

Material Extrusion Techniques for Biomedical Applications: Biomaterials and Their Performance - A Review

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Abstract. Material extrusion-based additive manufacturing (AM) is transforming the medical sector by enabling innovative, cost-effective, and highly customizable solutions. This review examines key material extrusion methods, namely Fused Filament Fabrication (FFF), Direct Ink Writing (DIW), and Direct Pellet Extrusion (DPE), highlighting their advantages, material versatility, and medical applications. These technologies support the development of personalized implants, prosthetics, tissue engineering, scaffolds, and drug delivery systems (DDS). A broad range of materials, like thermoplastics (e.g., PCL, PLA, PEEK), hydrogels (e.g., alginate, collagen), metals (e.g., titanium alloys), and bio ceramics (e.g., hydroxyapatite, zirconia), influence mechanical properties, biocompatibility, and degradation behavior. Thermoplastics provide durability, hydrogels promote cell growth, and bio ceramics aid bone regeneration. However, challenges like material limitations, mechanical strength, and degradation control require further research. Developments in composite printing, hybrid systems, and precision engineering are improving resolution, speed, and scalability. Innovations in smart polymers, nanocomposites, and bioactive hydrogels enhance functionality, while AI and robotics optimize design and fabrication. Despite these developments, regulatory and ethical concerns regarding safety and accessibility must be addressed. Future progress in custom organ printing and biodegradable implants holds promise for personalized healthcare, emphasizing the need for interdisciplinary collaboration to realize the full capabilities of material extrusion-based AM in medicine.

Keywords: Additive manufacturing, Material extrusion, Thermoplastics, Hydrogel, Metal, Ceramic, Biocompatible.

1. Introduction

Additive manufacturing (AM) is widely recognized for its resourcefulness and design flexibility in various fields, particularly in the medical sector [1,2]. AM technology builds products or prototypes layerwise from digital models [3]. According to the ISO/ASTM 52900:2021 standard, AM is a process of joining materials to make a part from 3D model data (typically from using standard tessellated language, a.k.a., STL), usually layer by layer, rather than using subtractive manufacturing and formative manufacturing techniques [4,5]. AM is categorized into seven classes according to their working principles and materials used: Material extrusion, Material Jetting, Binder Jetting, Direct energy deposition, Powder bed fusion, Sheet lamination and Vat photopolymerization (Figure 1)[6]. One of the main classes of interest in this manuscript is the material extrusion-based technique (indicated by the yellow box in Figure 1), which includes fused filament fabrication (FFF), direct ink writing (DIW), and direct pellet extrusion (DPE)[7,8,9].

Material extrusion found its application in the medical sector for prototyping implants and scaffolds due to its cost-effectiveness and material strength, which enabled design evaluation prior to sterilization, clinical trials, and regulatory approval[10,11]. Recent advancements have broadened the availability of materials for medical applications [12,13]. This reflected in the steep growth of research between 2014 and 2025, as illustrated in Figure 2a, and the percentage breakdown of various publication types in Figure 2b, which is derived from the Scopus database [14,15]. In medical applications, products are often personalized for individual patients, making traditional manufacturing processes time-consuming and expensive [16-18]. In contrast, additive manufacturing offers significant advantages by allowing for design freedom and

eliminating the need for extensive fabrication planning [19,20]. In particular, for small-scale production, AM offers a cost-effective alternative to traditional methods (e.g., injection molding, CNC machining and casting) [21,22]. Keywords analysis of 17,162 documents from the Scopus database (2014-2025) reveals that researchers focused on five primary domains (Figure 2c). Metal and alloy 3D printing has enabled the fabrication of efficient components for the aerospace and automotive industries, improving mechanical properties through optimized printing parameters [23-25]. In biomedical applications, additive manufacturing naturally lends itself to the complexity and high customizability required in sectors such as prosthetics, implants, and tissue engineering, and in turn offers patient-specific solutions [26,27]. Developing composite 3D printing materials has expanded the range of printable materials, enhancing strength, conductivity, and thermal properties for specialized applications [28,29]. Researchers have also improved the printing process and the structural optimization of parts to be 3D printed, using computational modeling and AI-driven tools to enhance precision and reduce defects [30,31]. Moreover, electrical applications of AM have facilitated the creation of conductive materials, sensors, and flexible electronics, driving innovations in wearable technology and smart devices [32,33]. These advancements highlight the interdisciplinary nature of AM and its transformative influence across several industries [29,34,35].

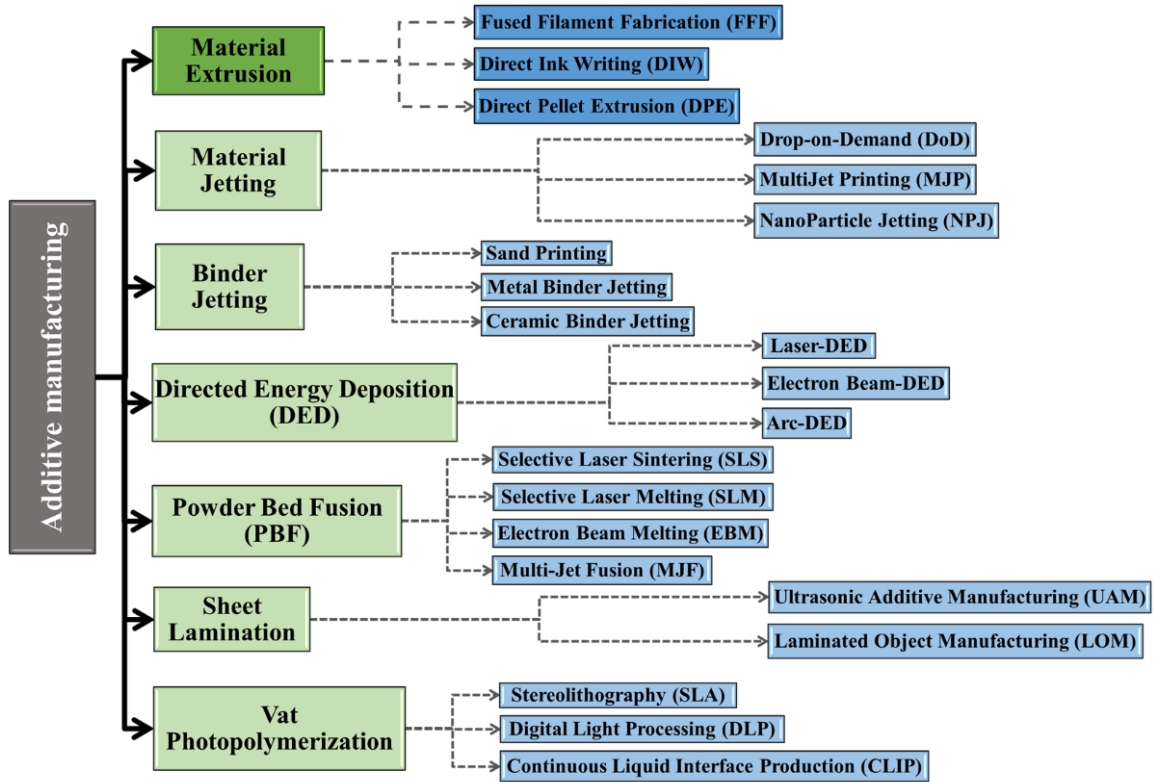


Figure 1. Additive manufacturing technology is classified based on the ISO/ASTM 52900:2021 standard, which includes some subclassifications.

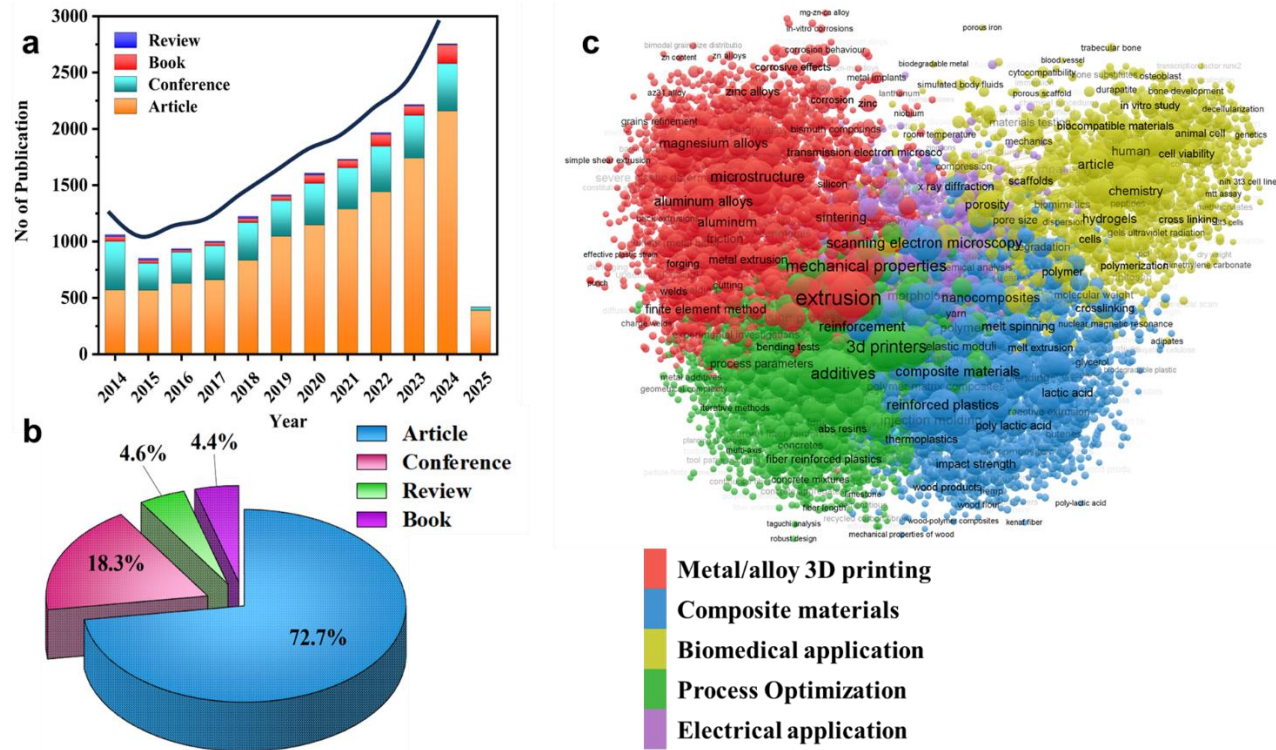


Figure 2. (a) The annual no of publications on material extrusion, (b) Percentage of publications distributed by document type, (c) Network mapping of keywords from 17,162 documents related to material extrusion (Scopus database 2014-2025).

According to the Global Market Insight 2024 report, the 3D printing market in healthcare will grow at a CAGR of 18.6% between 2024 and 2032, rising from \$2.9 billion in 2023 to \$13.8 billion by 2032 [36]. The rapid growth of this technology is driving its use in critical medical applications [37]. AM is transforming the way tissue engineering scaffolds, orthopedic implants, personalized medical apparatus, DDS, wound healing, and skin regeneration aids are developed [38,39]. Customized medical apparatus, including prosthetics, orthotics, and surgical equipment, is designed to meet patients’ specifications, enhancing comfort for patients and surgeons and improving functionality [17,40,41]. Implants, including joint replacements, dental implants, and cranial plates, are personalized to fit the patient's anatomy for efficient integration with the body [42,43]. AM is clearly an efficient production method that can potentially deliver high-quality products for healthcare [44,45]. Figure 3 shows some, but not all, AM medical prototypes.

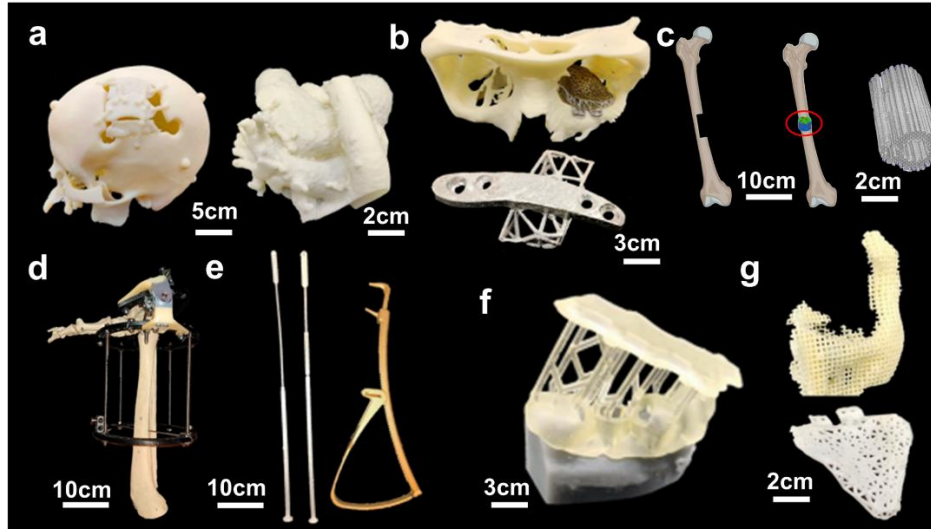


Figure 3. Some of the 3D printed Prototypes from the article are (a) medical models, (b) implants, (c) bone Scaffolds, (d) splints, supportive guides, medical aids, and prostheses, (e) tools, instruments for surgery, and (f) Parts for medical devices, (g) biomanufacturing available under the Creative Commons Attribution 4.0 (CC BY) guidelines [2,46,47].

Biocompatible AM materials ensure that implants and scaffolds, for instance, are safe and effective for long-term use.[48,49]. Similarly, AM has influenced Regenerative medicine and tissue engineering [50,51]. Tissue scaffolds, which serve as structural support for tissue formation and cell growth, can be accurately produced to replicate the complex architecture of living tissues and so enhance cell proliferation [52,53]. This technology offers potential for developing functional organs and tissues (at least in the long run) for transplantation, which is a step towards addressing the scarcity of organ donors. [54,55]. Drug delivery systems made with AM can be introduced into the body to control dosage release and targeting of drug delivery, enhancing safety and efficiency [56,57]. In wound healing and skin regeneration, a 3D printed wound scaffold for tissue regeneration can potentially heal damaged parts [58,59]. Figure 4 shows a list of some biocompatible, bioactive, or biodegradable materials utilized in material extrusion. This review work focuses on exploring and comparing various material extrusion-based AM techniques in light of the materials used and their suitability and performance in medical applications. We will explore how different extrusion materials and AM techniques advance personalized medical devices, implants, tissue scaffolds, DDS, and wound healing or skin regeneration aids. The review will analyze the material properties, biocompatibility and overall mechanical performance. We will highlight the most recent developments and challenges in extrusion-based AM. As such, this review will progressively identify the most promising extrusion-based approaches, along with their material collections, that can enhance the efficacy and safety of medical applications.

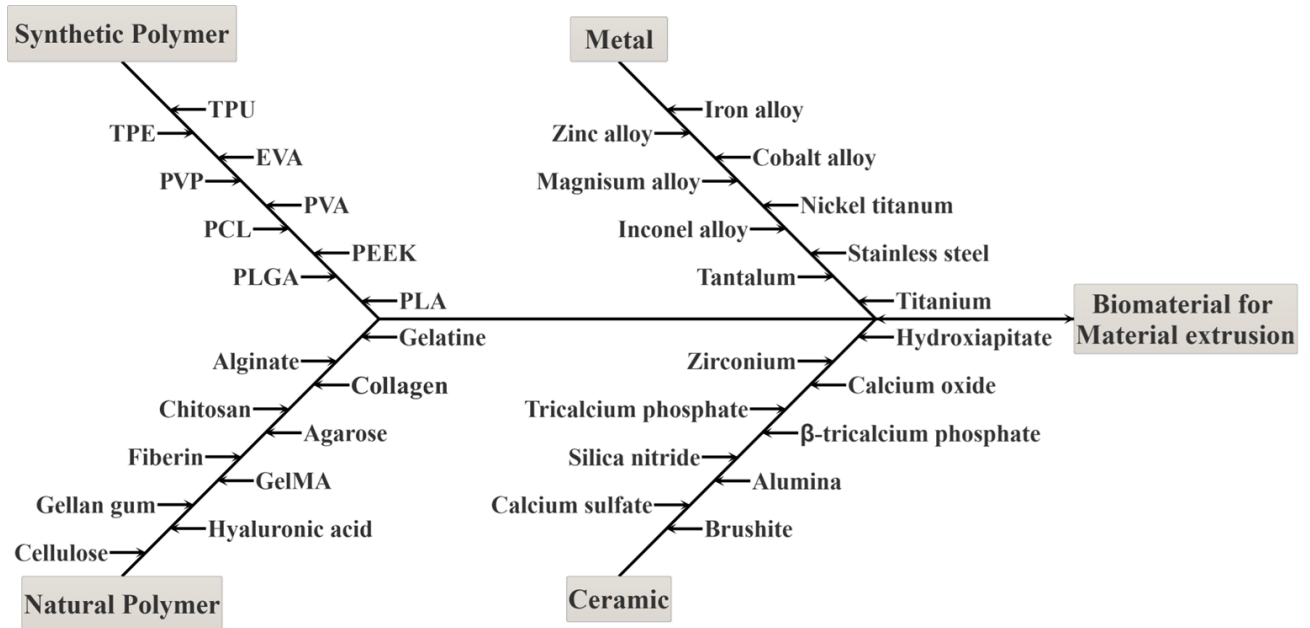


Figure 4. Fishbone diagram to illustrate the biomaterials utilized in the Material extrusion based on material type.

2. Material Extrusion Techniques

Material extrusion technology is easy to initiate, even in home settings, and features low apparatus and energy costs [60,61]. Because of this, it is widely used by hobbyists and small-scale manufacturers across various industries [62,63]. Figure 5 illustrates the general steps of the material extrusion method. Initially, a CAD model of the desired product is created using CAD modeling software or a 3D scanning system. The model is converted to an STL format, which is a widely accepted format for AM machines [64]. Slicing software, such as Ultimaker Cura, Simplify3D, or BambuStudio, is used to process the STL by slicing it into a stack of layers with a specific thickness and so generate the respective G-code that instructs the AM machine nozzle deposition path. Once the G-codes are uploaded to the AM machine, it constructs the part layer upon layer based on the specified printing parameters[65,66]. Several distinct factors affect the quality of products processed by ME techniques, as illustrated in Figure 6. These factors are categorized into six main groups: Environmental Factors, Design, Material, Machine, Process, and Post-Processing. This classification provides a comprehensive framework for identifying and optimizing the key variables involved in material extrusion-based 3D printing. After printing, any support structures or build-platform adhesion must be removed. Post-processing helps to enhance mechanical properties and surface quality [67]. Common methods include manual support removal, optical polishing, vapor smoothing, painting, tumbling, and CNC milling [68]. At the same time, advanced techniques like electroplating, ultrasonic abrasion, and laser finishing can further enhance the final product [69]. Here, we list out the three main types of material extrusion techniques in Table 1.

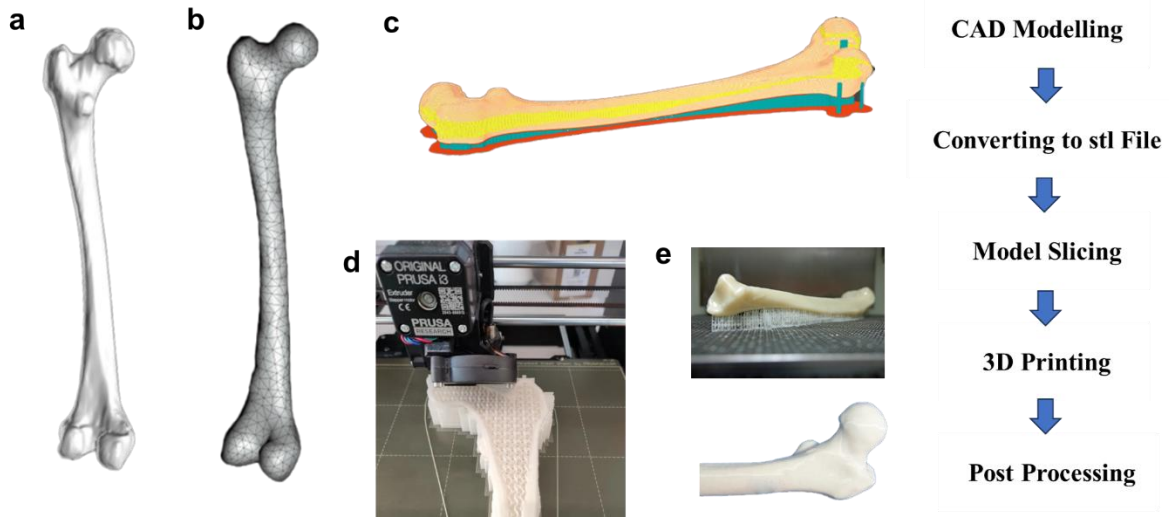


Figure 5. Generic process of the material extrusion AM technique: (a) CAD modelling, (b) stl file conversion, (c) model slicing, (d) 3D printing, and (e) post processing available under the Creative Commons Attribution 4.0 (CC BY) guidelines [70,71].

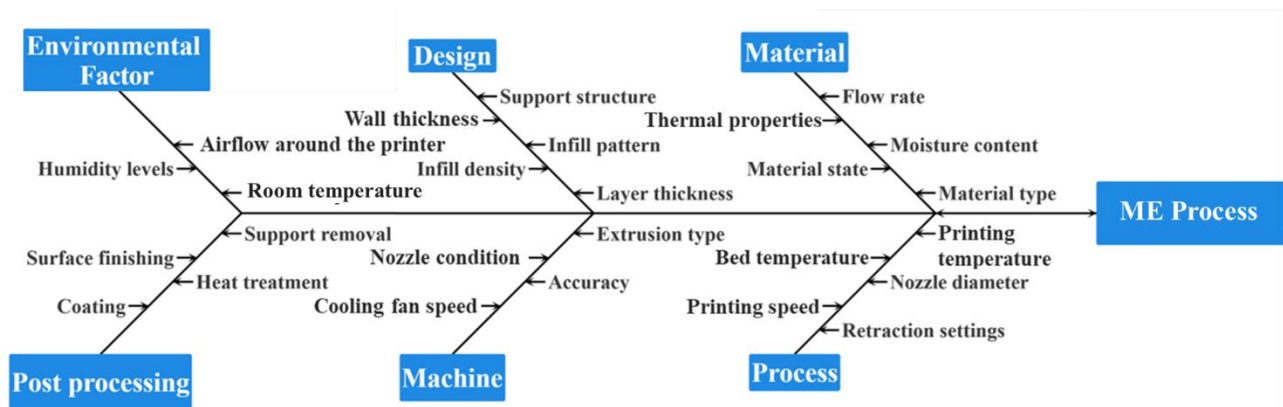


Figure 6. Fishbone diagram of factors impacting the product quality of the material extrusion process.

Table 1. Comparison table of various material extrusion techniques.

Technique		Principle and Mechanism	Materials Used	Medical Applications	Advantages	Limitations	Print Resolution (μm)	Bio-compatibility	Reference
Fused Filament Fabrication (FFF)		Molten thermoplastics are extruded through a nozzle to form structures	PLA, PEEK, TPU, EVA, PBAT, PVA	Prosthetics, implants, models, medical devices, Drug loaded scaffolds, Biomedical tools	Low cost, accessibility	surface finish, dimensional accuracy	100-300	Varies by material selection	[72,73,74]
Direct Ink Writing (DIW)	Gel-based (GDIW) or bioprinting	Layering bio-inks to create living tissues	Alginate, gellan gum, agarose, gelatin, collagen	Tissue engineering, organ scaffolds, organ construction, wound healing, drug delivery	Ability to print living tissues	Material instability, slow printing speed	50-100	High (for most bio inks)	[75,76,77,78]
	Ceramic-based (CDIW) or (DCE)	Extruding ceramic materials mixed with binders	Hydroxyapatite, zirconia, Silica nitride, tricalcium phosphate (TCP), β -TCP	Orthopedic implants, dental components, bone regeneration	complex geometries, high-strength	Complex machine calibration, brittleness	300-1000	High (for bioceramics)	[79,80,81]
Direct Pellet Extrusion (DPE)		Extruding polymer pellets through a nozzle	PEEK, UHMWPE, PLGA, POE, PCLF, TPE, EVA	Orthopedic implants, dental devices, Drug delivery, tissue engineering, scaffold	Broad material range, cost-effective	Complex calibration, lower precision	200-500	Varies by material selection	[82,83,84]

2.1. Fused Filament Fabrication (FFF)

FFF is a commonly exploited AM approach, particularly in the realm of material extrusion [85]. The basic principle of FFF involves selectively depositing molten thermoplastic polymers to build a 3D product by stacking layer upon layer [86]. The schematic of the Basic FFF machine is shown in Figure 7. STL file is processed using software specially made for slicing, which segments the design into horizontal layers and creates the printer's toolpath [87]. Thermoplastic filament spools, like Polylactic Acid (PLA), Polycarbonate (PC), or Polyether ether ketone (PEEK), are fed into the FFF machine [88]. The filament is directed into the print head, passing through the heater and subsequently to the nozzle. The heater heats the filament until it turns to a viscous state. Molten polymers are driven through the nozzle by the extruder head [89]. The nozzle follows the toolpath, moving along the horizontal (in-plane) and vertical axes (out-of-plane) to deposit molten or semisolid polymers on the bed. The material rapidly solidifies, creating the object's initial layer. Once a layer is finished, the bed lowers (or the print head rises) by a small increment, corresponding to the layer thickness (usually between 0.1 and 0.3 millimeters). Successive layers are deposited and fused, progressively building a solid 3D structure that replicates the digital model (i.e., the STL file).

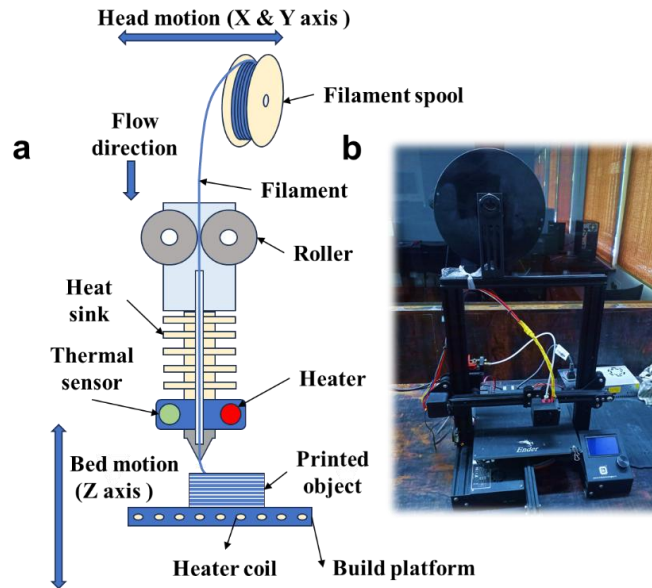


Figure 7. (a) Schematic model of FFF and (b) Basic FFF machine.

Fused Filament Fabrication (FFF) approach offers several benefits. This technology is economical, as the materials used are generally more affordable than those in other 3D printing methods, allowing it to be applied across a wide range of uses [90]. FFF also supports a range of thermoplastics, enabling the choice of materials with tailored properties, like strength, biocompatibility, and flexibility [91]. Additionally, FFF printers are user-friendly and require minimal maintenance, making them suitable for both experts and beginners. FFF is extensively utilized in the development of prototypes and the creation of custom medical devices, including prosthetics, orthotics, and surgical tools [92]. Custom implants tailored to patient-specific anatomical features can be produced using biocompatible thermoplastics [93]. FFF technology can also create complex scaffold structures supporting cell growth and tissue development, aiding regenerative medicine [94]. Several materials are commonly used in the FFF process. PLA is a biodegradable thermoplastic developed from renewable resources, including sugarcane, cassava, and corn. It is easy to

print, has low warping, and provides a moderate surface finish, making it ideal for creating anatomical models and temporary implants due to its biocompatibility and biodegradability [95,96]. PEEK is an efficient engineering thermoplastic with exceptional mechanical characteristics, chemical resistance, and thermal stability [97]. It is also biocompatible and can be sterilized, making it perfect for permanent implants like spinal implants, cranial plates, and dental implants [98]. ABS is a common thermoplastic as well, recognized for its toughness and impact resistance [99]. While it offers better mechanical properties than PLA, it is used in patient-contact applications like medical devices, surgical tools and fixtures. [100]. Biodegradable materials such as PCL and PGA are used in medical applications where the material is required to gradually break down over time within the body (i.e., resorbable) [101]. These materials are suitable for developing scaffolds and temporary implants that promote tissue regeneration and gradually degrade, that in turn removes the need for surgical extraction.

The FFF process has various applications in the medical sector. It helps create custom prosthetic limbs designed to fit patients' specific measurements for adequate comfort and usability. Organizations like e-NABLE use FFF technology to develop low-cost, customizable prosthetic hands for children [102]. FFF is also used to create implants that match patients' unique anatomical features, improving fit and integration with the body. For instance, the use of PEEK for spinal implants demonstrates the effectiveness of FFF in producing high-strength, biocompatible implants suitable for the human body [103]. Additionally, FFF is widely utilized to produce accurate anatomical models for medical education and surgical planning. These models accurately represent patient anatomy, permitting surgeons to plan intricate surgeries more effectively, reducing operation time, and improving outcomes [104]. However, there are some limitations to the FFF process. Various medical-grade polymers exist in the market, but FFF is limited to only a few due to filament availability [105]. FFF-printed objects typically undergo post-processing to attain a smooth surface finish, which is crucial for certain medical applications [67]. Moreover, the layer upon layer nature of FFF can lead to reduced resolution relative to other AM approaches, which may limit FFF's use in highly complex and fine biomedical implants and features [106].

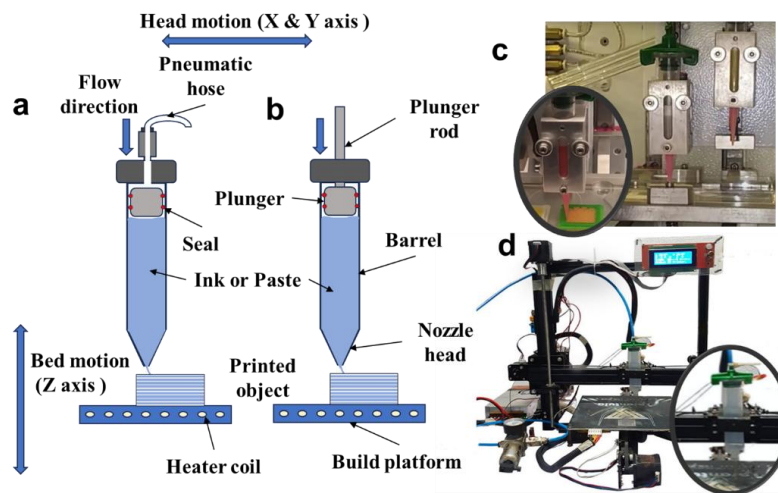


Figure 8. Schematic Diagram of (a) Pneumatic-based DIW and (b) Plunger-based DIW. DIW machines, (c) Gel-based DIW Fabforge bioprinter, and (d) DIY DIW printer available under the Creative Commons Attribution 4.0 (CC BY) guidelines.[107].

2.2. Direct ink writing (DIW)

DIW is an AM approach that allows the fabrication of complex 3D structures by precisely depositing a viscous ink layer upon layer schematic, as shown in Figure 8(a, b) [107]. Unlike other 3D printing methods like the FFF technique that rely on melting, curing, or sintering materials, DIW uses extrudable inks that solidify after deposition, making it highly versatile for a widespread of materials and applications. Those viscous inks are extruded via pneumatic, piston or a screw mechanism near room temperature. DIW has attracted growing attention for its capability to produce customized, multi-material, and functionally graded structures with high precision [108]. DIW can be applicable for materials with low melting points and that operate at low temperatures, thus can be adapted for heat-sensitive paste or ink in AM [8,109]. DIW can therefore be used for customized gel-like material and ceramic pastes, so DIW may subclassify into gel-based printing and ceramic-based printing.

2.2.1. Gel-Based DIW (GDIW)

Gel-based DIW is branched into 3D bioprinting that utilizes bioinks and soft materials integrated with cells to create structures that replicate natural tissues [110]. Bioinks are hydrogel-based materials typically loaded with living cells which are extruded through a nozzle to create 3D biological constructs while maintaining cell viability. [111]. The process starts by loading the bio-ink into a printing cartridge, which is then placed in the bioprinter. The printer employs a controlled extrusion system via either pneumatic, piston-driven, or screw-driven, finely tuned with the viscosity and shear-thinning behavior of the bioink, where the material's viscosity decreases with an increase in shear rate. In bioink 3D printing, the layered deposits can solidify through crosslinking agents, light exposure, and/or heat (Figure 8c)[112]. Nozzle diameter and control system of the moving frame is tuned to ensure that final structure closely resembles the target tissue or organ [113]. After printing, an additional cross-linking process is required to improve the mechanical characteristics and stability of the structure of the gel, which can involve using chemical agents, UV light, or thermal processes [114].

Alginate, collagen, and gelatin are prime base materials for bioinks used in a bioprinter. Alginate is natural polymer synthesized from seaweed and used in bioprinting for its biocompatibility and capability to undergo gelation upon interaction with divalent ions like calcium [115]. Collagen constitutes a significant portion of the extracellular matrix (ECM) across various tissue types and facilitates cell differentiation, adhesion, and growth. Collagen-based bioinks are often used to print skin, cartilage, and other connective tissues [116]. Gelatin is derived from collagen, a thermosensitive hydrogel that gels at lower temperatures. In addition, it is biodegradable and promotes cell proliferation and adhesion, thus of high utility for tissue engineering for skin and bone [117]. Other hydrogels like hyaluronic acid, fibrin, and polyethylene glycol (PEG) can also be utilized in bioprinting [118]. Novel formulations of different bioinks can potentially generate a spectrum of mechanical strengths and a wide range of bioactivities, thereby expand their biomedical applications: from vascular graft development to neural tissue regeneration. [119]. Embedded bioprinting approach supports the development of complex 3D structures by providing in-situ support during printing. These methods include omnidirectional printing, sacrificial writing, ghost writing, and Freeform Reversible Embedding of Suspended Hydrogels (FRESH) [120,121]. Decellularized ECM-based bioinks, derived from the extracellular matrix of different tissues, help create structures that closely mimic natural tissue environments. These biomimetic features support cell growth, guide differentiation, and promote tissue regeneration [122].

In particular, bioprinting applications include the production of layered skin tissues that closely resemble natural skin, which can be beneficial for treating burns and chronic wounds etc. It can also create cartilage scaffolds designed to repair joint injuries and degenerative conditions like osteoarthritis [123]. Bioprinting enables the development of intricate organ scaffolds that provide a framework for growing functional tissues for the heart, liver, and kidney [124]. In fact, researchers have successfully bioprinted mini-livers and heart valves suitable for disease modeling and drug testing [125]. Scaffolds embedded with osteogenic cells and growth factors, realized via bioprinting, can aid in bone regeneration for critical defects and fractures [126]. Bioprinting enables the fabrication of blood vessels and vascularized tissues, which not only replicate the overall shape of the organ but also endow it with functionality [127]. Besides, vascularization, the incorporation of viable living cells in bioprinting generates a functioning biological tissue that can integrate with the human body [128]. Moreover, it also enables the formation of patient-specific tissues and organs, enhancing treatment effectiveness and compatibility [129]. However, some bioinks and hydrogels may lack adequate mechanical stability, degrading too quickly or not providing sufficient support for tissue formation [130]. Bioink printing, however, is time-consuming and is not ideal for large-scale prints [131]. Furthermore, developing bioinks that maintain cell viability, promote tissue formation, and possess suitable mechanical properties is a challenging endeavor that requires extensive research and optimization [132].

2.2.2. Ceramic-based DIW(CDIW)

Direct ceramic extrusion is a manufacturing technique where ceramic materials, typically mixed with organic binders, are pushed through a nozzle to create intricate shapes. This process is similar to other extrusion methods but is specifically designed for ceramics. A mixture of ceramic powders, binders and additives to form a paste or slurry with the desired rheological behavior for extrusion, often containing polymers to maintain shape before sintering. The ceramic mixture is placed in a barrel, where a screw or piston mechanism forces the material via a nozzle. The nozzle diameter directly influences the cross-sectional profile of the deposited material. In some cases, heating is applied to reduce the mixture's viscosity, depending on the binder used [133]. As the material is extruded, it is deposited layer upon layer, thereby constructing intricate structural designs, commonly known as the green part (Figure 9a). The extruded shape remains stable until further processing, where it is transformed into the brown part through debinding by the removal of the binder materials (Figure 9b). In the final sintering phase, the extruded parts are heated and pressurized until the particles coalesce, forming a dense ceramic structure without fully melting (Figure 9c) [134].

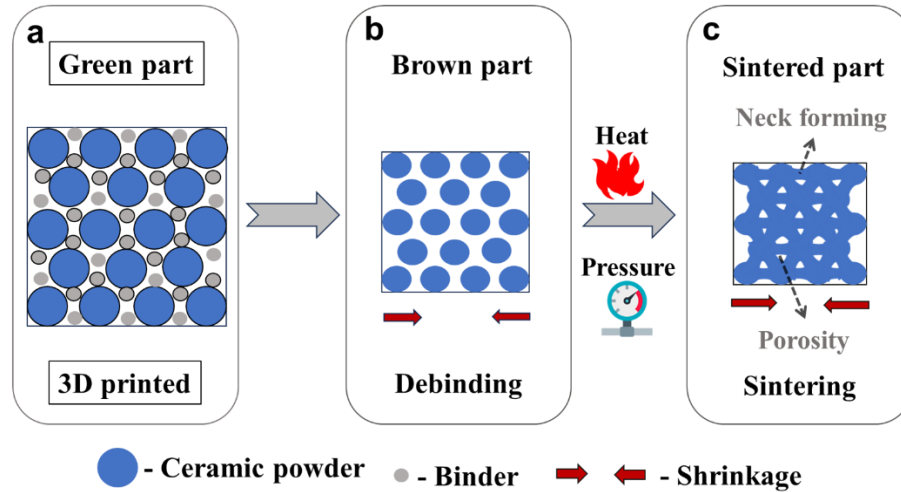


Figure 9. Post-processing Stages in Ceramic Additive Manufacturing. (a) green part, (b) brown part, and (c) sintered part.

Direct ceramic extrusion (DCE) uses high-performance bioceramics. For example, Hydroxyapatite (HA) that is a natural form of calcium apatite, is frequently utilized in bone regeneration owing to its high Osteo-conductivity and proven biocompatibility [135]. Tricalcium phosphate (TCP) is another bioceramic, which is biodegradable and known for promoting osteogenesis, and so is of utility in temporary bone scaffolds [136]. Recognized for its mechanical strength and resistance to wear, alumina is often applied in dental applications, such as crowns and bridges [137]. Calcium silicate, which promotes cell attachment, is useful in bone repair and regeneration [138]. This extrusion technique supports a variety of medical applications [139]. Alumina and zirconia are employed in dental restorations, like bridges and crowns, where aesthetics, strength, and durability are important [140]. Ceramic materials are also employed in surgical instruments requiring high wear resistance and biocompatibility. Additionally, HA or TCP scaffolds can be extruded to provide structural support for new bone growth in surgical repairs [141]. DCE is actually cost-effective compared to other advanced manufacturing methods. It is compatible with a broad spectrum of ceramic materials, enabling the combination of physical, biological, mechanical, and surface properties like strength, biocompatibility, and hardness, tailored for specific medical applications. As an additive manufacturing process, it actualizes complex shape, thus ideal for implants and scaffolds that mimic natural bone architecture and overall morphology. DCE however has some limitations. Precise calibration is required to maintain consistent material flow and accurate shapes, making the process more complex. Although it can create complex designs, DCE may lack the dimensional precision achievable with other 3D printing or CNC machining. The need for additional steps, like drying and sintering can extend production times [142,143].

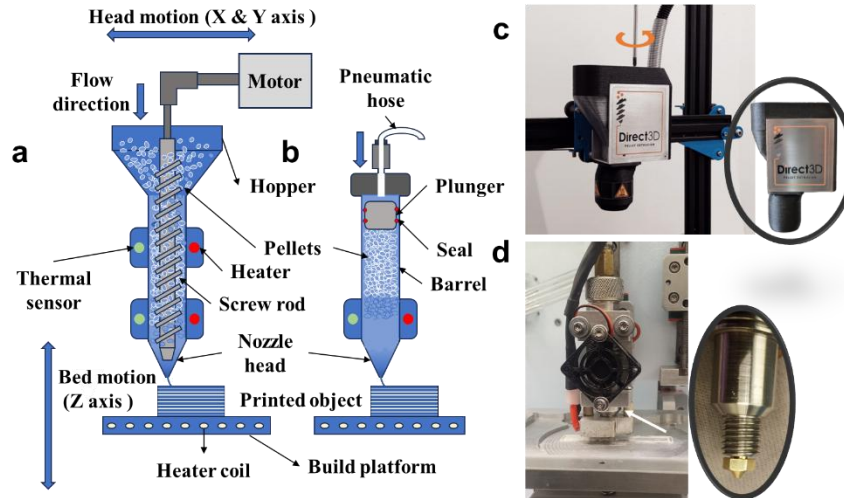


Figure 10. (a) Screw-based DPE, (b) Pneumatic-based DPE, (c) Screw-based DPE machines, and (d) Pneumatic-based DPE machines (Fabforge printer) [144].

2.3. Direct Pellet Extrusion (DPE)

DPE is an AM approach that utilizes polymer pellets as the feedstock instead of the more commonly used filament [145]. This method involves extruding molten polymer directly from the pellets, offering several advantages and unique characteristics compared to filament-based extrusion. In this process, polymer pellets are fed into a hopper, which guides them into the extrusion system. Unlike filament extrusion, which uses a continuous strand of filament, the pellets are transported into a heated chamber where they are melted. The temperature in this chamber is carefully controlled to ensure the polymer reaches the correct viscosity with the required shear-thinning properties for extrusion. A screw driven mechanism forces the liquefied polymer through a nozzle. This screw not only pushes the material but also mixes and homogenizes it, thereby achieving a consistent flow of molten polymer. Pneumatic pressure is an alternative as well. The nozzle deposits the material layer upon layer onto a build platform, similar to filament-based FFF (Figure 10d) [144]. The bed shifts along the z-axis to allow for the addition of subsequent successive layers. Like the FFF method, the object is built by layer. As each layer cools, it solidifies and bonds with the previous one, continuing this process until the entire structure is built as defined by the sliced CAD model. Materials used in the Direct Pellet Extrusion (DPE) process include PEEK, UHMWPE and PLGA, where each is chosen for its distinct properties and suitability for medical applications. PEEK stands out here because of its excellent mechanical characteristics, biocompatibility, and resistance to chemicals, making it very suitable for medical applications [146]. PEEK's durability and ability to be sterilized make it ideal for orthopedic implants, like spinal cages, joint replacements, and dental components. UHMWPE is widely recognized for its excellent resistance to impact, low friction, and biocompatibility, making it essential in applications where wear resistance is critical [147]. It is frequently utilized in orthopedic implants, especially in joint replacements like knee and hip implants. PLGA is a biocompatible and biodegradable copolymer utilized in medical applications where temporary support is needed and particularly gradual degradation is desired. PLGA is employed in scaffolds, tissue engineering, DDS, and temporary implants that promote tissue regeneration [148].

Direct pellet extrusion (DPE) bypasses the need for a filament and thus eliminates the need for large infrastructure (Filament maker). Accordingly, allows on-demand 3D printing of specialized formulae

and various mixtures of materials into the intended design, which is often the case with personalized orthopedic implants. A prime example is PEEK implants since PEEK has proven to be directly applicable in implants and is considered a viable alternative to metallic components [149], and is also applicable for crowns, bridges, and dentures as well [150]. Direct Pellet Extrusion (DPE) is particularly well-suited for PEEK printing, as its high-temperature heating chambers eliminate concerns associated with filament melting in traditional FFF printing. In DPE, the chamber temperature can be precisely set to exceed 343 °C, allowing PEEK to melt to various viscosity levels required to accurately realize the CAD model. By bypassing the need for filament use, DPE avoids common challenges such as maintaining uniform heat across the filament and the issues of warping and interlayer delamination, both of which are inherent to filament-based 3D printing. As such, DPE is better suited for the high-fidelity fabrication of high-strength polymers, including PEEK and UHMWPE-based prosthetics, dentures, and implants. DPE is also applicable in manufacturing surgical instruments, particularly those that require intricate designs or customization [151]. Materials like UHMWPE offer the necessary strength and wear resistance for these tools. Custom surgical guides and instruments made from PEEK or UHMWPE have been utilized in procedures that demand high precision and reliability [152].

In terms of affordability, DPE pellets are much more affordable than filaments. Thus, more suited for high-throughput production. A major edge of DPE is the ability to mix several polymers in the form of pellets with various additives at varied (powder) melting points prior to exposition into the building plate [83]. However, with the high adaptability of DPE comes a downside where requires cumbersome and precise calibration for the various combinations of polymers and additives that DPE permits. Therefore, each new mixture and/or material made via DPE will have its own unique protocol in terms of quantities (mass fractions), heating time, heat intensity, and heat adjustments during printing [153]. Because of the usual large nozzle discharge aperture of DPE that is mainly designed to accommodate various materials: fibers, polymers, and powder additives, there is therefore an inevitable compromise in resolution of the print. Thus, objects printed by DPE can have a rougher surface finish, which may necessitate additional finishing processes like polishing [154].

So far, we have outlined and elucidated the different extrusion-based 3D printing methods, along with their respective materials and applications. Next, we list how these techniques are applied across various biomedical fields. To this end, Table 2 highlights previous research studies that have utilized these 3D printing methods for diverse medical applications, presenting both the materials used and the key findings from each study. In summary, FFF has been widely applied in the fabrication of medical devices, implants, bone regeneration scaffolds, drug delivery systems, vascular implants, and dental components. GDIW has been utilized in biomedical sectors, like tissue engineering, organ fabrication, bone regeneration, wound healing, and scaffold development. CDIW has shown strength in bone regeneration, ceramic implant production, scaffold fabrication, and dental restorations. Finally, DPE has been employed in the creation of customized implants, drug delivery platforms, scaffolds, tissue engineering constructs, bioabsorbable devices, and skin-contact materials.

Table 2: Literature survey on material extrusion techniques in medical applications.

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
da silva siqueira, et al.	2024	FFF	PLA, HAP, Graphene oxide	Scaffolds	Evaluated bioactive materials for their effectiveness in scaffolds	[155]
Yohannan, Alex, et al.	2024	FFF	PLA/ Multiwalled carbon nanotubes	Medical device	Studied biopolymer composite materials for commercial medical devices.	[156]
Kökcü, İ., et al.	2023	FFF	PLA/halloysite nanotube	Drug loaded scaffold	Evaluated bioactive materials for their effectiveness in bone scaffold	[157]
Cecen, B., et al.	2023	FFF	PLA/PHA	Bone regeneration scaffolds	Evaluated TPMS structured bioactive materials for their effectiveness in bone scaffold	[158]
Mocanu, A. C., et al.	2023	FFF	PLA, Hydroxyapatite	Implantable structure	Studied the effectiveness of biomaterial in implantable structure	[159]
Borah, J., et al.	2023	FFF	PEEK	Implant	Discusses mechanical behavior and applications of 3D printed structure.	[160]
Ilyas, K., et al	2022	FFF	PCL/Bioactive glass, polydopamine	Scaffolds for bone tissue engineering	Studied the bioactivity of surface-coated 3D-printed structures for scaffolds.	[161]
Buj- Corral, I., et al	2022	FFF	PLA, Copper, bronze, steel	Bone scaffold	Studied the biomaterial composite interaction with stromal cells for scaffold	[162]

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
Kim, C. G., et al	2021	FFF	PCL, HAP	Bone tissue engineering scaffold	Evaluated the mechanical properties of composite biomaterial for scaffold	[163]
Alam, F., et al	2021	FFF	PLA, PCL, halloysite nanotube	Bone regeneration	Discussed the influence of composite biomaterial in bone regeneration scaffold	[164]
Mania, S. et al	2019	FFF	PLA, chitosan	Biomedical tools and implants	Studied the effectiveness of composite biomaterial in implant and biomedical tools	[165]
Bachtiar, E. O., et al	2020	FFF	Polycarbonate, urethane silicone	Vascular implant, heart valves and catheters	Evaluated the structural properties of biopolymer composite for vascular implanted	[166]
Thompson, C.,	2023	FFF	PLA, PEG, Mg, Zn	Implants	Evaluate the bioabsorbable polymer and metal composite for implants	[167]
Rossi, A. et al.	2024	GDIW	Alginate, gellan gum, agarose, gelatin, and collagen	Tissue and organ fabrication	Revised on various biomaterials for bioprinting of tissues and organs	[168]
Yogeshwaran, S, et al.	2024	GDIW	freeform reversible embedding of suspended hydrogels (FRESH)	Tissue engineering	Studied bio printability of fresh gel for tissue engineering.	[169]
Rodrigues, I. C. P., et al.	2024	GDIW	HAP, gelatin methacryloyl (Gel MA) hydrogel	Bone tissue engineering	Evaluated bioactive materials for their effectiveness in bone scaffold in bioprinting	[170]

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
Chen, P. H., et al.	2024	GDIW	Collagen maleate (ColME)	Tissue engineering	Evaluated bioprinting materials for their effectiveness in tissue engineering	[171]
Dharmaraj, J. J. J., et al.	2024	GDIW	Hydrogel	Tissue engineering	Discussed the efficiency of hydrogel bioprinting technique in tissue engineering	[172]
Karvinen, J., et al.	2023	GDIW	Hydrogel	Tissue or organ construction	Discusses the various technique of bioprinting for tissue or organ construction	[173]
Yang J., et al	2023	GDIW	Gelatin	Tissue construction	Studied the efficiency of gelatin-based bio-ink in bioprinting for tissue construction	[174]
Krishna, D. V, I., et al	2023	GDIW	Hydrogel	Tissue engineering	Revied on the various bio ink for bioprinting of tissue construction.	[175]
Li. Y., et al	2021	GDIW	Nano-hydroxyapatite /Polyethylene glycol diacrylate (nHA/PEGDA)	Bone tissue engineering scaffold	Studied the optimal printability of polymer ceramic biocomposite	[176]
Gillani, S. M., et al	2024	GDIW	carboxymethyl cellulose (CMC), polyvinylpyrrolidone (PVP), collagen, and oregano extract	Tissue constructs	Discussed the in mechanical and vivo assay of biopolymer composite with organo extract for tissue constructsscaffold	[177]

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
Silva, M., et al	2021	GDIW	Aliginate,chitosan,collgen, gelatin	Tissue regeneration, wound healing, drug delivery	Discussed on various materials of DIW for tissue engineering	[178]
Belyaeva, A. A., et al	2023	GDIW	Cellulose nanocrystals (CNC), poly(<i>N</i> -isopropyl acrylamide) (PNIPAM)	Tissue engineering	Studied the rheology of bio composite material for printability of DIW	[179]
Dai, Y. L.et al.	2024	CDIW	Silica nitride	Implant	Studied the mechanical behavior of 3d printed bioceramic material for implant.	[180]
Xu, C., et al.	2024	CDIW	Ti6Al4V	Scaffold	Discussed on the vitro assays of bioceramic material for scaffolds.	[181]
Buj-Corral, I., et al.	2024	CDIW	yttria-stabilized zirconia, mesenchymal stem cells	Bone tissue engineering	Evaluated bio ceramic materials for their printability and biocompatibility for bone scaffold	[182]
dos Santos, V. I., et al.	2024	CDIW	alumina-toughened zirconia (ATZ), carbon fiber	-	Discussed the optimization of DCE-printed ATZ	[183]
Wang, Y., et al.	2024	CDIW	-	Bone tissue engineering, Dental restorations	Discussed the applications of 3D printed structure-function integrated ceramics for bone tissue engineering and dental restorations.	[184]

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
Ghosh, R., et al.	2023	CDIW	Mg-doped calcium silicate ceramic diopside, lanthanum phosphate	Implant	Discusses the mechanical properties and biocompatibility of bio-ceramic material printed with DCE	[185]
Ravoor, J., et al	2023	CDIW	HAP, Calcium silicate, chitosan, glycerol, carboxymethyl cellulose	Bone regeneration	Studied the efficiency of various binders with HAP for optimal DCE printing bioceramic material for bone regeneration	[186]
Dong, J., et al	2022	CDIW	Mg, Zn, β -tricalcium phosphate (TCP)	Scaffold	Studied the in-vitro assays of bioceramic composite for scaffolds	[187]
Paul, D. B., et al	2025	CDIW	tricalcium phosphate (TCP),	Scaffold	Process Optimization of the mechanical properties of DCE printed bioceramic material for scaffold	[188]
DL, B. P., et al	2024	CDIW	β -TCP/Ti6Al4V, Pluronic gel	Bone regeneration	Process Optimization of the mechanical properties of DCE printed bioceramic composite material for Bone regeneration	[189]
Belgin Paul, D. L., et al	2023	CDIW	tricalcium phosphate (TCP), PVA	-	Discussed the rheology of DCE printed bio ceramic material for printing	[190]
Huang, R. et al	2021	CDIW	Zirconia	Scaffold	Studied the printability and mechanical characterization of bio ceramic for medical application	[191]

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
Ashwin, A. J. et al	2021	CDIW	Polycaprolactone (PCL), hydroxyapatite (HA), tricalcium phosphate (TCP)	Scaffold	Discussed the mechanical and bio properties of various bio ceramic material	[192]
Varsavas., et al.	2024	DPE	PLA, TPU, TPE	Skin contact material	Evaluated materials for their effectiveness in skin contact material	[193]
Luo, S., et al.	2024	DPE	EVA	Drug delivery and energy absorption	Studied biopolymer materials for drug delivery and energy absorption.	[194]
Whyman, S., et al.	2018	DPE	PLA	Scaffold	Evaluated mechanical properties of biopolymer materials for their effectiveness in scaffold	[145]
Karimi, A., et al.	2024	DPE	PBAT	Implant	Studied mechanical properties of biopolymer material for implant	[195]
Gradwohl, M., et al.	2021	DPE	PLA, PLGA	Bioabsorbable medical device	Studied the interaction bio-composite polymers with cells for medical device	[196]
Zhou, Z., et al.	2018	DPE	PVA	Drug delivery, tissue engineering	Discusses mechanical properties of biopolymers of 3D printed structure.	[197]

Author(s)	Year	Technique	Materials Used	Medical Applications	Key Work	Reference
Xiangyu, G., et al	2024	DPE	POE	-	Studied mechanical properties of 3D-printed polymer material	[198]
Gaihre, B., et al	2024	DPE	PCLF	Bone tissue engineering scaffold	Evaluated the interaction of biomaterial for scaffold	[199]
Bilgen, M. B., et al	2024	DPE	PEEK, carbon nanotube	Implant	Discussed the mechanical properties of 3D-printed bio-polymer composite material	[200]
Fontana.L., et al	2021	DPE	PLA	-	Discussed the mechanical properties of 3D-printed polymer material	[201]

3. Materials Used in Medical Applications

3.1. Thermoplastics in FDM and Pellet Extrusion

3.1.1. Biocompatible and Non-Biocompatible Polymers

Researchers utilize different polymer materials in AM for medical applications, each selected based on its biocompatibility and mechanical strength.

- i. PLA: A degradable polymer obtained from bio-based feedstocks (e.g., sugarcane and corn starch), frequently used for temporary implants and tissue scaffolds due to its moderate strength, rigidity, and notably easy processability due to its relatively low melting temperature (150–160 °C) [202, 203].
- ii. PEEK: An advanced thermoplastic with superior mechanical behaviors comparable to metals, along with proven chemical resistance and biocompatibility. It is well-suited for long-term implants (e.g., spinal and orthopaedic devices) and exhibits a comparatively high melting temperature of ~ 343 °C [204, 205].
- iii. ABS: A tough, impact-resistant polymer with high energy and shock absorption capacity, commonly used in medical device housings and surgical instruments. It exhibits a melting temperature in the range of 210–250 °C [206].
- iv. PC: A high-strength, transparent polymer with excellent thermal stability. Like ABS, it is used in medical equipment housings and optical devices. PC is not suitable for long-term implants. Its melting point is approximately 260 °C [207].

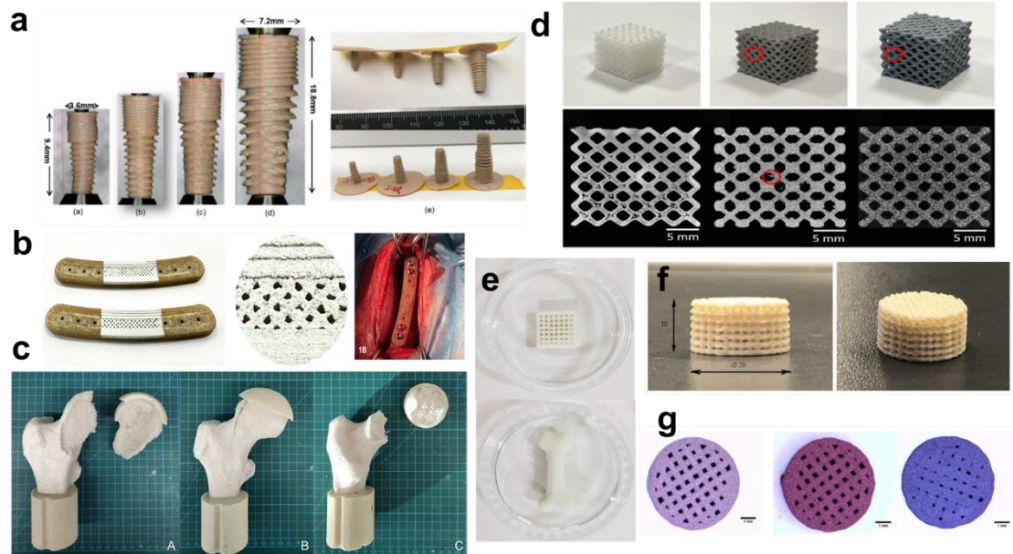


Figure 11. 3D-Printed Medical Applications Using the thermoplastic polymer material (a) FFF printed dental PEEK screw implant at various size [208], (b) 3D-Printed PEEK Implant following HAP coating, the implant was inserted into a femoral defect in a rabbit [209], (c) A 3D printed femoral model designed using human femoral bone geometry [70], (d) Cubic scaffolds with a face centered cubic (FCC) lattice structure were 3D printed using PLDL/PEG, PLDL/Mg/PEG, and PLDL/Zn [167], (e) PLA/HA printed bone scaffold and bone mimic structures [163], (f) PLA printed bone scaffold [210], (g) Disk-shaped PLA-based copper, bronze, and steel scaffold [162] available under the Creative Commons Attribution 3.0 & 4.0 (CC BY) guidelines.

Various in vitro and in vivo investigations have been carried out on 3D-printed implants and scaffolds fabricated using extrusion-based 3D printing prototypes. Wang et al. developed a PEEK dental implant made by AM, having both inner and outer threads. They optimized printing parameters of FFF method to produce screws of various sizes with high geometric accuracy, for accurate clinical integration (Figure 11a) [208]. Zhang et al. performed both in vivo and in vitro analyses of a 3D-printed PEEK implant, but coated with hydroxyapatite (HAP) for improved biocompatibility and osteogenic potential. They evaluated the implant's performance using a rabbit femur bone model (Figure 11b) [209]. Nagl et al. explored low-budget FFF 3D printing with PLA to fabricate femoral bone models, which surprisingly showed mechanical behavior like that of actual human bones (but not necessarily one-to-one strength values). This may open up new possibilities for employing FFF alone for highly affordable patient-specific biomechanical testing (Figure 12c) [70]. Thompson et al. fabricated medical-grade PLDL, PLDL/Zn, and PLDL/Mg filaments for controlled-porosity scaffolds. Those metal-polymer composites enhanced degradation rates while maintaining biocompatibility (Figure 11d) [167]. Kim et al. investigated FFF 3D-printed PCL/hydroxyapatite (HA) filaments for bone scaffolds (Figure 11e) [163]. Studie has also investigated the behavior of PLA scaffold under physiological media in vitro conditions until the bone tissue formation period. (Figure 11f) [210]. Metal-PLA composites can potentially exhibit good cytocompatibility and osteogenic differentiation, which support its potential use in bone scaffold fabrication (Figure 11g) [162].

3.2. Hydrogels and Bioinks in Bioprinting Biocompatibility and Degradability

Alginate is highly biocompatible and commonly used for encapsulating cells and creating tissue scaffolds. It degrades in the presence of calcium ions, allowing controlled release and integration with natural tissues. While alginate forms soft, flexible gels that support cell growth, it may need reinforcement for load-bearing applications [211]. Collagen, an essential structural protein found in the extracellular matrix, promotes cell adhesion and growth. It degrades enzymatically, enabling it to be suitable for applications where gradual tissue replacement is needed. However, collagen gels are soft and often require cross-linking or blending with other materials for added strength [212]. Gelatin, a collagen-derived material, is also biocompatible and supports cell proliferation and differentiation. It biodegrades under physiological conditions, and its degradation rate can be adjusted through cross-linking. Gelatin forms thermosensitive gels, useful for detailed structures but generally weaker than synthetic polymers [213]. Other hydrogels, like hyaluronic acid, fibrin, and PEG, exhibit high biocompatibility and support cell attachment and growth. Their degradation rates can be modified chemically, making them adaptable for different medical applications, with mechanical characteristics ranging from flexible to moderately stiff. Hydrogels like collagen and alginate closely resemble the ECM, creating ideal conditions for cell proliferation and tissue formation [214]. The mechanical behaviors of bioinks can be adjusted by modifying their composition and cross-linking, thus improving the printed structure ability to withstand physiological stresses [215]. Collagen and gelatin naturally promote cell adhesion and growth, while synthetic hydrogels like PEG can be enriched with cell-adhesive peptides to improve biocompatibility [216,217].

Direct Ink Writing (DIW) of hydrogels has been enhanced through interpenetrating network designs of different polymers, which improved mechanical characteristics and biocompatibility. As an example, Williams et al. developed self-reinforced homocomposite hydrogels (HHGs) using molecular alginate gels and soft dendritic colloids (SDCs), which turned out to have a threefold increased storage modulus and a fourfold increased Young's modulus. Higher storage modulus means a more solid-like material versus a liquid one and thus shape better after extrusion in the build plate during 3D printing (Figure 12a) [218]. In addition, Baniasadi et al. reinforced osteogenic hydrogel nanocomposites with mesoporous silica-calcia nanoparticles (MSNs) and icariin. These reinforcements enhanced bioactivity, mechanical strength (Figure 12b) [112]. Hull et al. explored viscoelastic bioinks with dynamic covalent cross-links that enabled cellular remodeling, particularly for breast cancer patients (Figure 12c) [219]. An advanced coaxial nozzle-based 3D printing technique has been developed for fabricating durable, cell-laden hydrogels with integrated microchannels, offering improved cell viability and tunable mechanical properties. This method holds potential for facilitating large-scale organ fabrication. (Figure 12d) [130].

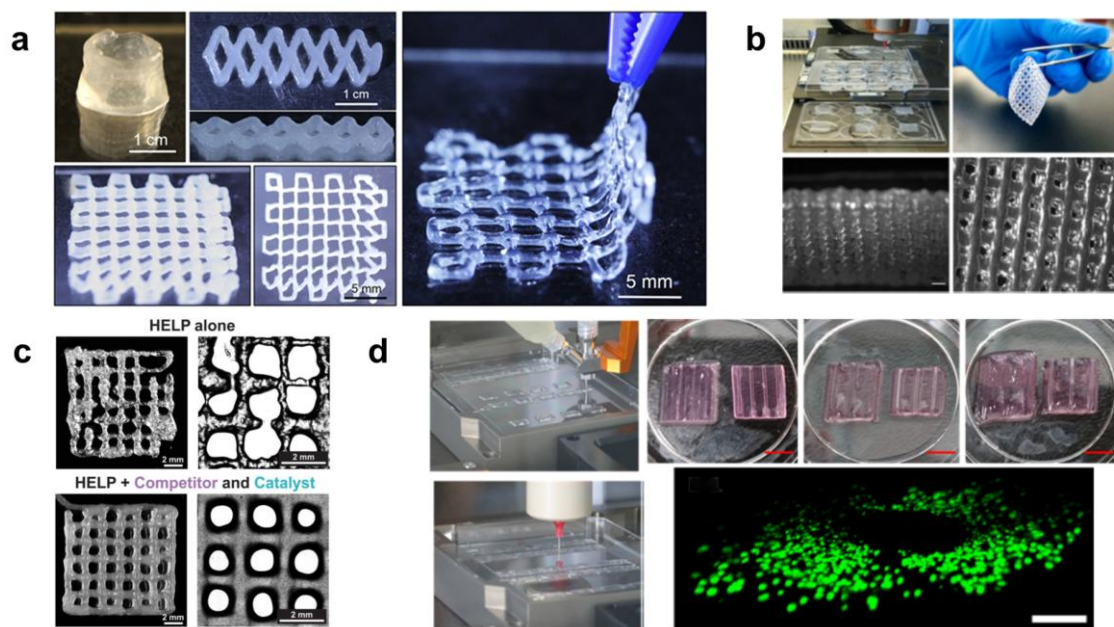


Figure 12. 3D-Printed Medical Applications Using Hydrogel and Bio-Ink-Based Structures (a) 3D-printed HHG paste with layered structures using different nozzle sizes and layer counts, followed by hydrogel removal from the substrate [218], (b) 3D-printed silica hydrogel with calcia-incorporated porous structures [112], (c) Bright-field microscopy images depicting 3D-printed lattice structures with HELP alone and HELP based ink formulated with a competitor and catalyst [219], and (d) 3D-printed gelatine-alginate structures with built-in microchannels. Live/ dead standing was employed to evaluate cell viability and survival for 1, 7, and 14 days [130] available under the Creative Commons Attribution 4.0 (CC BY) guidelines.

3.3. Metal and Ceramic Materials Utilized in the Medical Field

A variety of metal and ceramic materials are used in DCE, but only some exhibit biocompatibility, bioactivity, or biodegradability. Among metals, titanium alloys are the go-to material for implants due to their excellent strength relative to weight, superior resistance to corrosion, biocompatibility, and strong osseointegration properties, making them ideal for artificial joints, bone plates, and dental implants [220]. However, their high cost has led researchers to explore alternatives like stainless steel, which is more affordable and suitable, but for short-term implants [221]. Ceramics like alumina and zirconia have also garnered attention for their high strength, durability, and compatibility with human tissues. As a result, they help reduce the risk of adverse reactions within the human body [222]. Recent research on naturally derived ceramics like calcium oxide, β -tricalcium phosphate (β -TCP), and hydroxyapatite. sourced from animal bones, fish bones, or shells [223]. These materials closely resemble human bone composition, thus promote better integration with adjacent tissues and bones [224]. Unlike metal implants that may require removal, bioresorbable ceramic implants can remain in the body, supporting long-term bone regeneration and neglecting the need for additional surgeries [225]. For example, Zhu et al. studied the structural and biocompatibility behaviors of 3D-printed rabbit femur bone using zirconium oxide. They conducted in vivo tests on rabbits, and muscle tissue sections exhibited normal morphology, with no significant tissue abnormalities. Additionally, bone tissue sections showed signs of new bone regeneration (Figure 13a) [226]. Paul et al. studied DIW-based β -TCP/Ti6Al4V/Pluronic composite scaffolds, optimizing process parameters using the Box-Behnken method and ANOVA. Their study confirmed scaffold biocompatibility through cell viability tests over 14 days, showing effective cell colonization and growth through optical

imaging (Figure 13b) [189]. In addition, Zhang et al. reviewed the fabrication of human molar teeth and other structures for dental implants using 3 mol% yttria-stabilized tetragonal zirconia polycrystals, which showed that complex ceramic structures is realizable through direct ink writing (DIW) (Figure 13c) [227]. Wu et al. optimized the DIW of porcelain clay paste by adjusting sodium citrate content, improving rheology and mechanical properties after sintering (Figure 13d) [228]. Schult et al. developed porous barium titanate ceramics, highlighting their piezoelectric and biocompatible properties for bone tissue engineering, with material modifications enhancing printability and porosity for cell growth (Figure 13e) [229].

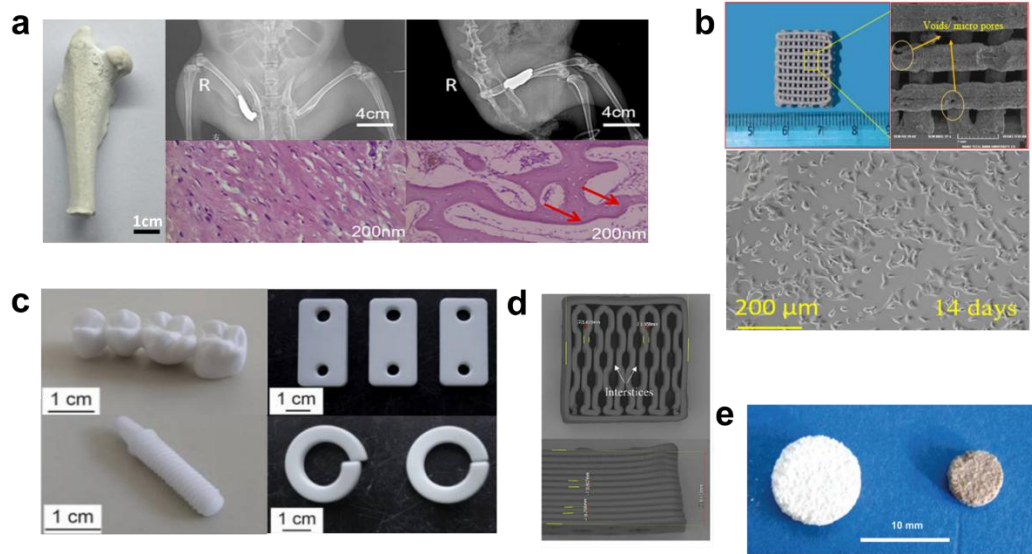


Figure 13. Medical Applications Using Ceramic Materials (a) Customization and Biocompatibility Assessment of 3D-Printed Zirconium Oxide Femur Implant in Rabbit Hip Joint [226], (b) Optimized 3D-printed scaffolds and their SEM images, with optical image of cell culture analysis at 14 days [189], (c) 3D-printed molar tooth and other prototype using 3Y-TZP [227], (d) Direct ink writing (DIW) 3D-printed green body incorporated with SC contents in a continuous honeycomb structure [228], (e) Extruded green part and sintered part of BaTiO₃ (Barium titanate) [229] available under the Creative Commons Attribution 3.0 & 4.0 (CC BY) guidelines.

As discussed previously, the material extrusion approach accommodates a diverse selection of materials, including polymers, hydrogels, metals, and ceramics. Researchers are also actively developing new materials to enhance performance in medical applications. Table 3 provides an overview of recently utilized materials in material extrusion, while highlighting their key characteristics and biocompatibility, including properties such as strength, elongation, and thermal stability of 3D-printed parts, in healthcare and biomedical fields. The biocompatibility levels in the table are categorized on a numerical scale from 1 to 4 to provide a consistent and comparable measure of a material's suitability for biological applications. Level 1 denotes low biocompatibility, where materials are generally unsuitable for direct contact with biological tissues due to potential toxicity or adverse reactions. Level 2 indicates moderate biocompatibility, suitable for limited or indirect contact but not ideal for implantation. Level 3 represents high biocompatibility, where materials are safe for temporary or partial in vivo use, such as short-term implants or biomedical devices. Level 4 signifies excellent biocompatibility, indicating implant-grade materials that can be used safely for long-term in vivo applications without causing harmful biological responses. This standardized scale enables a clear and systematic comparison of materials for biomedical and additive manufacturing purposes. Materials listed in the tables were 3 and 4 levels of biocompatibility.

Table 3. Comparison of the material's mechanical, thermal, biological behaviors, and compatible material extrusion techniques.

Material	Compatible ME Techniques	Tensile Strength	Strain	Thermal Stability of a Product (°C)	Biocompatibility	Reference
PLA	FFF, DPE	18-50 MPa	4-10%	~60	3	[230]
PEEK	FFF, DPE	Up to 98 MPa	20-30%	~290	4	[231]
TPU	FFF, DPE	25-50 MPa	>100%	~200	3	[232]
EVA	FFF, DPE	2-10 MPa	>100%	~100	3	[233]
PVA	FFF, DPE	10-20 MPa	>100%	~200	3	[234]
PMMA	FFF, DPE	40-70 MPa	2-5%	~150	3	[235]
Alginate	GDIW	<1 MPa	>50%	~90	3	[236]
Gellan gum	GDIW	<1 MPa	>60%	~90	3	[237]
Gelatin	GDIW	<1 MPa	>100%	~50	3	[238]
Collagen	GDIW	<1 MPa	~100%	~60	3	[239]
GelMA	GDIW	~0.5 MPa	~50-80%	~70	3	[240]
Carboxymethyl cellulose	GDIW	<1 MPa	>30%	~100	3	[241]
Polyvinylpyrrolidone	GDIW	<1 MPa	>30%	~150	3	[242]
Hydroxyapatite	GDIW, DCE	>100 MPa (sintered)	<1%	1300	4	[243]
Zirconia	CDIW	~900-1200 MPa (sintered)	<1%	~1500	4	[140]
Silica nitride	CDIW	~800 MPa	<1%	~1600	4	[244]
Tricalcium phosphate	CDIW	~60-90 MPa	<1%	~1300	4	[245]
β-TCP	CDIW	~70 MPa	<1%	~1250	4	[246]

Material	Compatible ME Techniques	Tensile Strength	Strain	Thermal Stability of a Product (°C)	Biocompatibility	Reference
Alumina-toughened zirconia (ATZ)	CDIW	~800-1200 MPa	<1%	~1400	4	[247]
Yttria-stabilized zirconia	CDIW	~1000 MPa	<1%	~1450	4	[248]
Ti6Al4V	CDIW	~950 MPa	~10-14%	~1600	4	[249]
Alumina	CDIW	~300-500 MPa	~0.1-0.3%	~1500	3	[250]

4. Performance Comparisons of Material Extrusion Techniques

Fused Filament Fabrication (FFF) typically achieves a layer height of 100-300 microns, with a nozzle diameter of around 0.4 mm, which limits the minimum feature size. Its dimensional accuracy is within ± 0.1 -0.2 mm, depending on machine calibration and material properties. FFF parts offer good structural integrity, but weak layer adhesion remains a concern in load-bearing applications. Post-processing methods like annealing can help improve strength [251]. Bioprinting achieves finer layer heights of 50-100 microns, depending on the bioink properties and nozzle size, with an accuracy of ± 0.05 -0.2 mm. However, this can vary based on bioink properties and cross-linking. However, printed structures generally have lower mechanical strength than thermoplastics, requiring careful handling and post-processing [252]. Direct Ceramic Extrusion (DCE) can create detailed parts but is limited by nozzle size and material flow, offering lower dimensional accuracy than other methods. Material shrinkage during sintering and drying can also affect final dimensions, often requiring post-processing for improved precision [253]. Direct pellet extrusion has a lower resolution than FFF, with layer heights of 200-500 microns and accuracy within ± 0.2 -0.5 mm, influenced by the extrusion system and pellet consistency. It produces strong parts using high-performance polymers but may result in surface roughness and inconsistencies [254]. Table 4 offers a brief comparison of the performance of the material extrusion technique.

Table 4. Performance comparisons of material extrusion techniques.

Technique	Resolution (μm)	Printing speed (mm/s)	Surface Finish (μm)	Accuracy (mm)	Reference
FFF	100-300	50/150 (Moderate)	10-25 (Moderate)	0.1-0.2	[251]
GDIW	50-100	5-20 (Slow)	5-15 (Good)	0.05-0.2	[252]
CDIW	300-1000	5-15 mm/s (Slow)	20-50 (Moderate/Rough)	0.5-1	[253]
DPE	200-500	20-80 (Moderate)	10-30 (Moderate)	0.2-0.5	[254]

5. Challenges and Limitations

5.1. Material and technical challenges

5.1.1. Key material challenges in material extrusions

In material extrusion processes, a range of biocompatible materials have been explored for diverse applications; however, these materials still face certain key challenges and limitations, as outlined below.

- i. **Anisotropic Properties:** In material extrusion, structures are built layer by layer, often leading to some adhesion issues between layers, especially along the Z-axis (out of the 3D printing plane). This results in a strength that depends on the loading direction.
- ii. **Biocompatibility and Toxicity:** Residual chemicals like monomers, solvents, or nanoparticles from the extrusion process can trigger immune responses. For example, the degradation products of PLA may cause inflammation in implant applications [255].
- iii. **Sterilization Challenges:** Many bioprinting materials, such as hydrogels, degrade when exposed to standard sterilization methods, including autoclaving or gamma radiation. Effective post-print sterilization remains a significant challenge.
- iv. **Mechanical Mismatch:** Synthetic polymers like PCL often lack the hyperelasticity of natural soft tissues. This mismatch can lead to the failure of implants when they are exposed to dynamic forces within the body.
- v. **Resolution vs. Speed Trade-off:** Achieving high-resolution in 3D printing (e.g., $< 50\mu\text{m}$) requires slowing down the extrusion speeds, thereby restricting the ability to scale up printing of large tissues or organs.
- vi. **Material Stability and Shelf Life:** Bioinks like collagen and alginate often gel too quickly or lose water (syneresis), reducing their printability and stability over time.
- vii. **Post-Processing Requirements:** Methods like Fused Filament Fabrication (FFF) and Direct Pellet Extrusion (DPE) often need surface finishing or support removal, which can damage delicate structures. In bioprinting methods like Direct Ink Writing (DIW), post-processing, such as crosslinking (UV, ionic, chemical, enzymatic), can harm living cells (if integrated). Extracting support materials from embedded structures also poses a risk to structural integrity.

Material-related challenges pose significant limitations for extrusion-based 3D printing methods, affecting their suitability for medical applications. Technique-wise impact printing speed, resolution, accuracy, and scalability, which are all critical for the production of high-quality biomedical components.

In Fused Filament Fabrication (FFF), the frequently utilized thermoplastics are not biocompatible. Materials such as PLA and PEEK are exceptions, as they are considered safe for contact with the human body. However, frequently used polymers like ABS and polycarbonate (PC) are limited to producing device casings or surgical tools, rather than implants or internal applications [256]. While PLA is biodegradable and biocompatible, it has relatively low strength and is brittle compared to PEEK, making it unsuitable for load-bearing implants. To enhance PLA's mechanical performance, it is often reinforced with biocompatible and non-cytotoxic additives to improve its strength, toughness, and fatigue resistance. Furthermore, PLA degradation can be inconsistent, risking the loss of structural integrity before proper tissue integration occurs [257]. FFF offers a suitable printing speed that is adequate for prototyping, but it becomes inefficient for larger or more complex structures, limiting its use in high-throughput or large-scale

biomedical production [258]. Additionally, FFF typically produces lower resolution prints, resulting in rougher surface textures and decreased dimensional accuracy.

Direct Pellet Extrusion (DPE) supports a broader range of materials, including high-performance polymers. However, medical-grade pellets are not widely available [259, 260]. This method is more intricate than FFF, as ensuring consistent material flow is challenging. Achieving optimal mechanical properties, particularly in biodegradable polymers, demands careful calibration of printing settings, a key factor in producing implants [261]. While DPE may offer faster production than FFF by utilizing bulk feedstock, the increased process complexity can reduce overall efficiency [262].

In bioprinting, gel-based bioinks such as hydrogels are commonly used due to their excellent biocompatibility. However, these materials have low mechanical strength, making them unsuitable for load-bearing applications without additional support. A major challenge is controlling the degradation rate of the bioinks to match the pace of tissue regeneration; any mismatch can lead to scaffold failure or prolonged presence of material in the body [263]. Bioink stability and functionality (rapid gelation or syneresis) must also be maintained during the printing process and cell culture, which can be difficult and may affect the quality of the final construct [264]. Bioprinting tends to be slower than other techniques because it requires precise deposition and careful handling to preserve cell viability, making it unsuitable for large-scale applications. Additionally, the soft nature of bioinks limits the achievable resolution, requiring a balance between maintaining structural integrity and ensuring cell health [265].

Direct Ceramic Extrusion (DCE) employs biocompatible materials like hydroxyapatite and tricalcium phosphate, making it well-suited for bone regeneration [266]. However, ceramics are brittle and lack the flexibility required for dynamic, load-bearing applications. Maintaining consistent ceramic paste extrusion and achieving uniform quality is technically challenging and demands precise printer calibration. Ceramics may experience shrinkage and warping during drying and sintering, which negatively impact the final structure and mechanical strength of the printed components [267]. These processes also significantly slow down production speed, making it more difficult to scale DCE for complex medical components [268].

5.2. Regulatory and ethical concerns

Regulatory and ethical considerations in medical 3D printing and bioprinting encompass safety, standardization, equity, and intellectual property rights. Regulatory agencies like the FDA and EMA confirm that AM medical devices comply with safety, effectiveness, and quality standards [269,270]. However, the regulations for bioprinted tissues and organs are still evolving, as maintaining consistent quality and functionality is difficult due to material variations, cells, and printing methods. Standardization is needed to establish testing protocols for both 3D-printed devices and bioprinted tissues to ensure safety and performance [271]. Ethical concerns arise with bioprinting human tissues, including questions about cell sourcing, the creation of human-animal hybrids, and the implications of printing entire organs. Another issue is ensuring equitable access to these advanced technologies, as they could increase healthcare inequalities. Intellectual property rights related to bioprinted tissues, organs, and the technologies used also present legal and ethical challenges around ownership and access [272].

5.3. Clinical Translation and Approval Barriers

Bringing material extrusion-printed products into clinical use as approved medical treatments presents numerous significant challenges. To advance to clinical trials, medical devices, implants, and bioprinted

tissues must show they are safe, consistent, and clinically effective. Regulatory bodies such as the U.S. FDA and EMA require comprehensive documentation, including material behaviors, mechanical performance data, sterilization validation, and biocompatibility assessments [269,270]. As detailed in Table 5, these agencies classify medical devices into three main categories: Class I, II, and III. Most extrusion-based medical products fall under Class II or Class III due to their intended use and potential risk. For extrusion methods such as FFF, DIW, and DPE, the use of medically approved and biocompatible materials, like PEEK, PLA, hydrogels, and bio-ceramics, is essential. The entire production pipeline must adhere to Good Manufacturing Practices (GMP) to ensure product quality and patient safety [273]. Even minor variations in extrusion parameters: Nozzle temperature, layer height, pressure, build orientation, and flow rate, can affect mechanical integrity and surface finish of the 3D printed part(s). Rigorous process validation and stringent quality control must be followed to ensure consistent part shape, surface finish, compatibility, function and overall performance [274].

Table 5. Classification of product risk based on FDA regulations.

Class	Risk Level of Products	Examples
Class I	Low risk	Bandages, tongue depressors, and exam gloves
Class II	Moderate risk	Implant, Infusion pumps, syringes, and contact lenses
Class III	High risk	Implant, Pacemakers, heart valves, and deep brain stimulators

In the case of bioprinting, especially involving living cells, regulatory pathways are even less established. Preclinical studies must assess not only structural properties but also immunogenicity, cell viability, and biodegradation behavior [271,275]. The personalization of many extrusion-printed products, particularly patient-specific implants and scaffolds, presents additional challenges for standardization and extensive regulatory approval. Gaining authorization to proceed to clinical trials often involves regulatory pathways such as Premarket Notification [510(k) or PMN], Premarket Approval (PMA), Investigational Device Exemption (IDE), Investigational New Drug (IND) application, or the De Novo classification process, all of which require comprehensive risk assessments and supporting clinical or performance data [276]. Overall, translating extrusion-printed products from research to clinical use is a time-intensive and resource-demanding process, typically spanning 3 to 7 years. The FDA provided a draft guidance titled “Technical Considerations for Additive Manufactured Devices” in 2017 to provide direction for manufacturers developing products via 3D printing [277]. While this guidance is still in draft form and open to public comment, it underscores the pressing need for more specific regulatory pathways and standardized evaluation methods tailored to extrusion-based AM. The FDA approval process for such devices is illustrated in Figure 14, and examples of recently FDA-approved 3D-printed products are summarized in Table 6. While drug delivery systems (DDS)-based therapies have been approved as Investigational New Drugs (IND) for patient treatment, the FDA has not yet approved any directly utilized material extrusion-based products, such as implants or scaffolds. There is still a long way to go, and further advancements are needed to improve the material extrusion process.

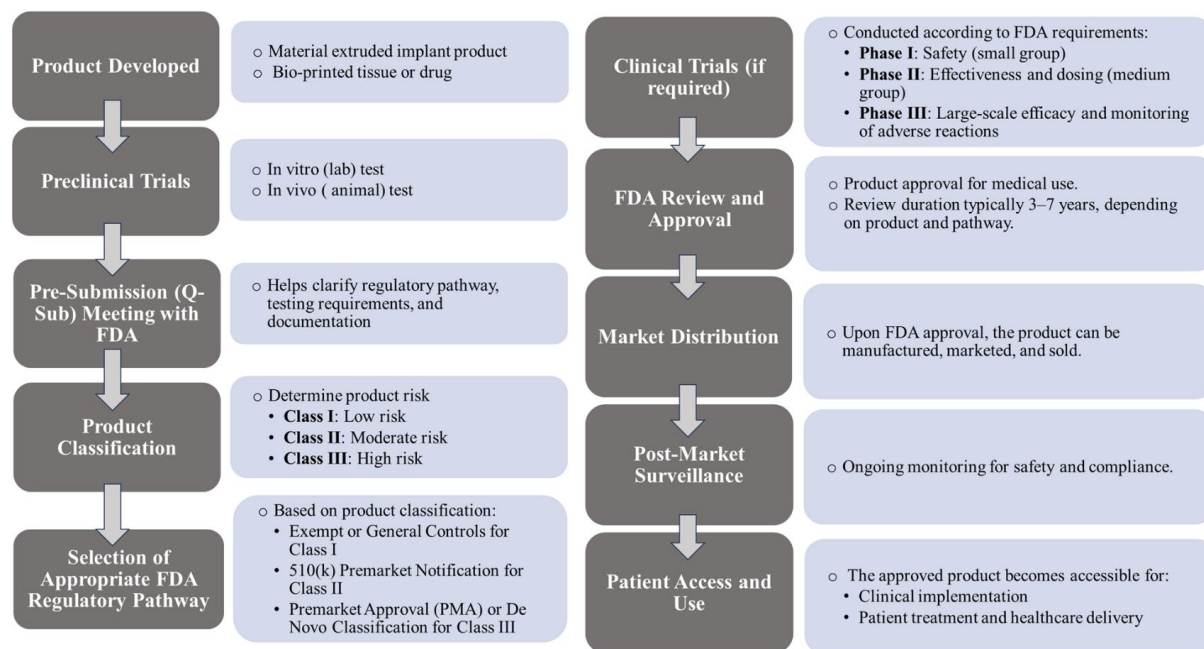


Figure 14. Workflow of FDA approval of medical products.

Table 6. Examples of US FDA-approved 3D printed products.

S.No	Product Name	Technique	Utilization	Year approved	Reference
1	T19	Melt extrusion deposition	3D printed Drug Delivery System - Provide treatment for individuals with rheumatoid arthritis	2023	[278]
2	T20	Melt extrusion deposition	3D printed Drug Delivery System - treatment for cardiovascular and clotting disorders	2023	[279]
3	T21	Melt extrusion deposition	3D printed Drug Delivery System - treatment for ulcerative colitis	2023	[280]

6. Recent Work in the Additive Manufacturing (AM) Field

Recent advancements in material extrusion and bioprinting have demonstrated significant progress across the medical sector. AI-based real-time defect detection is already being applied in AM approaches like Laser Powder Bed Fusion (LPBF) and Directed Energy Deposition (DED). Machine learning techniques such as K-Nearest Neighbors (KNN), Convolutional Neural Networks (CNN), Decision Trees (DT), and Artificial Neural Networks (ANN), are being utilized to detect process defects, optimize printing parameters, and enhance product quality [281,282]. In the context of sustainability, closed-loop recycling

systems are actively being developed to repurpose materials like PETG, including medical waste, into new products. This reduces environmental impact and supports circular manufacturing, particularly in the healthcare sector [283,284].

Self-healing polymers are under active study for biomedical applications, where their intrinsic and extrinsic healing mechanisms contribute to extended device lifespans and increased reliability of implants [285]. Hand-held extruders, such as the Penn State Bioprinter, are currently being studied in medical settings to apply regenerative material directly to wound sites, enabling fast and precise treatment [286]. Additionally, 4D bioink materials that respond to stimuli like temperature, pH, or light by altering their shape or structure are proving promising in regenerative medicine, tissue engineering, and advanced biomedical systems [287].

Embedded bioprinting techniques like omnidirectional printing, ghost writing, sacrificial writing, and Freeform Reversible Embedding of Suspended Hydrogels (FRESH) have been successfully used to create complex structures by offering in-situ support during printing [120,121]. Conductive bioinks, particularly those based on graphene or PEDOT/PSS, are being explored for neural scaffolds and bioelectronic interfaces because they can replicate the electrical conductivity of neural tissue [288]. Circular economy practices are gaining traction, with the recycling of ocean plastics, agricultural waste, and sterilized medical waste into high-quality 3D printing feedstock becoming increasingly common [289].

Biodegradable polymers derived from algae and mushroom mycelium are emerging as sustainable alternatives to recently used biopolymers like alginate, gelatine, etc. [290]. These materials are examined for use in packaging, disposable products, and temporary medical implants. In the food sector, extrusion is being leveraged to produce personalized nutrition products. Companies like Redefine Meat are creating plant-based protein blends tailored to individual dietary needs, opening new possibilities for health-conscious consumers [291].

7. Future Directions in Additive Manufacturing (AM)

Looking ahead, the future of material extrusion and bioprinting is undergoing transformative developments. Table 7 summarizes potential future directions and advancements for the material extrusion technique [8]. Artificial intelligence and robotics will play an increasingly central role in optimizing 3D printing processes. AI-driven designs will enhance part performance, while robotic systems will facilitate precise handling and automated assembly of printed components [292,293]. Advancements in smart polymers that react to physiological stimuli will enable controlled drug release and improved integration with tissues, thereby significantly enhancing patient outcomes [294]. Biocompatible thermoplastics and bioactive materials that promote cell growth are also expected to become standard in medical applications.

Nanocomposite polymers incorporating nanoparticles are being engineered to improve strength, antimicrobial resistance, and bioactivity [295]. These advancements will enable the development of stronger, superior functionality, and more durable biomedical devices. Functionally Graded Material (FGM) printing, enabling the simultaneous use of multiple materials in a product, will facilitate the fabrication of complex, multifunctional parts tailored to specific applications [296,297]. Hybrid printing systems that combine various techniques will further expand the capabilities of AM, making it possible to create intricate structures with multiple integrated functions [298].

In bioprinting, one of the most groundbreaking directions is the potential to print entire organs with complex vascular systems using a patient's own cells [299]. This could help address the global organ shortage and minimize the risks of transplant rejection. Similarly, advances in tissue engineering are leading to the development of multi-tissue constructs that more closely replicate the functions of real biological tissues. Biodegradable implants are also being designed to offer temporary support during healing and then degrade safely within the body, eliminating the need for surgical removal [300,301].

Another promising area is the fabrication of metamaterials through extrusion. By precisely controlling lattice geometry and internal structure, materials can be created with tunable properties such as thermal conductivity, stiffness, or impact resistance [302]. These materials have high potential in the medical sector as well as in aerospace, protective wearables, and soft robotics. As technology continues to evolve, these innovations will collectively redefine the capabilities and applications of extrusion-based manufacturing in both industrial and biomedical fields [303]. Lastly, the rise of low-cost desktop extruders is democratizing access to manufacturing, enabling startups, researchers, and hobbyists to experiment with custom formulations, recycle household waste, and develop innovative solutions locally with the developing AM DIY community [304,305,306].

Table 7. Potential advancements and future directions for the material extrusion technique.

Technique	Future Innovations	Predicted Impact
Fused Filament Fabrication (FFF)	New biocompatible polymers and composite	Enhanced patient-specific solutions
Direct Pellet Extrusion	Multi-material printing	More complex implants
Gel-Based DIW (Bioprinting)	Advanced bioinks	Improved tissue integration
Ceramic-Based DIW (DCE)	High-performance ceramics	Greater longevity of implants

8. Conclusions

Material extrusion (ME)-based AM has become a groundbreaking approach in the medical sector, providing exceptional design flexibility, cost efficiency, and the capability to create patient-specific solutions. This review has explored the various material extrusion approaches like Fused Filament Fabrication (FFF), Direct Ink Writing (DIW), and Direct Pellet Extrusion (DPE), highlighting their unique advantages, material capabilities, and applications in medical contexts, from personalized prosthetics and implants to tissue engineering scaffolds and DDS. Rheological properties of materials are crucial for the material extrusion process. During extrusion through the nozzle, the shear rate increases, and for materials exhibiting shear-thinning behavior, this results in a temporary decrease in viscosity, allowing smooth flow. Once the material exits the nozzle, the shear rate decreases, causing the viscosity to rise again, which helps maintain the deposited shape. Controlling shear forces is therefore key to achieving stable non-planar deposition. After deposition, print stability can be further ensured through post-processing, such as cooling for thermoplastics, UV curing for UV-curable resins, or chemical curing for gels that solidify through chemical reactions. Material extrusion has shown great promise in revolutionizing healthcare by permitting the fabrication of complex, customized, and biocompatible structures. Even though the SLS and DED have a higher printing resolution than ME, the ME process offers greater material versatility, particularly in accommodating a wider range of functional materials suitable for biomedical applications. Additionally, ME is generally more cost-effective due to lower equipment and operating costs, and it allows easier customization of multi-material or composite structures during the printing process.

The performance of materials used in these techniques, such as thermoplastics (e.g., PLA, PEEK, TPU, EVA, PBAT, PVA, UHMWPE, PLGA, POE, PCLF etc.), hydrogels (e.g., alginate, collagen, gellan gum, agarose, gelatin etc.), metals (e.g., titanium alloy, tantalum, magnesium alloy, Inconel, Stainless steel etc.), and bioceramics (e.g., hydroxyapatite, zirconia, Silica nitride, tricalcium phosphate (TCP), β -TCP etc.), has been critically evaluated. While thermoplastics like PEEK offer excellent mechanical properties and biocompatibility for long-term implants, hydrogels and bio-inks provide ideal conditions for cell growth and tissue regeneration. Conversely, bioceramics are ideal for bone regeneration due to their osteoconductive and biodegradable characteristics. However, challenges like limited material biocompatibility, mechanical strength, and degradation control remain, necessitating further research and development.

Technological advancements in precision, multi-material printing, and hybrid systems are addressing some of the limitations in resolution, speed, and scalability. Innovations in smart polymers, nanocomposites, and dynamic hydrogels are helping to progress in more functional and responsive medical devices. Additionally, integrating AI and robotics improves the design and fabrication processes, enabling the development of highly optimized and intricate structures. Similarly, the AI-related works of LPBF can be adapted for use in the material extrusion (ME) process development. Despite these advancements, regulatory and ethical concerns, including safety, standardization, and equitable access, must be resolved to guarantee the broad adoption of these technologies. The evolving regulatory landscape for bio-printed tissues and organs, in particular, requires careful consideration to balance innovation with patient safety.

Looking ahead, the future of material extrusion in medical applications is promising. The development of custom organ printing, functional tissue constructs, and biodegradable implants holds the potential to address critical healthcare challenges like organ shortages and the need for personalized

treatments. As material science, printing technologies, and regulatory frameworks continue to evolve, material extrusion-based AM is anticipated to be instrumental in progressing regenerative medicine, personalized healthcare, and the overall efficacy of medical treatments. Hybrid and dual techniques, such as the integration of additive and subtractive methods, or multi-material and multi-process systems, indeed represent a promising direction in the field of additive manufacturing. Ongoing interdisciplinary collaboration and innovation are crucial for identifying obstacles and unlocking the potential of this groundbreaking technology.

Competing interests

The authors declare that they have no competing interests.

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Nomenclatures

S.No	Nomenclature	Description
1	AM	Additive Manufacturing
2	FFF	Fused Filament Fabrication
3	DIW	Direct ink Writing
4	DPE	Direct Pellet Extrusion
5	DDS	Drug Delivery System
6	PLA	Polylactic Acid
7	PEEK	Polyether ether ketone
8	3D	Three Dimensions
9	ISO	Indian Organization for Standardizations
10	ASTM	American Society for Testing and Materials
11	FDM	Fused Deposition Modelling
12	AI	Artificial Intelligent
13	CAGR	Compound Annual Growth Rate
14	PLGA	Poly (lactic-co-glycolic acid)
15	PCL	Polycaprolactone
16	PVA	Polyvinyl alcohol
17	PVP	Polyvinylpyrrolidone
18	EVA	Ethylene vinyl acetate
19	TPE	Thermoplastic Elastomer
20	TPU	Thermoplastic polyurethane
21	PMMA	Polymethylmethacrylate
22	GelMA	Gelatine Methacrylate
23	CAD	Computer Aided Design
24	STL or .stl	Standard Triangle Language (or) Standard Tessellation Language
25	G-code	Geometric code
26	CNC	Computerized Numerical Control
27	ME	Material Extrusion
28	PBAT	Polybutylene adipate terephthalate
29	TCP	Tricalcium phosphate
30	UHMWPE	Ultra-High Molecular Weight Polyethylene
31	POE	Polyolefin elastomers
32	PCLF	Poly (caprolactone fumarate)
33	PC	Polycarbonate
34	ABS	Acrylonitrile Butadiene Styrene
35	PGA	Polyglycolic acid
36	GDIW	Gel- Direct ink Writing
37	CDIW	Ceramic- Direct ink Writing
38	PEG	Polyethylene Glycol

39	HA or HAP	Hydroxyapatite
40	MWCNT	Multi-wall carbon nanotube
41	HNT	Halloysite nanotubes
42	PHA	Polyhydroxyalkanoate
43	BG	Bioactive glass
44	Mg	Magnesium
45	Zn	Zinc
46	FRESH	Freeform Reversible Embedding of Suspended Hydrogels
47	nHA	Nano-hydroxyapatite
48	PEGDA	Polyethylene glycol diacrylate
49	CMC	carboxymethyl cellulose
50	PNIPAM	Poly (<i>N</i> -isopropyl acrylamide)
51	Si ₃ N ₄	Silica Nitride
52	Ti6Al4V	Titanium Alloy (90% titanium, 6% aluminium and 4% vanadium)
53	ATZ	Alumina-Toughened Zirconia
54	PLDL	Poly (L, DL-Lactic acid)
55	PCU-Sil	Polycarbonate-based urethane silicone
56	CF	Carbon Fiber
57	HHGs	Homocomposite hydrogels
58	SDCs	Soft dendritic colloids
59	MSNs	Mesoporous silica-calcia nanoparticles
60	HELP	hyaluronan elastin-like protein
61	ANOVA	Analysis of Variants
62	SEM	Scanning Electron Microscope
63	SC	Sodium Citrate
64	BaTiO ₃	Barium titanate
65	FDA	Food and Drug administration
66	EMA	European Medicines Agency
67	FGM	Functionally Graded Material
68	3Y-TZP	3 mol% yttria-stabilized tetragonal zirconia polycrystals
69	GMP	Good Manufacturing Practices
70	PMA	Premarket Approval
71	PMN	Premarket Notification
72	IDE	Investigational Device Exemption
73	IND	Investigational New Drug
74	DED	Directed Energy Deposition
75	LPBF	Laser Powder Bed Fusion
76	CNN	Convolutional Neural Networks

77	KNN	K-Nearest Neighbors
78	DT	Decision Tree
79	ANN	Artificial Neural Networks
80	4D	Four dimensions
81	pH	Potential of Hydrogen
82	PEDOT	Poly(3,4-ethylenedioxythiophene)
83	PSS	Poly(styrenesulfonate)
84	DIY	Do It Yourself
85	ECM	Extracellular Matrix
86	°C	Degree Celsius
87	μm	micrometer (or) micron
88	mm	millimeter