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Review

Applications of 3D printing in healthcare

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Abstract:
3D printing creates a physical product from a digital file by layering various materials to form a single structure. Computer-aided design (CAD) files are necessary for the procedure. Due to its innovative and research-focused nature, 3D printing is well-suited to the medical industry. High-resolution anatomical images from MRI, X-ray, CT, or 3D ultrasound scans (3D scanning techniques) can create patient-specific models. Patients can receive inexpensive customized implants, prosthetics, and medical devices. 3D printing enables surgeons to operate more efficiently using personalized instruments and anatomical models. It also accelerates the development of new products for medical device manufacturers. In the pharmaceutical field, 3D printing allows for complex drug delivery systems, patient-specific implants, and tissue or organ creation. It facilitates telemedicine and tele-pharmacy by enabling the remote prescription and delivery of personalized medications. Additionally, personalized dosage forms simplify prescription regimens and enhance patient comfort. Besides this, key medical applications of 3D printing include tissue engineering, medical devices, drug delivery, and veterinary medicine.

Keywords: 3D printing, Additive Manufacturing, Medical Devices, Healthcare applications

1. Introduction

There is already a booming sector using 3D printing for medical implants. This is because advances in material design have expanded the range of materials that can be 3D printed, and the development of 3D printer technology has made it possible to create intricate biological structures at the microscopic level. Complex objects, including metals and plastics, can be made from less material due to 3D printing. Physiological models are currently one of the most widely used 3D printing applications in the medical field (1,2).

For most 3D printing applications, a CAD-generated design is often exported to the specific 3D printing (or slicing) tool using a Standard Tessellation Language (STL). For a particular 3D printing program, the 3D model is cut into layers of the right thickness, which are then divided into components. After being sliced, the 3D printer builds them into the appropriate shape and size. This technique is being employed in several industries, such as electronics, automobile, agriculture, medical, engineering, construction, and aerospace. In addition, 3D printing has significantly impacted academic research in fields that require rapid product development and prototyping (3,4).

For several reasons, 3D printing is quite appealing. First, it is now reasonably priced and available to many consumers. Second, the materials related to diverse applications can be printed using a variety of printing techniques. In comparison to earlier times, the manufacturing time and printing quality are also favorable (5,6). It is a rapidly developing technology, and it has numerous useful uses in the medical field, such as in orthopedics. Here, the technology serves as a pre-operative planning tool for orthopedic surgery, particularly when intricate 3D thinking is required to determine the size of the implant that may be employed intraoperatively and to consider the underlying anatomy. It enables you to create 3D models before surgery that, in every way, match the patients' real anatomy and pathology as they would be experienced in the operating room. It improves this by giving the surgeons a 3D perspective of anatomy, which is essential for a seamless surgical process and raises the standard of care (7,8). Besides this, in both human and veterinary orthopedics, 3D printing has emerged as a very promising method for producing personalized implants for each receiver's unique needs. "Receiver specific" describes traits such as the receiver's distinct bone geometry or bone density as determined by medical imaging of the receiver. In veterinary practice, the need for customized therapy and a specific implant for the recipient is even more remarkable. This is mostly because veterinary receivers differ from humans in terms of size and shape both within and between breeds and species (9). This overview discusses several uses of 3D printing in healthcare, particularly how technology is revolutionizing surgery planning, orthopedics, and pharmaceuticals.

2. 3D printing

The technique of turning a digital file into a tangible product by layering various materials to form a single structure is known as 3D printing. It is also known as additive manufacturing (AM). A computer-aided design (CAD) file directs the construction procedure by providing 3D printer-compatible file formats. Through its research-oriented quality, 3D printing enables the medical industry to operate innovatively at high speed. This approach creates a volumetric anatomy image using 3D scanning methods such as MRI, X-ray, CT, or 3D ultrasound (10). Nowadays, 3D printing is commonly accepted to create tangible neo-objects using CAD or imaging methods. It can create items with unique structures that are not possible with traditional (subtractive) manufacturing since it fabricates in layers. From creating molds and small tools to the automotive, aviation, dental, biomedical, and even food industries, 3D printing finds use in nearly every sector of manufacturing.

Research data shows that current advancements in 3D printing technology will produce a revolutionary change in healthcare that will reshape medical practice. As a result, clinical treatments will shift away from "one size fits all" and toward personalized medications, which will vary in dosage or combinations of dosages based on the patient's needs. However, 3D printing technologies may be able to produce drugs and drug-loaded medical devices on demand and in a clinical setting. Besides this various treatment approaches that have been made available are Orally disintegrating systems, controlled release formulations, formulations with unique shapes and specialized functionalities, multi-drug combinations, pediatric-friendly formulations, and medical devices (11) .

This technology serves as our present-day solution to assist pharmaceutical and medical industries in creating new medical products, rapid production of medical implants, and superior planning methods for specialists and authorities. 3D medical printing started as an expensive futuristic concept before becoming available to the medical sector across the globe. Current medical organizations, together with medicine, benefit from 3D printing technology, which made professional planning methods revolutionize through developing precise pharmaceutical products and medical devices. It enables makers to access exact physical models of anatomy as well as patient-specific models which guide surgery while also producing stents, prosthetic implants and drug delivery systems (12).

Every 3D printing method contains two essential procedures, which include design software generation of virtual objects and physical printer formation of materials through printing operations. A range of software tools such as AutoCAD (computer-aided design), 3D Slash, SketchUp, Fusion 360, and Solid works permit users to record 3D model designs. Any slicer program, including KISSlicer, Slic3r, Octo-Print, Simplify3D, and Cura, helps execute this operation on the respective part. The G-code transformation of the identical STL 3D design file concludes this process to allow the printer to execute the deposition operations. A slicer program configures the printer parameters, which consist of layer quantity and infill percentage and initial head-to-stage distance along with layer spacing and printing speed and final print time. The printer executes this generated G-code after receiving a print order to produce an object of the correct dimensions. The processing methods of 3D printers depend on the printer type. The three basic operating systems employed are **inkjet-based system, extrusion-based system, and laser-based system.** (13).

3. Types of processes in 3D printing technology

The need to print intricate geometric models at high resolutions has led to the development of additive manufacturing techniques. Rapid prototyping has played a major role in the development of additively made technologies. The three main techniques upon which AM methods are based are sintering, which creates intricate, high-resolution prototypes by increasing the temperature of the material without melting it; melting, which uses electron beams to melt the powders; and stereolithography, which employs a process known as photopolymerization, which uses an associated ultraviolet laser. For torque-resistant ceramic components to withstand the highest temperatures possible, this laser is directed across a photopolymer resin vat (14).

In the following sections, the most significant 3D printing methodologies will be covered, which include the effort involved in each process, its benefits and drawbacks, materials for various procedures, and applications of various 3D printing techniques.

a) Stereolithography (SLA)

One popular kind of VAT polymerization that is crucial to additive manufacturing (AM) is SLA. Most of the time, thermoset photopolymer material is used to make parts. Photopolymer conducts a chemical reaction and changes both chemically and mechanically when exposed to sunshine. Because it uses wavelengths that fall into the ultraviolet (UV) or infrared bands, this light is typically invisible, however, it can sometimes originate from visible wavelengths. Its parameters are usually resistant to modification and set to preset requirements. Achieving surface quality requires careful consideration of the layer's height and the light source's resolution (15).

Chuck Hull first proposed the contemporary stereolithography process in 1986. Its basic idea is to use computers to train a laser to a pool of liquid that has frozen under exposure. The build platform would place itself as close to the liquid's surface as it could at the beginning of the printing process, leaving only a very thin coating of liquid on it (the initial printing location). The first layer of the object is then formed by a 2D pattern created by laser scanning the liquid. Every time a new layer is printed over the first one, the platform slowly descends, immersing the 2D design in the resin. Until the part's printing is finished, the hardened layers continue to cross-link and adhere to one another (16–19).

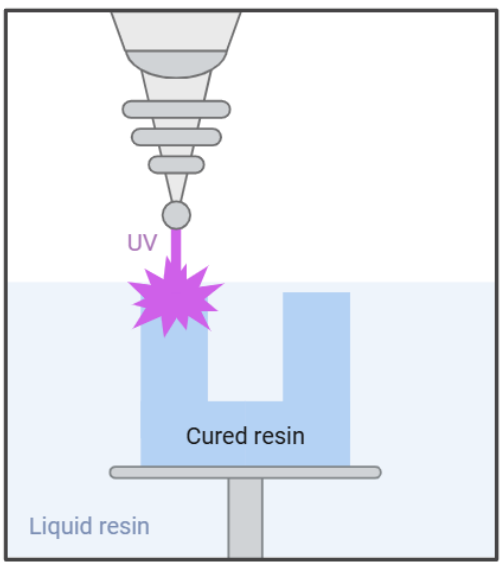

Figure 1: Stereolithography 3D printing (Created from Biorender)

b) **Fused Deposition Modeling-FDM**

The study indicates that, after stereolithography, FDM is the second most sophisticated RP method. This FDM makes it easier to produce intricate designs in hygienic, secure settings like offices. Poly-lactic acid (PLA), reinforced PLA, polycarbonate (PC), polyurethanes, acrylonitrile butadiene styrene (ABS), and PC-ABS mixes are among the thermoplastics frequently utilized in FDM (20–22).

A liquefier is used in an FDM machine to melt thermoplastic materials, which are subsequently deposited layer by layer via nozzle movement along the supplied CAD model in standard triangulation language (STL) format. After melting, the material cools and hardens inside the heat bed before being placed on top of it. For easier solidification, the heat bed temperature is maintained at a lower level. The goal of the post-processing is to achieve a nearly net form (22–28).

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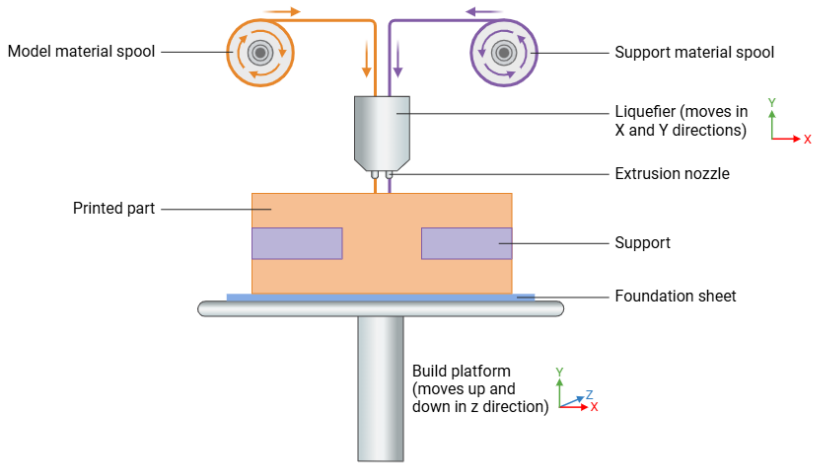

Figure 2: FDM 3D printing (Created from Bio Render)

c) Selective laser sintering (SLS)

Around the middle of the 1980s, Drs. Carl Deckard and Joe Beaman of the University of Texas at Austin are credited with creating this method. By stacking layers of powdered material on top of one another, Selective Laser Sintering (SLS), a rapid prototyping technique, aids in the formation of intricate structures. Depending on the type of surface end and fusion required, layers are solidified with the aid of CO2/Nitrogen lasers. To create the product, the powder employed in this procedure must be a solid chemical compound. This powder may be classified under metals, glasses, ceramics, thermoplastics, etc. Direct Metal Laser Sintering (DMLS) is the procedure used when metal-based powder is used. Two additively created chambers make up a typical SLS printer, with the first chamber supplying power to the second chamber, which is where the actual generation takes place. Just below its melting point, the powder is heated. The powder is dispersed into layers by the leveler or roller at the top. After production is finished, finishing operations are required (11,12(29,30).

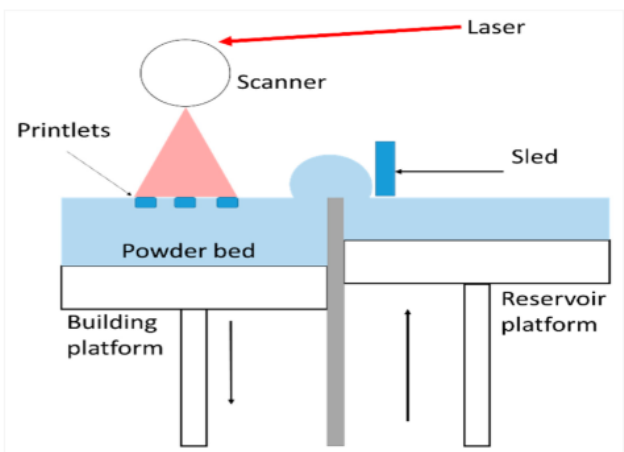

Figure 3: SLS 3D Printing

d) Binder jetting (BJ)

An in-house variant of binder jetting is an inkjet technology system. Researchers from the Massachusetts Institute of Technology created this novel procedure. It ink-jets the binding rather than using laser punctuation, as is the case with other methods. Additionally, it creates the 3D model by stacking the process above and using 2D printer technology in inkjet. Here, a printhead moving in two axes accurately deposits a liquid binder. This procedure begins with the creation of a 3D drawing, which is then imported into the printer's software, just like any other 3D printing procedure. Because printing necessitates a constant supply, a dispenser is set up to guarantee supply by filling it with powder. using the powder sheet of different thickness after filling up the binder material according to the specifications programmed into the printing head. Before moving on to the next layer, the solvent and binder should be cured with electric or fluorescent lamps. A second layer of powder is applied once the powder bed has been dumbled down. After this cycle, the binder will be placed in a furnace.

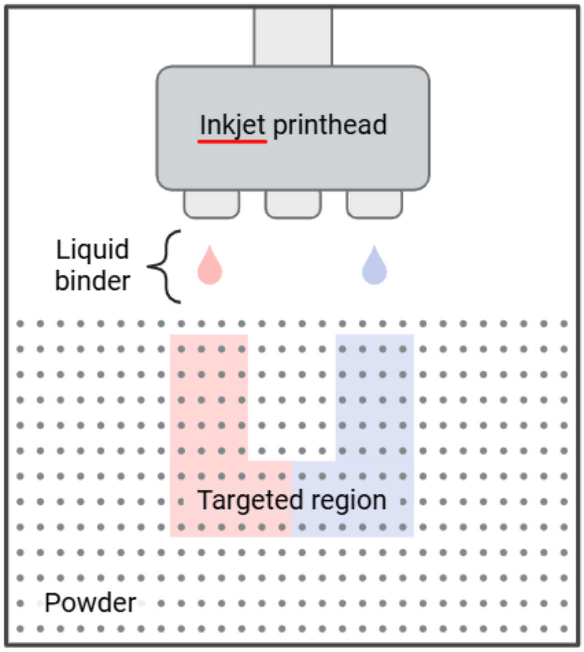

Figure 4: Binder jetting (Created from BioRender)

The type of binder used affects the temperature and amount of time required. Before being made available to end users, metals and ceramic pieces must undergo one of the following processes: sintering, infiltration, heat treatment, or hot isostatic pressing. Most metals and polymers do not require any further post-processing after printing (5,31–34). Table 1 below comparatively lists the different techniques, materials used, and their applications.

Table1: Various 3D printing techniques, materials used and their applications

S.No.	3D Printing Technique	Materials Used	Medical Applications	References
1.	Stereolithography (SLA)	Photopolymers, Biocompatible resins	Dental models, surgical guides, hearing aids, Implantable devices, prosthetics, orthodontics	(35,36)
2.	Fused Deposition Modeling (FDM)	Thermoplastics (PLA, ABS, PCL)	Dental implants, hearing aids, pharmaceutical applications, and surgical instruments or tools.	(35,37)
3.	Selective Laser Sintering (SLS)	Nylon, Polyamide, Metal powders	Customized implants, prosthetics, surgical instruments, and tissue engineering	(38,39)
4.	Binder Jetting (BJ)	Metal powders, Ceramics	Drug tablets, bone scaffolds, anatomical models	(40–42)

4. Applications of 3D printing in healthcare

i. Pharmaceutical Application of 3D Printing in Hospitals and Pharmacies

Using 3D printing technology in pharmacies, clinics, and hospitals offers a great chance to improve drug discovery, customize medication, create new medical goods, and improve drug delivery. To improve drug solubility, controlled-release profiles, advanced medical devices, and the potential to further ensure the reality of telepharmacy, researchers and pharmaceutical companies can use additive manufacturing capabilities to create patient-specific drug formulations and dosage forms. In addition, 3D printing made it possible to customize dosage forms and medication according to patient needs and provide a systematic pharmaceutical administration method. It has also transformed the field of medical equipment, and today, 3D printing is mostly used to create anatomically accurate models for planning surgical procedures as well as a few patient-specific implants that enhance comfort and quality of life. Drug release rates, dosages, and spatial distribution can all be economically managed by using technologically sophisticated drug delivery devices, such as patches resembling microneedles and inhalation formulations. Furthermore, 3-D printing is utilized to create short-term, real prototypes and is quite beneficial for ongoing research projects that test several novel formulas; Animal experiments are not necessary because it is utilized to create tissues that are comparable to human physiology. The technique offers an automated method of taking advantage of compounding in a pharmacy, guaranteeing that medications are more precisely dosed, more target-specific, and have value integration. Although 3DP is a promising technology for advances in pharmaceutical sector improvements brought about by its research progressing daily, regulatory considerations and material selection also create limits, especially in the pharmaceutical industry (43–45).

Patients who need medication customized for their specific needs can benefit from such technology while treating cases of extremely complex diseases. For instance, the narrow therapeutic index of warfarin necessitates dose adjustments. The international normalized ratio test of a person is used to determine the dosage titration. The strengths of commercial warfarin tablets range from 2 to 10 mg, as this is allowed for consumer-purchased tablets. Considering this, it is usually quite acceptable and routine practice in medical wards to break the tablet in two to give a patient the dosage they want. According to reports, warfarin 3D printing was used to create the right dosage materials for oral films and tablets.

Binder jet printing was used to create Warfarin oral disintegrating tablets (ODTs). These tablets were found to be ideal when compared to other factors, including precise medication content, appropriate mechanical strength, and high disintegration time. The fact that a powder bed fusion was used to create a commercial 3D printed tablet for the first time is notable and unquestionably a sign of its potential use in the pharmaceutical industry. However, there is still a significant drawback to using powder bed fusion technology in pharmacies and hospitals: it is not easily accessible; the costs are prohibitive because of the costly processing equipment, and the transfer of processing units became a major issue when the technology was used in hospitals and healthcare facilities (3,46).

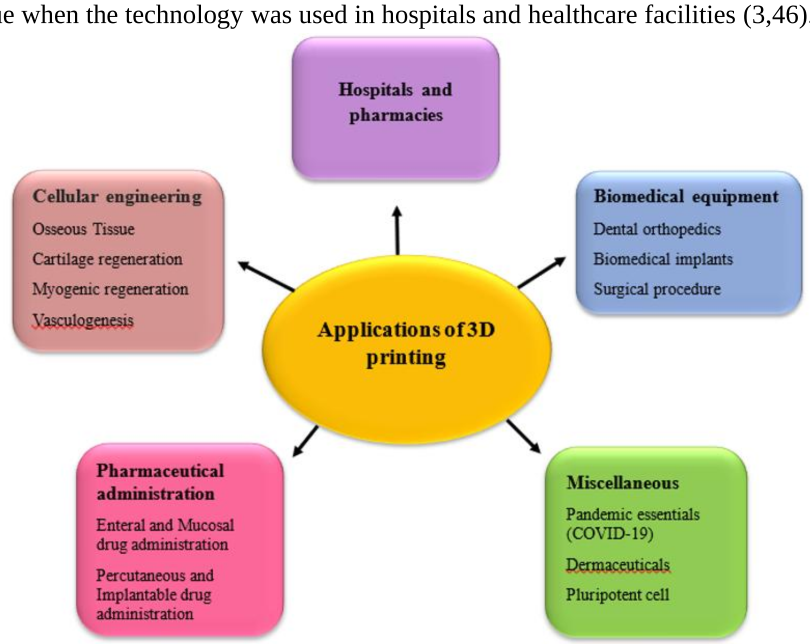

Fig 5: Different applications of 3D printing technology in healthcare

ii. Cellular engineering

Organ failure cannot be avoided and is a universal concern. Although organ transplantation is a great strategy to prevent the failure of specific organs, there is still more work to be done. Advanced technologies are also requested because of the organ shortage and the long-term requirement for immunosuppressive treatments. Thus, the use of bioinks as building materials in additive printing is becoming widespread in the fabrication of various tissues, such as skin, bone, and cartilage, in addition to other vascularized organs like the liver, kidney, and heart. Various bioinks result in good tissue compatibility. Choosing the right polymer is only one aspect of the situation; in most situations, the characteristics of the bioinks should also be considered. Therefore, the researcher's ability to properly classify material in the process of developing as long as possible is crucial. Various tissue/organ models can be used for drug design, high-throughput screening (HTS), in vitro disease modeling, and the elucidation of new platforms such as tissue/organ on a chip. Together with the polymer components, generated computer models are guided inside the printer. The scaffold will be constructed once it has been made according to specifications (47).

a) Osseous tissue

Bone, a hard connective tissue with an interior structure made of a highly cross-linked matrix, can regenerate and remodel to restore or repair damaged bone matrix structure and function, such as in cases of osteoporosis, tumor treatment, and bone trauma. Research on bone regeneration focuses on two primary goals: improving regeneration capabilities and simulating natural human bone conditions. Many research teams often use hydrogel-based scaffolds due to their easily adjustable properties.

Seong et al. described the development of a sodium alginate-based hydrogel scaffold. In terms of compatibility and workability, this sodium alginate has been excellent, despite delaying the sealing and showing poor mechanical ability. These hydrogels would serve as systems for bone remodeling. Unexpectedly, the inhibition caused by crosslinked structures would be overcome. Finally, the retard was irritated by the combination of sodium alginate and hyaluronic acid, which now gives sodium alginate a physicochemical property and combining strength. As a result, the scaffold combination of sodium alginate and hyaluronic acid has been effectively used to create bone-like models for effective structure creation, opening a new avenue for tissue engineering (48).

b) Cartilage regeneration

Many of the body's small organs are supported by the malleable tissue known as cartilage. Because chondrocytes lack blood arteries and neurons, nutrients enter them by a diffusion mechanism. Collagen was used to create a high-density mortar hydrogel for the cartilage scaffold model. The integration of cartilage in that application was motivated by its high biocompatibility. Researchers have looked at how collagen polymer could be appraised in between in vitro and in vivo characteristic tests. In contrast to the latter, which showed a presence of modest inflammation with the production of connective fibers and macrophages at nucleoli, the former implied that the cells were unable to survive environmental conditions. Thus, they claimed that the number of chondrocytes required to initiate cartilage tissue formation was lacking (49).

c) Myogenic Regeneration

Myofibril is the fundamental structural and functional unit of skeletal muscle. 3D printing was the only way to organize this structure in a laminated method. The muscular contraction model was examined by Dickman et al., who noted that it was a significant issue to achieve in most disorders, such as intestinal illness or asthma. A 3D muscle model that was bio inked with collagen polymer was demonstrated as a solution to this issue. The human respiratory channel and the muscle that is connected to it were part of the model's structure. For the 3D model that was produced, drugs that reduce histamine and salbutamol prevented constriction and a relaxed state. Muscle contractions were observed for one day, and with time, the speed of contraction increased daily. This was a highly specialized, agonist-dependent mechanism found in adult muscles. Through fibrosis, it carries out the effect of encouraging the long-term alteration and maintenance of muscle disposition. Therefore, from a scientific perspective, it is presumed that the model is highly like biological muscle in terms of muscular motions, which may lead to the application of the model for medication administration on muscles (50).

d) Vasculogenesis

The movement of nutrients, gases like oxygen, and other internal organs depends on blood arteries. In a sense, blood serves as the "connective tissue" for the entire development. Therefore, it is quite evident that most of the major vasculatures are damaged or blocked in many trauma and disease circumstances, which makes it more difficult for the heart or kidney to exchange gases and nutrients with the other organs. Therefore, with more simple tissue engineering, 3D printing technology is seen as a glimmer of hope for vessel regeneration.

In tissue engineering, Hann et al. used two fabrication techniques to create a vascularized bone tissue model. Numerous factors, including trauma and accidents, can result in bone disorders and deformations. This is where the benefits of using 3D printing for modeling and the miracles of tissue engineering come into play. As a result, this study suggested the most effective model, which combined SLA and FDM to include bone and vascular. First, a polyvinyl alcohol (PVA) scaffold hollow model was created. The formation of bone tissue was accomplished within the core through the proliferation of human bone marrow mesenchymal cells, while endothelial cells from the umbilical vein were integrally integrated into the capillaries. This method produced bone tissue with capillaries that resembled human blood vessels (51).

iii. Healthcare equipment

A common and preferred technique for producing many medical devices is 3D printing technology. Most of these devices are challenging to make using traditional techniques, but most importantly, 3D printing makes it inexpensive to create devices that fit the patient's anatomical structure. For instance, this process is widely used to produce hearing prosthesis specifically for the patient, such as hearing aids, which need to fit into the ear's structure. Moreover, this technique is not limited to prospective medical equipment in the future. Also, it will be beneficial for producing devices like stethoscopes, goggles, and contact lenses designed for the visually impaired (1,2). Besides this The Food & Drug Administration's (FDA) market access grant for a total of three medical device products made using 3D printing to facilitate people's exhibited faith is a very smart marketing (52).

a) Dental orthopedics

In respect to the dentition's occlusal plane reference system, three-dimensional medical imaging aids in precise diagnosis and construction of orthodontic appliances. Orthodontics and dentistry are undergoing a revolution due to advancements in medical imaging, 3D printing, and appliance and gadget personalization. As a result, this method reduced treatment times, enhanced comfort, and removed the need to create dental models out of various materials (53).

Redaelli *et al*. used the 3D printing process to evaluate the orthodontic braces' applicability. It was found that the polymer utilized in the manufacturing process was modified polyethylene terephthalate glycol (PETG). Therefore, the printed model was compared to thermoformed polymers like polyethylene and polypropylene. Tensile properties, affordability, mechanical strength, cost, and patient acceptability of the prosthesis were among the criteria considered. In this instance, the findings indicated that the suggested method meets the patient's present needs. The structural model's mechanical strength was discovered to be improved for improved patient compliance, and I did not find any morphological features lacking. This modular structure can also be used in therapeutic medications to demonstrate the pharmacological mechanism, such as sedation (54).

Thurzo *et al*. successfully constructed an orthodontic power arm model using 3D printing. The model was updated to include biomaterials made of biocompatible polymers. Because of the porous alloys it encountered, the titanium material type found there was appropriate for use in biomedical applications. The researchers used finite-element modeling to enhance designs for power-arm robustness. After that, the model may be affixed to the tooth's shape, enabling the construction of the researched design. The construction was accomplished with an 82% reduction in stress and a 7% improvement in tensile arm strength, demonstrating the enhanced characteristic over the traditional procedure (55).

b) Biomedical implants

In this modern world, prosthetics are manufactured using conventional techniques such as casting processes. However, recent years have seen the successful application of 3D printing technology in prostheses production. It is difficult to distinguish between a prosthetic hand manufactured with 3D printing technology and one made with traditional methods, even though the latter is better suited for individual use.

In the last few years, a lot of businesses have begun utilizing the idea of 3D printing for prosthetic designs. This has allowed them to rapidly create a few favored designs and begin testing them as soon as feasible and at the lowest possible cost. The technique enables you to quickly create prostheses with the proper mechanical and physical properties that are completely compatible with the patient using a 3D printer. Prosthetics for the hands, feet, nose, teeth, and bones are designed to resemble the patient's anatomy as closely as possible. They are acceptable for usage as the original part and have characteristics that are comparable to those of the original component.

Additionally, multi-material printing technology enables customization of the prosthesis's skin color to match the patient’s skin tone. Despite its advantages, this technology has certain limitations. For instance, the prosthesis is harder than the patient’s natural skin. Firstly, the prosthesis is harder than the original person's skin. Furthermore, because these prostheses are not flexible, they will no longer suit the patient as they get older. Only these limitations must be removed to maximize the technology's potential for use. The weight of the prosthesis is yet another problem that has been successfully predicted as a solution. Furthermore, prostheses are hefty, particularly sophisticated ones. In the near term, weight might not seem important, but it hinders the prosthesis's ability to be used for daily tasks. To satisfy the mechanical and physical needs of people of various ages, races, genders, and sizes, the prostheses can then be manufactured in a variety of colors (15)

c) Surgical procedure

The vast process of physiological operation is defined by numerous combinations of problems. By incorporating innovative technologies, the danger was reduced both during and after surgery. The overall goal is to increase process conformity and quality while reducing the amount of time required to do the work and the amount of exposure made possible by using one's position. Therefore, 3D printing serves as the foundation for surgeries that are optimized under challenging circumstances. This technology piqued the curiosity of surgeons and academics, and its applications were redirected in many sectors (56).

Chen et al. performed right hemi colon cancer surgery and employed 3D printing to repair the mesenteric arteries. Three distinct groups participated in the randomized clinical studies, which included imaginary division, 3D printing, and 3D image. The primary quantitative measurements were the length of the procedure, the amount of blood loss, and the number and density of lymphatic system nodes; the secondary qualitative data collection observations included possible postoperative complications, the amount of time required to return to normal functions, and patient compliance. The findings showed that the number of lymphatic system nodes has increased, and the overall operating time has been reduced by technological advancements like 3D printing. Additionally, the surgery's cost was significantly decreased, complications and postoperative mortality also improved after the procedure. Consequently, experts concluded that the technology continues to lower the cost and danger of surgery while also improving its availability (57).

iv. Pharmaceutical administration

a) Enteral and Mucosal Drug Delivery

Hsu et al. reaffirmed that the use of the 3D concept in conjunction with the specific methodology could produce solid dispersion systems with incredibly precise API dosage management. The study successfully developed a system with homogeneous composition and controlled release properties using naproxen, an anti-inflammatory medication, and PEG, which has high biodegradation properties.

The rectal and vaginal suppository molds were created using CAD software and a General commercial 3D printer. The polypropylene molds were then filled with silicone polymers and medications. The scientists noted that the drug-polymer system affected the mechanical properties of the drug-containing silicone elastomer and the rate of drug release. Additionally, Tudela et al. used the same technique to cast a cervical cerclage pessary to treat cervical incompetence and prevent preterm labor.

Together, the latest research on 3D printing technologies offers viable methods for creating oral, vaginal, and rectal drug administration systems that give regulated, desired drug release patterns, degradation rates, and geometric shapes that improve patient satisfaction and performance. The commercialization of the first FDA-approved

3D printed medication, Spritam, in 2015 and ZipDose® by Aprecia® Pharmaceuticals are examples of how these beneficial applications of 3D printing have been realized (58–60).

b) Percutaneous and Implantable Drug Delivery

An attempt has been made to integrate 3D printing into pharmaceutical programs to create topical drug delivery systems. The skin is a protuberant anatomical development on the human body's outermost layer. In place of a standard method, a fabrication strategy that can deliver various drug forms and dosages while accounting for the unique characteristics of individual patients must be developed.

Using two different printing techniques, Goyanes et al. directly converted the patient's facial characteristics from a 3D scanner model for polymers into a CAD format for usage in a unique nose patch for acne therapy. A biodegradable synthetic polymer was melt-processed at an elevated temperature using the extrusion method, and a nose-shaped mask loaded with salicylic acid was 3D printed. Salicylic acid was dissolved in a photo cross linkable polymer to create a nasal patch using the STL technique. Compared to the nasal patch made using the extrusion approach, this patch showed superior surface morphology and drug encapsulation capabilities with no drug deterioration (58).

v. Miscellaneous

a) Pandemic Essentials (COVID-19)

The global pandemic known as COVID-19 was primarily defined by the virus's propagation through the respiratory system. A great backstep to stop the spread among people was the lack of N95 masks, personal protective equipment, face shields, testing kits, etc. Therefore, in the context of the pandemic, 3D printing technology offered an opportunity to produce these materials quickly and efficiently to satisfy the needs of patients, doctors, and others in need. Face shields are modeled via 3D printing using polyester, polycarbonate, and polyvinyl chloride polymers. N95 masks are created using 3D laser scanning. For this reason, thermoplastic polymers, such as the styrene complex, are made using the material extrusion technique (61).

Commonly used medications for controlling COVID-19, such as lopinavir/ritonavir, chloroquine, and hydroxychloroquine tablets, were also manufactured at a faster pace of layer-by-layer drug deposition using fused filament, ink jet, and powder extrusion (62).

b) Dermaceuticals

The public's stakes in eliminating or preventing several visual impairments are starting to rise thanks to cosmetic medicine. As a result, the greater surge has been shown to require a lot more technological advancements and application in this specific industry. As a result, 3D printing advances this technique while offering patients additional benefits. The main cause of these light-related limitations is the sun's UV rays, which harm the environment and most skin-related limitations. To produce reactive oxygen species, alter genes, DNA, and cells, and in the worst cases, cause skin cancer, a specific percentage of the rays must pass through the normal skin aperture. Reducing exposure to radiation or using sunscreen, which typically reduces penetration into skin layers, are the most common ways to avoid negative effects. To provide readers with additional reference, the following study material elaborates on the use of 3D printing in the cosmeceutical industry (63).

c) Pluripotent cell

Feng et al. used stem cells in the current production process. The stability and cost-effectiveness of the many models used in the 3D method are also enhanced by the real-time monitoring. Alginate and gelatin were used to create scaffolds in a straightforward manner. A comparison between the hydrogel and model forms of the same polymers was conducted. The generated model was found to have a higher tensile strength and a better pattern based on the parameters.

Because of this culture, HepaRG cells and ESCs were examined for a certain architecture and cell division capacity. The results were validated since the pluripotent cells improved liver differentiation and proliferation. To ensure the safety of the involved structure, the scaffold was designed to gel and un-gel when removed. A new and scalable method for creating 3D printed scaffolds for large-scale cell growth and secure storage for potential future applications was presented in this study (64).

5. Challenges of 3D printing technology

Although 3D printing technology has several advantages over conventional production techniques, there are often obstacles to overcome before it can be widely used in the medical field. The medical field encounters material selection as its greatest implementing barrier for AM technology at present. Anything that is created with additive manufacturing needs to be human-safe, biocompatible, and sterilizable. It also needs to have mechanical qualities like durability, toughness, and frictional resistance that are suitable for the specific use. Further research is therefore required to locate and create suitable biocompatible and sterilizable materials that can work effectively in such a tough environment as the human body (65).

Medical applications that use 3D printing must achieve both precise and accurate results by design. High tolerances should be present in medical parts. Acceptable criteria defined by these standards would endanger the patient's health. Enviable operation and printer design emerges from tedious material examination and detailed design assessments and print errors analysis alongside highly demanding superior quality control criteria. High accuracy and tight tolerances represent the main production objective (66).

Another significant issue that must be resolved for 3D printing in medical applications is regulatory compliance. To guarantee both safety and effectiveness, medical devices made via 3D printing must closely follow regulatory procedures during their use. Depending on the nation or area in which the device is being used, these rules may change. To guarantee that the final product satisfies all regulatory standards, any modifications to the design or manufacturing processes must be assessed and recorded. Medical field AM technology needs appropriate norms and guidelines, which can be achieved through regulatory agency collaboration. Additionally, quality control methods must be developed to guarantee that the 3D-printed components fulfill the required standards and are safe for human use (65).

Contamination is a concern while creating edible 3D items. Every drug printer that encounters edible printed materials or products must have easy-to-clean surfaces. When medication formulation materials are combined with those from 3D printing operations, there is an additional risk of contamination due to the material's exposure to previously used drug formulation inks or processing conditions. Additionally, FDM printers come with typical brass nozzles, which are known to contain lead; these parts can also cause contamination. For medical purposes, stainless steel nozzles must be used instead (67,68). Expenses are yet another significant obstacle for 3D printing, particularly in medical applications. Many medical facilities may be limited by the expenses of purchasing or renting equipment, materials, the time required to produce the gadget, and software. Additionally, 3D-printed item processing and finishing can significantly raise overall costs (69,70).

Widespread medical acceptance of additive manufacturing technology depends on solving existing obstacles before its introduction can become standard practice. Researchers and manufacturers are working to solve these issues through research into new materials, printing parameter improvements, and post-processing refinement. Accelerating the medical adoption of AM technology will be achieved through combined government-business-academic research endeavours (71,72).

6. Future Prospects and Emerging trends

The modern world is evolving daily, and the unmet requirements of time are changing along with it through helpful technologies. There are many successful examples of 3D printing technology in its various uses, and it has a lot of potential going forward. It is anticipated to be quite helpful in resolving some of the issues we have recently encountered. The masks created with this technology to combat COVID-19, which have gained attention in recent years, are among the most well-known examples in this respect. The lack of face masks during pandemic emergencies has been problematic, particularly for medical professionals, including paramedics, doctors, and nurses. In the context of mask production, this technique might be applied to help produce masks that are quickly made available all over the world. The benefits of this technology during times of crisis have drawn attention due to its application in both preventing the spread of the disease and offering environmentally friendly and sustainable support for the future (73–79).

Scientists predict that within a few years, science will be able to replace badly damaged tissue with biologically functional tissue that has been 3D printed. These days, 3D printing is being developed for use in regenerative medicine as well as industry. To restore irreparably injured tissue, scientists want to employ this 3D printing model to create customized biocompatible tissue scaffolds. 3D printing has the potential to improve and save the lives of patients in several ways. Furthermore, clinicians can use 3D printing to help them choose the right percutaneous devices, evaluate procedure risk, optimize deployment technique, and train in vitro with challenging or uncommon situations. Additionally, this technology can support potential human body functions or better cosmetic surgery outcomes. In the future, this technology might be sufficiently developed to replace failing organs with custom structures created inside, eliminating the need to wait for a healthy organ and perhaps even for organ donors (1).

In the future, transplantable organs like kidneys, livers, or hearts might be made from the patient's own stem cells with the help of 3D printing technology and advancements in stem cell research. Compared to donated organs, printed organs have several major advantages, including the possibility of producing healthy organs and the absence of rejection. At present, this manufacturing method is used in many other industries, including medicine (80). Besides this, future studies will also concentrate on improving AM technology to increase efficiency and utility, discover more medical uses, and verify the quality and security of printed goods. Creating novel printing materials and techniques that are biodegradable, bioresorbable, and capable to mimic the properties of human tissues and organs will be one of the main research goals in AM for the medical industry (81).

Enhancing printing quality and safety is another focus of AM research for the medical field. The correctness and uniformity of the printed goods will be guaranteed by new advancements in hardware and software AM solutions, such as sensors and monitoring systems that can identify and fix printing mistakes. To ensure that printed items meet the necessary safety and quality standards and are compatible with the current medical systems and procedures, further key efforts will involve creating new guidelines and standards about AM in the medical sector.

Conclusion

In conclusion, the medical industry benefits greatly from 3D printing technology since it can be used to create customized medical equipment and complex implants that meet patient needs while keeping costs down. This solution is being used by businesses in this sector in a number of other everyday applications. Medical 3D printing's primary capability of adapting designs enables medical practitioners to produce personalized medical equipment. Veterinary medicine, tissue engineering, the pharmaceutical industry, and organ bioprinting—which is still in the testing stage—are among the expert fields that use surgical bio-models or templates with imaging models to comprehend diseases and develop medical devices before developing patient-specific implants or prostheses. This technology is frequently used to produce prosthetics and implants that can be customized. This medical method creates prostheses and implants that are anatomically suited, improving many patients' quality of life. For pharmaceutical and bioprinting applications, this revolutionary technological advancement lies in the interim between active testing and partial approval. Once extensively adopted, this technology is still predicted to bring about a completely revolutionary shift. This field's ongoing developments will spur more advancements in healthcare that improve patient outcomes and treatment modalities.

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