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Research Progress of Bone Implant Additive Manufacturing

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Abstract

Bone implants are currently a solution for the treatment of large bone defects. The structural design and manufacture of complex bone tissue engineering scaffolds can be realized by using additive manufacturing technology. Advances in additive manufacturing techniques and the continued emergence of related materials provide different opportunities for new bone implant techniques to achieve the challenging requirements of proposed bone implants. The purpose of this review is to present the current status and analyze the advantages and disadvantages of various additive manufacturing for the manufacturing of bone implants. Five different manufacturing techniques (multilayer deposition forming, ink direct writing, laser melting, laser sintering, and light curing are reviewed.) and the currently required bone implants technology, and thus put forward the research and development direction of additive manufacturing suitable for bone implants.

Keywords: bone implant, additive manufacturing, bone scaffold

1. Introduction

As one of the most important components of the human body, the basic function of bones is to support the body while protecting the internal organs (Reza MM, Subramaniyam N, Sim CM, et al, 2017). For people, bone defect is a very serious and common disease. Although the human skeleton has a certain self-repair ability, if it encounters a serious defect, it needs the intervention and help of external forces, such as large areas of bone loss and Repair has become a difficult problem often encountered in surgery. Therefore, certain new technologies and materials are needed to replace the missing bone parts in the human body (Lin S, Yang G, Jiang F, et al, 2019; Duan H, Cao C, Wang X, et al, 2020).

Additive manufacturing (3D printing technology) has been developed as a revolutionary technology for more than 30 years. Compared with traditional subtractive technology, additive manufacturing is based on software for three-dimensional structure and continuous accumulation of materials. It can be used flexibly after processing different parts and materials, and has the characteristics of low cost and short cycle. Additive manufacturing technology has emerged in recent years as a powerful method for fabricating biomaterials, including metallic biomaterials for bone tissue regeneration. Additive manufacturing technology enables high-precision fabrication with high flexibility of internal and external macro- and micro-structures of orthopedic implants. The geometrical and topological porous properties of metallic biosalts can be precisely tuned through a controlled fabrication process, resulting in improved mechanical properties for bone simulation, altered biodegradation kinetics, increased bone tissue regeneration rates, and the formation of scaffolds with extensive, interconnected osteoblastic luminal-tubular networks of biomaterials. The current methods of additive technology for bone implantation are under further research, mainly including fused deposition modelling (FDM), direct ink writing (DIW), selective laser melting (SLM), selective laser sintering (SLS), light curing (stereolithography, SLA), digital light processing (DLP), etc. (Figure 1) (Shi Y.S., Wu H.Z, Yan C.H, Yang X, Chen D.B. & Zhang C, 2020; Wei S, Ma J.X, Xu L, et al, 2020; Rezwan K, Chen QZ, Blaker JJ, et al, 2006). Compared to traditional manufacturing techniques, additive manufacturing technologies can customize complex and fine porous structures for each patient with different diseases, and even provide certain additional functions. This paper will provide a comprehensive overview of the current technological advances in biodegradable bone implant research materials.

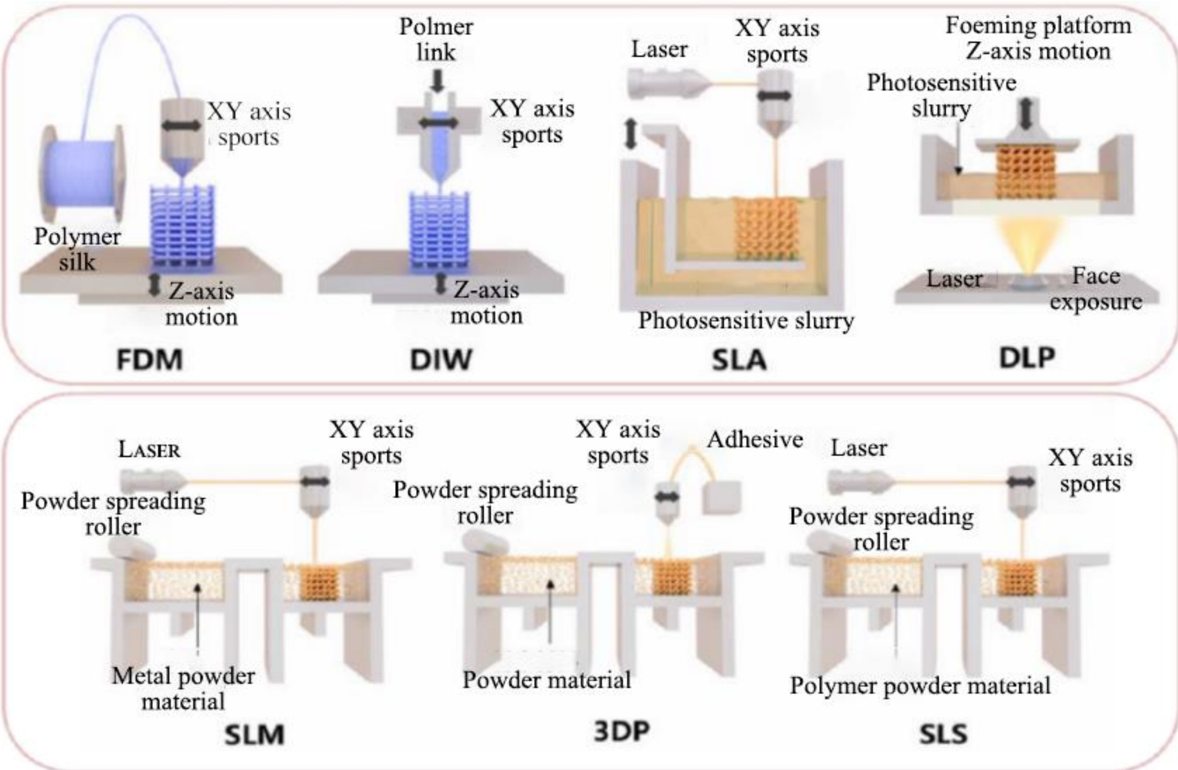

Figure 1. Map of common additive manufacturing techniques for biodegradable bone implants (Wei S, Ma J.X, Xu L, et al, 2020)

2. FDM Technology

FDM is the abbreviation of "Fused Deposition Modeling", that is, fused deposition modeling. This rapid prototyping process is a kind of rapid prototyping process that does not rely on laser as a molding energy source, but heats various filaments (such as engineering plastics ABS, polycarbonate PC, etc.) Melting and deposition molding method, referred to as FDM. FDM technology appeared in the late 1980s. The basic principle of fused deposition modeling technology is shown in Figure 1. The liquid metal is fed into the laser generator at high speed. Under the action of the laser, the liquid metal is heated to the melting point and sprayed onto the laser focal plane at a very high speed. Due to the high energy density of the laser, the wire melts into a molten state, and the molten metal flows rapidly downward under the action of gravity. Since the free length of the metal wire is not constant, but changes exponentially with time, when the laser energy density reaches the melting point, the molten metal wire will continue to solidify and accumulate at the laser focus to form a solid part. By controlling the laser energy density in the laser generator, the melting rate of the molten metal wire can be adjusted, thereby controlling the forming accuracy. After the accumulation of one layer of fuses is completed, the fuses of the next layer begin to flow downward again, and so on until the entire bracket is completed. FDM printing works on the principle of high-temperature nozzles to melt the filament material, and then through software control nozzles along the part cross-sectional contour and filling trajectory movement, and extrusion of the filament material, the filament material in the printing platform stacked, cooling, curing, so that layer by layer stacked to form a three-dimensional entity, as shown in Figure 2 (Ji Hf, 2023).

Degradable materials suitable for FDM include polylactic acid (PLA), polycaprolactone (PCL), polycaprolactone-hydroxyapatite (PCL-HA) and polycaprolactone - Tricalcium phosphate (PCL-TCP), etc. Zein et al. (Iwan Zein, Dietmar W. Hutmacher, Kim Cheng Tan et al., 2002) used thermoplastic degradable PCL wire to prepare a porous scaffold with a honeycomb structure. The scaffold has completely through channels and high porosity. The pore size can be controlled at 160-700 μm, and the yield strength is 0.4-3.6 MPa, suitable for the repair of cancellous bone. Jonas et al (Jensen J, Rolfing J H D, Svend Le D Q, et al, 2014) used rapid prototyping technology to establish a three-dimensional fusion deposition model (FDM-PCL). The FDM-PCL scaffold showed good osteoconductivity and osseointegration after 8 and 12 weeks in a study of porcine cranial defects, emphasizing that this scaffold can serve as a basis for testing other 3D printed scaffolds in the future. Yiwen Xuan et al. (Xuan Y, Tang H, Wu B, et al, 2014) fabricated polycaprolactone/hydroxyapatite (PCL/HA) tissue scaffolds with personalized grooves to repair sternal defects using fusion deposition modeling (FDM) technology. Experiments have proved that the scaffold made by FDM technology can be designed in combination with the specific information of the patient and specific grooves, which is suitable for repairing partial sternal defects in large animal models and shortens the operation time (Figure 3). Margaret et al (Nowicki M A, Castro N J, Plesniak M W, et al, 2016) used FDM-based 3D bioprinting and nanocrystalline hydroxyapatite to improve the adhesion, growth and osteochondral differentiation of bone marrow mesenchymal stem cells (HMSC). The application of cartilage matrix was also evaluated to prepare a three-dimensional bioactive scaffold for cartilage tissue repair and regeneration. Fangzheng Li et al (Li F, Liu C, Song X, et al, 2018) used a structured light scanner and a fused deposition modeling (FDM) printer to produce high-precision animal skeletal models, and confirmed the accuracy and reliability of the digital and printed models through anatomical feature analysis, dimensional measurements (Figure 4). Sa et al. (Sa M W, Nguyen B N B, Moriarty R A, et al, 2018) prepared BCP/ZrO2 blended scaffolds with the FDM system, and proposed that the BCP/ZrO2 scaffolds manufactured by the innovative technology of FDM may provide applications for various types of tissue regeneration, including bone and cartilage. Hsu et al. (Hsu C P, Lin C S, Fan C H, et al, 2020) used fused deposition modeling (FDM) to print an acrylonitrile butadiene styrene (ABS) canine tibia model. The tibia model fabricated on an FDM printer had high geometric accuracy and low RMS values. The surface deviations in EFDM-CT show that the errors that occur during manufacturing are larger than those that occur during sterilization. Therefore, this model can be used for further clinically relevant applications in surgical rehearsal and bone surgery. Bernardo et al. (Bernardo M P, da Silva B C R, Hamouda A E I, et al, 2022) developed a 3D printed high ceramic content (above 20%) polylactic acid/hydroxyapatite (PLA/HA) composite porous scaffold by FDM, and the results showed that the 3D printed PLA scaffold with high concentration of HA Suitable for future applications in bone tissue engineering. Eichholz et al. (Eichholz K F, Freeman F E, Pitacco P, et al, 2022) used Fused Deposition Modeling (FDM) to study how scaffold microstructure affects the healing of large bone defects. Experiments proved that FDM scaffolds have lower porosity and larger fiber diameters, and proposed that the 3D microfiber environment has a great influence on cell The importance of outgrowth and 3D printed framework design in developing bone TE scaffolds is shown in Figure 5. Foroughi et al. (Foroughi A H, Valeri C, Jiang D, et al, 2023) investigated the effect of fused deposition modeling (FDM) process parameters, including printing speed, printing temperature, and layer thickness, on the compressive viscoelastic properties of polylactic acid (PLA) scaffolds. Fabricate modified face-centered cubic (MFCC) scaffolds using FDM, and change the FDM process parameters to achieve a compressive viscoelastic response that matches natural trabecular bone tissue, and design bone-inspired scaffolds with optimized mechanical properties by controlling the FDM process parameters, as shown in Figure 6. Mona et al. (Mona Alizadeh-Osgouei, Yuncang Li, Alireza Vahid, et al, 2021) successfully prepared a PLA degradable scaffold with a three-period minimal curved surface structure with higher compressive strength, and the porosity of the scaffold was 86%-90%. However, FDM technology also has many disadvantages, such as long cooling time and low forming accuracy, and it still has certain defects for precision bone grafting.

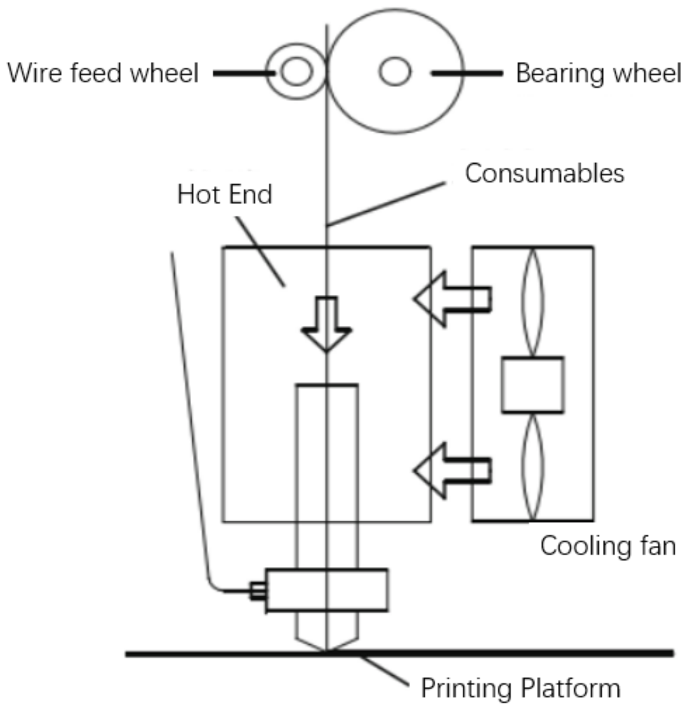

Figure 2. Principle diagram of FDM printing technology (Ji Hf, 2023)

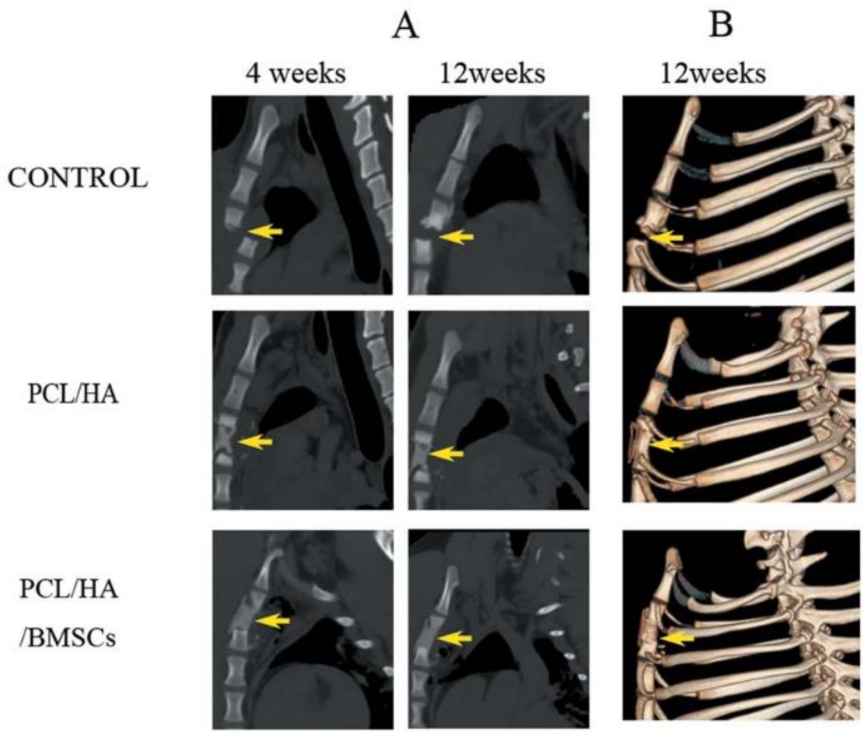

Figure 3. Radiological evaluation of sternal bone regeneration. (A) Representative radiographs at 4 and 12 weeks after implantation (B) Three-dimensional reconstruction of the sternum. Yellow arrows point to defective sites. (Xuan Y, Tang H, Wu B, et al, 2014)

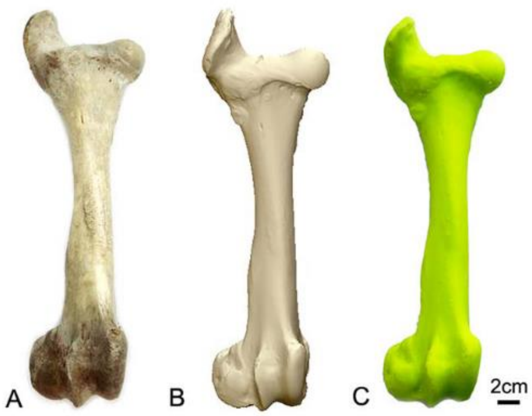

Figure 4. Anatomical features of the dorsal view of the adult bovine femur. (A) bone specimen; (B) digital model; (C) 3D printed model. (Li F, Liu C, Song X, et al, 2018)

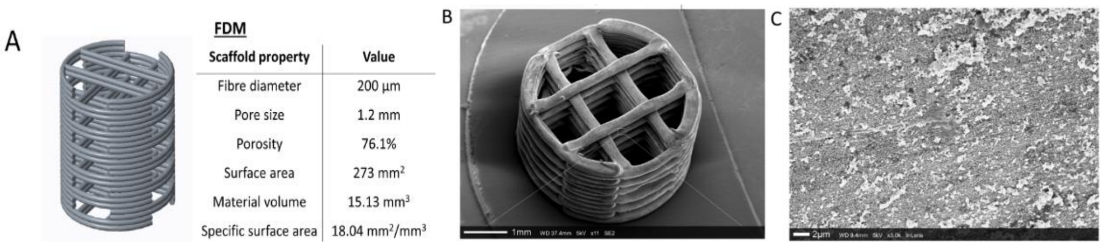

Figure 5. FDM and the new scaffold design and construction. (A) CAD model of the scaffold and list of scaffold properties. (B) SEM image showing the FDM scaffold structure and (C) nanomorphology of the NNHA coating. (Eichholz K F, Freeman F E, Pitacco P, et al, 2022)

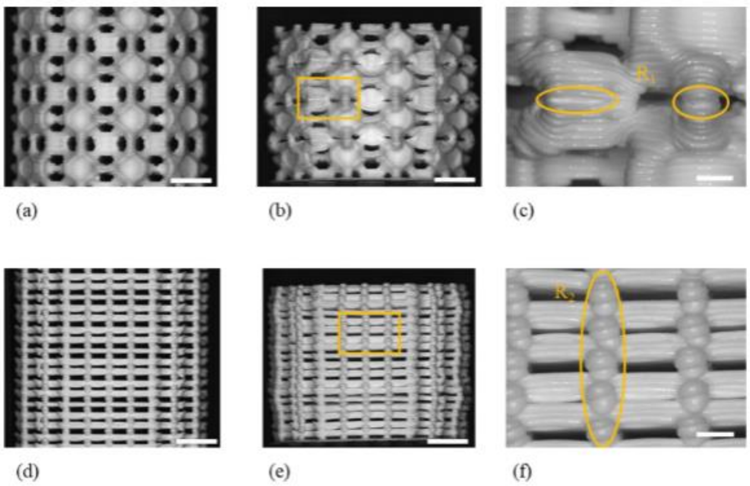

Figure 6. Side view of a PLA holder fabricated by FDM. (Foroughi A H, Valeri C, Jiang D, et al, 2023)

3. DIW Technology

Direct Ink Writing (DIW) (Lakhdar Y, Tuck C, Binner J, et al, 2021) is an additive manufacturing technology based on flowable slurry extruded through a needle and then stacked to form. It can achieve rapid and moldless forming, with simple equipment and easy operation. Different printing models can be designed, and customized manufacturing can also be realized. Therefore, DIW technology is considered to be the simplest and most cost-effective ceramic additive manufacturing technology (Wei X, Peng E, Xie Y, et al, 2017; Tang S, Fan Z, Zhao H, et al, 2018; Peng E, Zhang D & Ding J, 2018), as shown in Figure 7. DIW technology has high requirements for printing inks, which need to have good shear dilution behavior, maintain smooth flow past the nozzle, and require sufficiently high yield stress and storage modulus to keep the extruded ink in continuous filamentary form (Chang P, Mei H, Zhou S, et al, 2019). Generally speaking, DIW technology is simple in structure, low in cost and easy to operate, but it can only be formed as a filamentous accumulation for manufacturing, and it is not suitable for fine bone production.

Konka et al (Konka J, Buxadera-Palomero J, Espanol M, et al, 2021) formed spherical pores on the fiber surface by adding gelatin microspheres as an auxiliary material in self-curing calcium phosphate ink, and the porosity increased from 0.2% to 67.9%, and the increased porosity on the scaffold surface could provide a good environment for effective adhesion and proliferation of osteoblasts. Lin Kuan-Sheng et al. (Lin K.S, Liu J, Liu F.Z, et al, 2020) used 10% sodium alginate as a cross-linking agent for DIW printing ink and added it to nano-hydroxyapatite (nano-HA)/PLA composites, and the formed parts had both the osteoinductivity of nano-HA and the biocompatibility and degradability of PLA. Moncal et al. (Moncal KK, Heo DN, Godzik KP, et al, 2018) developed a composite ink-polycaprolactone/polylactic acid-glycolic acid/hydroxyapatite (PCL/PLGA/HA), and studied its printability and biocompatibility. The degradation performance is better than ordinary PCL stents. The team of Professor Liu Ren from Jiangnan University reported a 3D printing strategy triggered by near-infrared (NIR) photopolymerization (Zhu J, Zhang Q, Yang T., Liu Y, & Liu, R, 2020). The integration of NIR light-curable materials with DIW 3D printing technology enables in-situ curing of thick filaments with high penetration rates. This increases the scalability of DIW, enabling deposited filaments up to 4 mm in diameter, far exceeding any existing UV-assisted DIW, as shown in Figure 8. The NIR effect range can be extended to tens of centimeters and provides embedded writing capability. The authors also demonstrate its parallel fabrication capabilities, simultaneously curing multi-colored filaments and independent objects. This strategy has the further advantage of being widely applicable in combination with other ink-based 3D printing techniques. NIR-DIW ink preparation and real-time FTIR photorheological analysis For DIW printing, a good print structure depends on the proper rheological properties of the ink. Yunhui Chen et al. (Chen Y, Han P, Vandi L J, et al, 2019) used direct ink writing (DIW) technology to print a new thermosetting biopolymer titanium artificial bone scaffold, and demonstrated that thermosetting biopolymers can be used as inkjet adhesives for direct ink writing in hard tissue engineering. Excellent potential in the fabrication of porous titanium scaffolds. Raymond et al. (Raymond S, Maazouz Y, Montufar E B, et al, 2018) explored the consolidation of different hydrothermal treatments on DIW scaffolds prepared with α-tricalcium phosphate/Pluronic F127 ink and compared them with biomimetic treatments. Experiments have proved that the bionic scaffolds and hydrothermal treatment scaffolds manufactured by DIW technology have a good supporting effect on the adhesion and proliferation of rat bone marrow mesenchymal stem cells, and have good application prospects in bone tissue engineering. Mondal et al. (Mondal D & Willett T L, 2020) demonstrated that extrusion direct ink writing (DIW) technology enhanced the mechanical properties of a novel AESO-PEGDA-NHA nanocomposite biomaterial for biomedical applications. These enhanced mechanical properties are the result of reduced defects and increased crystallinity. A method of achieving mechanical properties suitable for repairing bone defects is provided. Konka et al. (Konka J, Buxadera-Palomero J, Espanol M, et al, 2021) used the direct ink writing (DIW) technique to print calcium phosphate scaffolds, proposing to add gelatin microspheres as a dissolving material in the self-curing calcium phosphate ink, because the partial dissolution of gelatin during scaffold printing leads to the formation of the entire fiber surface Spherical pores and exposed on the surface, the presence of concave pores on the surface of these microfilaments can dissolve at low temperature and have biocompatibility, and provide a good environment for cell adhesion and proliferation, and the porosity also helps to improve the bone density. The osteogenic performance of the scaffold is shown in Figure 9. Das et al. (Das M, Jana A, Mishra R, et al, 2023) made a biosourced ink from calcium extracted from the discarded bones of animals. Nanoscale calcium is extracted from bone and mixed with different biocompatible binders to make ink. This ink utilizes DIW to print a scaffold with controllable porosity, which enables cells to grow better, and has good mechanical properties and biocompatibility. It is proposed that DIW technology is an ideal method for repairing and regenerating deformity or loss in tissue engineering. Organ and tissue techniques for the repair or replacement of bone-related diseases in the field of bone defects. As shown in Figure 10.

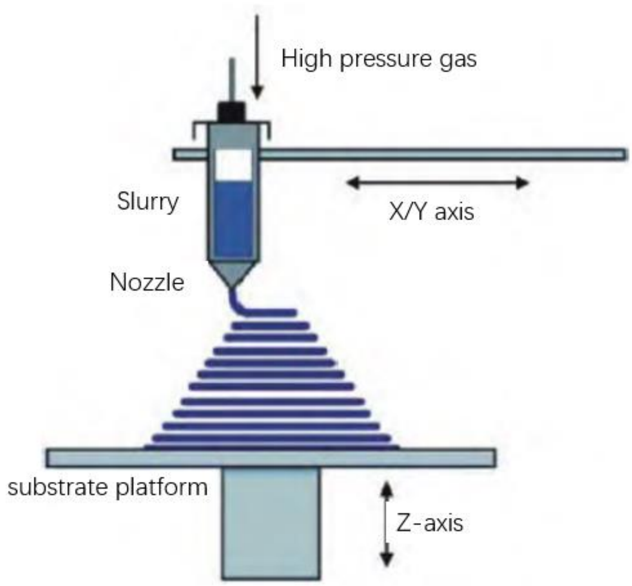

Figure 7. Schematic diagram of DIW printing technology

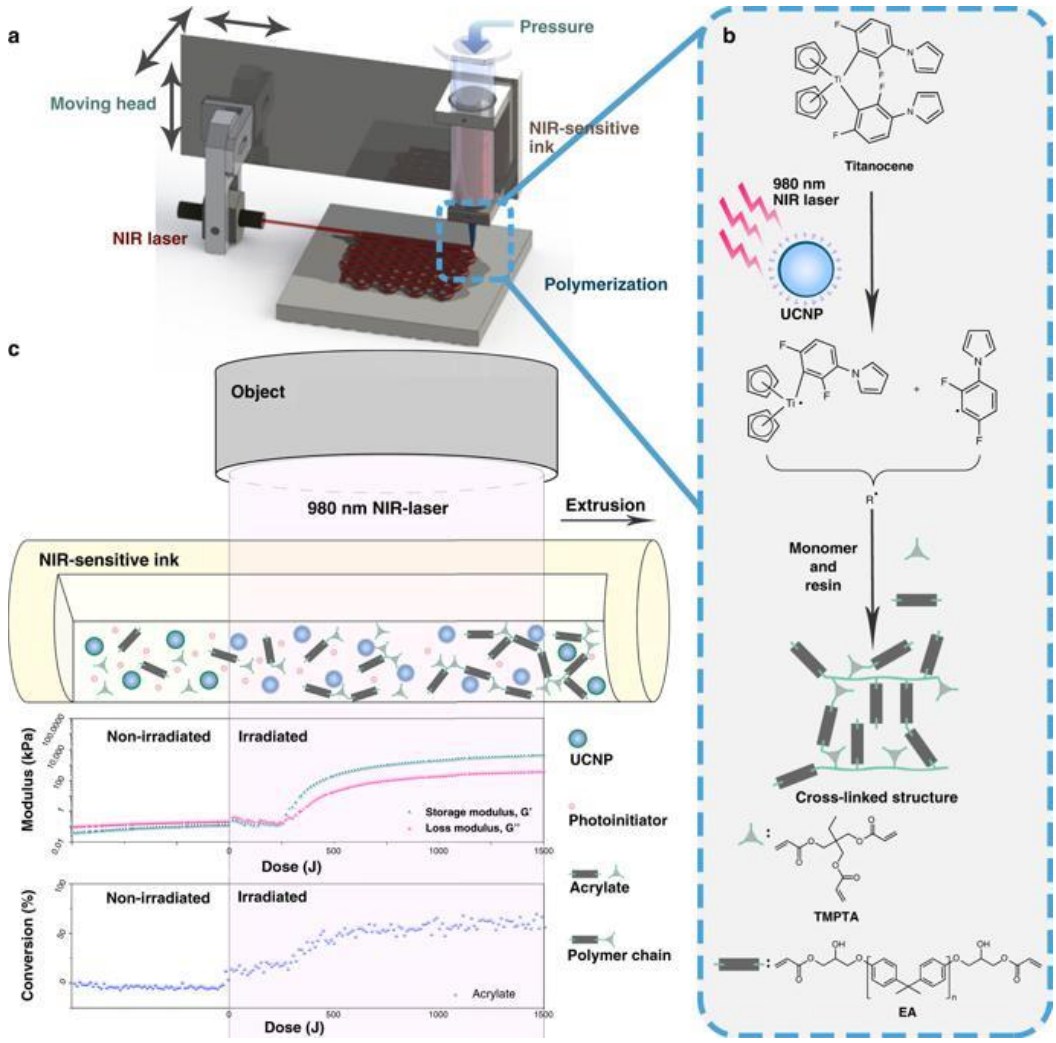

Figure 8. Schematic diagram of NIR-DIW and real-time FTIR photorheology analysis. (a) Configuration of NIR-induced DIW; (b) Structures and reactions used for NIR-DIW printing; (c) Monitoring of NIR-induced photopolymerization by real-time FTIR rheology analysis. (Zhu J, Zhang Q, Yang T., Liu Y, & Liu, R, 2020)

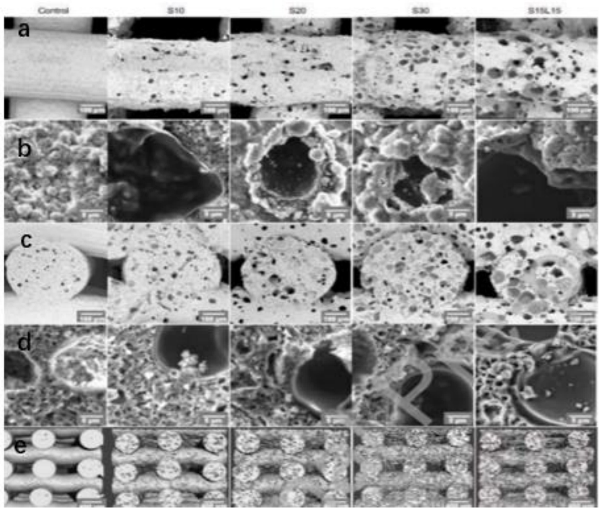

Figure 9. Morphology of the concave pores formed by the 3d scaffold after partial dissolution of gelatin microspheres in scanning electron microscopy images of: (a) the surface of the filament and (b) the pores covered with gelatin on the surface at higher magnification; (c) the cross-section of the filament and (d) the pores covered with gelatin- at magnification cross-section. (e) Three-dimensional reconstruction of μ-CT images of the specimen (Konka J, Buxadera-Palomero J, Espanol M, et al, 2021)

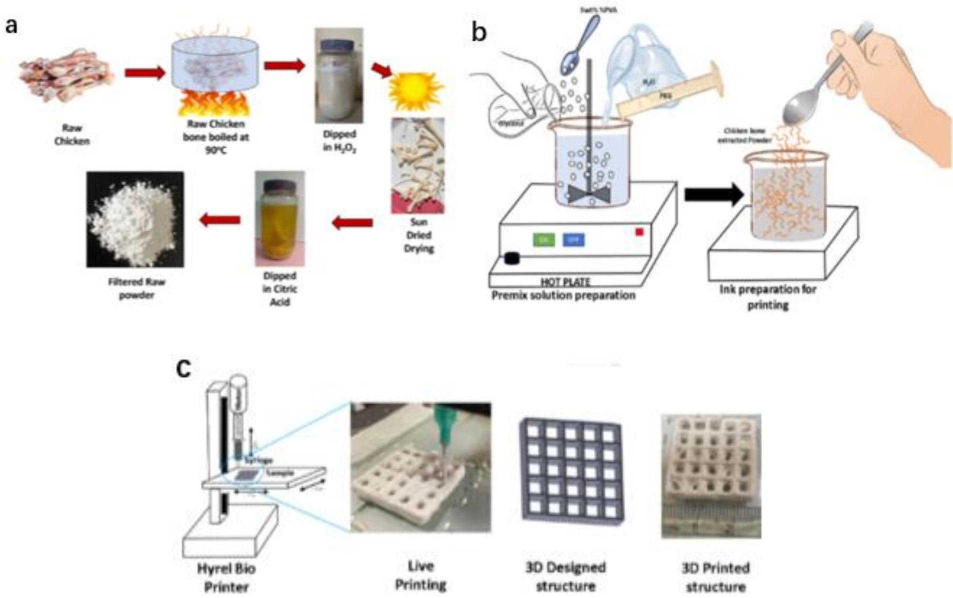

Figure 10. (a) Schematic diagram showing the different processes involved in extracting chicken bone powder, (b) pre-ink solution preparation and ink preparation, and (c) 3D printing of complex structures using chicken bone extract ink (Das M, Jana A, Mishra R, et al, 2023)

4. SLM Technology

Selective laser melting technology (SLM) is an important part of additive manufacturing (Zhang W.X, 2008). Figure 11 is a schematic diagram of selective laser melting technology. SLM technology integrates laser melting technology and rapid cooling solidification technology to selectively melt the metal powder and melt the metal powder material into molten liquid for additive forming, and the obtained metal specimens have uniform metallographic organization, and the densities can meet the requirements of use, and the mechanical properties are close to those of forged metal specimens (Wu W.H, Zhang L, He B.B & Lu L, 2016; Shi Y.S, Lu C.L, Zhang C.L, Huang S.W & Chen G.Q, 2006). SLM technology is currently the mainstream method for the production of medical degradable metal materials. The production precision is very high, and it is widely used in the manufacture of precision medical appliances with good performance. This technology has successfully realized the preparation of degradable metal implants such as magnesium (Mg) alloy, iron (Fe) alloy and zinc (Zn) alloy (Jin S, Zhao D.L & Wang H.Z, 2021). Compared with some formed inert metals such as stainless steel, cobalt (Co-Cr) alloy and titanium (Ti) alloy, some alloys with low melting point such as Mg alloy and Zn put forward higher requirements and challenges for SLM technology (Qing, Y, Wen, P, Xia, D, Zheng, Y, Jauer, L, et al, 2019). If the processing conditions are not suitable, many defects will appear, such as large gaps, insufficient fusion, rough surface and even deformation. Even for Fe, evaporation can occur at high laser intensities (Kruth, J. P., Froyen, L., Van Vaerenbergh, J., Mercelis, P., Rombouts, M. & Lauwers, B, 2004). Precise control is therefore crucial for the successful fabrication of ordered porous implants from resorbable metals by SLM.

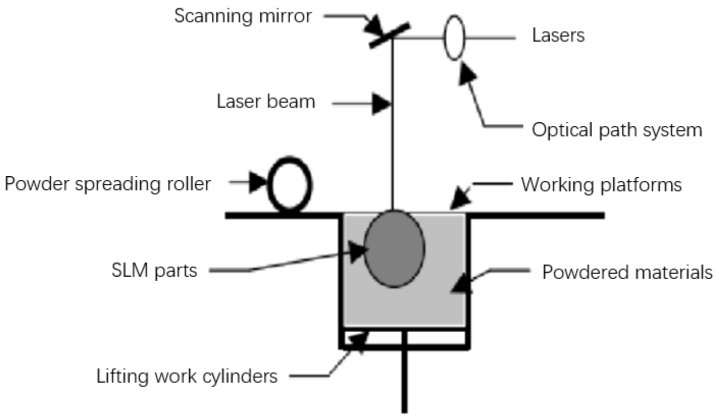

Figure 11. Schematic diagram of SLM technology

The advantages of SLM manufacturing are very many, mainly the following two points: First, through the ultra-fast forming solidification rate compared to FDM can be manufactured with fine-grained crystals of the alloy, reducing the traditional process on the complex manufacturing process, the laser melt pool internal convection and solidification rate can inhibit the occurrence of severe segregation, significantly improving the preparation of the performance of uniformity; second can be free to achieve different needs of the manufacturing function, flexible and versatile, but also to achieve complex functional requirements. Flexible and versatile, it can also achieve complex functional requirements formulation. The preparation of porous structures of Mg alloys, Fe alloys and Zn alloys was achieved (Figure 12) (Qin Y, Wen P, Guo H, et al, 2019; Hai B.S, 2022).

There is a large body of relevant experimental data and literature investigating the use of SLM technology to fabricate biodegradable bone implants and conditioning implants, as well as the use of a three-dimensional fully coherent linkage network to induce targeted bone tissue regeneration, promote bone growth to the interior of the implant, and enhance the integration between implant and bone for better customization of the structure.

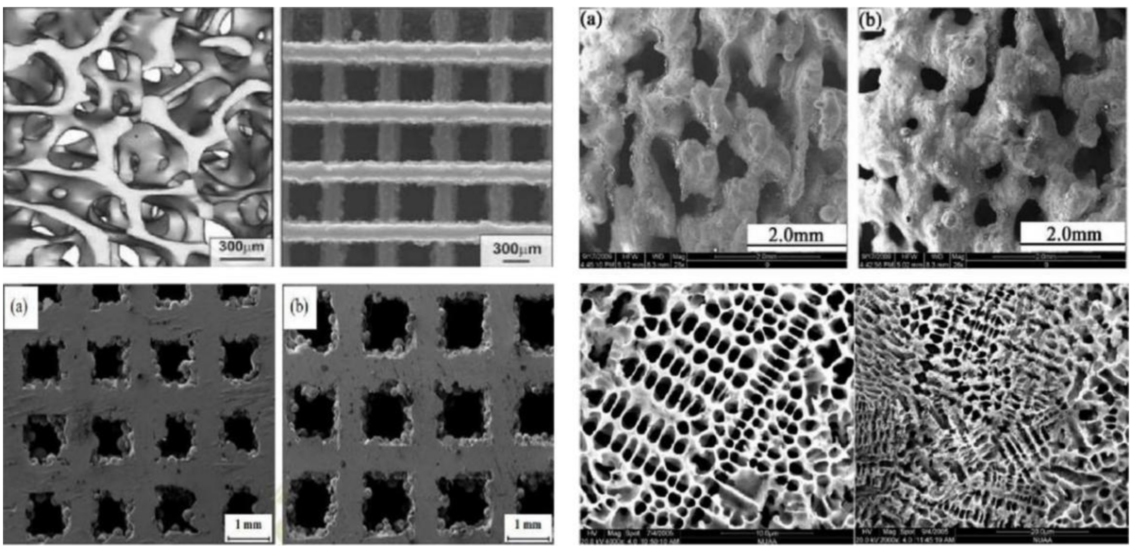

Figure 12. Microstructure of the porous structure of the SLM printed support alloy (Hai B.S, 2022)

For SLM technology, the emergence of degradable metals has brought great opportunities to the research and discovery of degradable implants manufactured in clinical medicine, leading the development trend of orthopedics. Li et al. (Li Y, Zhou J, Pavanram P, et al, 2018; Li Y, Pavanram P, Zhou J, et al, 2019; Li Y, Lietaert K, Li W, et al, 2019) successfully realized Mg-RE alloy, Fe alloy and Zn alloy porous scaffolds through additive manufacturing technology, and verified the feasibility of SLM technology to prepare degradable metal implants. Qin et al. (Qin Y, Wen P, Voshage M, et al, 2019) successfully realized the in-situ alloying of Zn alloy and Mg alloy by using SLM technology, which greatly broadened the scope of Zn alloying and proved the richness of SLM technology in material design. Wen et al (Wen P, Voshage M, Jauer L, et al, 2018) used SLM technology to prepare a cardiovascular stent with a diameter of 2-5 mm and a support rod of 200-500 μm, which proved the ability of this technology to prepare complex structures. Kanazawa et al (Kanazawa M, Iwaki M, Minakuchi S, et al, 2014) used a selective laser melting system (SLM) to fabricate thin titanium alloy brackets for maxillary complete dentures and evaluated their hardness and microstructure, and found that the mechanical properties and microstructure of the printed brackets were suitable for clinical use. Shaoki et al. (Shaoki A, Xu J, Sun H, et al, 2016) evaluated the osseointegration ability of SLM implants in vivo. The study proved the ability of SLM implants to integrate with living bone. SLM technology is expected to become a new dental implant manufacturing technology. Peng et al. (Peng W, Liu Y, Jiang X, et al, 2019) used selective laser melting (SLM) to prepare LSRCMS porous implants with different parameters and porosity, as shown in Figure 13. The microstructure characterization method was used to evaluate the printed samples, the mechanical properties were analyzed by mechanical tests, and the stress characteristics of LSRCMS under loading force were numerically calculated by using the finite element analysis method. The results show that the porous Ti6Al4V scaffold prepared by SLM based on LSRCMS is a promising bone implant material, which can be applied in the field of bone defect repair. Carluccio et al. (Carluccio D, Xu C, Venezuela J, et al, 2020) conducted a microstructural, mechanical, corrosion and biological characterization of the properties of Fe-Mn bone scaffolds prepared by SLM, and experimentally demonstrated the promising application of porous Fe35Mn implants fabricated by SLM in biodegradable load-bearing bone scaffolds. Liao et al. (Liao B, Xia R F, Li W, et al, 2021) used Ti6Al4V as material to prepare TPMS scaffolds with different radial gradient porosity by selective laser melting (SLM) performance and cell behavior, improving understanding of the impact of SLM design parameters on scaffold mechanical properties and cell growth. Pei et al. (Pei X, Wu L, Lei H, et al, 2021) combined SLM with a hydrothermal process to prepare three-level inhomogeneous porosity titanium implants, as shown in Figure 14, providing a multifaceted pathway to modulate the biological function of biomaterials by optimizing the design and preparation of scaffolds. Shi et al. (Shi C, Lu N, Qin Y, et al, 2021) prepared four sets of model samples using selective laser melting (SLM) and Ti6Al4V materials. The static performance of the scaffold was comprehensively evaluated by mechanical compression simulation and mechanical compression test, the manufacturing error of the scaffold sample was evaluated by scanning electron microscopy (SEM), and the permeability of the scaffold was predicted and evaluated by computational fluid dynamics (CFD) simulation analysis. All of them match with human cancellous bone, indicating that they have great research and application potential in the field of artificial bone scaffolds. Suresh et al. (Suresh S, Sun C N, Tekumalla S, et al, 2021) demonstrated that selective laser melting (SLM) technique can be used to fabricate Ti-6Al-4V ultra-low interstitial (ELI) pores to reduce their stiffness while enhancing cell adhesion and proliferation. The results provide mechanical information and biological understanding for the application of SLM-printed porous Ti-6Al-4V ELI and SLM-printed dense Ti-6Al-4V ELI in the biomedical field.

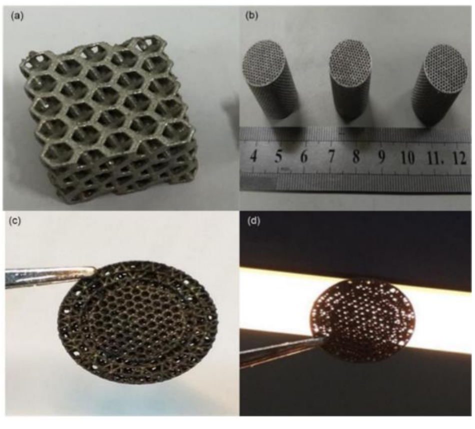

Figure 13. Selective laser melting (SLM) printing of Ti6Al4V porous structures (a) enlarged image of a porous structural unit; (B) standard porous specimen prepared for mechanical properties testing; (c) internal structure of a porous specimen; (d) internal pores of a porous specimen (Peng W, Liu Y, Jiang X, et al, 2019)

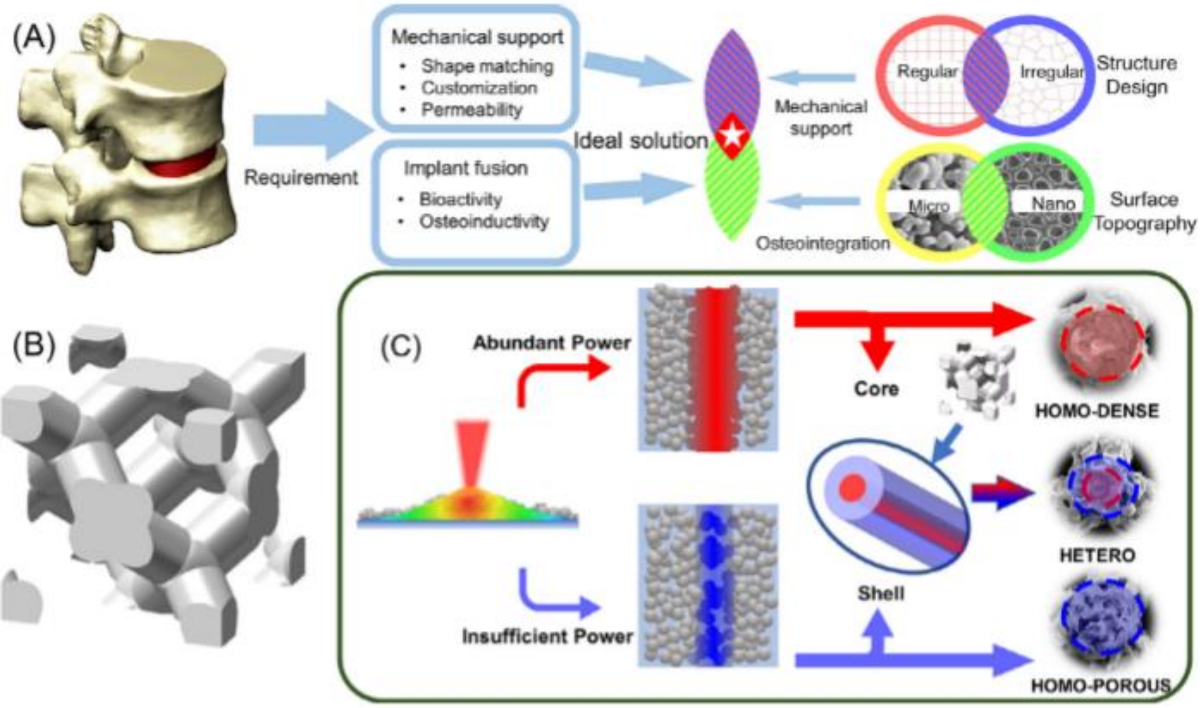

Figure 14. (A) Schematic representation of the critical mass of an ideal bone engineered scaffold; (B) single monolithic macroscopic structure used in this study; (C) core-shell inhomogeneous structure prepared by SLM (Pei X, Wu L, Lei H, et al, 2021)

5. SLS Technology

Different from the forming principles of other additive manufacturing technologies, SLS technology sinters powder materials into shape by scanning and forming layers of laser heat sources. SLS equipment mainly includes: lasers, scanning galvanometers, temperature control boxes, forming cylinders, and powder supply cylinders. powder spreading roller and recovery cylinder, the working principle of which is shown in Figure 15 (Song B, Cai YS, Xu H, Xia JQ, et al, 2017). The SLS process can work with a variety of materials including nylon, polymer and ceramic plaster. Its advantage is that most powdery materials can be formed without organic binders, and the utilization rate is also very high, and more complex geometric objects can be manufactured. However, the volume of the equipment is relatively large and the process is complicated. Inert flame-retardant gas needs to be added into the forming cavity of the equipment, and the forming cavity needs to be preheated before sintering, so it is difficult to clean the remaining powder.

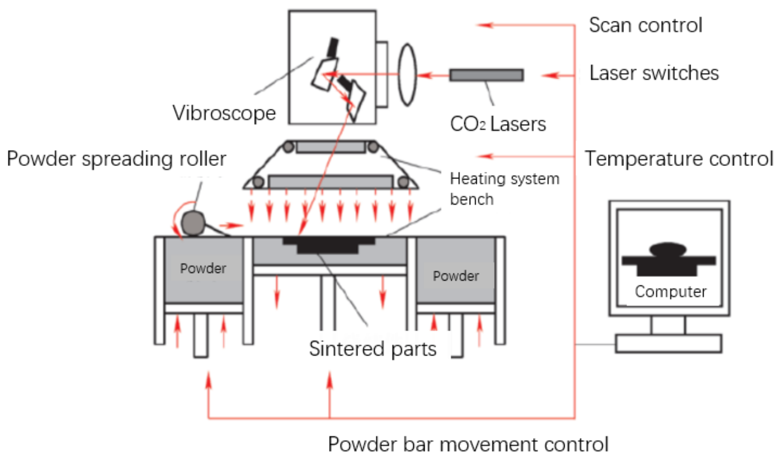

Figure 15. Schematic diagram of the operation of the SLS (Song B, Cai YS, Xu H, Xia JQ, et al, 2017)

Meng et al. filled the PCL scaffold into NaCl particles for recasting and solidification, and transformed it into a metal implant with fine and dense appearance and powerful mechanical properties through the SLS process. The treated PCL has been implanted in animals for 24 weeks, and the results show that it has good osteoinductivity and good compatibility with other organisms in the body. During the degradation process, its original appearance and Performance is also very well maintained (Meng Z, He J, Cai Z, et al, 2020). Yan et al. (Yan D, Zeng B, Han Y, et al, 2020) prepared biodegradable PLA and nano-HA composite microsphere powder by emulsion solvent evaporation method, and prepared biocompatible PLA/nano-HA composite parts by SLS process, and modified parts It has been verified by in vitro cell experiments that it has no cytotoxicity, and has good biocompatibility and the ability to promote osteoblast differentiation. Du et al. (Du Y, Liu H, Yang Q, et al, 2017) prepared an articular cartilage/bone tissue bionic structural scaffold consisting of PCL and HA/PCL microspheres using the SLS process and achieved regenerative repair of articular cartilage bone tissue defects without the attachment of any live cells and growth factors. Diermann et al. (Diermann S H, Lu M, Zhao Y, et al, 2018) prepared a biodegradable polyhydroxybutyrate-hydroxyvalerate (PHBV) interconnected porous scaffold with a large specific surface area and a relative porosity of up to 80% using the SLS process. The scaffold has a unique Microstructure, consisting of pores, islands, and bridges. Its unique microstructure provides great potential for further in vitro and in vivo testing of scaffolds. Diermann et al. (Diermann S H, Lu M, Edwards G, et al, 2019) investigated the degradation behavior of high molecular weight PHBV scaffolds prepared using selective laser sintering (SLS) without the use of pre-designed porous structures. The prepared scaffold has a high surface area and a strong water absorption capacity. The PHBV scaffolds prepared with SLS exhibited adequate mechanical properties and good structural integrity after testing. This indicates that the scaffolds have great potential for clinical applications. Zeng et al. (Zeng H, Pathak J L, Shi Y, et al, 2020) used selective laser sintering (SLS) to print three-dimensional microporous BCP scaffolds for bone tissue engineering. As shown in Figure 16, the physicochemical properties, cell adhesion, biocompatibility, and in vitro The osteogenic potential and healing potential of critical-sized calvarial defects in rabbits were studied, and it was found that the BCP scaffold prepared by SLS printing maintained the physicochemical properties of BCP, had the ability to concentrate host precursor cells to the defect site, and possibly activated ERK1/2 signaling Promote endogenous bone regeneration. Tortorici et al. (Tortorici M, Gayer C, Torchio A, et al, 2021) studied the effect of SLS process parameters on sintered scaffolds, and prepared high-porosity (>70% porosity) PCL scaffolds. The effects of laser power, beam compensation and laser beam diameter on the dimensional accuracy and mechanical stiffness of the fabricated PCL stent were specifically studied. The applicability of SLS as a production technology for bone TE PCL scaffolds under various SLS process parameters was confirmed. Du et al. (Du Y, Liu H, Yang Q, et al, 2017) evaluated the feasibility of SLS to fabricate gradient multilayer scaffolds. Using the SLS technique, multilayer scaffolds containing HA were produced and implanted in a rabbit cartilage defect model. Six to 12 weeks after the placement of the multilayer scaffold, the repair ability of the bone defect was enhanced, and smooth cartilage tissue was found in the multilayer scaffold. The results showed that the multilayered scaffolds containing HA could effectively enhance osteochondral repair, and newly formed tissues were articular cartilage, subchondral bone, and reconstructed osteochondral interface. In addition, Shuai et al. (Shuai C, Gao C, Nie Y, Hu A, Qu H & Peng S, 2010) investigated the effects of different preheating temperatures and laser speeds on the surface properties of SLS-printed nano-HA-based artificial bone scaffolds. They suggested that scaffolds meeting bone mechanical and biological performance requirements could be obtained by optimizing sintering time. In addition, Roskies et al. (Roskies M, Jordan JO, Fang D, et al, 2016) used SLS to print PEEK scaffolds and co-cultured with rat BMSCS and adipose-derived stem cells (ADSCS). The results showed that ADSCS had higher osteogenic differentiation ability than BMSCS.

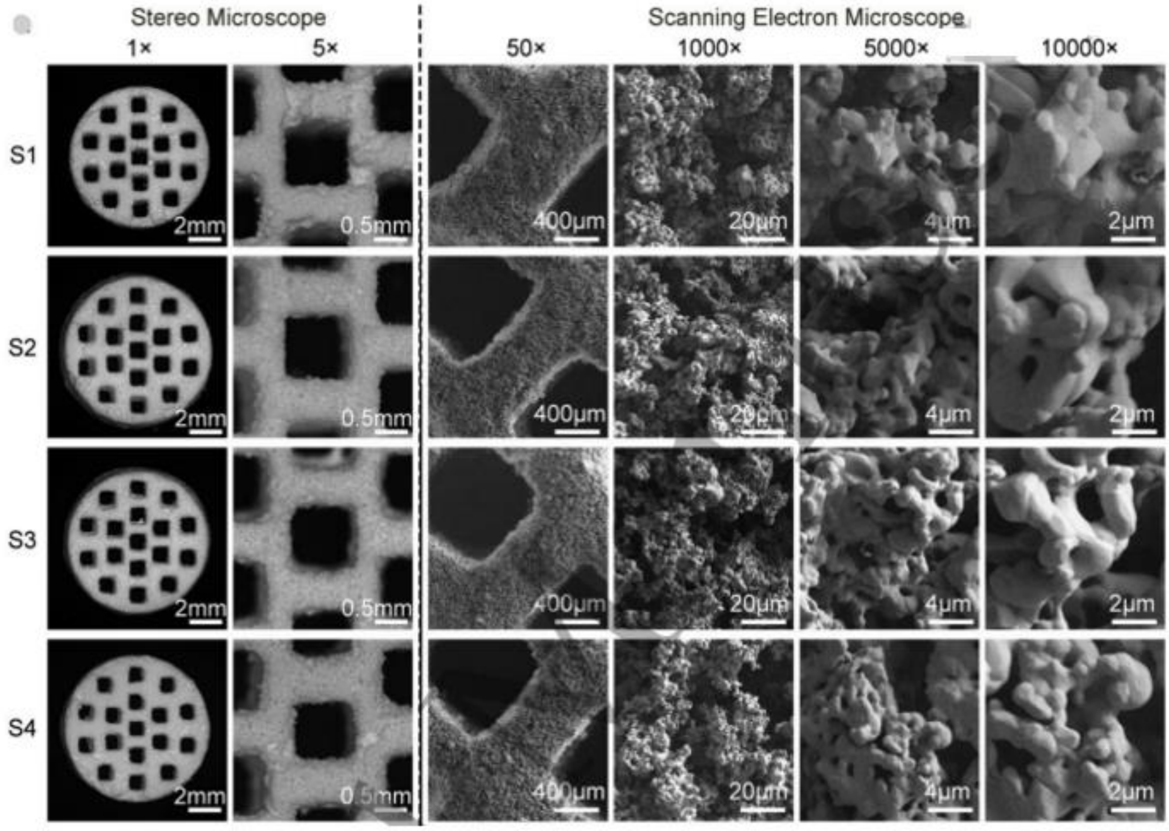

Figure 16. Surface morphology of the BCP scaffold observed on a stereomicroscope and scanning electron microscope (Zeng H, Pathak J L, Shi Y, et al, 2020)

6. SLA Technology

SLA (Solid Laser Array) technology, that is, fused deposition modeling technology, is a technology that uses metal powder as a raw material to realize solid forming by layer-by-layer accumulation and layer-by-layer melting. SLA technology has been widely used in medical fields, such as oral cavity, heart, bone, tooth, orthopedics and prosthesis manufacturing, etc. The basic principle of SLA technology is to send the powder material directly into the hot bed, and accumulate layer by layer through the rapid prototyping equipment, so that the material is melted and solidified, and finally forms a three-dimensional entity. There are usually three forming processes in SLA technology: (1) layer-by-layer accumulation, achieved by controlling layer thickness and support structure; (2) synchronous scanning, achieved by controlling the speed of laser scanning; (3) Layer-by-layer printing, which is achieved by adjusting parameters such as support structure, layer thickness and laser scanning speed. One of the most common SLA technologies is layer-by-layer stacking. The materials currently used in SLA technology mainly include metal materials, polymer materials and bioceramics. Among them, metal materials are the main application of SLA technology at present. The metal materials are mainly nickel-titanium alloy and pure titanium, etc.

The most widely used SLA technology is nickel-titanium alloy. Nickel-titanium alloy has good mechanical properties, and its compressive strength can reach 2000 MPa. However, due to its high surface hardness, it requires high precision of processing equipment. Pure titanium is a high-strength, corrosion-resistant metal material, its compressive strength can reach 1500 MPa, but its tensile strength is low, which is not suitable for SLA technology applications. Bioceramic is a bioceramic material with excellent performance, which has high hardness and elastic modulus.

At present, there are many studies on the application of bioceramics in SLA technology, but its application in SLA technology remains to be studied. The high price of bioceramics has a certain restriction on the promotion of SLA technology. SLA belongs to the light-curing additive manufacturing, and the light-curing molding has the characteristics of high precision compared with other rapid prototyping technologies. This technology uses the ultraviolet laser beam under the control of the computer to scan the layered sections of the computer model point by point, and the resin thin layer in the scanned area produces a curing reaction to form the thin layer section of the part. After a liquid resin curing layer is completed, a new layer of liquid resin is applied on the surface of the cured resin to repeat scanning and curing, and so on until the curing of the entire part is completed (Figure 17) (Zhang D, Jin T P & Huang C M, 2013). Melchels et al. developed a light-curable resin without reactive diluents, using ethyl lactate as a non-reactive diluent, and successfully prepared racemic polylactic acid Poly (D, L -lactide) PDLLA scaffold, cell experiments proved that mouse preosteoblasts are more likely to adhere and proliferate on this structure (Melchels FPW, Feijen J, Grijpma DW, et al, 2009).

For SLA technology, the scope of application is also relatively wide. Not only can degradable polymer materials be used, but also some other composite materials such as composite ceramic materials can be used for forming. The precision is high and complex parts can be manufactured. Mangano et al. (Mangano C, Mangano F, Gobbi L, et al, 2019) compared laser stereolithography (SLA) 3D printed scaffolds with traditional sintered biphasic calcium phosphate scaffolds by comprehensive morphological, morphometric, and mechanical analysis. The study found that SLA-3D printed biomaterials had properties comparable to, and in some cases superior to, conventional sintered materials, with higher average thicknesses of pillars and pores. Micro-CT and scanning electron microscopy imaging results showed that the studied biomaterial exhibited a structure closer to that of the human jaw than the sintered biomaterial. Chen et al. (Chen Q, Zou B, Lai Q, et al, 2019) prepared SLA-3D hydroxyapatite scaffolds in order to investigate whether SLA-3D printed hydroxyapatite scaffolds are toxic or not, using thermogravimetric analysis (TG), differential scanning calorimetry (DSC), in vitro cytotoxicity test, and rabbit parietal bone implantation pre-experiment, and the final prepared microporous HAP samples showed good biosafety in the rabbit parietal bone implantation pre-experiment. Le. et.al. (Le Guéhennec L, Van Hede D, Plougonven E, et al, 2020) evaluated the in vitro and in vivo biocompatibility and osteoinductive properties of two calcium phosphate (CAP)-based scaffolds fabricated using SLA printing. This study highlighted the potential of SLA 3D printed CAP-based biomaterials for intraoral Relevance to bone regeneration, fabrication precision needs to be improved, and further experiments should be performed using biomimetic scaffolds. Pan et al. (Pan Y, Zheng R, Liu F, et al, 2014) used computed tomography (CT) combined with computer-aided design (CAD) and stereolithography (SLA) to design and manufacture a full-geometric canine rib prosthesis (Figure 18), and evaluated the accuracy of the method. Experiments have proved that it is feasible to design and manufacture rib prostheses with full geometric shapes by using CT scanning technology combined with CAD and SLA technology. Kakarala et al. (Kakarala G, Toms A D & Kuiper J H, 2006) investigated whether the stability and cortical strain of SLA implants allowed the bone to match the stiffer artificial bone, and if not, whether compensating for the lower modulus with a thicker cortex would result in a better match. Provides a strong indication for the SLA tibia as a valid model for the evaluation of new techniques in knee surgery and compares well with previously used models. Cooke et al. (Cooke M N, Fisher J P, Dean D, et al, 2003) proposed a new method of using SLA to prepare biodegradable polymer scaffolds for tissue engineering. A biodegradable resin mixture of diethyl fumarate (DEF), polypropylene fumarate (PPF) and photoinitiator bisacylphosphine oxide (BAPO) was used in the experiment. The PPF was cross-linked with a UV laser (325-nm) from SLA. Successfully fabricated DEF/PPF scaffolds, which have certain application value in tissue engineering of bone matrix. As shown in Figure 19 (Kim K, Dean D, Wallace J, et al, 2011) found that in the three-dimensional PPF/DEF scaffold prepared by SLA, the continuous open pore geometry may be a more favorable environment to promote the expression of early osteogenic signals and subsequent osteoblast differentiation.

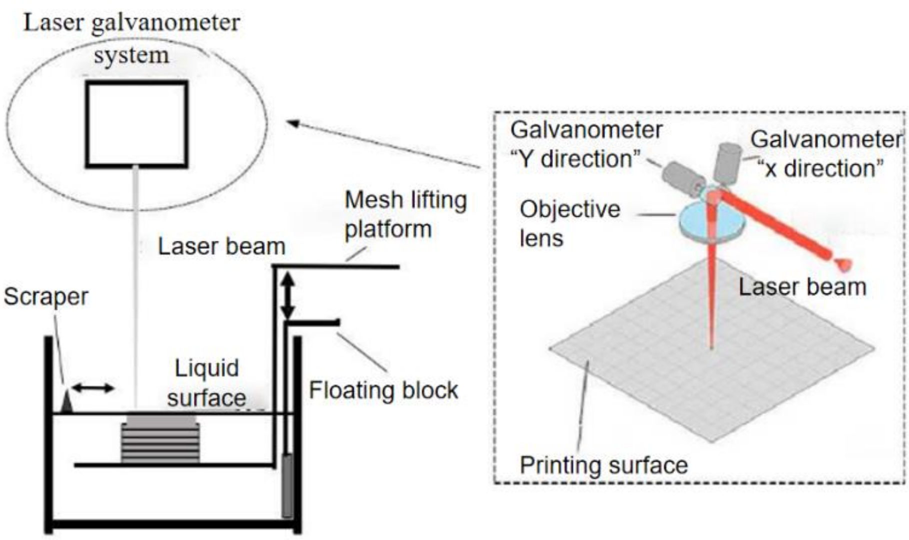

Figure 17. Model of SLA light-curing additive technology (Zhang D, Jin T P & Huang C M, 2013)

Figure 18. Rib prosthesis (upwards) and rib prototype (downwards) (Pan Y, Zheng R, Liu F, et al, 2014)

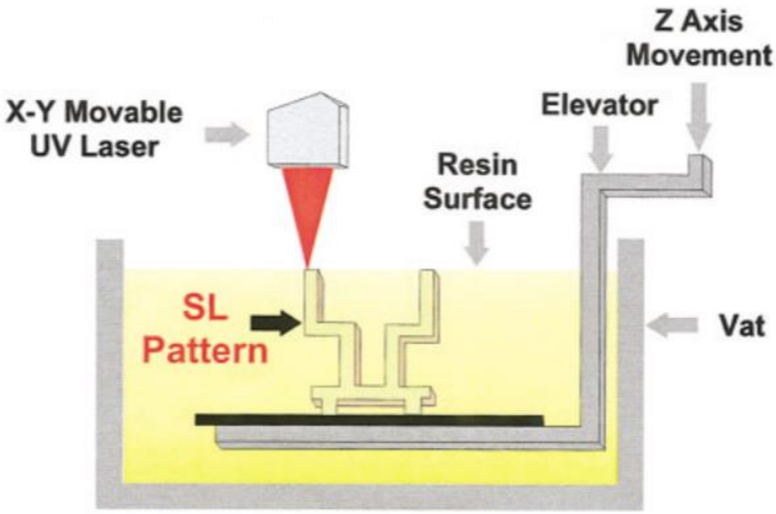

Figure 19. Laser curing unit (3d Systems 250/40SLA): conversion of CAD files into slice data. A high-resolution laser beam moves over a barrel of resin. The resin is hardened to a defined depth of 0.1 mm (100 μm), one slice at a time. The lift platform is moved down by 0.1 mm after each layer is polymerised. Adjacent layers were polymerised to each other and kept in alignment by means of supports fixed to the lift (build) platen (Cooke M N, Fisher J P, Dean D, et al, 2003)

7. Discussion

Regarding the current status of clinical treatment of bone defects, this paper discusses and studies from the aspect of additive manufacturing technology, and believes that with the continuous updating and iteration of its technology, coupled with the continuous emergence of new biometal materials used to replace bone defects, it will be a revolutionary boost to additive technologies for bone replacement. At present, biodegradable bone implants have been widely spread in related medical and engineering fields, because these degradable bone implants can be decomposed and eliminated in the human body without secondary surgery. It can effectively prevent patients from being subjected to the risk of surgery again, and it also points out a new way out for the future manufacturing and technology of current clinical metal stents. Additive manufacturing technologies mainly include fused deposition modeling (FDM), direct ink writing (DIW), selective laser melting (SLM), selective laser sintering (SLS), and stereolithography (SLA). Among them, SLM, as a relatively mainstream bone material additive manufacturing technology, has not only successfully realized the printing of bone implants of new materials such as magnesium (Mg) alloy, iron (Fe) alloy, and zinc (Zn) alloy, the manufacturing process of bone implant materials also performed well. With the development and research of additive manufacturing in the past 30 years, some scholars have not been satisfied with the technology of 3D printing, and proposed forming smart components (4D printing) and even life components (5D printing), these technologies can realize the formation of active biological Cell materials are used to manufacture relevant life organ components in the human body, making additive manufacturing develop in a higher dimension.

8. Conclusion

With the development of the times, the demand for alternative bone implants is constantly developing in a better, newer, and more environmentally friendly direction. New materials and processes are needed to ensure that the corresponding biological environmental adaptability and mechanical properties are met. For the current bone implant additive manufacturing, a large number of new technologies and materials have emerged, as well as some new research directions including degradable bone implants. But generally speaking, the current biological additive manufacturing is still in the development stage. Compared with the traditional additive manufacturing, it will take a certain amount of time for the formulation of materials, methods, manufacturing standards and ethical issues related to biological additive. In order to improve it, multi-disciplinary and multi-party organizations are required to conduct discussion and research. At the same time, bio-augmentation technology can produce engineering scaffolds that meet the various needs of the human body, and can even endow the native skeleton with more functions, which is of great significance for future bone tissue research and clinical applications.

Conflict of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical Approval

Not required.

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