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(Review Article)

3D Printing in Medicine: Revolutionizing Modern Healthcare: A Comprehensive Review

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Abstract

3D printing is transforming healthcare by providing customized and affordable medical components such as prostheses and implants. This technology enables surgeons to work more efficiently with tools and models specifically designed for individual patients, while also allowing medical device manufacturers to develop new products more quickly. Additionally, 3D printed tissues have the potential to enhance drug research and development, which could lead to lower costs and greater accessibility to medications. In the realm of education, 3D printing offers realistic anatomical models that improve hands-on learning experiences compared to traditional models. This paper reviews the role of 3D printing and bio-printing in healthcare, outlining the necessary steps for implementation and the facilities that support this technology. It also highlights significant applications of 3D printing in the medical field, demonstrating its potential to improve patient care and medical training.

Keywords: 3D printing, implants, Medical device, Bio-printing, medical training

INTRODUCTION

3D printing is an impressive technology that is expanding across nearly all areas of healthcare. It merges medical and technological applications to address the current needs of the health system. This technology originated in the late 1980s with a process known as stereolithography and has rapidly gained popularity since then. This incredible technology utilizes fabrication science along with various construction techniques to build different materials, referred to as inks, layer by layer in a variety of shapes and forms. It is centred on additive manufacturing (AM) and rapid prototyping. Traditional manufacturing methods have played a key role in the industrialization that shaped modern society, but they come with fundamental flaws that call for new approaches.

Additive manufacturing encompasses a range of new technologies that create objects from scratch, adding one cross-sectional layer at a time. This process begins with computer-aided design (CAD) software, which creates a 3D model of the item. Specialized software then slices this model into multiple layers, generating a file that the AM machine can interpret. The machine then builds the object by layering the inks. Some of the most notable printing technologies include selective laser sintering (SLS), stereolithography (SLA), inkjet 3D printing, extrusion, laser-assisted printing, and selective laser melting (SLM). 3D printing has numerous applications, particularly in healthcare sectors such as therapeutics, orthodontics, and medical devices, and these innovative technologies are increasingly streamlining the process. Three-dimensional (3D) printing, particularly bioprinting, is quickly becoming a significant innovation in the pharmaceutical industry. In the past decade, it has expanded into various fields, including aviation, defence, automotive, architecture, film, and healthcare. Its relevance in pharmaceuticals has notably increased in recent years. During this process, computer-aided drug (CAD) models are created using specialized software and then sent to bioprinters. These printers interpret the material inputs to construct the model scaffolds. Techniques such as stereolithography, selective laser sintering, and inkjet-based printing help accelerate the printing process. The advantages of 3D printing include rapid prototyping, flexible designs, on-demand production, lightweight yet strong components, cost-effectiveness, and environmental sustainability.

3D Printing Techniques

3D printing is based on additive manufacturing (AM), which constructs objects layer by layer, in contrast to traditional manufacturing methods. This technology represents a significant breakthrough that has the potential to transform industries and establish new business models. The process begins with creating a 3D model using software such as computer-aided design (CAD). This model is saved in a format known as .stl, which converts it into a series of triangles that the printer can understand. During the printing phase, the model is divided into sections, and the material is layered to produce the final object.3D printing has revitalized various fields, enabling the production of items that are challenging or impossible to create using conventional methods. The choice of printing technique depends on how the layers are formed and the types of materials used, which can include solids, liquids, or powders, such as metals, ceramics, and polymers. Metals have several advantages over other construction materials, such as their ability to absorb laser energy and their stability at higher temperatures. As a result, metals are becoming increasingly popular in this technology, where polymers have been predominantly used for many years.

Fused deposition modelling [FDM]

Stereolithography [SLA]

Selective Laser Sintering [SLS]

Selective Laser Melting [SLM]

Material Extrusion

Bio-printing Fused Deposition Modelling

Fused Deposition Modelling (FDM) is a 3D printing method that uses two heated nozzles. One nozzle extrudes melted thermoplastic material, while the other adds temporary support material. The thermoplastic is melted and laid down in layers on a build platform where the layers stick together. It uses molten thermoplastic polymers, such as acrylonitrile butadiene.

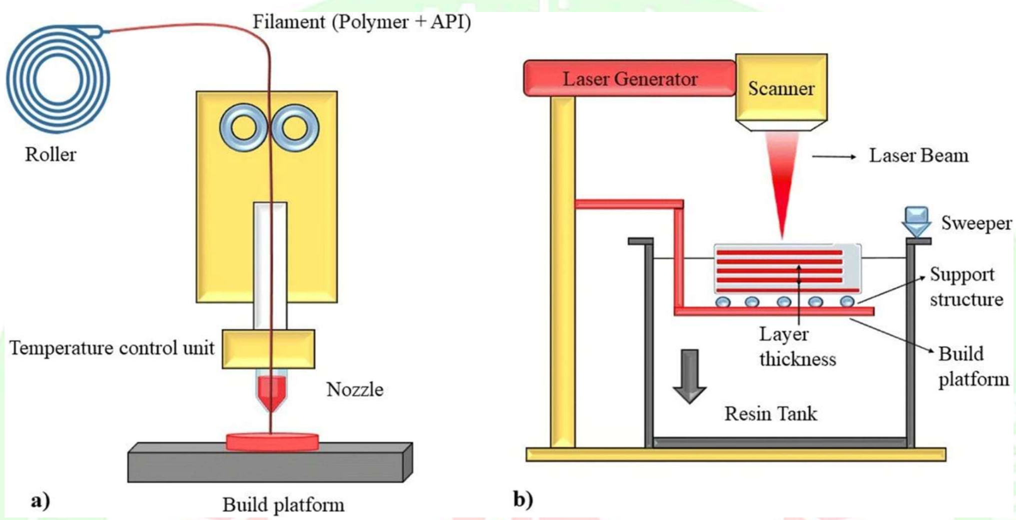

Figure 1: Bio-printing Fused Deposition Modelling

styrene (ABS) and polylactic acid (PLA), which are heated above their glass transition temperature and applied in layers. This process builds up the desired 3D model, with each layer fusing together.

FDM's effectiveness depends on factors like filament feed rate, plotting speed, and layer thickness. Stewart et al. developed an implantable system using 3D printing to deliver different samples, with varying release rates based on implant design and sample characteristics. They also created a rate-controlling membrane to extend the release, highlighting its potential for treating serious illnesses. FDM can use multiple nozzles with different materials, which allows for varied compositions, although this hasn't been fully achieved yet. Important factors for choosing materials in FDM include how well they transfer heat and how they flow. Common materials used include PVC, nylon, ABS, and casting wax because they have low melting points. For medical applications, polycaprolactone (PCL) is commonly used because it melts at around 60°C and has a low glass transition temperature of -60°C. Poly(lactic-co-glycolic acid) (PLGA) is also used, but it is more challenging to process because it requires higher temperatures (110-140°C) due to its glass transition temperature of 40-60°C. Bhupendra Raj Giri, Eon Soo Song, Jaewook Kwon, Ju-Hyun Lee, Jun-Bom Park, and Dong Wuk Kim proposed a method for producing gastro-retentive floating tablets using theophylline as a model drug. These tablets demonstrated sufficient buoyancy for about 10 hours and followed zero-order drug release patterns, proving to be an efficient and cost-effective solution for gastro-retentive dosage forms with improved controlled release rates. Important factors that influence the strength of the printed parts include the thickness of each layer, the orientation of the filaments, their width, and the air gaps between layers. Mechanical weaknesses often arise from distortion between layers.

FDM has several advantages, such as being relatively fast, cost-effective, and straightforward to operate. However, it also has some drawbacks, including weak mechanical properties, poor surface finish, a visible layer structure, and a limited range of materials. The use of fiber-reinforced composites can enhance the strength of FDM-printed parts, but challenges like bonding issues and fiber orientation persist.

Stereolithography (SLA): Stereolithography (SLA) is the first technology for rapid prototyping, developed in the late 1980s. It uses a laser to cure liquid resin layer by layer. In the bottom-up method, the platform that holds the cured part lowers, allowing new resin to spread over it. In the top-down method, light shines through a transparent plate to cure the resin. To speed up the process for larger parts, a technique called masked lamp curing allows an entire layer to be cured at once. After the part is built, any leftover liquid resin is drained, and post-curing in a UV oven strengthens the final product. The speed and thickness of the curing process depend on the chemical reactions involved, which can be adjusted for better results. This technique involves using a special polymer known as photopolymer, which alters its characteristics when exposed to UV or infrared light. It offers advantages such as high surface quality and the ability to produce very detailed 3D prints. However, it also has significant drawbacks, including brittleness, low impact strength, and limited resistance. Additionally, photopolymers have a short lifespan as their properties can degrade over time.

Healy and his team developed a new formulation of photopolymer resin using the SLA method, testing it with aspirin and paracetamol. They experimented with different ratios of the polymers and drug dosages, discovering that the medications were released gradually over time. The 3D printing process enhanced both the therapeutic loading capacity and the release kinetics. Xu and his colleagues also applied this technique to create 3D printed dosage forms for several antihypertensive medications, including irbesartan, atenolol, hydrochlorothiazide, and amlodipine. They successfully achieved polymerization but observed an unusual dark reaction between the photopolymer and the drugs. They concluded that a more effective screening process is necessary to ensure compatibility between the drugs and the polymer. SLA (Stereolithography) is utilized in the medical field for creating detailed anatomical models that assist in surgical planning and for making moulds for medical devices. For instance, titanium dental implants can be produced by machining titanium based on SLA models

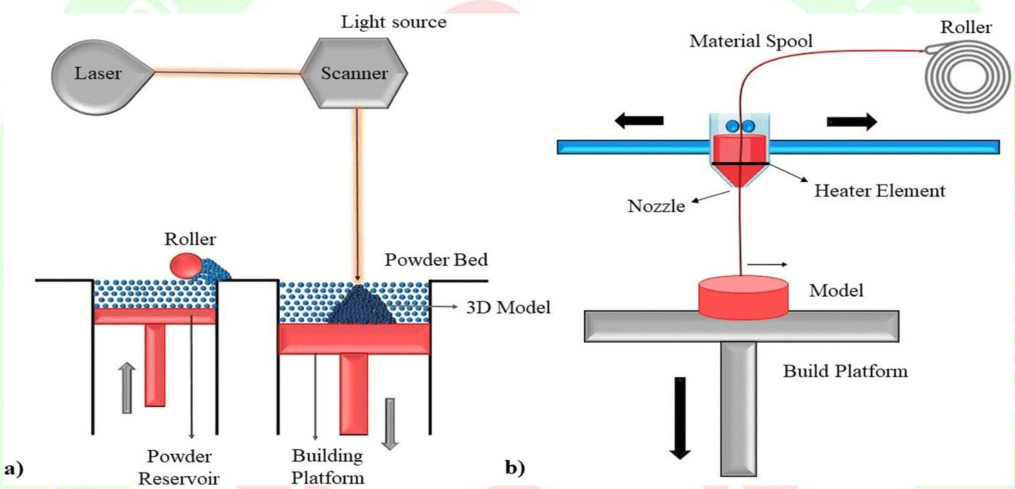

Figure 2: Stereolithography

The advantages of SLA include its capability to create intricate shapes with internal structures, the ease of removing excess resin, and achieving very high detail resolution (around 1.2 micro meters). However, there are some drawbacks, such as the limited availability of biocompatible resins, and certain materials used can be toxic to cells. Additional challenges include the presence of unreacted materials and difficulties in designing certain features without support structures, which can be tough to remove. Recent advancements have focused on expanding the range of available resins and enabling the use of multiple types of resins within a single build.

Selective Laser Sintering (SLS):

Selective laser sintering (SLS) falls under the category of powder bed fusion (PBF). In this process, a laser is used to melt a mixture of polymers that contains medication. SLS printers typically utilize CO2 lasers, which are effective for a variety of thermoplastic polymers.

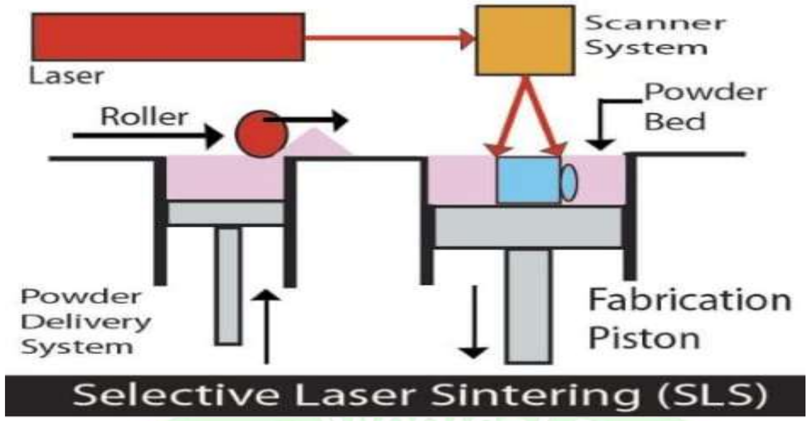

Figure 3: Selective Laser Sintering

The quality of the final product is influenced by factors such as temperature, laser intensity, scanning speed, and layer density. SLS is capable of producing detailed models at room temperature, although there are concerns regarding the mutagenic properties of some polymers. Research conducted by Fina and all. Demonstrated that SLS can create high-resolution objects loaded with paracetamol from different polymers, enabling personalized medication without the need for redesigning the formulation for each case. Thakkar and all applied SLS to develop a three-dimensional dosage form for nifedipine, a light-sensitive medication. They investigated how varying polymer concentrations affected the drug's stability and transitions during the SLS process.

Selective Laser Melting (SLM):

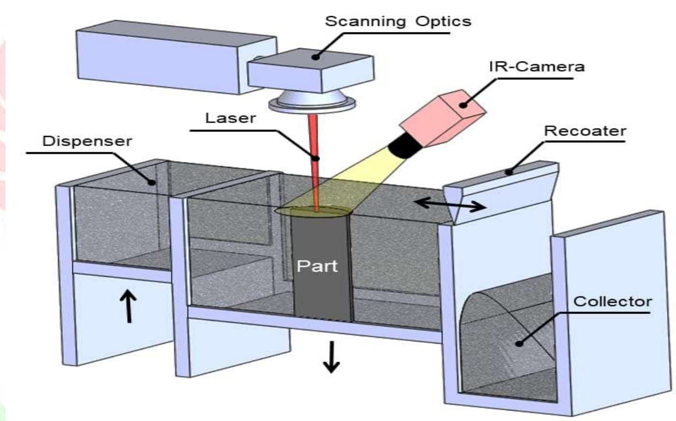

Figure 4: Selective Laser Melting (SLM)

Selective laser melting (SLM) is a form of powder bed fusion that is similar to selective laser sintering (SLS). This method involves using a bed of powder granules with a specific density. A laser serves as a heat source to melt the powder particles, and as the temperature decreases, the molten material solidifies into the desired shape. Some of the powder remains un melted to provide support for the object during the process. Once the fabrication of the object complete, the unused powder is removed.

Material Extrusion: Fused deposition modelling (FDM) is a widely recognized 3D printing technique that involves melting thermoplastic polymers and depositing them layer by layer to form a model. A nozzle moves across the work area, extruding the melted polymer, which then cools and solidifies

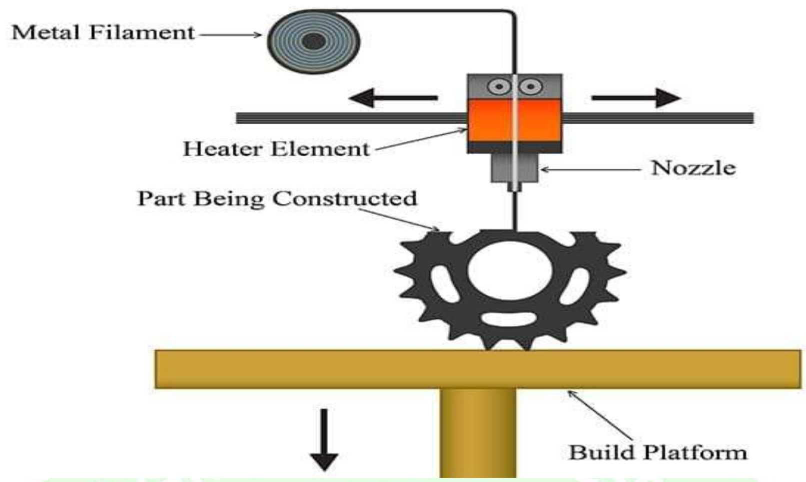

Figure 4: Bio-printing

This method is particularly effective for creating scaffolds and hydrogels. Researchers, such as Burdick, have demonstrated that incorporating special networks into hydrogels can enhance the printing process. These networks feature strong connections that provide stability to the printed structures and improve the fusion of layers. However, FDM does have some drawbacks, including the need for cross-linkers, the requirement for heat, and a slower printing speed compared to other methods. Bio-printing: Bioinks are a crucial component in the 3D printing process, particularly in the fields of tissue engineering and organ creation. This technique is especially beneficial for addressing issues related to bone fractures and defects. The application of bioink technology holds significant promise in areas such as the implantation of metal prostheses, bone grafting, biomineralization, and the formation of new bone tissue. One of the primary advantages of this method is its potential to reduce costs, minimize waste, and decrease production time when compared to synthetic approaches. The fabrication techniques can be divided into two main categories: extrusion and laser-based methods. Extrusion involves the use of mechanical or pneumatic systems to deposit layers, while laser-based methods utilize lasers to induce thermal stimulation. Kondiah and his colleagues utilized this technology to develop a bone model aimed at evaluating the strength, resilience, and porous characteristics of the bone matrix. They incorporated Simvastatin, a model drug, into the scaffolds and conducted a thorough characterization of the results.

Their optimized formulation demonstrated effective therapeutic delivery for over 20 days and resulted in the generation of a pseudo-matrix. The findings confirmed that the model's strength, resilience, and morphology closely resembled those of human bone. Recent advancements in bioplotting materials include substances like PLGA, TCP, collagen, and chitosan, as well as composites made from collagen, alginate, and silica that are coated with hydroxyapatite (HA), soy protein, and a mix of agarose and gelatin. In vitro studies have utilized mouse pre-osteoblasts and human mesenchymal stem cells, while in vivo studies have focused on defects in sheep skulls. These materials are primarily applied in bone tissue engineering and tissue regeneration. In the context of bio-printing, materials such as agarose containing human umbilical vein smooth muscle cells (HUVSMCs), gelatin-HA-tetraPEG-DA combined with NIH 3T3 cells, and alginate droplets are commonly used. The main applications here are related to vascular tissue engineering. Recent research has shown the ability to bio-print single cells and cell-laden hydrogel-PCL scaffolds. Techniques like "Block-Cell-Printing" enable high-throughput printing of single-cell arrays. Microfluidic arrays are used to capture individual cells, allowing for the study of cell communication. In one study, primary rat cortical neurons that were trapped exhibited typical neuronal shapes when cultured.

Application

3D printing is being utilized in healthcare, particularly in drug research and manufacturing. One important area is personalized medication. Researchers are exploring the use of 3D printing to create customized medicines on demand. This approach allows for unique structures that are difficult to replicate with traditional methods. It is especially beneficial for patients with seizures, children, the elderly, and those who have difficulty taking their medications. Another significant development is the creation of "polypills," which combine multiple medications into a single pill. These polypills can release the appropriate medication at the right time, reducing the number of tablets a patient needs to take. This is particularly advantageous for older adults, as it can decrease the likelihood of medication errors and side effects while enhancing treatment effectiveness. 3D printing also shows potential for personalizing dosages, which is important for patients on complex medication regimens. Overall, this technology could lower costs, improve patient care, and accelerate innovation in the medical field.

3D printing is also being used to address challenges in drug delivery. With a 3D printer, drugs can be manufactured in various forms and sizes, allowing for adjustments in how the drug is released. Medicine delivery systems can be created using 3D printers, utilizing scans of a patient's body as a template. This enables the design of devices that optimize contact with the treated tissue, making it easier to deliver the right amount of medication. The availability of pharmaceutical components in powdered form plays a crucial role in this process. Patients would no longer need to rely on large capsules and tablets, making it possible to choose treatments that are easier to swallow. This flexibility is especially important for individuals who have difficulty swallowing tablets, such as those with physical challenges. For tissue engineering and controlled drug release applications, 3D scaffolds with well-defined external and internal structures are necessary. This technology can produce scaffolds from various materials, including soft hydrogels, polymer melts, hard ceramics, and metals. The approach involves depositing materials in three dimensions using pressure. Additionally, medication efficacy and side effects can be evaluated using customized models by printing small segments of patient-specific tissue. In contrast to a one-size-fits-all approach to medication, adopting a personalized strategy would help us avoid using ineffective or potentially harmful treatments, thereby increasing the chances of recovery.

Advanced pharmaceutical research is another unique area where 3D printing is making a significant impact. 3D bio printers offer substantial advantages for drug testing and clinical trial applications. The rise of 3D printing enables manufacturing to be brought closer to those in need, allowing for the creation of better and more individualized pharmaceuticals. This technology has the potential to greatly influence the pharmaceutical industry.

With the introduction of more affordable consumer-grade 3D printers, clinics, pharmacies, and even patients' homes can now provide on-demand drug printing services. This capability allows for the development of customized dosage regimens. As 3D printing technology advances, the safety and regulatory concerns surrounding these therapies will also be addressed. Furthermore, the decreasing cost of this technology may give early adopters a significant competitive advantage in their supply chains.

Developing a better treatment system is becoming possible due to the technological potential of 3D printing, which offers opportunities across various use cases. This shift moves away from a "one-size-fits-all" approach toward decentralized production and personalized products and services at the point of care. 3D printing uniquely enables high patient participation by allowing a collaborative approach to developing treatments, surgeries, and drugs that cater to individual needs.

Data shows that healthcare providers and life science companies that have adopted or plan to use 3D printing are more likely to incorporate cloud, robotics, and IoT technologies. This trend indicates that digitally mature organizations that utilize cloud infrastructure and invest in innovation are ahead in recognizing manufacturing opportunities. They can scale, decentralize, and design more efficient production processes through the intelligent use of data and technological resources.

Reducing medical risks and complications is a priority for doctors who are working on challenging surgeries by creating new surgical instruments that can simplify procedures and enhance patient outcomes. 3D printing has allowed designers to create more efficient medical devices at a lower cost

CONCLUSION

3D printing technologies are being effectively used in medicine and healthcare. Many traditional manufacturing methods are being replaced by 3D printing due to its advantages in controllability, accuracy, and the ability to create patient-specific devices. However, challenges exist when printing with tough or thick materials, which may require modifications or replacements of certain components. The commercialization of these technologies remains uncertain. Some may only be suitable for research and might never receive approval for healthcare use, particularly devices that have not been cleared by the Food and Drug Administration. It is essential to evaluate the stability and consistency of the final products produced by 3D printing. Although there has been significant progress in 3D printing applications in medical and healthcare fields, these technologies still need thorough assessment to ensure they meet standards for efficiency, energy consumption, and sustainability. Furthermore, support from related industries is crucial for academic developments in this area, as their financial backing is necessary for the technology to advance effectively.

Additive manufacturing is expanding into areas like lightweight engineering, energy, and medicine. A significant development is 3D bio printing, which creates structures filled with cells that can grow. Personalized implants and medications can help reduce side effects and improve effectiveness. Although this technology and the materials used can be quite expensive, prices are expected to decrease, making large-scale production more feasible. This progress benefits medical professionals and patients alike. However, maintaining the stability of bio printed tissues over time is still a challenge. Overall, the future of 3D bio printing looks very promising.

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