Two categories of commercially available smart materials exist: 1) Shape Memory Alloys (SMAs) and 2) Shape Memory Polymers (SMPs). The transformation of SMAs occurs when two phases, martensite (low temperature) and austenite (high temperature), are in equilibrium; the transformation of SMPs occurs in a bi-directional manner to a temporary shape when exposed to a variety of external stimuli such as temperature. A researcher named Hiltz determined the results of a comparison between Nitinol, an extremely popular in the aerospace industry Titanium/Nickel SMA developed at the Naval Ordinance Lab, and an SMP, both of which have been 4D printed.

Table 1 SMA and SMP comparison

Material Property	Ti/Ni Shape Memory Alloy	Shape Memory Polymer
Recovery Stress	200-400 MPa	1-3 MPa
Recovery strain	6%	50-600%
At low temperature	Soft	Hard
At high temperature	Hard	Soft
Density	6-7 g/cm^3	1 g/cm^3
Phase transformations	Martensitic, R-phase	Glass Transition
Shaping	Difficult	Easy
Cost	Expensive	Cheap
Heat conductivity	High	Low

4.2 Defense science

There are numerous advantages of 3D printing for the defense industry. Now, the sector is seeking further applications for 4D printing.

One of the most exciting applications of 4D printing could involve uniforms that can change their camouflage or provide enhanced protection against toxic gases or shrapnel.

Researchers are also investigating how the military could utilize self-assembling things, including the prospect of self-assembling shelters and bridges.

During the projected period, the military 3D and 4D printing market is anticipated to grow at a CAGR of more than 10 percent (2020 - 2025). The growing requirement to simplify the process of manufacturing parts and components, as well as weapons and equipment, in the defense industry is currently driving the expansion of the military 3D and 4D printing market over the forecast period.

In addition, the increasing investments by the armed services for the reduction of production cost maintenance of military equipment, as well as the high demand for lightweight components, are anticipated to increase the penetration of additive manufacturing for military applications.

With the changes in battlefield requirements, the equipment that changes (shape or properties) in accordance with the environment is likely to help armies gain an upper hand. To have this tactical advantage, investments in 4D printed weapons are anticipated to grow rapidly in the future.

4.3 Automotive industry

The automobile industry requires systems and subsystems that are cost-effective, lightweight, and sustainable [14] due to the emergence of several technologies and the global trend toward pursuing sustainable solutions and products. In the automotive industry, 4D printing technology can be utilized for a wide variety of components. The diverse properties of 4D printing, such as shape-memory and self-healing materials, can be exploited widely in the vehicle industry. Figure 4 demonstrates several automobile applications where 4D printing technology can be applied.

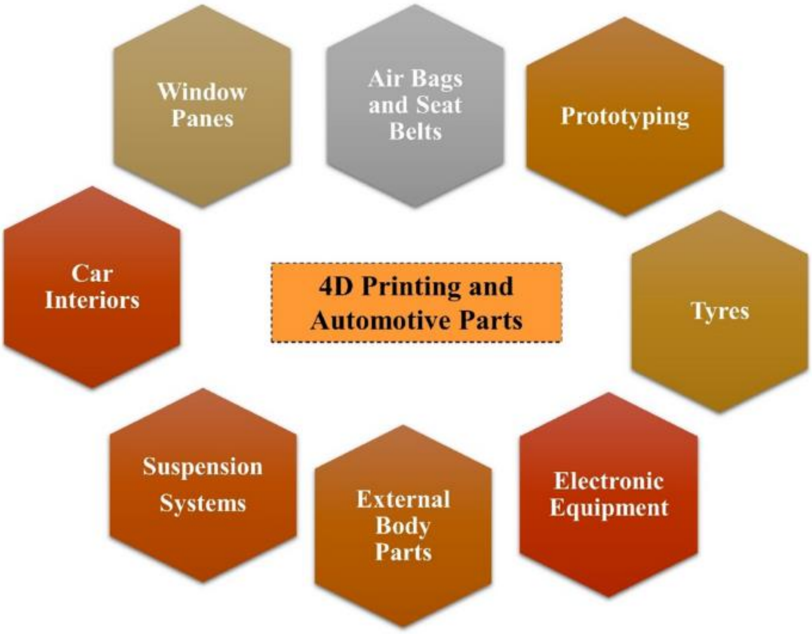

Figure 4 Application areas of 4D printing within the automobile industry

In 2016, BMW celebrated 100 years with a 4D printed VISION NEXT 100 concept car. According to BMW, 4D printed self-driving cars with augmented reality windshields and shape-shifting fenders might be the answer. To celebrate its centennial anniversary, the German car giant today unveiled the VISION NEXT 100, the first in a series of conceptual car designs that invite us into BMW's vision for the next 100 years of driving.

Figure 5 Exterior Design for BMW Vision Next 100 (2016).

4.4 Consumer goods

The creation of consumer goods is another sector that 4D printing could revolutionize. For instance, the technology might be utilized to produce flatpack chairs and tables that self-assemble upon being activated.
Once purchased, 4D-printed furniture would self-assemble, eliminating the need to open a box and physically assemble each component. This could ultimately result in products that require less storage space and are easier to move.

Figure 6 Programmable Table designed as a result of MIT's Self-Assembly Lab, the prototype is able to transform to full functionality.

4.5 Constructions

This should not come as a surprise. Together, 4D technology and SolidFace would change the housing and construction industries. The utilization of enormous 3D printers to manufacture dwellings is of particular interest to engineers, especially as a means of reducing the suffering of thousands of people in undeveloped nations.
4D would significantly improve the global response to natural catastrophes and emergencies, which might otherwise devastate a region.

5. 4D printing applications in healthcare

This part of this paper provides a detailed overview of the current state-of-the-art healthcare applications. Recent research has investigated a new field that combines 3D and 4D printing with medicines. As a result, numerous pharmaceutical and medical device and formulation ideas that can be printed and possibly individualized have developed. Figure 7 shows some 4D printing techniques and their applications in Healthcare
Numerous developments have occurred in the healthcare profession because of the advent of 3D printing. However, because 3D printing outputs are rigid in nature, the flexible products of 4D printing technology allow organ parts to be tailored based on the patient's look. 4D printing can therefore be used to construct bones, ears, exoskeletons, windpipes, jawbones, eyeglasses, cell cultures, stern cells, blood vessels, vascular networks, tissues, and organs, as well as novel dosage forms and medicine delivery devices. The use of 4D printing in healthcare permits the customization and individualization of medical items, medications, and equipment, which is advantageous for both healthcare practitioners and patients. Personalized 4D-printed implants, fixtures, and surgical instruments, for instance, can shorten the time required for surgery and patient recuperation while enhancing the success of the implant or surgery.
The basis of 4D printing technology is intelligent material, which enables printed objects to be more flexible, expandable, and deformable in reaction to specific stimuli [15]. In medical devices, responsive structures, such as soft robotics and printed actuators, have gained increasing interest in 4D printing. The 4D printing concept investigates a new area of additive manufacturing research that has the potential to increase the capabilities of both 3D and 4D printing technologies. This section seeks to provide a concise overview of the essential aspects of 4D printing technology and their expanding medical applications. As 4D printing may facilitate the adoption of soft robotic technology, such as flexible sensors and actuators.
4D printing is an emerging technique, where a time of usage is also integrated with 3D printing, in which printed medical models become capable of changing their shape and functionalities. This time-dependent shape model also provides a high potential for biomedical scaffolds and various other essential purposes. It has various emerging applications in medicine, and Table 2 discusses important ones.

Table 2 4D printing applications in the medical field [16].

Healthcare application	Description
Complex surgery	• It could produce a haptic model to represent the movement of the body as well as appearance. • In future, it can well be adopted for quite complicated surgery, which is not possible, by other manufacturing technologies. • It can produce a model by using a smart material with the help of CT and MRI scan that accurately replicate hand or another body movement. • It can represent anatomical details in a precise and accurate manner.
Manufacturing of smart medical devices	• This technology can manufacture 3D-printed complex smart medical devices, which have excellent functional properties. • Adjusted as per requirement of surgery concerning time
Skin Graft	• It has great possibilities to print skin graft like original colour of the patients. • Also useful for the burn patient which will easily implant in the patient body and grows like an original
Printing of heart, kidney and liver	• In the future, 4D printing can print heart, kidney and liver by using the smart material. • Ability to print these parts which have great flexibility with precise fit and perfect genetic match
Dyspnea (Breathing problem)	• 4D printing technology save lives of babies, which are suffering from Dyspnea (breathing problems). • It quickly creates a medical implant which can change shape over time as babies grew and helped them keep breathing
Smart medical implants and tissue engineering	• 4D printing creates exciting possibilities of the shape-shifting material. • Its potential application could use for medical implants and tissue engineering that change their shape inside the body. • Used for regeneration of those tissues where mechanical properties vary dynamically as our body gets active, such as muscle, bone, and cardiovascular tissues.
Smart multi-material printing	• Use UV curable polymer to layer-by-layer technique. • It is a new process for printing customizable smart multi-material printing of medical implants. • Clearly, show multi parts of the body in the 3D printed body
Smart stent	• 4D printing could develop stents, which can be expanded, and take required shape with the help of heat of the patient body. • This latest solution act quickly to save a patient's life for complicated surgery. • A shape gets changed w.r.t time and temperature
Organ printing	• This emerging technology applies to fabricate complex 3D organ. • Used to print organs where own cells of the patient are applied and save a life. • It is a promising solution for organ shortages.

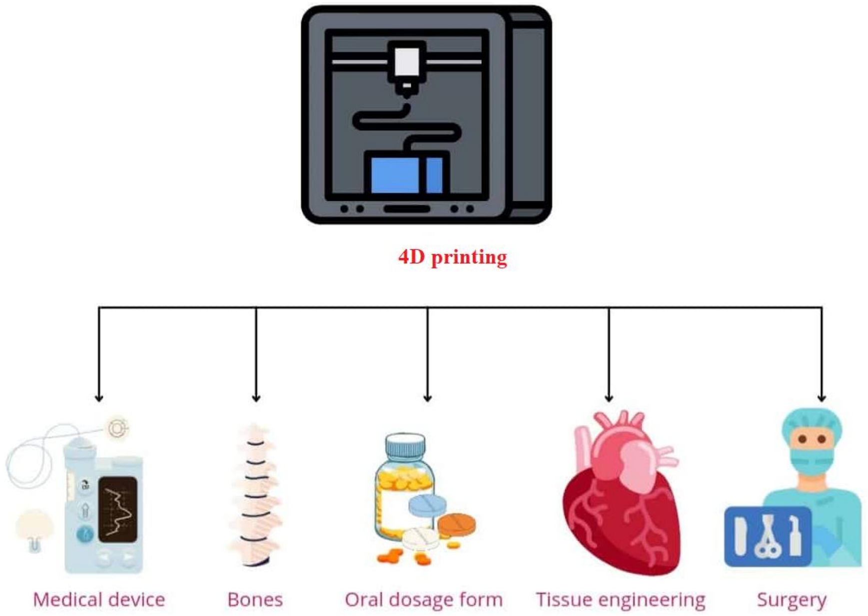

Figure 7 4D printing techniques and their applications in Healthcare.

6. Global 4D Printing in Healthcare Market Size and forecasting

The North American region, particularly the United States, is among the lead innovators and pioneers, in terms of the adoption, of additive manufacturing. It is expected to retain its position as the market leader, over the forecast period. Figure 8 illustrates the 4D printing market- growth by region (2020-2025).

Figure 8 4D printing market- growth by region (2020-2025), Source: Mordor Intelligence

4D Printing In Healthcare Market size was valued at USD 17.99 Billion in 2020 and is projected to reach USD 73.81 Billion by 2028, growing at a CAGR of 19.20 % from 2021 to 2028.
Global 4D Printing In Healthcare Market is likely to witness exponential growth due to its extensive application in the industry and constant technological innovations. 4D printing is an up-gradation of 3D printing technology based on a similar production method with one difference being in the materials utilized for the production process. It is the latest technology in healthcare that is going to revolutionize the artificial organs and prosthetics industry. The 4D printing is evolved in 3D prints where the fourth dimension is the time and shape of the product that can change within time. 4D printed models possess the advantage that changes the shape of the 3D printed model after its publication**.** Figure 9 shows 4D printing in healthcare market growing in the world from 2021 to 2028.

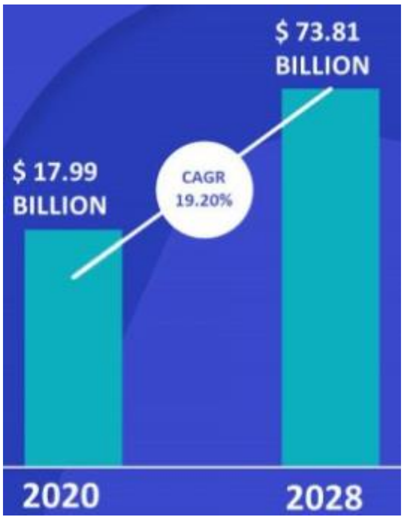

Figure 9 4D printing in healthcare market growing from 2021 to 2028.

Conclusion

As it was presented in this paper, there has been a rapid and significant development in 4D printing, especially for healthcare applications. This paper presented a comprehensive overview of the basic mechanism of 4D printing technology and its application in addition to the use of this technology in healthcare fields and other applications. Also, this paper showed that the 4D printing market size will grow exponentially over 2020-2028, because it is driven by the rapid deployment of the technology across the manufacturing sector due to its self-assembling and reshaping capabilities, alongside the increasing R&D activities to broaden its application scope in industries like construction and electronics..

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