Journal of Phase Change Material

J-PCM

Article

Check for updates

A Review on 3D Bioprinting Materials and Technique

Vinay Kumar Soni [1], Sudip.K. Sinha [2,*], Hemant Kumar Sharma [3]

[1] Department of Mechanical Engineering, Columbia Institute of Engineering & Technology, Raipur 492010, India

[2] Department of Metallurgical and Materials Engineering, National Institute of Technology, Raipur 492010, India

[3] Department of Health, Dau Kalian Singh Post Graduate Institute & Research Centre Raipur 492001, India

E-mail: : vnysny@gmail.com

Published from the Department of Computer Engineering, Modeling, Electronics and Systems - DIMES, Italy by Royallite Global UK

Volume 2, Issue 2, 2022

Article Information
Submitted: 14 October 2022
Accepted: 20 November 2022
Published: 01 December 2022

Additional information is available at the end of the article

How to Cite:

Soni, V., Sinha, S., Sharma, H., (2022). A Review on 3D Bioprinting Materials and Technique. *Journal of Phase Change Materials*, 2(2), 1-18.

DOI: https://doi.org/10.58256/jpcm.v2i2.26

Abstract

As a fabrication technique for developing scaffolds for tissue engineering, three-dimensional printing has a lot of potential. The range of biomaterials that can be utilized in this method affects the uses of 3D printing in the fields of tissue engineering and regenerative medicine. To facilitate their usage in 3D printing techniques, numerous researchers have created novel biomaterials and compositions. There are many benefits to making scaffolds with 3D printing, such as the capacity to design complicated geometries, porosities and co-culture of numerous cells. The present review emphasizes on innovative biomaterials utilized in various 3D printing methods for clinical applications. The most prevalent types of medical 3D printing technologies like extrusion-based bioprinting, inkjet, and Laser-assisted bioprinting as well as their clinical applications, various types of biomaterials currently employed by researchers, and significant drawbacks are discussed in detail.

Keywords: 3D bioprinting, Biomaterials, bioinks, Synthetic polymers, Additive manufacturing

Public Interest Statement

While many of the advances in materials science have been driven by breakthroughs in material design and fabrication, understanding the changes that occur in a material during its utilization or operation in devices is of immense importance for its successful integration. Considering these aspects and the continued growth in materials research, there is a clear need for new topical journals which can serve researchers to understand the phase transitions and exploit the phenomena to current, state-of-the-art research in the field of materials science, moreover with full accessibility.

1. Introduction

People are dealing with tissue and organ failure difficulties such as renal failure, coronary artery disease, bone tumours biliary atresia, ear abnormalities, and more. Severe kidney failure, chronic infections, heart failure and other disorders have been on the increase in recent years. In India, heart disease resulted in the deaths of about 4.77 million people in 2020. This was mostly due to a scarcity of organ donors and the failure of transplanted organs. In the case of renal transplantation, it has been reported that around 20% of patients develop acute rejection within 5 years of implantation, and more than 40% of people die or lose donor functionality within 10 years [1]. These traumas have a significant impact on human lives and necessarily require organ or tissue transplantation. Patients with damaged tissue have two options: organ transplantation or repair, depending on context and severity of the damage. However, the number of donors is restricted. There are extremely long organ transplant waiting lists all across the world. Scientists are eager to find alternate strategies to compensate for the organ scarcity in these circumstances.

The issue of a lack of tissue or organs may one day be resolved with the use of tissue biofabrication technologies. It is necessary to create new organ transplantation techniques that are more dependable and cost-effective than existing ones **[2]**. Three-dimensional (3D) printing, commonly referred to as rapid prototyping or additive manufacturing, has the potential to completely change how this issue is resolved.

By using this approach, the likelihood of organ rejection is reduced, as is the need for lifelong restrictive medications. In order to create a 3D scaffold using 3D bioprinting, living cells can be suspended in a liquid polymer called "bioink" (living cells, biomaterials, and growth factors). Additive manufacturing, popularly known as three-dimensional (3D) printing, is a base manufacturing method that includes depositing and acquiring raw materials and fabricating actual product with the help of software and CNC systems **[3]**. Manufacturing, architecture, energy, and healthcare are just a few of the fields where 3D printing has been applied.

Given the intricacy and customized character of human tissues and disorders, it has gotten a lot of interest in the biomedical profession. Customized products, such as orthopedic implants and client implants can be 3D printed for surgical supervision and restorative reasons by modelling a tissue utilizing image reconstruction following a computerized tomography (CT) scan and magnetic resonance imaging (MRI) **[4]**. Using nucleic acids, living cells , growth factors, medications, and proteins, 3D bioprinting has proven to be an effective method for tissue synthesis, development, and organ patterning. There are several uses of 3D bioprinting in the medical field using the various approaches suggested **Fig.1**.

In this context, our review offers a background on 3D bioprinting in general, emphasizing the inclusion of living cells in the process of production. The most current developments in novel bioinks and bioprinting methods are then introduced. Moreover, we will give a general overview of 3D tissue and organ printing with an emphasis on applications and the state of the art in bioprinting. We conclude by offering viewpoints on the clinical uses of designing functional tissues or organs.

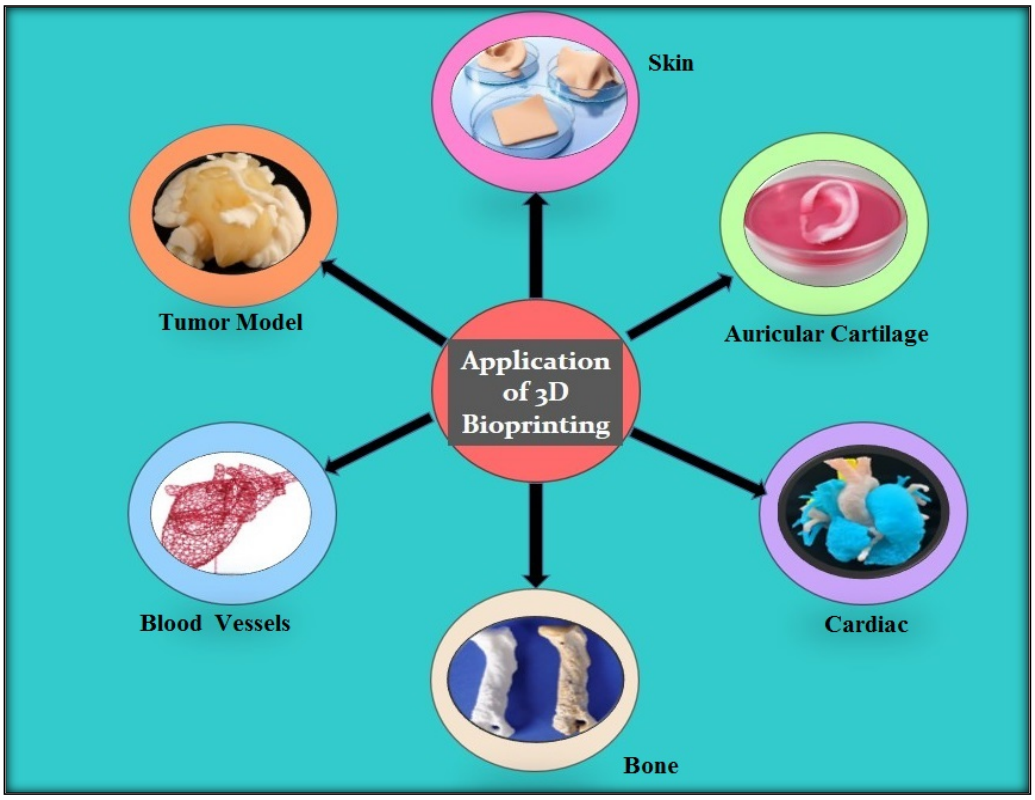

Fig.1 Applications of 3D bioprinting in various medical field

2. Bio-ink:

Bioink is a significant term in the organ bioprinting and tissue manufacturing. Bioinks are made up of biomaterials and living cells in a biological matrix. Bioinks must have nontoxic bioactive constituents and a printing temperature below biological temperatures, as opposed to conventional 3D printing materials **[5]**. Bioinks are divided into four categories based on their functions, according to the literature: functional bioinks, support bioinks, fugitive bioink and structural bioinks. Due to the wide range of materials that can be used in bioinks, both natural and synthetic polymers are being used. Polycaprolactone (PCL), polyvinylpyrrolidone (PVP), pluronic and polyethylene glycol (PEG) are synthetic polymers, while hyaluronic acid, gelatin, collagen, and matrigel are natural polymers **[6-8]**.

3. Common materials used in 3D Bioprinting

The most crucial aspects for biomaterials used in 3D bioprinting are biocompatibility, homogeneity in degradation, and printability. Biomaterials are generally defined as organic or synthetic materials employed in biological equipment for organ replacement or repair. They are divided into four divisions based on their chemical makeup: metals, polymers, ceramics, and composites. While ceramics and composites have stronger corrosion resistance than other types of materials, metals and composites offer excellent mechanical strength **[9-10]**. In contrast to other materials, polymers are

notable for being biocompatible and biodegradable.

The most practical materials for 3D bioprinting are thermoplastic polymers. They are divided into two main categories for 3D bioprinting, though: synthetic polymers and natural polymers. Better structural and mechanical qualities are found in synthetic polymers, and their production is subject to fewer constraints. Natural polymers have a high molecular weight, which results in limited solubility and high viscosity. Due to the qualities they offer, such as high strength, dominating microstructure, and regulated degradability, synthetic polymers have made a significant contribution as high applicability materials in 3D bioprinting **[11-12]**. Here is a list of a few important synthetic polymers with a brief description.

3.1. Acrylonitrile Butadiene Styrene (ABS):

The triblock copolymer Acrylonitrile Butadiene Styrene (ABS) has petrochemical roots. ABS belongs to the styrene terpolymer chemical family, which has acceptable strength and hardness. Applications for this material are increased by its low melting point (105℃). The ABS is composed of three separate monomers, each of which contributes a variety of useful properties, such as powerful impact strength from butadiene, imparted stiffness from styrene, and heat endurance from acrylonitrile. In processes like fused deposition modelling (FDM) and selective laser sintering (SLS) printing, ABS is employed as a precursor. In cartilage engineering technologies, it is also used. The applicability of this material is constrained by its partially identical cell integration, biodegradable nature and polylactic acid-like processing capabilities (PLA) **[13-15].**

3.2. Polylactic Acid (PLA)

The widely used polymeric bioink known as PLA is an aliphatic polyester that is hydrolytically degradable and has printing capabilities among other qualities. The primary polymer utilized as a precursor in the FDM (Fused Deposition Modeling) process is PLA. In musculoskeletal tissue engineering, generated filaments from PLA can be utilized to replace ligaments and non-biodegradable fibers. Its long-term biocompatibility is harmed by the production of acidic byproducts caused by PLA decomposition, which also causes tissue inflammation and cell death. Furthermore, PLA's brittleness restricts its use by lowering its overall strength below that of bone. It can be used with inexpensive ceramic materials, like calcium phosphate, to get around the restriction. It builds stronger bone scaffolds and lessens acid production **[16-18]**.

3.3. Poly-D, L-Lactic Acid

Poly-D, L-lactic acid is a noncrystalline polymer having lactic acid as its source (PDLLA). Due to its innate hydrophobicity, practical biodegradability, and robust mechanical qualities, it is well suited for biomedical applications, particularly in Stereolithography (SLA) techniques. One of the polymers that is widely utilized to make biocompatible porous scaffolds is this one. It is utilized in tissue engineering devices and resorbable orthopedic treatments as a result. Due to PDLLA's hydrophobic properties,

water cannot diffuse through its matrix, which slows down the deterioration process. However, the presence of hydrophilic groups increases the water absorption, which stops the degradation. In the meantime, the presence of hydrophilic groups can lower the pH, causing the polymer to break down into monomers, as well as adverse allergic and inflammatory reactions in the body **[19-22]**.

3.4. Polyethylene Glycol (PEG)

Radical polymerization forms the hydrophilic polymer recognized as polyethylene glycol (PEG). It features an asymmetric or dissymmetric hydroxyl ion as its tail groups and a linear or branching structure. PEG is now more frequently utilized in drug delivery systems. The construction of tissue engineering scaffolds, and surface changes that result in the production of amphiphilic lock copolymers and ionomers. PEG mostly forms hydrogel and is not susceptible to protein adsorption or cell adhesion in nature. They exhibited poor mechanical strength and are not biodegradable. Their inability to degrade is also linked to the presence of a C-C polymer backbone. However, hydrolytic and enzymatic degradation are frequently to blame for PEG's degradability **[23-25]**.

3.5. Polyether Ether Ketone (PEEK)

A nonbiodegradable polymer with higher biocompatibility, radiolucency, little heat conductivity, and equivalent bio-inertness is polyether ether ketone (PEEK). The material's semi-crystalline structure offers acceptable chemical stability and thermal resistance. By reducing stress shielding, it possesses strength and elasticity that are comparable to cortical bone, which lowers the risk of osteopenia following implementation. PEEK is a material that is frequently utilized in FDM and SLS technologies, as well as in bioinks for the prototyping of craniofacial implants and bone substitution **[26-28]**.

By enabling radiographic examination, the distinctive radiolucent feature benefits orthopedic applications. The bioinert's submissive nature inhibits osteointegrative abilities, which consequently restricts its suitability for tissue engineering. Additionally, it has the ability to catalyze bodily processes that could impact the tissues, such as extrusion, encapsulation, and dislodging. Additionally, the SLS process cannot use it due of its high melting point of 345°C **[29-31]**.

3.6. Poly-glycolic acid (PGA)

Poly-glycolic acid (PGA) is a major synthetic polymer in 3D scaffold design because of its chemical variety, ease of processing, biocompatibility, and biological properties. Glycolic acid monomer is created during the biodegradation of PGA and is then simply excreted from the body via certain catabolic pathways as carbon dioxide and water. Additionally, PGA's copolymers can preserve their mechanical and physical characteristics. PGA is used to make resorbable sutures and internal fixation devices for bones. The breakdown products of PGA are less hazardous than PDLLA. The surface modification of PGA through ester bond hydrolysis can increase cell seeding density and spreading. Although the hydrolysis method has certain advantageous properties, its

surface shape and mechanical strength can limit it. It is prone to bulk erosion, which can cause the scaffold to collapse and release body-harming acidic breakdown products **[32-33]**.

3.7. Polybutylene Terephthalate (PBT)

Biocompatible thermoplastic polyester called Polybutylene Terephthalate (PBT) is used in fused deposition modeling (FDM) printing techniques. PBT exhibits excellent elasticity, simple processing, and allowable strength and toughness. PBT is a typical polymer that is frequently utilized in the biomedical industry for in vivo and in-vitro biocompatibility. The printing of canine trabecular bone scaffolds and tissue regeneration continue to be two applications for it. Orthopedic surgery also uses it as filler. It has comparable physical and chemical characteristics as PCL or PLA and doesn't have any unique advantages. Like other polymers, PBTs break down in aqueous medium via oxidation or hydrolysis. Its high melting point (225°C) and nonbiodegradable nature, which result in the formation of crystalline substances during in-vivo application, restrict its applicability **[34-37]**.

3.8. Poly Caprolactone (PCL)

PCL is a less expensive polymer that has excellent bioink properties like rigidity, biocompatibility, and degradability. One non-toxic polymer that can endure remarkable stability is PCL. The stability typically lasts for six months with a three-year biological half-life. SLS printed PCL scaffolds have features such a porous structure that promotes connectivity, a rough surface, and bone-like compactness that promote bone regeneration and cell ingrowth. The prolonged biological half-life of the scaffold, however, creates an additional barrier in scaffolds designed for uses other than bone tissue engineering. Additionally, the higher hydrophobicity of the substance results in low bioactivity, which slows down tissue adhesion and cell proliferation **[38-40]**.

3.9. Polyurethane (PU)

Polyurethane (PU) is regarded as a promising biodegradable elastomer due to its thermosetting properties, strong biocompatibility, and mechanical strength. The type of solvent it employs allows it to be separated from traditional PU and water-based PU. In the latter, water is used as a solvent, whereas volatile organics are utilized in the former. SLA and DLP printing techniques use PU, and PLA can be used to determine how well it degrades. High printing resolution and superior cytocompatibility strengthen 3D bio printing's features. Chondrocytes are required for cartilage tissue engineering as well as the manufacture of scaffolds for the bones, muscles, and nerves. It demonstrates an exceptional ideal elastomeric quality that withstands repeated contraction and relaxation and makes a good option for muscle development **[41-42]**.

3.10. X Poly-vinyl alcohol (PVA)

Vinyl alcohol and acetate are used to create the synthetic polymer known as poly-vinyl alcohol (PVA). These monomers are really the causes of the semi-crystalline character, biocompatibility, biodegradability, and bioinertness of these polymers. PVA, a polymer that dissolves in water, is utilized in the SLS printing process. PVA has a tensile strength comparable to human articular cartilage. With the right adhesive, PVA can develop intricate structures and offer an ideal matrix for the ingrowth of bone cells. Due to its preferred hydrophilicity and chemical stability, it can withstand high pH and temperature changes, and the semi-crystalline structure ensures that oxygen and other nutrients are efficiently transported into the cell PVA is extensively helpful in a variety of load-bearing treatments, such as bone tissue engineering applications, correction of craniofacial defects. Since PVA is water-soluble, controlling its swelling in the presence of water is difficult **[43-44]**.

3.11. Polylactic-co-glycolic acid (PLGA)

The polymer known as Polylactic-co-glycolic acid (PLGA) is remarkably cytocompatible and has a dependable biodegradable nature. It is osteoconductive and possesses mechanical properties comparable to those of calcareous bone in humans. Additionally, PLGA is utilized in numerous tissue-restoration systems and animal models for bone regeneration. However, the hydrophobic property delays its use. Additionally, due of its linear structures' weak stiffness and rapid disintegration, it is not widely used as a scaffolding material. In-vivo testing of the shattered PLGA debris shows a propensity for an escalating inflammatory response, although this fracturing can be reduced by blending it with PCL **[45-46]**.

4. Method used in 3D Bioprinting

4.1. Fused deposition modeling (FDM)

Fused deposition modeling (FDM), also referred to as 3D printing, is one of the earliest AM techniques. According to the printing procedure, a thermoplastic polymer is fed into a liquefier and then a filament is extruded to create the melted thermoplastic utilized as a support for bioinks **[47]**. As seen in **Fig.2**, a variety of variables affect the traits of parts made using FDM.

Researchers tried to focus on important factors in order to enhance the manufactured pieces and ultimately acquire the combination of them nearly all researches have attempted to use characterization methods to evaluate the researched factors and their impact on the accuracy and geometry of printed components with regard to the applied materials and parameters **[48-49]**.

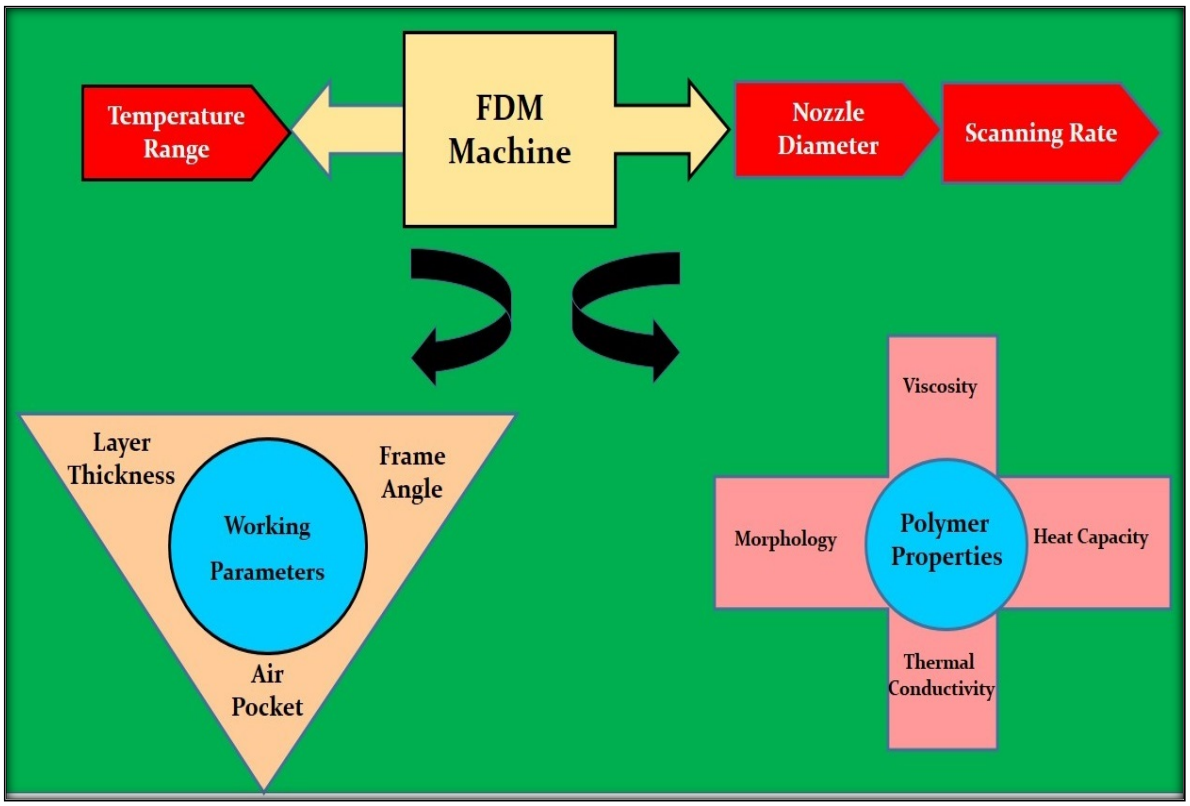

Fig. 2 Illustration of FDM-based study taking process aspects into consideration

4.2.Extrusion Printing

Extrusion-based printing is the most widely utilized, affordable, and accessible form of 3D bioprinting. It comes in mechanical and pneumatic versions. In mechanical systems, the printing process is started by vertical and rotational forces, whereas air pressure in pneumatic systems drives the dispensing mechanism. **Fig. 3** depicts extrusion-based bioprinting schematically.

Both screw-driven and piston-driven motors are used in the mechanical dispensing method. The distribution of bioink at higher viscosities and additional dimensional control are made feasible by screw-driven systems, while direct control of the bioink flow is available with a piston-driven system. Bioink is used during the liquid phase to prevent nozzle blockage. The minimum nozzle size is normally above 100 m since smaller nozzle sizes can result in cell damage and death or higher shear stress. Furthermore, utilizing a mechanical device to apply a lot of pressure can cause the cell membrane to break, which can kill the cells. The hydrogels can contain cells, which can then be added and extruded from a nozzle onto a substrate where solidification takes place. The substrate is then utilized to replace or repair damaged tissue or organs. It is crucial to pick a material for hydrogel synthesis that is printable and offers a 3D structural matrix **[50-52]**.

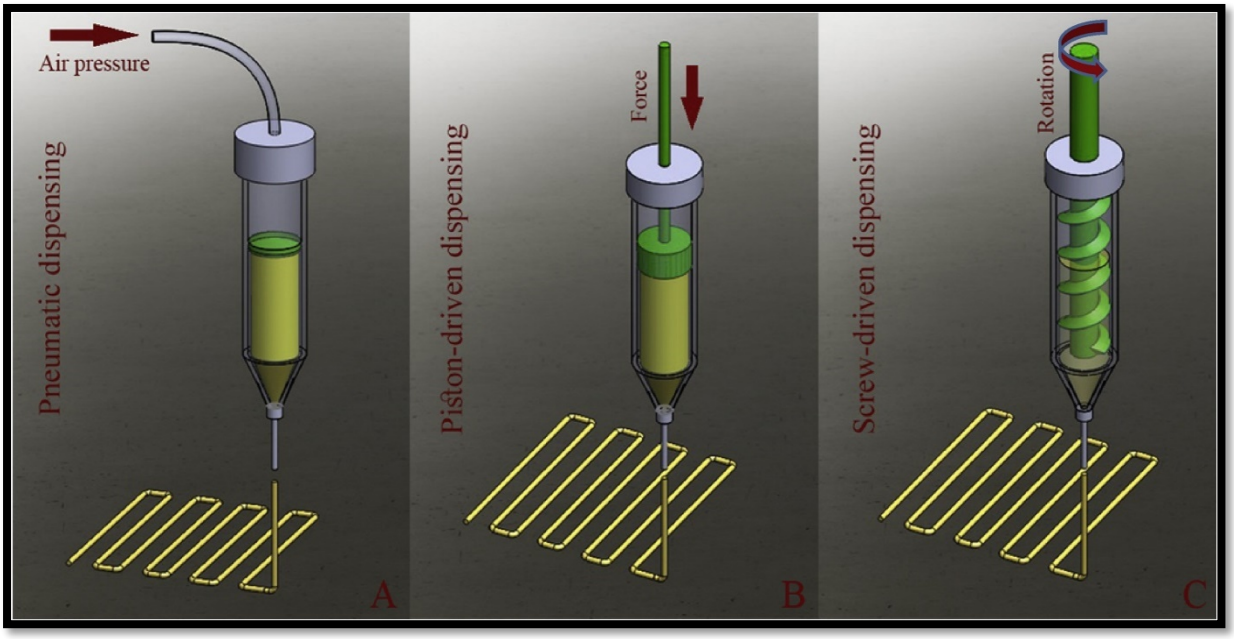

Fig. 3 Extrusion-based bioprinting methods: (A) pneumatic, (B) Piston-driven, and (C) screw-driven dispensing method **[53]**

For extrusion bioprinting, there are three important aspects for printability: A material-specific biofabrication window, bioink phase before extrusion, and viscosity adjustability are three key concepts. Viscosity are sometimes affected by temperature or shear thinning, so it must be adjusted for various printing techniques. Additionally, bioink must be in a liquid state to prevent nozzle blockage. Finally, not all biomaterials can be printed, and those that can depend on the processing conditions in which they are printed. The most recent extrusion bioprinting studies are listed in the following sentences to show the state of the art at the beginning **[54]**.

Rees et al. [55] initially thought of two varieties of 3D printed oxidized nanocellulose structures as wound dressings. The first kind was synthesized using (2, 2, 6, 6-tetramethylpiperidin-1-yl) oxidanyl (TEMPO), and the second type was synthesized using a combination of carboxymethylation and periodate oxidation. After being utilized to print 3D porous structures and tested for its ability to support bacterial development, the developed nan cellulose bioink was found to have the ability to carry and release antimicrobial components while not promoting bacterial growth.

4.3.Inkjet

In this method, pressure is used to drop droplets containing cell-loaded hydrogels onto the substrate (volume between 1 and 150 pL). The bioink is dependent on a number of physical characteristics, including viscosity, density, and surface tension, for the successful deposition of droplets onto a substrate. Continuous-inkjet bioprinting, electro-hydrodynamic jet bioprinting, and drop-on-demand inkjet bioprinting are three categories of inkjet printing techniques **[50] [56]**.

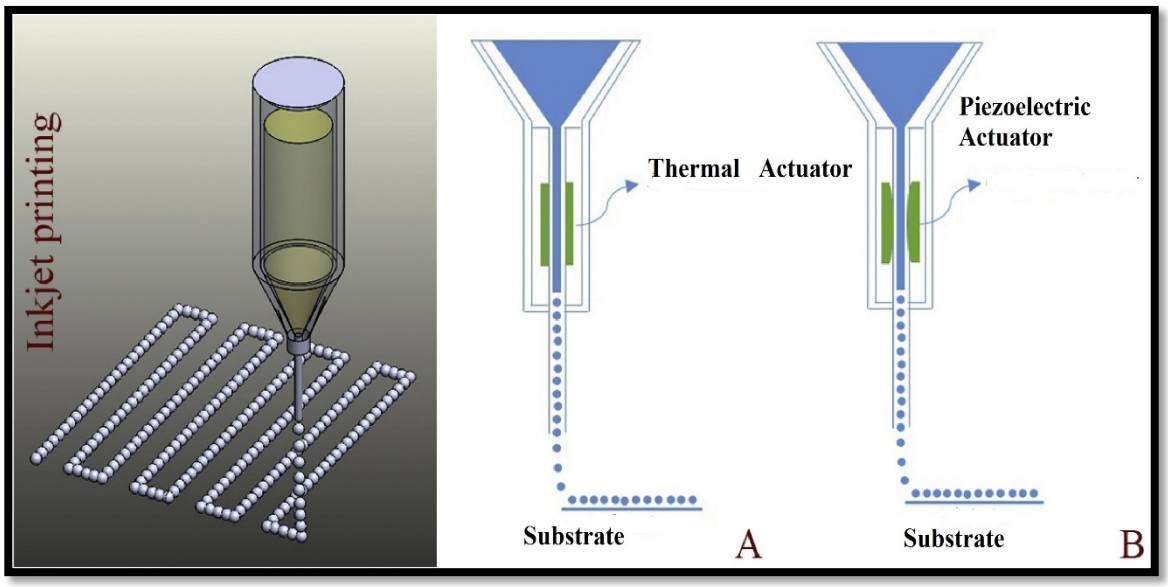

Fig.4 Representation of the drop-on-demand inkjet printing technique using thermal and piezoelectric actuators, respectively. A heating element is used in a thermal printing head to locally increase the temperature and produce a bubble that forces droplets into the nozzle. Utilizing a substance that transforms shape when voltage is applied and forces droplets out, a piezoelectric head is used **[53]**

The latter category, which includes thermal, piezoelectric, and electrostatic inkjet bioprinting, is actually the biggest and most prevalent one. In **Fig. 4**, schematic representations of thermal and piezoelectric inkjet printing are provided. Either continuous inkjet bioprinting or drop-demand (DOD) inkjet bioprinting is categories for it. Thermal and piezoelectric controls in the DOD method control the deposition of bioink. By creating bubbles that drive the bioink to exit the nozzle, the heating components in the thermal controller increase the temperature of the substance. When voltage is provided to the piezoelectric controller, acoustic waves are produced inside the print head and quickly alter the structure of the droplets **[57-58]**.

4.4. Stereolithography (SLAs)

The basis of stereolithography printing is the accurately controlled polymerization of light-sensitive polymers by light glinted from digital micro mirrors. Stereolithography has a high printing quality, speed, and cell survival when compared to other technologies. However, utilizing this strategy has been said to have downsides. For instance, it has been observed that the popular polymerization process, UV light source, is bad for DNA cells and can potentially lead to skin cancer **[59]**. Visible light stereolithography bioprinting methods have drawn attention as a solution to this problem.

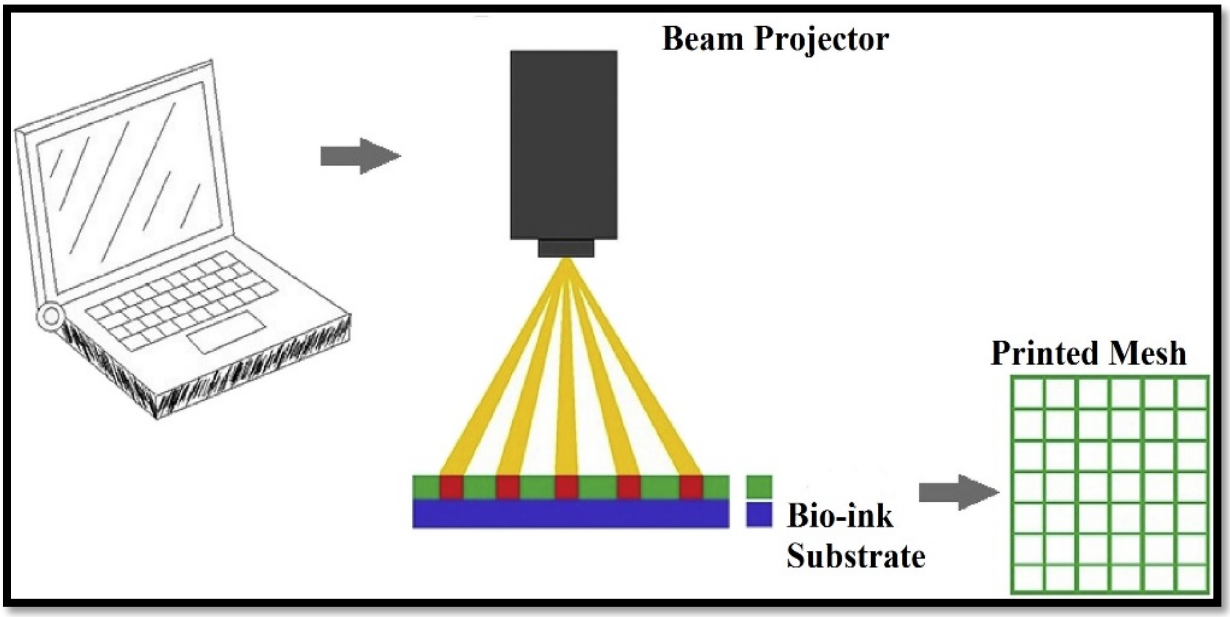

Fig. 5 Diagrammatic representation of stereolithography utilizing a beam projector. Using concentrated laser beams, layers of light-sensitive polymer can be precisely photo polymerized to apply any desired design to the bioink **[62]**

Wang et al. used a bioprinting system that included a beam projector and mixtures of PEGDA, GelMA, and erosion Y-based photo initiator as bioinks as an example. The results of this study's NIH 3T3 cell bioprinting experiment showed that the suggested low-cost technology can print and cure hydrogels with visible light with a 50 mm resolution and a comparatively high cell survival. A beam projector is used to depict stereolithography in **Fig. 5**.

The photo polymerization of bioink, which comprises a light-sensitive polymer, is used in this technique to achieve the spatial solidification of resin (in liquid form). Compared to the extrusion process, it offers a higher resolution and more cell survival. High-speed photopolymers are cured using a UV light source, and the energy creates a covalent link between neighboring polymer chains, turning liquid into solid **[60-61]**.

4.5.Laser-assisted bioprinting

This approach focuses on pulsed laser beams that exhibit ribbon-like behavior. The ribbon is mostly formed of glass, has a gold or titanium donor convey support layer, a layer of biological material that contains cells or hydrogel, and is assembled on a substrate that is facing the ribbon. Using this technique, the gold layer of the ribbon is bio printed also results in a high-pressure bubble that is then gathered on the substrate **[68-69]**.

The primary factors affecting bioprinting resolution are surface tension, the

distance between the substrate and the ribbon, substrate wettability, the amount of energy delivered per square inch, viscosity, and the thickness of the biological layer. Although the LIFT approach for cell transfer has been successful, the cell survival percentage is frequently under 85%. The primary cause of cell death was identified as radiation injury brought on by nanosecond laser irritancy. Using femtosecond lasers, the damage to the cells was reduced **[65]**. **Hopp et al. [66]** focused on the absorbing film-assisted LIFT (AFALIFT) approach, an enhanced LIFT technique, as a way to manage the transfer of living cells onto different acceptor surfaces. The powerful photomechanical effects of the laser pulse were mostly to blame for the greater fatality rates in cells generated by femtosecond AFA-LIFT compared to nanosecond AFA-LIFT, according to experimental findings of this work.

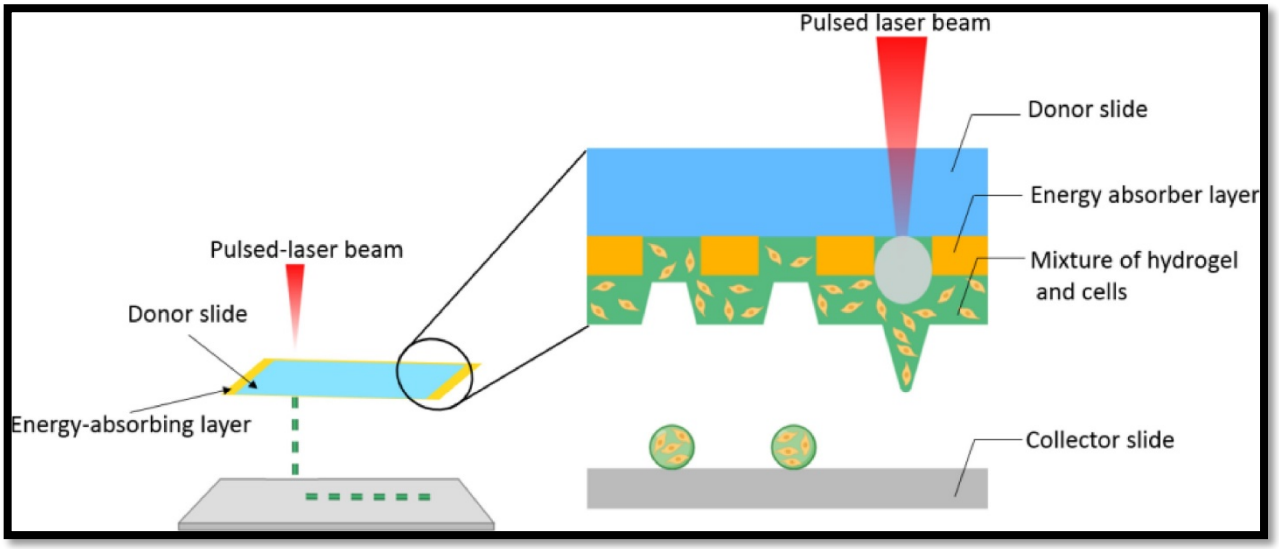

Fig. 4 Schematic diagram of laser-assisted bioprinting **[62]**

5. Limitations

The lack of variety in biomaterials prevents 3D printing from being used in a wide range of medical applications, having its capacity to produce complex designs on demand and at low cost. Considering the availability of a wide range of biomaterials, including metals, ceramics, polymers, and composites, medical 3D printing is still constrained by factors like biomaterial printability, acceptable mechanical strength, biodegradation, and biocompatible characteristics.

Higher polymer concentrations are typically employed in the fabrication of bioinks in extrusion-based bioprinting to ensure the structural integrity of the final product. The cellular network and functional integration of the scaffold are constrained by the dense hydrogel environment. Vascularization is essential for any moderately large biological scaffold to operate, but it is currently unable to do so using 3D printing. A life-size functional organ requires extensive vascularization, unlike the small scale scaffolds that

are currently printed in research labs, which can easily survive through diffusion. Many researchers have employed the addition of sacrificial elements during the scaffold manufacturing to solve this issue. Following the synthesis of the structures, these components are eliminated using post-processing techniques. These materials cover the blank areas and give the printing materials mechanical support. Numerous sacrificial/fugitive substances are being studied right now, including gelatin micro particles, carbohydrate glass, and pluronic glass.

6. Conclusions

3D printing has completely transformed the medical industry and is still growing quickly. Manufacturing patient-specific implants and prostheses, building scaffolds for tissue regeneration and bio artificial organs, individualized drug delivery systems, and anatomical modeling for perioperative simulations are all common therapeutic applications. Because of its possibilities, including the personalization of medicine, cost effectiveness, speed, and increased productivity, 3D printing is increasingly being used in the medical industry. With the help of finite element analysis, it is possible to simulate how the printing parameters will affect the final product's mechanical qualities and acquire the most suitable printing settings in advance. Considering all these developments, 3D printing for medical purposes is still in its infancy and has enormous potential.

There are now just a few biodegradable polymers that can be used in 3D printing. The majority of these biomaterials utilized in 3D printing are implanted or used to provide medicines. Therefore, there is a critical need for research to create innovative biopolymers that can restore functionality at the application site and have customizable bio-properties. We concentrate on inexpensive, easily accessible lactic acid-based polymers (such PLA and PCL) because they work well with the majority of 3D printing processes. They also offer great mechanical and biodegradable qualities. Moreover, these polymers are combined with conventional biomaterials (such HA, TCP) to create composites that have superior mechanical stability, printability, and tissue integration for artificial joint.

This review introduces the sophisticated procedures that are frequently properly considered by researchers and gives an overview of the most widely popular and new biomaterials in 3D bioprinting technique. Furthermore, by highlighting the most significant achievements, an attempt has been made to pass along the most relevant applications of 3D bioprinting technology, such as tissue regeneration, medical research, etc. In order to conduct a comparison using existing biomaterials and 3D bioprinting processes, we focused our attention to highlighting their advantages and disadvantages.

More research is required to maintain 3D bioprinting technology as a feasible fabrication method in biomedical systems given its rapid development.

Acknowledgements

Authors are thankful to Columbia Institute of Engineering and Technology Raipur for providing platform for this research.

Conflict of interest: The authors declare that there is no conflict of interest.

References

[1] Muskan, D. Gupta, and N. P. Negi, "3D bioprinting: Printing the future and recent advances," Bioprinting, vol. 27, 2022, ***doi: 10.1016/j.bprint.2022.e00211****.*

[2] C. L. Ventola, "Medical Applications for 3D Printing: Current and Projected Uses," D Printing, Vol 39, 2014, PMID: 25336867; PMCID: PMC4189697, ***www.ncbi.nlm.nih.gov/pmc/articles/PMC4189697/.***

[3] Y. Fang et al., "Advances in 3D Bioprinting," Chinese Journal of Mechanical Engineering: Additive Manufacturing Frontiers, vol. 1, 2022, ***doi: 10.1016/j.cjmeam.2022.100011****.*

[4] L. Ma et al., "3D printed personalized titanium plates improve clinical outcome in microwave ablation of bone tumors around the knee," Sci Rep, vol. 7, Dec. 2017, ***doi: 10.1038/s41598-017-07243-3****.*

[5] P. S. Gungor-Ozkerim, I. Inci, Y. S. Zhang, A. Khademhosseini, and M. R. Dokmeci, "Bioinks for 3D bioprinting: an overview," Biomater. Sci., vol. 6, 2018, ***doi: 10.1039/C7BM00765E****.*

[6] W. Ng, W. Yeong, and M. Naing, "Polyvinylpyrrolidone-Based Bio-Ink Improves Cell Viability and Homogeneity during Drop-On-Demand Printing," Materials, vol. 10, 2017, ***doi: 10.3390/ma10020190****.*

[7] T. Xu et al., "Hybrid printing of mechanically and biologically improved constructs for cartilage tissue engineering applications," Biofabrication, vol. 5, 2012, ***doi: 10.1088/1758-5082/5/1/015001****.*

[8] M. Müller, J. Becher, M. Schnabelrauch, and M. Zenobi-Wong, "Nanostructured Pluronic hydrogels as bioinks for 3D bioprinting," Biofabrication, vol. 7, 2015, ***doi: 10.1088/1758-5090/7/3/035006****.*

[9] F. Raza et al., "A Review on Recent Advances in Stabilizing Peptides/Proteins upon Fabrication in Hydrogels from Biodegradable Polymers," Pharmaceutics, vol. 10, 2018, ***doi: 10.3390/pharmaceutics10010016.***

[10] S. V. Murphy, A. Skardal, and A. Atala, "Evaluation of hydrogels for bio-printing applications," J. Biomed. Mater. Res., vol. 101A, 2013, ***doi: 10.1002/jbm.a.34326****.*

[11] K. Tappa and U. Jammalamadaka, "Novel Biomaterials Used in Medical 3D Printing Techniques," JFB, vol. 9, 2018, ***doi: 10.3390/jfb9010017****.*

[12] M. K. DeBari, M. N. Keyser, M. A. Bai, and R. D. Abbott, "3D printing with silk: considerations and applications," Connective Tissue Research, vol. 61, 2020, ***doi: 10.1080/03008207.2018.1553959.***

[13] S. Vanaei, M. S. Parizi, S. Abdolhosseini, and I. Katouzian, "Spectroscopic, molecular docking and molecular dynamic simulation studies on the complexes of β-lactoglobulin, safranal and oleuropein," International Journal of Biological Macromolecules, vol. 165, 2020, ***doi: 10.1016/j.ijbiomac.2020.10.139****.*

[14] M. Guvendiren, J. Molde, R. M. D. Soares, and J. Kohn, "Designing Biomaterials for 3D Printing," ACS Biomater. Sci. Eng., vol. 2, 2016, ***doi: 10.1021/acsbiomaterials.6b00121.***

[15] D. Rosenzweig, E. Carelli, T. Steffen, P. Jarzem, and L. Haglund, "3D-Printed ABS and PLA Scaffolds for Cartilage and Nucleus Pulposus Tissue Regeneration," IJMS, vol. 16, 2015, ***doi: 10.3390/ijms160715118.***

[16] D. Garlotta, "A Literature Review of Poly (Lactic Acid)," Journal of Polymers and the Environment, Vol. 9, 200, ***doi.org/10.1023/A:1020200822435.***

[17] T. Serra, M. A. Mateos-Timoneda, J. A. Planell, and M. Navarro, "3D printed PLA-based scaffolds: A versatile tool in regenerative medicine," Organogenesis, vol. 9, Oct. 2013, ***doi: 10.4161/org.26048.***

[18] J. Suganuma and H. Alexander, "Biological response of intramedullary bone to poly-L-lactic acid," J. App. Biomater., vol. 4, 1993, ***doi: 10.1002/jab.770040103****.*

[19] V. E. Santo, A. R. C. Duarte, M. E. Gomes, J. F. Mano, and R. L. Reis, "Hybrid 3D structure of poly(d,l-lactic acid) loaded with chitosan/chondroitin sulfate nanoparticles to be used as carriers for biomacromolecules in tissue engineering," The Journal of Supercritical Fluids, vol. 54, 2010, ***doi: 10.1016/j.supflu.2010.05.021.***

[20] H.-J. Sung, C. Meredith, C. Johnson, and Z. S. Galis, "The effect of scaffold degradation rate on three-dimensional cell growth and angiogenesis," Biomaterials, vol. 25, 2004, ***doi: 10.1016/j.biomaterials.2004.01.066.***

[21] H. Li and J. Chang, "Preparation and characterization of bioactive and biodegradable Wollastonite /poly (D,L-lactic acid) composite scaffolds," Journal of Materials Science: Materials in Medicine, vol. 15, 2004, ***doi: 10.1023/B:JMSM.0000046390.09540.c2.***

[22] X. Zhang, H. Hua, X. Shen, and Q. Yang, "In vitro degradation and biocompatibility of poly (l-lactic acid)/chitosan fiber composites," Polymer, vol. 48, 2007, ***doi: 10.1016/j.polymer.2006.12.028.***

[23] J. Zhu, "Bioactive modification of poly (ethylene glycol) hydrogels for tissue engineering," Biomaterials, vol. 31, 2010, ***doi: 10.1016/j.biomaterials.2010.02.044.***

[24] J. Ulbricht, R. Jordan, and R. Luxenhofer, "On the biodegradability of polyethylene glycol, polypeptoids and poly (2-oxazoline)" Biomaterials, vol. 35, 2014, ***doi: 10.1016/j.biomaterials.2014.02.029.***

[25] B. Romberg et al., "Enzymatic Degradation of Liposome-Grafted Poly (hydroxyethyl L -glutamine)," Bio conjugate Chem., vol. 16, 2005, ***doi: 10.1021/bc0497719.***

[26] W. Wu, P. Geng, G. Li, D. Zhao, H. Zhang, and J. Zhao, "Influence of Layer Thickness and Raster Angle on the Mechanical Properties of 3D-Printed PEEK and a Comparative Mechanical Study between PEEK and ABS," Materials, vol. 8, 2015, ***doi: 10.3390/ma8095271.***

[27] D. W. Hutmacher, M. Sittinger, and M. V. Risbud, "Scaffold-based tissue engineering: rationale for computer-aided design and solid free-form fabrication systems," Trends in Biotechnology, vol. 22, 2004, ***doi: 10.1016/j.tibtech.2004.05.005****.*

[28] K. H. Tan et al., "Scaffold development using selective laser sintering of polyetheretherketone–hydroxyapatite bio composite blends," Biomaterials, vol. 24, 2003, ***doi: 10.1016/S0142-9612(03)00131-5.***

[29] M. Vaezi and S. Yang, "Extrusion-based additive manufacturing of PEEK for biomedical applications," Virtual and Physical Prototyping, vol. 10, 2015, ***doi: 10.1080/17452759.2015.1097053****.*

[30] M. C. Sobieraj and C. M. Rimnac, "Fracture, Fatigue, and Notch Behavior of PEEK," in PEEK Biomaterials Handbook, Elsevier, 2019,. ***doi: 10.1016/B978-0-12-812524-3.00005-3.***

[31] M. Schmidt, D. Pohle, and T. Rechtenwald, "Selective Laser Sintering of PEEK," CIRP Annals, vol. 56, 2007, ***doi: 10.1016/j.cirp.2007.05.097.***

[32] A. Asti and L. Gioglio, "Natural and Synthetic Biodegradable Polymers: Different Scaffolds for Cell Expansion and Tissue Formation," Int J Artif Organs, vol. 37, 2014, ***doi: 10.5301/ijao.5000307.***

[33] X. Liu and P. X. Ma, "Polymeric Scaffolds for Bone Tissue Engineering," Annals of Biomedical Engineering, Vol. 32, 2004, ***doi: 10.1023/b:abme.0000017544.36001.8e.***

[34] B. C. Tellis, J. A. Szivek, C. L. Bliss, D. S. Margolis, R. K. Vaidyanathan, and P. Calvert, "Trabecular scaffolds created using micro CT guided fused deposition modeling," Materials Science and Engineering: C,. 2008, ***doi: 10.1016/j.msec.2006.11.010.***

[35] L. Moroni, G. Poort, F. Van Keulen, J. R. de Wijn, and C. A. van Blitterswijk, "Dynamic mechanical properties of 3D fiber-deposited PEOT/PBT scaffolds: An experimental and numerical analysis," J. Biomed. Mater. Res., 2006, ***doi: 10.1002/jbm.a.30716.***

[36] J. M. Bezemer, D. W. Grijpma, P. J. Dijkstra, C. A. van Blitterswijk, and J. Feijen, "A controlled release system for proteins based on poly(ether ester) block-copolymers: polymer network characterization," Journal of Controlled Release, 1999, ***doi: 10.1016/S0168-3659(99)00170-4.***

[37] A. A. Deschamps et al., "In vivo and in vitro degradation of poly(ether ester) block copolymers based on poly(ethylene glycol) and poly(butylene terephthalate)," Biomaterials, 2004, ***doi: 10.1016/S0142-9612(03)00495-2.***

[38] C. Murphy, K. Kolan, W. Li, J. Semon, D. Day, and M. Leu, "3D bioprinting of stem cells and polymer/bioactive glass composite scaffolds for tissue engineering," Int. J. Bioprint., vol. 3, 2017, ***doi: 10.18063/IJB.2017.01.005.***

[39] M. A. Woodruff and D. W. Hutmacher, "The return of a forgotten polymer—Polycaprolactone in the 21st century," Progress in Polymer Science, vol. 35, 2010, ***doi: 10.1016/j.progpolymsci.2010.04.002.***

[40] Q. Pan et al., "Investigation of bone reconstruction using an attenuated immunogenicity xenogenic composite scaffold fabricated by 3D printing," Bio-des. Manuf., vol. 3, 2020, ***doi: 10.1007/s42242-020-00086-4.***

[41] M.-Y. Shie et al., "3D Printing of Cytocompatible Water-Based Light-Cured

Polyurethane with Hyaluronic Acid for Cartilage Tissue Engineering Applications," Materials, vol. 10, 2017, ***doi: 10.3390/ma10020136.***

[42] K.-C. Hung, C.-S. Tseng, and S. Hsu, "Synthesis and 3D Printing of Biodegradable Polyurethane Elastomer by a Water-Based Process for Cartilage Tissue Engineering Applications," Adv. Healthcare Mater., vol. 3, 2014, ***doi: 10.1002/adhm.201400018.***

[43] C. K. Chua, K. F. Leong, K. H. Tan, F. E. Wiria, and C. M. Cheah, "Development of tissue scaffolds using selective laser sintering of polyvinyl alcohol/hydroxyapatite bio composite for craniofacial and joint defects," Journal of Materials Science: Materials in Medicine, vol. 15, 2004, ***doi: 10.1023/B:JMSM.0000046393.81449.a5.***

[44] C. Shuai, Z. Mao, H. Lu, Y. Nie, H. Hu, and S. Peng, "Fabrication of porous polyvinyl alcohol scaffold for bone tissue engineering via selective laser sintering," Biofabrication, vol. 5, 2013, ***doi: 10.1088/1758-5082/5/1/015014.***

[45] Z. G. Tang, J. T. Callaghan, and J. A. Hunt, "The physical properties and response of osteoblasts to solution cast films of PLGA doped polycaprolactone," Biomaterials, vol. 26, 2005, ***doi: 10.1016/j.biomaterials.2005.04.013.***

[46] J.-H. Shim, J. Y. Kim, M. Park, J. Park, and D.-W. Cho, "Development of a hybrid scaffold with synthetic biomaterials and hydrogel using solid freeform fabrication technology," Biofabrication, vol. 3, no. 3, p. 034102, Sep. 2011, ***doi: 10.1088/1758-5082/3/3/034102.***

[47] P. Chennakesava and Y. S. Narayan, "Fused Deposition Modeling - Insights," Conference: International Conference on Advances in Design & Manufacturing (ICAD&M'14), 2014.

[48] O. A. Mohamed, S. H. Masood, and J. L. Bhowmik, "Optimization of fused deposition modeling process parameters for dimensional accuracy using I-optimality criterion," Measurement, vol. 81 2016, ***doi: 10.1016/j.measurement.2015.12.011.***

[49] H. Vanaei et al., "Influence of process parameters on thermal and mechanical properties of POLYLACTIC ACID fabricated by fused filament fabrication," Polym Eng Sci, vol. 60, 2020, ***doi: 10.1002/pen.25419.***

[50] K. Hölzl, S. Lin, L. Tytgat, S. Van Vlierberghe, L. Gu, and A. Ovsianikov, "Bioink properties before, during and after 3D bioprinting," Biofabrication, vol. 8, 2016, ***doi: 10.1088/1758-5090/8/3/032002.***

[51] A. Pfister, R. Landers, A. Laib, U. Hübner, R. Schmelzeisen, and R. Mülhaupt, "Biofunctional rapid prototyping for tissue-engineering applications: 3D bioplotting versus 3D printing: Biofunctional Rapid Prototyping," J. Polym. Sci. A Polym. Chem., vol. 42, 2004, ***doi: 10.1002/pola.10807****.*

[52] F. P. W. Melchels, M. A. N. Domingos, T. J. Klein, J. Malda, P. J. Bartolo, and D. W. Hutmacher, "Additive manufacturing of tissues and organs," Progress in Polymer Science, vol. 37, 2012, ***doi: 10.1016/j.progpolymsci.2011.11.007.***

[53] S. Derakhshanfar, R. Mbeleck, K. Xu, X. Zhang, W. Zhong, and M. Xing, "3D bioprinting for biomedical devices and tissue engineering: A review of recent trends and advances,"

Bioactive Materials, vol. 3, 2018, ***doi: 10.1016/j.bioactmat.2017.11.008.***

[54] M. Kesti et al., "A versatile bioink for three-dimensional printing of cellular scaffolds based on thermally and photo-triggered tandem gelation," Acta Biomaterialia, vol. 11, 2015, ***doi: 10.1016/j.actbio.2014.09.033.***

[55] A. Rees et al., "3D Bioprinting of Carboxymethylated-Periodate Oxidized Nanocellulose Constructs for Wound Dressing Applications," BioMed Research International, 2015, ***doi: 10.1155/2015/925757.***

[56] I. Ozbolat and Y. Yu, "Bioprinting towards Organ Fabrication: Challenges and Future Trends," IEEE Trans Biomed Eng , 2013, ***doi: 10.1109/TBME.2013.2243912.***

[57] H. Gudapati, M. Dey, and I. Ozbolat, "A comprehensive review on droplet-based bioprinting: Past, present and future," Biomaterials, vol. 102, 2016, ***doi: 10.1016/j.biomaterials.2016.06.012.***

[58] J. D. Kim, J. S. Choi, B. S. Kim, Y. Chan Choi, and Y. W. Cho, "Piezoelectric inkjet printing of polymers: Stem cell patterning on polymer substrates," Polymer, vol. 51, 2010, ***doi: 10.1016/j.polymer.2010.03.038.***

[59] R. P. Sinha and D.-P. Häder, "UV-induced DNA damage and repair: a review," Photochemical. Photobiol. Sci., vol. 1, 2002, ***doi: 10.1039/b201230h.***

[60] F. R. de Gruijl, H. J. van Kranen, and L. H. F. Mullenders, "UV-induced DNA damage, repair, mutations and oncogenic pathways in skin cancer," Journal of Photochemistry and Photobiology B: Biology, vol. 63, 2001, ***doi: 10.1016/S1011-1344(01)00199-3.***

[61] Z. Wang, R. Abdulla, B. Parker, R. Samanipour, S. Ghosh, and K. Kim, "A simple and high-resolution stereolithography-based 3D bioprinting system using visible light crosslinkable bioinks," Biofabrication, vol. 7, 2015, ***doi: 10.1088/1758-5090/7/4/045009.***

[62] S. Vanaei, M. S. Parizi, S. Vanaei, F. Salemizadehparizi, and H. R. Vanaei, "An Overview on Materials and Techniques in 3D Bioprinting Toward Biomedical Application," Engineered Regeneration, vol. 2, 2021, ***doi: 10.1016/j.engreg.2020.12.001.***

[63] H. Gudapati, J. Yan, Y. Huang, and D. B. Chrisey, "Alginate gelation-induced cell death during laser-assisted cell printing," Biofabrication, vol. 6, 2014, ***doi: 10.1088/1758-5082/6/3/035022.***

[64] J. A. Barron, P. Wu, H. D. Ladouceur, and B. R. Ringeisen, "Biological Laser Printing: A Novel Technique for Creating Heterogeneous 3-dimensional Cell Patterns," Biomedical Microdevices, vol. 6, 2004, ***doi: 10.1023/B:BMMD.0000031751.67267.9f.***

[65] C. B. Arnold, P. Serra, and A. Piqué, "Laser Direct-Write Techniques for Printing of Complex Materials," MRS Bull., vol. 32, 2007, ***doi: 10.1557/mrs2007.11.***

[66] B. Hopp, "Femtosecond laser printing of living cells using absorbing film-assisted laser-induced forward transfer," Opt. Eng, vol. 51, 2012, ***doi: 10.1117/1.OE.51.1.014302.***