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Review Article

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Fundamentals of 3D Printing in Medical & Pharmaceutical Sector and its Approaches

Nikita M*, Sakshi G, Kshitija A, Amit k, Hemant R and Shaikh MRN

MET's Institute of D Pharmacy, India

***Corresponding author:** Nikita Maske, MET's Institute of D Pharmacy, Adgaon, Nashik, India, Email: amitkakad12@gmail.com

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Abstract

As the fourth industrial revolution approaches, the technological revolution has a tangible impact on every production sector. In this new environment, three-dimensional (3D) printing has already demonstrated its promise with impressive uses in the creation of medicine delivery systems. Global research efforts have been focused on the notion of personalising the dosage form through better formulation functions or individualised medicinal doses. To encourage the real-time manufacture of pharmaceutical goods in dispersed locations, important elements that go beyond the manufacturing level must be taken into account. The majority of current research efforts are devoted to developing 3D-printed medicine delivery systems and illustrating various installation possibilities for 3D printers in the pharmaceutical, community, and hospital sectors as well as in patients' homes. A wide range of factors are presented by this research that need to be taken into account in order to incorporate 3D printing into a future healthcare system. Of particular importance are regulatory concerns, drug shortages, product quality assurance, and the public's and healthcare professionals' acceptance of these scenarios. This review's goal is to critically show the range of possibilities that might lead to the use of 3D printing in healthcare in the future and to talk about the concerns that will inevitably come up.

Keywords: 3D Printing; Medical Applications; Healthcare

Abbreviations: SLS: Selective Laser Sintering; SLA: Stereolithography; FDM: Fused Deposition Modelling; UCL: University College London.

Introduction

Some media, like the Financial Times, have stated that 3D printing, or additive manufacturing, may surpass the size of the Internet. For some, this is the case. It is urged by several others that this is only a product of the incredible hype around this thrilling field of technology. Thus, what exactly is three-dimensional printing, and for what purposes are they typically used? Through the process of layering down consecutive layers of material, 3D printing is a type of additive manufacturing technique that creates three-dimensional objects. A machine that is suitably sized and linked to a computer that has the object's blueprints is used to quickly produce 3D items using a process also known as fast prototyping. Almost everyone finds the idea of personalised manufacturing through 3D printing appealing. This ground-breaking approach of using inkjet technology to create 3D models saves time and The fundamental ideas are that of material cartridges, output flexibility, and code translation into observable patterns [1-3].

3D printers are devices that use digital data to create physical 3D objects layer by layer. It may create physical representations of items that have been scanned using a 3D scanner or developed with a CAD programme. It is utilised in many different sectors, such as consumer goods, automotive, aerospace, dentistry, and medical, jewellery, footwear, industrial design, architecture, engineering, and construction.

Perhaps more than any other sector, technology has had an impact on modern human history. Consider a lightbulb, a steam engine, or, more recently, automobiles and aircraft. The World Wide Web is another example. In many respects, these technologies have improved our lives and created new opportunities, but it sometimes takes time-sometimes even decades-for the really disruptive aspects of the technology to show! Many people think additive manufacturing, or 3D printing, has a great deal of potential to be one of these technologies. Nowadays, 3D printing has been widely covered by television networks [2,3].

What exactly is 3D printing, according to many who have predicted it will revolutionise design, eliminate conventional manufacturing as we know it, and have an impact on our daily lives in terms of geopolitics, economics, social issues, demographics, the environment, and security? The fundamental idea that sets 3D printing apart is that it is an additive manufacturing technique. And this is really crucial because 3D printing is a completely new kind of manufacturing that uses cutting-edge technology to manufacture items at the sub-millimeter scale, layer by layer. This differs radically from all other conventional production methods now in use! Traditional manufacturing, which has historically relied heavily on human labour and the "made by hand" mentality dating back to the French term for manufacture's etymology, has a variety of drawbacks. But, the industrial landscape has evolved, and automated procedures like forming, casting, machining, and moulding are now (relatively) novel, intricate operations requiring equipment, computers, and robotics. But all of these technologies require removing material from a bigger block in order to build a tool for casting or moulding operations, or to create the final product itself. This poses a significant challenge to the production process as a whole [3,4].

Traditional design and manufacturing methods impose a variety of undesirable limits for many applications, such as the necessity for intricate part assembly, fixtures, and the costly tooling noted above. In addition, up to 90% of the initial material block may be lost during subtractive manufacturing procedures like machining. On the other hand, depending on the technology being utilised, 3D printing is a method of directly producing items by adding material layer by layer in a number of methods. Simplifying the philosophy underlying 3D printing, it may be compared to the automated construction of anything out of Lego blocks for those who are still struggling to grasp the idea (which is a lot of people) [1,2].

Every designer is aware of the magic involved in turning an amazing concept into a real, usable product that you can touch in your hands. It might be a consumer product that is displayed on a store shelf, a vital part of a manufacturing device, or even a tangible prototype that first shows off your innovative concept to the public.

Physical prototypes may dramatically convey your concept in a way that goes beyond drawings or computer models. They might be simple and blocky or perfectly realised in shape, texture, and colour. Instead than just making assumptions about the product, they enable the viewer to learn more about it and engage with it. People will be able to touch, feel, spin, and even turn the object upside down before it is ever manufactured. They have plenty of time to test, operate, and thoroughly assess it before the final product is released into the market. For some of the most brilliant and demanding designers and engineers in the world, this ideal is really a reality.

On-demand prototypes, which can be obtained in a matter of hours from the moment the "print" button is pressed on a sleek, silent machine in an ordinary office setting, improve communication within the product development team, shorten design cycles, launch superior products ahead of the competition, stretch R&D budgets, increase accuracy, reduce costly errors, generate unexpected ideas, drive innovation and quality, and enhance coordination between engineering, sales, marketing, and the executive team.

This paper will first discuss the origins and development of 3D printing, then go into great detail on how a 3D printer creates a physical model, and then look at the characteristics that set a 3D printer apart and the technological choices that led to those characteristics [1,3,4].

History

The concept of 3D printing originated in the early 1970s, when Pierre A. L. Ciraud published a description of a process for applying powdered material and then using a high-energy laser to solidify each layer. Meltable materials, such metals or polymers, might hypothetically be utilised in this situation to prepare the thing. Early in the 1980s, Carl Deckard developed a technique for solidifying powdered bed by laser beam known as selective laser sintering (SLS), and Ross Housholder described an idea of sand binding by different materials in a patent titled "A moulding process for forming a three-dimensional article in layers" [1,5].

Stereolithography (SLA) was the first technology developed by Chuck Hull that was made available for purchase. The

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photopolymerization of liquid resin by UV light served as the basis for this technique. Scott Crump applied for a patent towards the close of the 1980s for fused deposition modelling (FDM), a method of preparing objects using thermoplastic material. "Three-dimensional printing techniques" were developed in the 1990s by Emanuel Sachs, an MIT scientist, and his colleagues. These techniques used binding material to link specific powder areas [5,6].

Gradually Changes in these Years

Older people or those on complicated dosage schedules where polypharmacy is prevalent and results in a high pill load may benefit from 3D printing. Research has shown that polypharmacy increases the likelihood of dosage mistakes by causing patients to become confused and noncompliant.

Low-dose antihypertensive polypills including atenolol, ramipril, pravastatin, aspirin, and hydrochlorothiazide were created using FDM 3D printing in a 2015 study. It should be mentioned that, although it is possible to print polypills using 3D printing, this will probably only work for medications with modest therapeutic dosages (microgram to milligramme dose strength) in order to guarantee that the formulation's size is appropriate for administration.

A partnership was announced in June 2021 between Gustave Roussy, a world-class oncology hospital in Paris, and FabRx, a biotech spin-out from University College London [UCL] with the goal of bringing multi-drug 3D printed formulations into the clinic. Under this partnership, customised, multi-drug 3D printed dosage forms will be created to treat patients with early-stage breast cancer by combining anti-side effect and anticancer medication into a single tablet. In contrast to the conventional treatment regimen, the printed medications will be evaluated in a multi-center clinical investigation to see how well they improve patient outcomes, adherence, and acceptance [7].

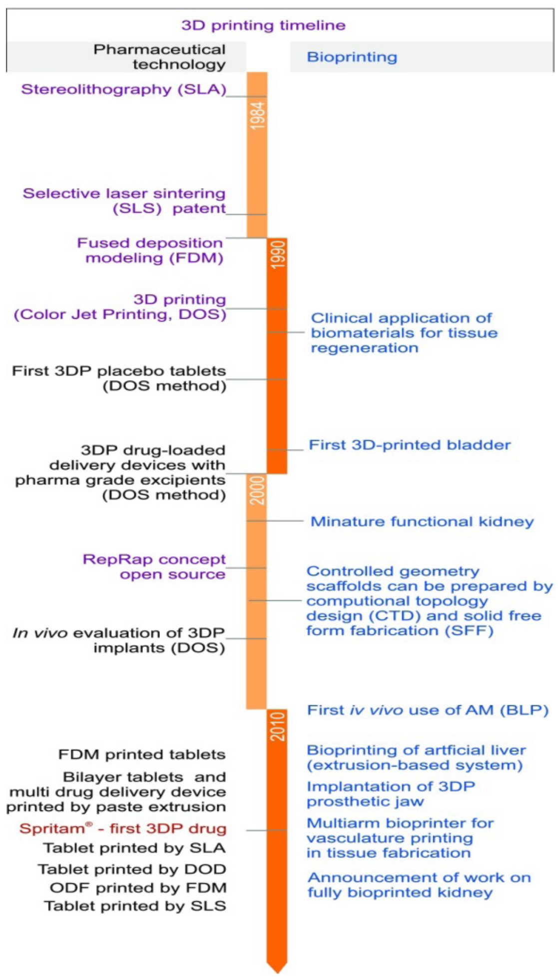

Figure 1: Presents the Most Significant Advancements in 3D printing for use in Biomedical and Pharmaceutical Applications.

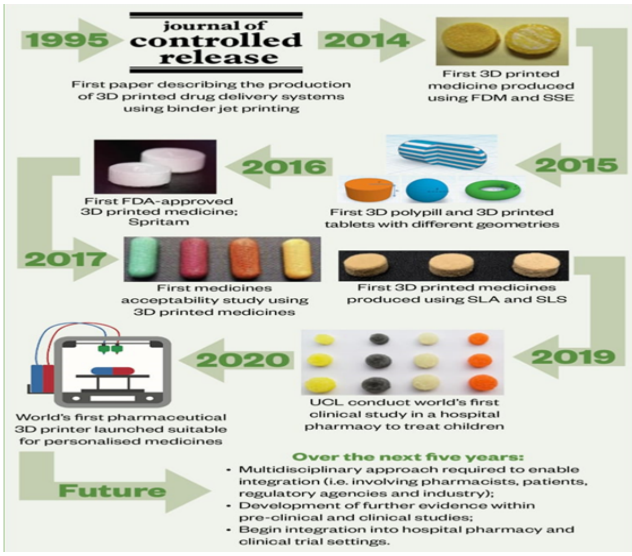

Figure 2: Development of Drug with Years.

Working

Over the course of the nearly 40 years that 3DP has existed, several approaches have been created and have advanced along with technology.

The main methods are based on:

- Powder solidification,
- Liquid solidification,
- Extrusion.

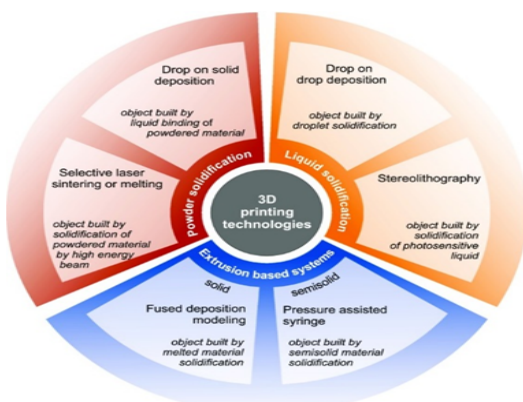

Figure 3: 3DP Methods Applied for Drug Formulation.

3D printing in pharmacy revolutionizes medicine manufacturing by employing innovative techniques such as powder solidification, liquid solidification, and extrusion. In powder solidification, pharmaceutical ingredients are deposited layer by layer and solidified using heat or adhesive agents, enabling precise control over drug composition and dosage. Liquid solidification involves the deposition of liquid formulations onto a substrate, followed by solidification through processes like photopolymerization, yielding complex drug delivery systems with tailored properties. Extrusion, on the other hand, utilizes a continuous flow of material, allowing for the fabrication of intricate drug-loaded filaments or implants [5-7]. These methods not only enhance the efficiency and accuracy of medicine production but also pave the way for personalized medication tailored to individual patient needs.

Despite the Variety of 3DP Techniques, there is Various Steps Involved in getting a 3D-Printed Object Ready

The process of designing a three-dimensional object using computer-aided design software and optimising the geometry to meet printer specifications; exporting the three-dimensional model to a common file format that is recognised by printers, such as STL, which contains only three-dimensional geometry in the form of each vertex position data, or OBJ, which contains additional information about polygonal faces or colour texture coding; importing the file into the software and creating printing layers, the height of which significantly affects both the quality and time of printing the object; the object is then created by applying (or solidifying) material layers specific to the chosen printing technique [6,8].

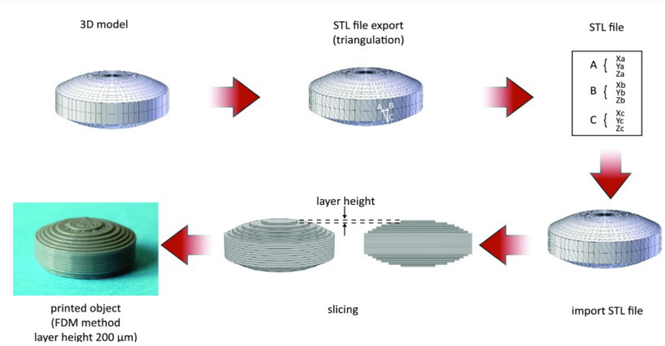

Figure 4: The development of 3D Printed Object.

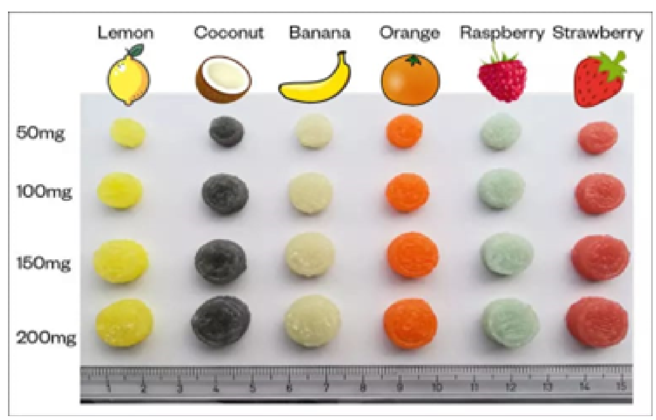

Figure 5: Different Types of Tablet.

Dosage form	API	Excipients	Effect	Ref
Implant	Isoniazide	Powder: PLLA Ink: Acethone, Ethanole, Water	Sustained release	10
Tablets	Captopril	Powders: maltitol, maltodextrin, Ink: Water Polyvinylpyrrolidone	Rapidly dispersing tablets	11
Tablets	Paracetamol 4-Aminosalicylic acid	Poly(ethylene glycol) diacrylate, Poly(ethylene glycol) 300, diphenyl(2,4,6-trimethylbenzoyl) phosphine oxide	Controlled release	12
Microneedles	Insulin	Dental SG resin Xylitol, Mannitol, Trehalose	Insulin skin delivery	13
Drop on drop	Tablets	Ropinirole HCl	Irgacure 2959 Poly(ethylene glycol) diacrylate	14
Orodispersible films	Aripiprazole	Polyvinyl alcohol	Fast disintegration and dissolution	15
Tablets	Theophylline	Hydroxypropyl cellulose, Triacetin, Sodium starch glycolate, Croscarmellose sodium, Crospovidone,	Immediate release	16
Floating tablets	Dipyridamole	Hydroxypropyl methyl cellulose, Microcrystalline cellulose, Lactose, Polyvinyl pyrrolidone	Sustained release, gastrofloating dosage form	17
Multi-compartment tablet	Nifedypine,	Polyethylene glycol 6000, Microcrystalline cellulose,	Controlled release	18
	Captopril,	Hydroxypropyl methylcelloluse,		
	Glipizide	D-Mannitol, Lactose, Sodium starch glycolate, Croscarmellose sodium, Sodium chloride, Tromethamine		

Table 1: Examples of 3D Printed Medicines Prepared with Different 3D Printing Methods.

Medicinal Application

Since the early 2000s, when the technology was initially utilised to create personalised prostheses and dental implants, 3D printing has been employed in medical [6,9]. Since then, 3D printing's medicinal uses have significantly expanded. Reviews that have recently been published discuss the use of 3D printing to create innovative dosage forms and medication delivery systems, as well as bones, ears, exoskeletons, windpipes, a jaw bone, eyeglasses, cell cultures, stem cells, blood vessels, vascular networks, tissues, and organs.

Three main areas may be used to group the present medical applications of 3D printing: the production of tissues and organs; the development of prostheses, implants, and anatomical models; and pharmaceutical research pertaining to dosage forms, drug transport, and discovery. These medicinal uses are then discussed [9-19].

Bio Printing Tissues and Organs

The shortage of organ donors for transplant surgery poses a significant medical challenge, with thousands of patients waiting for life-saving organs each year. Traditional treatments rely on finding compatible donors, which is often difficult and costly. However, advances in tissue engineering and regenerative medicine offer hope for a solution. 3D bioprinting technology, which constructs tissue-like structures layer by layer, shows promise in creating replacement organs using a patient's own cells [18,20]. This method provides precise control over cell placement and can use various biomaterials tailored to different tissues. Although still in its early stages, bioprinting has shown success in creating tissues like knee menisci and heart valves, as well as assisting in unique medical cases, such as fabricating a tracheal splint for a baby with tracheobronchomalacia. Additionally, biotech companies are exploring the use of bioprinted tissues for drug screening purposes, potentially reducing research costs and time. While challenges remain, the development of bioprinting technology holds great potential for addressing the organ donor shortage and improving personalized medicine [20].

Challenges in Building 3D Vascularized Organs

Although bioprinting has proven successful in producing small, straightforward organs, the vascularization required for bigger, more complicated organs like kidneys, livers, and hearts presents difficulties. Blood arteries are necessary for these organs to get oxygen, nutrition, and waste removal. The exact integration of circulatory networks required for these organs to operate has not yet been accomplished by current bioprinting techniques. But encouraging progress has been made in the field of bioprinting, especially with TIJ printers, which hold the promise of producing complex vascular systems [18,20]. A major step towards resolving this obstacle in organ bioprinting has been taken recently with the successful bioprinting of functional capillary networks through cooperation between academic institutions [21].

Anatomical Models for Surgical Preparation

Because 3D-printed models may give realistic representations of a patient's anatomy, they are helpful for surgical preparation and training. These models provide surgeons with a deeper grasp of intricate systems, such neuroanatomy and spinal abnormalities, than 2D MRI or CT images, which lack depth. They are very helpful in practicing difficult situations and figuring out the best surgical pathways, which lowers the possibility of surgical mistakes. Furthermore, 3D models support training for operations such as colonoscopies, which are essential in the fight against colorectal cancer. These models have been successfully utilised by forward-thinking surgeons to design complex surgery, including liver transplants, with improved accuracy and less tissue loss. Because they are constructed from materials that mimic actual tissues, these models improve patient outcomes by enabling realistic surgical simulation [22,23].

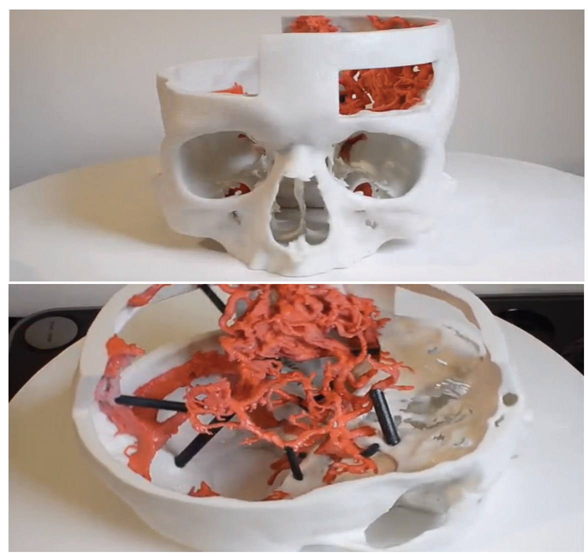

Figure 6: A 3D model used for surgical planning by neurosurgeons at the Walter Reed National Military Medical Centre.

Custom 3D-Printed Dosage Forms and Drug Delivery Devices

Pharmaceutical research and production presently use 3D printing technologies, which present a huge transformational opportunity. The capacity to construct dosage forms with complex drug-release patterns, great repeatability, and exact control over droplet size and quantity are some of the main benefits. Furthermore, the standardisation, simplification, and viability of complicated medication production procedures are also potential benefits of 3D printing. It is also expected that the technology would play a significant role in the development of personalised medicine [8,24].

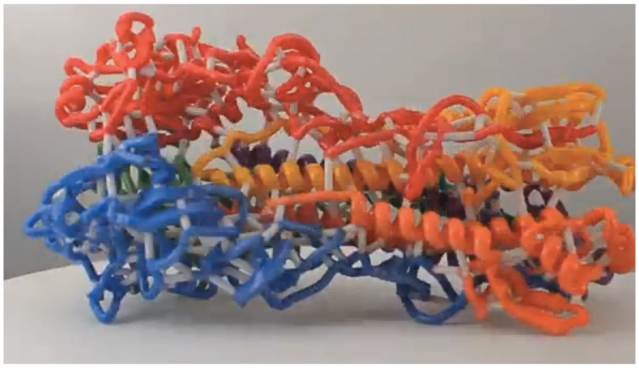

Figure 7: 3D-Printed Representation of an Influenza Hemagglutinin Trimer.

Unique Dosage Forms

Inkjet-based and inkjet powder-based 3D printing technologies are the primary ones used in the pharmaceutical industry. In powder-based printing, ink is sprayed onto a powder foundation to create layer-by-layer solid dosage forms; in inkjet printing, drugs and binders are sprayed as precise droplets onto a substrate. These techniques allow a variety of active and inert components to be used in the production of different dosage forms, such as microcapsules, matrices, and drug delivery systems. pharmaceuticals such as vitamins, antibiotics, and anti-inflammatory pharmaceuticals may be used in ink compositions; inactive substances include solvents, polymers, and surfactants [8,24].

Future Trends

Personalised medicine might be revolutionised by 3D printing, which would make it easier to customise medications, organs, and nutritional goods. It is anticipated that 3D printing will proliferate, especially in pharmacy settings, and might completely transform current approaches to the production and delivery of pharmaceuticals. One possible situation is that pharmacies get databases of drug formulations by email from pharmaceutical corporations, allowing for on-demand drug printing. This change might significantly transform current procedures, making them more affordable and accessible [24,25].

Furthermore, 3D printing presents exciting opportunities for customised medicine in the future, such as printing a patient's tissue to evaluate the efficacy of a treatment. Furthermore, cutting-edge concepts such as using a child's baby tooth stem cells to generate new tissues and organs for life hint at the technology's transformational potential. The bioprinting of intricate organs is made possible by the progress of 3D printing technology; experts predict that in the next 20 years, a printable, completely functioning heart will be possible. Considerable progress has been achieved in printing vascular networks despite current obstacles, providing encouraging signs for the development of organ fabrication in the future. It is expected that complex heterogeneous tissues, such liver and renal tissues, would be effectively produced as technology advances. This finding may pave the way for printed tissue and organ models that are essential for enhancing drug development, as well as functional living implants [24,25]. Another fascinating frontier is in situ printing, which allows for the direct printing of implants or living organs within the body while surgery is being performed. With the use of digital control and developments in robotic bioprinters, this method has the ability to precisely treat a variety of lesions. With potential to expand this technique to the repair of sick or partially damaged internal organs, in situ bioprinting has already shown promise in the healing of external organs such as the skin. Advances in robot-assisted surgery and the creation of portable 3D printers for direct tissue repair hold promise for expanding the applications of 3D printing in personalised medicine [25].

Conclusion

Including the medical area, 3D printing has emerged as a practical and maybe revolutionary instrument. Six Applications have grown along with printer capability, resolution, and material availability. Six Scholars persistently strive to enhance current medical applications utilising 3D printing technology and investigate novel ones. Six Even though 3D printing has already produced substantial and fascinating medical advancements, some of the most ground-breaking uses, like organ printing, will take some time to develop.

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