



3D Printing: A Review of Recent Breakthroughs and Emerging Applications.

Running Title: Recent Breakthroughs and Emerging Applications in 3D Printing

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ABSTRACT:

Three-dimensional (3-D) printing has become a popular printing technique in many different industries. In the upcoming years, this technology may potentially replace traditional production. It is becoming more and more popular because to its design versatility, which allows for the construction of objects without any creative limitations. The evaluation provides insight into how 3-D printing is being used in various industries. However, the typical single-type raw 3-D printed products are frequently too fragile, resulting in fragments that break easily. Nowadays, three-dimensional (3-D) printing is a widely utilized printing method in various industries. In the years to come, this method might take the place of traditional production. Its design flexibility, which allows products to be made without creative limits, is the reason for its increasing attention. The review offers a viewpoint on how 3-D printing is being used in various businesses. Standard single-type raw 3-D printed products, on the other hand, are frequently excessively fragile and break into pieces. A 3-D printed object must have better mechanical properties in order to be used in a variety of industries.

Sr.No	Abbreviation	Meaning
1.	CAD	Computer Aided Design
2.	RP	Rapid prototyping
3.	SLA	Stereology apparatus
4.	MIT	Massachusetts Institute of Technology
5.	FDA	Food and Drug Administration
6.	US	United state
7.	FDM	Fused deposition modeling
8.	DLP	Digital Light Processing
9.	SLS	Selected Laser Sintering
10.	MJ	Material jetting
11.	EBM	Electron Beam Melting
12.	MJF	Multi Jet Fusion
13.	PLA	Poly(lactic acid)
14.	PLGA	Poly(lacti-co-glycolic acid)
15.	PGA	Poly(glycolic acid)
16.	(β -TCP)	Beta tri-calcium phosphate
17.	HA	Hydroxyapatite



18.	Ti	Titanium
19.	MPa	Megapascal
20.	CLIP	Continuous Liquid Interface Production
21.	Wire+arc AM	WAAM
22.	Polycaprolactone	PCL
23.	Extracellular matrix	ECM
24.	Twophoton Polymerization	TPP

1. Introduction about 3D printing technology

Three-dimensional (3D) printing technology, a pharmaceutical and formulation production technique, uses computer-aided designs (CAD) and printing settings to give the pharmaceuticals that are produced flexibility [1, 2]. 3D printing is the process of stacking layers on top of each other using a 3D printer. The additional layers are the reason it's frequently called additive manufacturing technology. With the correct

excipients, the desired product can be printed using a computer file that contains all of the design parameters, including the infill %, geometry, printing speed, layer height, thickness, extrusion, and platform temperature. They send this file to a printer in the.stl format. To meet each patient's specific needs, 3D printing is a bespoke formulation development technique. Accurate dosage administration is one of the most crucial components of targeted drug delivery. [1, 3, 4].

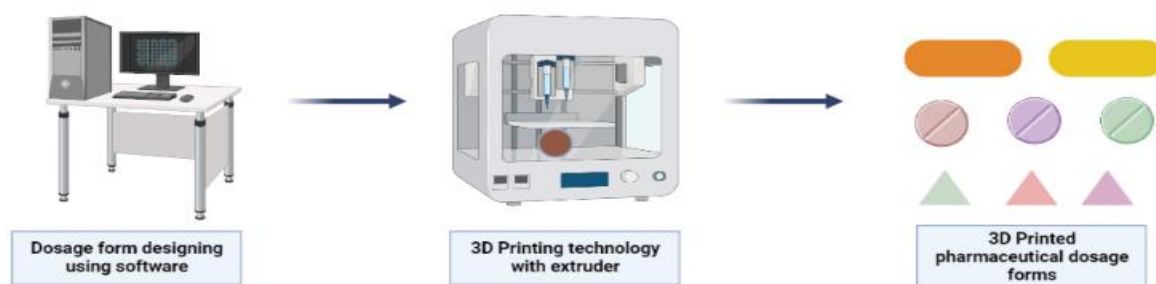


Figure 1: 3D Printing technique.

The capacity of this technology to accurately create dose forms is advantageous for drug product creation. It also allows for patient-centric treatment, including personalized doses to treat certain disease states or patient populations, and offers a variety of release mechanisms to meet therapeutic requirements [5]. A new technique known as three-dimensional (3D) printing has the potential to be very beneficial to the pharmaceutical industry. It can provide patients and the pharmaceutical industry creative solutions, and it has been used for more than 30 years in a variety of fields, including robotics, automotive, chemical sciences, and prototyping. [3, 5]. Currently, the pharmaceutical sector markets its products through conventional or traditional means [3]. The process of mixing, blending, or changing materials to make drugs in response to

particular patient circumstances that require certain excipients, drug strengths, or dose formats is known as traditional pharmaceutical compounding. 3D printing technology has the potential to revolutionize the customized pharmaceutical sector as we work to abandon the "one size fits all" strategy [2]. Customizing pharmaceuticals to each patient's needs while taking into consideration differences in age, gender, race, genetic profiles, epigenetics, and environmental factors is the primary objective of customized medicines [2].

2. History

Contrary to popular belief, the 3D printing technique is not a recent development. Since its introduction nearly 30 years ago, 3D printing has transformed production with an unmatched range of applications. 3D printing



originally appeared in the 1980s when Japanese researcher Dr. Hideo Kodama created a rapid prototyping (RP) process [1,2]. Charles Hull was a furniture manufacturer who invented stereolithography apparatus (SLA) in 1984. He started his own business, 3D Systems, in California in 1986 after being granted a patent for this technology. In 1988, they unveiled the SLA-1, their first product to be sold commercially [1, 2, 3]. Scott Crump filed a patent application in 1989 for fused deposition modeling, an alternate 3DP approach. The 3DP technology was created and patented in the

early 1990s by Emanuel Sachs and his associates at the Massachusetts Institute of Technology (MIT) using inkjet printing in the pharmaceutical sector. The particles on the powder bed have been bound together with a binder solution. This method has to be repeated several times before the desired structure was obtained [1, 2, 4]. The number of businesses vying for the rapid prototyping technique skyrocketed in the 1990s [2]. In 2016, Aprelia Pharmaceuticals used inkjet printing to release Spritam® (levetiracetam), the first 3D-printed pill to receive FDA approval.

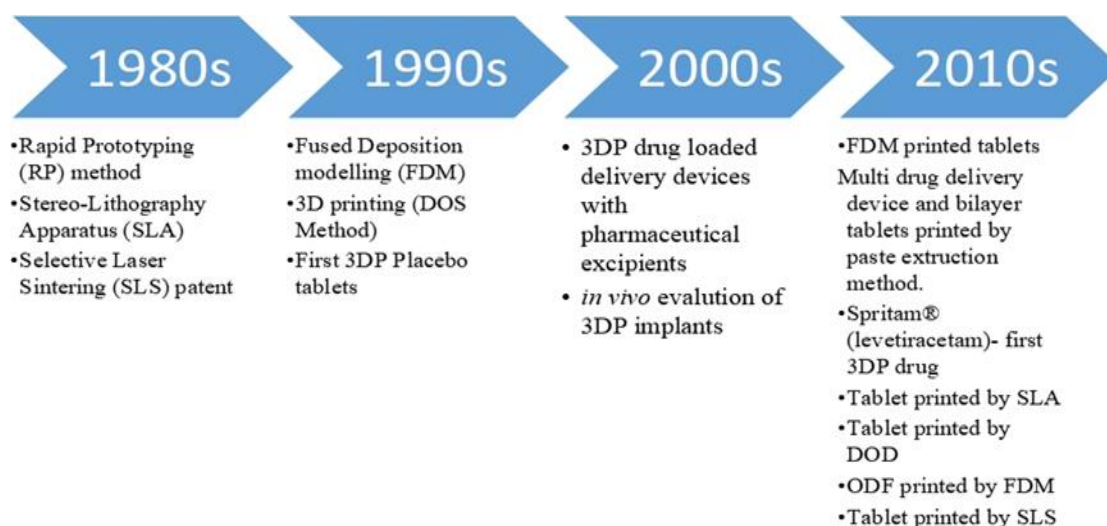


Fig 2: The important breakthrough of 3D Printing in Pharmaceutical field.

Table 1 Historical Development in 3D Printing Field [6,7].

YEAR	MAJOR DEVELOPMENT
1980	The first patent by Japanese researcher Dr. Hideo Kodama for Rapid prototyping (RP)
1984	Stereolithography by French engineers was then abandoned due to improper funding.
1984	Charles Hull invented the stereolithography apparatus (SLA).
1986	Charles Hull got his patent for Stereolithography apparatus (SLA).
1986	Carl Deckard invented an apparatus for producing parts by selective sintering.
1989	A patent was granted to Carl Deckard for SLA.
1989	Fused deposition modeling (FDM) by Scott Crump
1992	By using the 3D system, the first SLA machine was produced.
1993	A 3D printing patent was granted to E.M. Sachs.
1996	Clinical application of biomaterials for tissue regeneration
1999	Luke Massella received his first 3D-printed bladder, which was an amalgamation of 3D-printed biomaterials and his own cells.



2000	MCP Technologies introduced the SLM technology.
2002	A miniature functional kidney was fabricated.
2004	Dr. Bowyer conceived the RepRap concept of an open-source, self-replicating 3D printer.
2005	Z Crop introduced the first color 3D printer.
2009	Organovo, Inc., announced the release of data on the first fully bioprinted blood vessels.
2012	Extrusion-based bio-printing for an artificial liver A 3D-printed prosthetic jaw was implanted.
2014	Implementation of a multi-arm bio-printer to integrate tissue fabrication with printed vasculature
2015	The first 3D-printed pill was approved by the US FDA. Organovo announced the release of data on the first fully bio-printed kidney.

3. Types of 3-D printer

Generally speaking, 3-D printers can be categorized based on the printing method and materials. Cost, printing quality, printer capabilities, printing speed, user expectations, and practicality are some of the factors that must be considered in the development of the 3-D printer. When selecting a printer, the elements might be balanced.[8] For instance, you can use Digital Light Processing (DLP) to print a polymer, which has a high resolution and can be generated fast, while also using Fused Deposition Modelling (FDM), which is substantially less expensive than FDM. Table 2 provides a list of the advantages and disadvantages of the various types of 3-D printers. The most popular 3-D printing method in additive manufacturing, stereolithography (SLA), is perfect for producing prototypes due to its high precision and smooth surface finish. But the material used in this kind of printer, liquid resin, is

expensive, ranging from \$50 to \$400 per liter [9]. Fused Deposition Modelling (FDM) is a potentially superior alternative due to its lower cost compared to other 3-D printing technologies and its convenient home use. But with an FDM 3-D printer, you can only utilize thermoplastic materials. Additionally helpful is Selected Laser Sintering (SLS), which may produce objects with complex forms. Compared to other 3D printing technologies, the main advantage of SLS printers is that they don't require any post-processing during the manufacturing process or extra supports, which minimizes scrap. However, the final product.

With an emphasis on popular technologies, their procedures, benefits, drawbacks, and common applications, this table summarizes the primary kinds of 3D printers. Based on broad knowledge about 3D printing, the data is unique.

Table 2 : Summarizing the main types of 3D printers

Sr.No	3D Printing Technology	Process	Materials Used	Advantages	Disadvantages	Typical Applications
1.	Fused Deposition Modeling (FDM)	Extrusion of thermoplastic material through a heated nozzle	PLA, ABS, PETG, Nylon, TPU	Low cost, widely available, easy to use	Lower resolution, limited material variety	Prototyping, hobbyist projects, low-cost manufacturing
2.	Stereolithography (SLA)	UV laser cures liquid resin layer by layer	Photo-polymer resins	High resolution, smooth surface finishes	Expensive materials, post-processing required	Dental models, jewelry, high-detail prototypes



3.	Selective Laser Sintering (SLS)	Laser fuses powdered material layer by layer	Nylon, TPU, metals, ceramics	Strong, durable parts, no need for support structures	Expensive, complex setup	Functional parts, aerospace components, medical devices
4.	Digital Light Processing (DLP)	Projector cures resin with digital light source	Photopolymer resins	High resolution, fast printing	Resin handling can be hazardous, limited build size	Dental applications, small detailed parts, jewelry
5.	Material Jetting (MJ)	Droplets of material are jetted and cured with UV light	Polymers, waxes, ceramics, metals	High precision, multi-material printing	High cost, brittle parts, complex maintenance	Prototypes, visual models, casting molds
6.	Binder Jetting	A liquid binder is deposited onto powdered material	Sand, metals, ceramics, polymers	Low cost, large build volume	Low mechanical strength, post-processing required	Casting molds, large-scale architectural models
7.	Electron Beam Melting (EBM)	Electron beam melts powdered metal in vacuum	Titanium alloys, cobalt-chrome	Strong, fully dense metal parts, biocompatible materials	Very expensive, limited materials, slow	Aerospace, medical implants, high-performance metal parts
8.	Multi Jet Fusion (MJF)	Fusing agent selectively deposited on powder bed	Nylon, TPU, polymers	High strength, fast production, smooth finishes	Expensive machines, limited material variety	Functional parts, small batch production, consumer goods

4. Base materials in 3-D printing

A small number of material types are frequently utilized. The majority of printing materials are pliable or have a high degree of plasticity and permeability. The primary benefits of employing plastic in 3-D printing are its affordability and portability. Because not all powders can be revived, the dispersed form of nanoparticles requires a later separation, increasing the process cost. For this reason, a polymer is chosen to hold the nanoparticles in the application of 3-D printed nanocomposites.[10]

3.1 Polymer/plastics

The majority of consumer goods are primarily constructed of thermoplastics. 3-D printing has made extensive use of plastics to produce prototypes and consumer goods. Compared to standard 3-D printing applications, the polymers employed in tissue engineering applications may differ. Choosing the right polymer is crucial because bio-compatibility is a key component of medical applications. Natural, synthetic, bio-composite, metal-based, and bio-ceramic polymers are the groups of polymers utilized in 3-D printing in the medical field. [11].



Biological elements including collagen, polysaccharides, gelatin, etc. were utilized to create a scaffold in order to create a natural polymer that could be used as the material for 3-D printing. Utilizing natural polymers has several benefits, including the ability to preserve the extracellular matrix of the host tissue [12] and a minimal risk of an immunological rejection reaction [13]. Nevertheless, natural polymers frequently lack mechanical strength, which limits their use in load-bearing applications. Additionally, it breaks down so quickly that the mending tissues aren't supported. Because synthetic polymers are more biodegradable, have higher mechanical qualities, and have a longer breakdown period, they are therefore a better option for supporting tissues. Poly(lactic acid) (PLA), poly(lacti-co-glycolic acid) (PLGA), and poly(glycolic acid) (PGA) are a few instances of synthetic polymers [14]. Because of their desirable qualities, including biocompatibility, chemical and

physical stability, and antibacterial action, hydroxyapatite (HA) and beta tri-calcium phosphate (β -TCP), which fall under the category of bio-ceramic materials, are also frequently used in 3-D printing, particularly in bone tissue engineering [15, 16]. Bio-ceramics have many benefits, but they also have disadvantages, such as low elasticity, fractures, and excessive rigidity [17]. Its clinical applicability had been hampered by this. In order to create the perfect scaffold, it was proposed that bio-ceramics may be mixed with other raw materials. On the other hand, metal-based polymers are particularly helpful in replacing bone in the human body. It is resistant to corrosion, has a high mechanical strength, and can stimulate tissue growth. Due to its strength and biocompatibility, titanium (Ti) alloy can be used to replace bone, hip, femur, skull, and knee. However, the low bioactivity of the metal may also make using metal-based polymers more difficult.

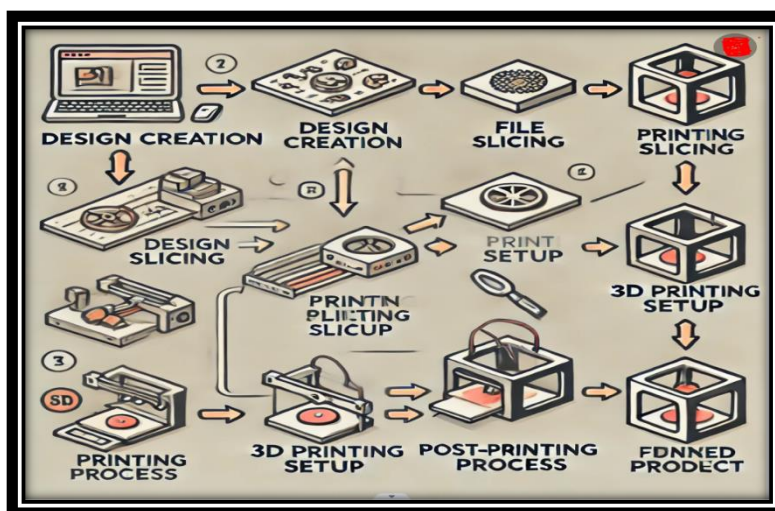


Fig. 3: Process of 3-D printing

3.2 Metals

Since metals have strong strength and thermal qualities, they are occasionally employed in 3-D printing. They can be used to print anything that must be able to support weight, such as auto and aircraft parts. Table 3 lists the metals used in 3-D printing in summary form. When it comes to engine parts that need to withstand high levels of stress, a blend of cobalt-chrome metal is advantageous because it has a higher tensile strength than other metals. Since the majority of display

devices can be produced using plastic materials, metals are typically used for practical purposes rather than display applications. Titanium, maraging steel, cobalt-chrome, tungsten, and nickel all have high tensile strengths above 1000 MPa, as illustrated in Fig. 3. Tensile strength is a straightforward method of assessing a metal's mechanical characteristics. High tensile strength metals can withstand wear and tear in harsh environments, which is particularly helpful in automotive and aerospace applications. In the aerospace industry, choosing the right metal is essential to



lowering weight, consuming less fuel, and improving performance [18]. Aluminum is nevertheless utilized extensively in the automotive and aerospace industries despite having a lower tensile strength [19]. Its low density, which led to lighter parts, and its low cost in comparison to other metals are the key causes of this. The wire+arc AM (WAAM) hybrid-AM method can be used to correct surface flaws, refine grain size, and remove metallurgical defects in aluminum parts [20]. On the other side, titanium is quite expensive, but it has low density and is roughly twice as strong as aluminum. Due to its ability to reduce vibration, tungsten metal is unique in its use and may be used to make a variety of items, including battle blades, ballast weight, and missile components.

3.3 Ceramics

Among its many outstanding qualities are their low density, strength, high electrical insulating capacity, corrosion resistance, chemical stability, and dimensional stability. They can therefore be used in a variety of applications due to these qualities. The chemical industry, biomedical engineering, aerospace, and machinery are all included in this. As previously said, these characteristics enable its application in numerous industries. The shapes are formed using the traditional process, which involves gel casting and molding techniques. Binders and other additives may or may not be added with the powder. The green portions must be sintered at a high temperature in order to produce densification. However, the lengthy processing time and expensive cost of these conventional ceramic forming methods limit their use. Furthermore, using molding techniques to create objects with intricate geometries and interconnected holes is not feasible. Additionally, the machining of ceramic components presents a challenge since the exceptional hardness and brittleness of the ceramic material exposes the cutting tools to significant wear and flaws. As a result, achieving precise surface finishing and dimensional accuracy is challenging. The substitution of 3-D

printing technology could solve the issues caused by traditional technologies. Depending on the shape of the preprocessed feedstock, the technology can be divided into two categories: slurry-based and powder-based. The fine ceramic particles in slurry-based ceramic feedstock are distributed across a liquid or semiliquid medium. The semi-liquid takes the shape of the system's solid loading, while the liquid takes the form of inks, depending on the viscosity [69]. For this feedstock, the item can be printed using Binder Jetting (BJ), Inkjet Printing (IJP), Direct Ink Write (DIW), Digital Light Processing (DLP), Two photon Polymerization (TPP), and Selective Laser (SL) [21]. Conversely, powder beds containing loose ceramic particles are used as feedstock in powder-based ceramic feedstock. Using thermal energy from the laser beam or dispersing liquid binders, ceramic particles can be fused together via powder fusion [22]. Selective Laser Sintering (SLS) and Selective Laser Melting (SLM) are the two 3-D printer types utilized for this feedstock. As previously said, ceramic 3D printers are used to make green parts. The initial step is comparable to the normal 3-D printing procedure, which involves slicing the intended object in aslicing software until it is prepared for production. Since ceramic 3-D printing is still in its green condition, it needs to undergo extra treatments because it is still brittle and delicate. Before reaching their final structure—glazing and fring—these green components will go through a number of steps to create a stronger ceramic final product. The final ceramic prototype's bending strength, for example, significantly improved from 17 MPa for the green state to 220 MPa [23].

5. Recent advances in 3D printing technology:

Current developments in 3D printing technology have had a big impact on a number of industries, expanding the realm of what is feasible in construction, manufacturing, healthcare, and even food production. An overview of some significant developments is provided below:[24]



Figure 4: Illustrating the recent advances in 3D printing technology. It covers key developments such as materials innovation, speed and precision, large-scale 3D printing, customization and personalization, and sustainability.

5.1. Materials Innovation

5.1.1. Multi-material Printing: Multiple materials can now be printed in a single process because of developments in materials science. The use of 3D printing has increased as a result of these capabilities, especially when it comes to producing intricate parts like integrated circuit circuitry.

5.1.2. Bio-compatible Materials: In the medical field, 3D printing implants, prosthetics, and even tissues and organs is now possible because of the discovery of bio-compatible materials. The likelihood of rejection is decreased because these materials are made to blend in perfectly with the human body.[25]

5.2. Speed and Precision

5.2.1. Faster Printing Technologies: The time needed to create objects has significantly decreased thanks to new 3D printing technologies like Multi Jet Fusion (MJF) and Continuous Liquid Interface Production (CLIP). By increasing production efficiency, these technologies increase the viability of 3D printing for large-scale manufacturing.

5.2.2. Enhanced Precision: Advances in stereolithography and laser sintering have improved the accuracy of 3D-printed items, enabling smoother finishes and finer details. This has been especially helpful in fields where accuracy is essential, like aerospace and healthcare.

5.3. Large-scale 3D Printing

5.3.1. Construction Applications: Entire buildings or other massive constructions can now be printed using large-scale 3D printers. Businesses like Apis Cor and ICON have shown that they can use 3D printing to build houses and structures, which can drastically cut down on construction time and expenses.

5.3.2. Automotive and Aerospace: Large-scale 3D printing has been embraced by the automotive and aerospace sectors to produce lightweight, long-lasting parts for vehicles, aircraft, and spacecraft.[26]

5.4. Customization and Personalization

5.4.1. Healthcare Solutions: 3D printing makes it possible to customize medical products, like orthodontic and prosthetic devices, to meet the unique demands of each patient. A degree of customization like this improves efficiency and comfort.

5.4.2. Consumer Goods: 3D printing makes it possible to produce personalized goods for the consumer market, such as eyewear and shoes, giving customers one-of-a-kind and customized options.[27]

5.5. Sustainability

5.5.1. Reduced Waste: Since 3D printing is an additive process that only consumes the material required to build the object, it is by nature more sustainable than traditional manufacturing techniques. Waste is greatly reduced as a result.



5.5.5.2. Recycled Materials: Recycled materials are becoming more and more popular for 3D printing. Businesses are looking into ways to promote a circular economy by recycling plastics and other resources into 3D printing filaments.[28]

6. Role of 3D Printing in Nanocomposites

3D printing is revolutionary in the field of nanocomposites because it makes it possible to precisely design and fabricate intricate structures that are embedded with nanoparticles. The mechanical, electrical, thermal, or optical properties of materials are improved by adding nanoparticles to create nanocomposites. A number of benefits come with using 3D printing to produce these cutting-edge materials:

6.1. Precision and Customization: Nanocomposites can be used in a variety of applications due to their high accuracy layer-by-layer fabrication of geometrically complicated structures.

6.2. Enhanced Properties: The uniform dispersion of nanoparticles (such as metallic, graphene, or carbon nanotubes) within polymers results in enhanced mechanical strength, electrical conductivity, thermal stability, and chemical resistance in 3D-printed nanocomposites.

Customized Performance: Through the manipulation of nanoparticle concentration and location, 3D printing enables the fine-tuning of material properties, which can be crucial in industries like as electronics, biomedicine, and aerospace.[29]

6.3. Sustainability and Resource Efficiency: By facilitating the efficient use of materials, cutting waste, and possibly permitting the recycling of discarded components, 3D printing of nanocomposites helps to promote more environmentally friendly production techniques.

7. 3D Printing in the Design and Application of Biopolymers

Bio-polymer 3D printing promises revolutionary breakthroughs in the environmental and biomedical domains. Bio-polymers are eco-friendly, biodegradable polymers that come from nature. These materials can be used in a number of creative ways with 3D printing:

7.1. Medical Applications: Biocompatible polymers including alginate, poly-lactic acid (PLA), and

polycaprolactone (PCL) are frequently utilized in 3D printing for medical implants, drug delivery, and tissue engineering.[30]

7.2. Customized Scaffolds for Tissue Engineering: Extracellular matrix (ECM)-like scaffolds made of 3D-printed biopolymers can promote tissue regeneration and cell proliferation. It is possible to customize these scaffolds to meet the demands of the patient.

7.3. Eco-Friendly Packaging: Biodegradable 3D-printed bio-polymer goods are becoming more popular in sectors like packaging because they provide a sustainable substitute for conventional plastic packaging.

Food Industry: Personalized nutrition solutions can be achieved by using edible bio-polymers to 3D print bespoke food items.

8. 3D Printing and Bio printing Methods for Cardiovascular Tissue Engineering

Biological tissues, including those for cardiovascular uses, can be created via bio-printing, a specialized type of 3D printing. 3D printing has transformed cardiovascular tissue engineering, enabling the creation of synthetic tissues for application in drug testing, research, and even implants:

8.1. Vascular Scaffolds:

In order to create scaffolds that resemble blood arteries and offer a surface for cell adhesion and proliferation, 3D printing techniques are employed. For the development of engineered vascular tissues, these scaffolds are necessary.[31].

8.2. Cardiac Tissue Models:

The development of intricate cardiac tissue models for medication testing and heart disease research is made possible by 3D bioprinting. These models can replicate the pathological and physiological states of the tissues found in the human heart.

8.3. Heart Valve Engineering:

To create heart valves with accurate anatomical characteristics, 3D printing and bio-printing are used. These devices can be used as implants or as models for surgical planning and instruction.



8.4.Cell-laden Hydro-gels:

Bioprinting technologies commonly use hydrogels called bioinks that include living cells. Tissue-engineered structures for heart regeneration and repair can be further enhanced by printing functional cardiac tissues with them.[31]

9. 3D Printed Grafts in Animal Models

Preclinical studies are using 3D-printed grafts more frequently to evaluate their effectiveness in tissue regeneration and repair. With the aid of CAD software, these grafts are created and then manufactured from biocompatible materials such as hydrogels or polylactic acid (PLA) utilizing processes like bio-printing, selective laser sintering (SLS), or fused deposition modeling (FDM).

To assess biocompatibility, tissue integration, and mechanical stability, the grafts are surgically implanted in animal models, usually mice, rats, or rabbits. Following implantation, the animals are observed to make sure the transplant stimulates tissue growth without triggering an immunological reaction. Imaging and histological examination are frequently used in post-implantation studies to evaluate graft function.

The materials and graft design are improved for possible therapeutic uses in humans thanks to the findings of these investigations. The advancement of tissue engineering and regenerative medicine depends on this study.

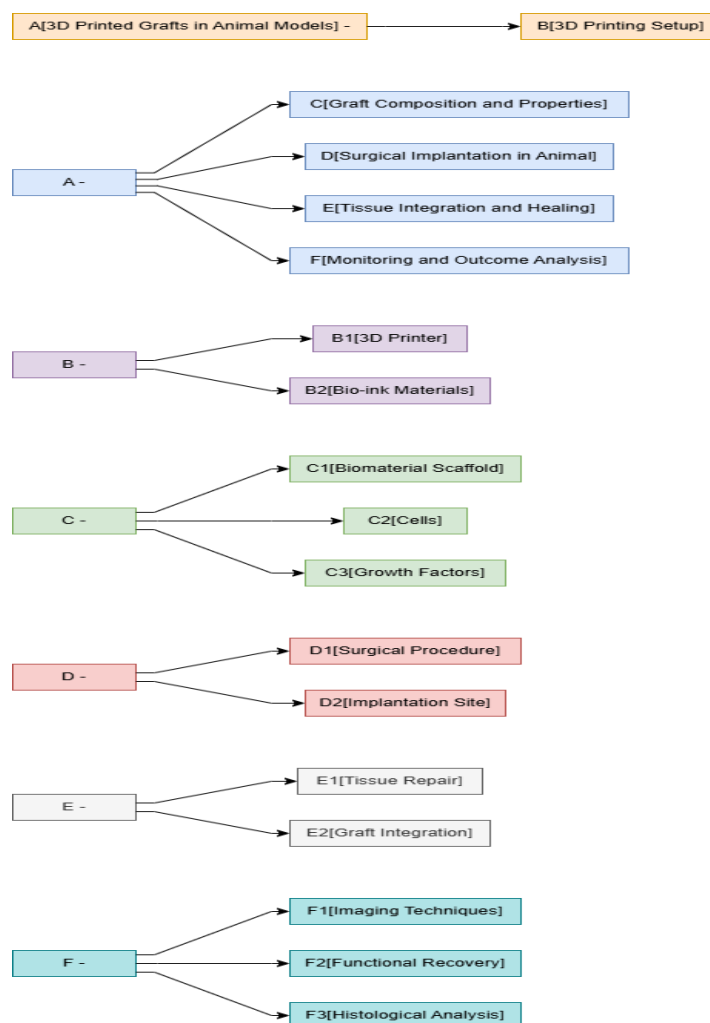


Fig 5:3D Printed Grafts in Animal Models



This diagram shows the overall process from 3D printing the graft to its implantation, healing, and the final outcome analysis.

Conclusion:

In this review, 3-D printing's progress in a number of fields has been noted in this study. Because 3-D printing has so many potential uses, it is important to allow and encourage ongoing study, particularly in the area of 3-D printed nanocomposites. It has been demonstrated that adding nanoparticles to items can make them more functional. Numerous benefits come with adding nanoparticles, including the ability to enhance the printed items' mechanical, dielectric, and even biological qualities. The information in this evaluation also helps researchers and manufacturers promote the improvement of 3-D printing in terms of system recyclability and sustainability. Finally, research should continue to address the issues raised by the limitations of 3-D printed nanocomposites. It is thought that engineers' creativity and innovation in creating a specialized 3-D printer for nanocomposites could lessen or prevent the issues that have become beyond the current boundaries of limitation. Since 3-D printing will transform development in the future and has the potential to produce significant revenue across a range of industries, it is crucial to investigate this topic. Current constraints, however, include the expense of manufacturing 3-D printed objects and a lack of operational experience. We hope to see more incredible 3-D technology applications in the years to come.

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Conflict of Interest

The authors declare no conflict of interest.

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