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An Overview of Additive Manufacturing Methods for Biomedical Applications

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An Overview of Additive Manufacturing Methods for Biomedical Applications

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Abstract

Additive Manufacturing (AM) is rapidly developing technology in biomedical implant manufacturing area. It provides the opportunity to produce custom-made implants from 3D digital modeling of the desired prosthesis with complex geometries and different materials such as metal, ceramic and polymer. Although the researches are going on vigorously, there are still some gaps about manufacturing implants with in desired surface quality and dimensional accuracy. In this study the most widely used AM methods in biomedical implant manufacturing, such as Stereolithography, fused deposition modeling (FDM), selective laser sintering (SLS), selective laser melting (SLM) and electron beam melting (EBM) are explained. Application and recent studies in this area are reviewed in terms of orthopedic and dental prosthesis. Moreover, recent trends and future directions about AM for manufacturing more precise and accurate biomedical implants are discussed.

Keywords: 3D printing, Additive manufacturing, Dimensional accuracy, Hip implants, Knee implants, Orthopedic prosthesis.

Introduction

Additive Manufacturing (AM) is the process that produces parts by adding materials layer-by-layer according to 3-dimensional model data of the product. In conventional manufacturing such as, milling, turning or stamping, the final shape of the product is obtained by removing material from the bulk or sheet form of the raw material. AM processes give opportunity for reduction of raw material waste. Moreover, it provides possibility for obtaining final product from 3D model of the part without any molding, fixture or tool. Therefore, manufacturing of complex geometries is easier than by conventional methods (Srivatsan and Sudarshan, 2016). With these superiorities, AM processes are tremendously growing technology that finds a wide range of application area from aerospace, automotive industries to medical sector (Gibson Rosen and Stucker, 2015).

For layer-based manufacturing, at first CAD model of the part is divided in to 2D slices and 3D printer uses these slice information and create the 3D geometry of the product layer by layer (Bandyopadhyay and Bose, 2016). It makes possible to control and modify the design if needed. Also it gives the opportunity to create customized parts according to customer demand especially custom made implants for medical applications (Srivatsan and Sudarshan 2016).

There are different types of additive manufacturing methods that can be classified according to the power source (laser, electron beam etc.), material type (plastic, metal, and ceramic) and the form of the feedstock (powder, filament, bar, resin). American Society for Testing and Materials (ASTM) group, ASTMF42-Additive Manufacturing committee has classified AM methods basically in seven categories. These categories are; Vat photo polymerization (Stereolithography, bioplotters), Powder bed fusion (Selective Laser Sintering (SLS), Selective Laser Melting (SLM), Electron Beam Melting (EBM), Direct Metal Laser Sintering (DMLS)), Material extrusion (Fused Deposition Modeling (FDM)), Material jetting (Multi-jet Fusion Technology), Binder jetting, Directed energy deposition (Laser Engineered Net Shaping, Direct Metal Deposition) and Sheet lamination (Bandyopadhyay et al., 2015).

Being a direct manufacturing method, production of surgical implants and reconstruction of a model for desired assembly is more practical than conventional methods. Using 3D digital data of desired geometry provides flexibility in design and fabrication of complex geometrical features. Intricate shapes, hallow structures and thinner channels can be manufactured easily by AM methods without any tools, moulds, press or punches and so with minimum human error. It gives opportunity to build up the parts with different densities. For example, according to the function of the manufactured part it is possible to study with different filling ratios in FDM process. Materials that used in biomedical applications are expensive rather than that used in mechanical applications. AM technology provides maximum material saving by adding materials without subtracting. It is reported that, in metal industry wastage of raw material was reduced up to 40% by using AM technologies instead of conventional machining (Petrovic et al., 2012; Hollister and Bergman, 2004).

This paper summarizes the AM methods used in biomedical industry such as Stereo lithography, Fused Deposition Modeling, Selective Laser Sintering, Selective Laser Melting, and Electron Beam Melting. It explains basic principles of these systems, give examples about applications and used materials. Moreover, the paper presents advantages and limitations of the methods and gives future directions about the application of AM for biomedical implants.

Additive Manufacturing Methods for Biomedical Applications

In medical application, 3D modeling and additive manufacturing have become most preferred way for preoperative planning and surgical training in complex orthopedic cases such as total joint arthroplasty, reconstructive surgery, spine, hand, shoulder or any other orthopedic cases (Ju and Choi, 2010, Paiva et al., 2007, Tetsworth et al., 2017). Different imaging methods such as X-ray computed tomography (XCT) (Thompson et al., 2017), magnetic resonance imaging (MRI) and computed tomography (CT), have been used for medical imaging and obtaining 3D data for the development of patient specific devices. At present, AM methods are widely used for obtaining 3D physical template models of the medical parts for surgical guides and medical education (Huotilainen et al., 2014, Salmi et al., 2013, Hurson et al., 2007, Youssef, 2017). Moreover, rapid developments and researches are going on for obtaining custom based net shape implants ready for usage in patient body with different materials and different AM methods. Comparison of AM methods can be seen in Table 1.

Stereo Lithography

Stereo lithography, in the Vat polymerization category, is the oldest 3D printing method. It was developed and patented by Charles Hull in 1986. It converts liquid photosensitive resin into a solid part by exposing it selectively to an ultraviolet (UV) light or an ultraviolet laser by 3D printing machine called stereolithograph apparatus (SLA) (Bandyopadhyay and Bose, 2016; Bandyopadhyay et al., 2015).The process uses photo sensitive polymeric resin called as photopolymer, but for producing metal or ceramic parts, suspensions that contain metal or ceramic particle in a photo curable monomer are used in the SLA process.Complex shaped parts for tissue engineering can be manufactured by this method but its usage is restricted just with photopolymers (Ronca et al., 2013).

In medical applications, the SLA system is generally used for manufacturing anatomical models for preliminary training, pre-surgical planning and medical education (Poukens et al., 2003). Besides, molds, patterns and prototypes can be prepared by SLA method for indirect manufacturing of medical devices (Park et al. 2014). More over the stereolithographic model can be used for evaluating ideal dimensions of components such as screws, plates and some other orthopedic implants. It also makes possible to visualize tumors and its relationship with surrounding tissues by representative models. It serves surgeons to clarify the complexity of the case, simplify making decisions about treatment and making preliminary planning to reduce risks of unexpected situations during the surgery (Paiva et al., 2007).

Micro-stereolithography system (MSTL, μSL or MSL) has been derived for manufacturing highly intricate inner surfaces for tissue engineering applications with biodegradable or biocompatible materials. The system has been developed for complex three-dimensional micro structures and geometries with high aspect ratio. It offers high resolutions from sub microns to a few tens of microns while the resolutions of stereolithography are generally greater than 50 μm. With development of micro-stereolithograpy systems, different commercial materials and laboratory-based synthesized resins have been used for different applications (Srivatsan and Sudarshan, 2016).

The SLA system presents advantages about ability of manufacturing complex shapes that have internal surfaces and holes. However, exiguity of biocompatible resins, cytotoxic radicals with long processing time, residual photo initiator are the main restrictions about the biomedical applications of the system. Poor mechanical properties of the photo-polymerized resin are also a disadvantage for hard tissue engineering applications. Beside these, necessity of incorporation support structures for overhangs and cantilevers of the manufactured part and removal of these supports after manufacturing creates extra processing steps and make the SLA method as time consuming(Chia and Wu, 2015).

Table 1. *Comparison of AM Methods in terms of Material, Feedstock and Energy Source*

AM Method	Material	Feedstock	Heat Source	Application
Stereo lithography	Photo polymers	Resin	UV laser	Molds, patterns, prototypes
Fused deposition modeling	Thermoplastic polymer	Filament	Heating chamber	Antibiotic delivery systems, porous structures, scaffolds
Selective laser sintering	Metal, polymer, ceramic materials	Powder	Laser	Craniofacial and joint implants, scaffolds for tissue engineering
Selective laser melting	Metal materials	Powder	Fibre laser source	Cervical, vertebral body replacement, porous dental implants
Electron beam melting	Metal materials	Powder	Electron beam	Knee and hip implants, press fit

Source: Gibson et al., 2015; Probst et al., 2010;Korpela et al., 2013; Wu et al., 2013;Tunchel et al., 2016.

Fused Deposition Modeling (FDM)

Fused Deposition Modeling (FDM) is another AM method used in biomedical applications. It is the most common extrusion based method and developed by Stratasys, USA (Gibson et al., 2015). The system uses a heating chamber to bring thermoplastic polymer into semi-liquid form that is fed through heated extrusion head with a small orifice in filament form. The system contains two nozzles; one of them deposits main material in to the substrate while the other feeds the support cantilevers. The deposited layers are fused together and built up 3D shape of the designed part (Chia and Wu, 2015). Application of FDM is easy and can be used with a large variety of thermoplastic polymer such as structural and biopolymers, ceramic and metal polymer composites (Gebhardt and Hötter, 2016). The method gives opportunity to obtain porous structured part that mimics natural bone and serves osseointegration of the implant to bone tissue. For controlling, pore size and morphology of the scaffolds and implants manufactured by FDM method, raster angle, raster gap width and raster thickness are the controllable parameters (Chia and Wu, 2015).

Biocompatible polymers with low melting temperature are generally used in FDM process. In clinical applications polylactic acid (PLA), polycaprolactone (PCL), poly lactic-co-glicolic acid (PLGA), PLGA-three calcium phosphate (TCP), poly methyl methacrylate (PMMA), poly-ether–ether–ketone (PEEK), polyglycolic acid (PGA), polypropylene (PP) and polydioxanone (PDO) are most commonly used biopolymers. Antibiotic delivery systems, osseous craniofacial defects repairing, scaffolds for tissue engineering and bone tissue engineering are the general applications of FDM in biomedical field (Probst et al., 2010; Korpela et al., 2013; Yen et al., 2009; Teo et al., 2011; Shim et al., 2012; Kim et al., 2009;Ramot et al., 2016; Evans et al., 2015;Teo et al., 2016).

FDM isrestricted with thermoplastic polymer. The extruded molten polymer must be hot enough to fuse through previous layer. So viscosity of the polymer is very important material property that effects the extrusion of the material from the nozzle. Because of high processing temperature, FDM method is not suitable for build up living cells and temperature sensitive biological agents (Chia and Wu 2015). Moreover, build speed, material density and accuracy are limitations of the method and need to improvement (Gibson et al., 2015).

Selective Laser Sintering (SLS)

SLS, invented at the University of Texas and patented by Carl Deckard in 1989 (Brandt, 2017), is a kind of powder bed AM processes based on powder spreading and laser sintering to build up desired 3D shape of the product layer by layer (Gu, 2015). The basic elements of the system consists of a laser (such as; CO_2, Nd:YAG, fiber lasers, disc lasers, etc.) (Schleifenbaum et al., 2010; Kaiser and Albrecht, 2007) an automatic apparatus for powder layering, a computer system to control the process, inert gas protection system and powder bed preheating system (Gu 2015). In SLS processing, the material powder is deposited repetitively on to the build platform and these powder selectively sintered by laser beam according to the data taken from 3D CAD model of the part (Brandt, 2017).

In sintering step, the powder is heated above its glass transition temperature and molecular diffusion occurs between the neighboring powder particles. After building one layer (<100 µm), the build platform lowers and a new powder layer is feed across the top surface of the part. The new layer is bound to the previous layer and builds up 3D shape of the designed part. The excessive, unbounded powder is removed after the part is finished. Because these unbound powder particles serves as support to cantilever structures, there is no need of any temporary supports. The porosity between original powder particles can be preserved because there is no complete melting of the powder particles in sintering process (Chia and Wu 2015).

The particle size of the powder, heat transfer in the powder bed and the diameter of the focused laser beam determine the resolution of the system. A wide range of materials can be used in SLS process such as polymers, metals, ceramics (PCL, HA, PLLA, tricalcium phosphate, and poly(3-hydroxybutyrate)) and polymer coated ceramics (Chia and Wu, 2015). Craniofacial and joint implants were manufactured by SLS method with water soluble polyvinyl alcohol (PVA) polymer coated hydroxyapatite (HA) particles (Chua et al., 2004). Moreover, polymer coated calcium phosphate bone implants (Tan et al., 2005) and porous polycaprolactone (PCL) scaffolds for tissue engineering, with desired mechanical properties were manufactured by SLS AM method (Williams et al., 2005; Lohfeld et al., 2010; Yeong et al., 2010).

Selective Laser Melting (SLM)

Metals such as pure titanium or its alloys; Ti-6Al-4V, NiTi and Co-Cr-Mo alloys are most widely used in orthopedic prosthesis. Powder bed fusion AM processes such as selective laser melting (SLM) and electron beam melting (EBM) methods are commonly used for manufacturing load bearing metal implants (Zadpoor and Malda, 2017).

Selective laser melting (SLM) is one of the additive manufacturing method, that works with powder bed fusion principle. In this method the product is manufactured by melting and fusing the material in powder form (Kruth et al., 2005). Fibre laser energy source is used for melting selective region of the powder layers. The fusion region is pre-defined in CAD model of the work piece. When melting of one layer completed, the powder bed is lowered by a predetermined distance, which specify the layer thickness. Then a new layer of powder is deposited on top and the process is repeated until the object is completed. The entire process is carried out in an inert gas atmosphere to ensure high purity (Taniguchi et al., 2016; Sing et al., 2015).

Biomedical implants surfaces, especially used in orthopedic applications, need bioactive, porous surface coatings such as hydroxyapatite or bioactive class for increasing osseointegration between bone-implant interfaces. For this reason different coating techniques are used after manufacturing the implant.

Although bioactivity of implants are increased by surface coating, hydroxyapatite particles that break away from the implant surface may go through the bearing surfaces such as in total hip and knee joints. These particles acts as third body wear particles and fasten the implant wear mechanism.

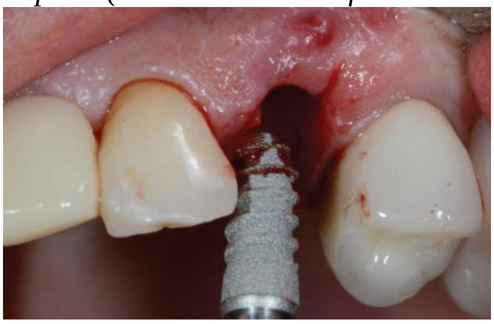
SLM process is able to manufacture complicated three-dimensional dense or porous structures. Moreover, it is possible to create porous surface coatings on additively manufactured titanium implant surfaces. In literature studies complex shaped implants that mimics the porous structure of human cancellous bone were manufactured by AM method from metal powder for joint artroplasty (Pattanayak et al., 2011).

Pattanayak et al. (2011) studied about the investigation of optimal SLM processing parameters such as scanning speed, hatching pattern and laser power for obtaining titanium product that can be used as orthopedic implant. They heat treated to the titanium samples under argon atmosphere and subjected them to NaOH and HCl for providing bioactivity. They reported that bone-like apatite formed on the treated surface of the samples in simulated body fluid within 3 days (Pattanayak et al., 2011).

Wu et al. made an in vivo study about cervical vertebral body replacement. They implanted an AM manufactured porous metal implant into anterior cervical defects in sheep and compared it with poly-ether-ether-ketone cage. They reported that porous metal showed higher mechanical bone -implant stability and that stability was enhanced by bone ingrowths (Wu et al., 2013).

In another paper, Tunchel et al. conducted 3-year follow-up prospective clinical study about titanium dental implants, which are manufactured by SLM method. They evaluated the survival and success rates of AM manufactured titanium dental implants and they followed up eighty-two patients during the study. They reported that the followed titanium implants showed 94.5% of survival rate and 94.3% of implant-crown success rate. By considering these results, the authors concluded that the additively manufactured titanium dental implants represent successful clinical results and they offered that further long term clinical studies were necessary for approving their results (Tunchel et al., 2016). An example of the clinical application of additively manufactured titanium implant can be seen in Figure 1.

Figure 1.*Placement of the Additively Manufactured Porous Titanium Dental Implant (with Permission of Tunchel S.)*

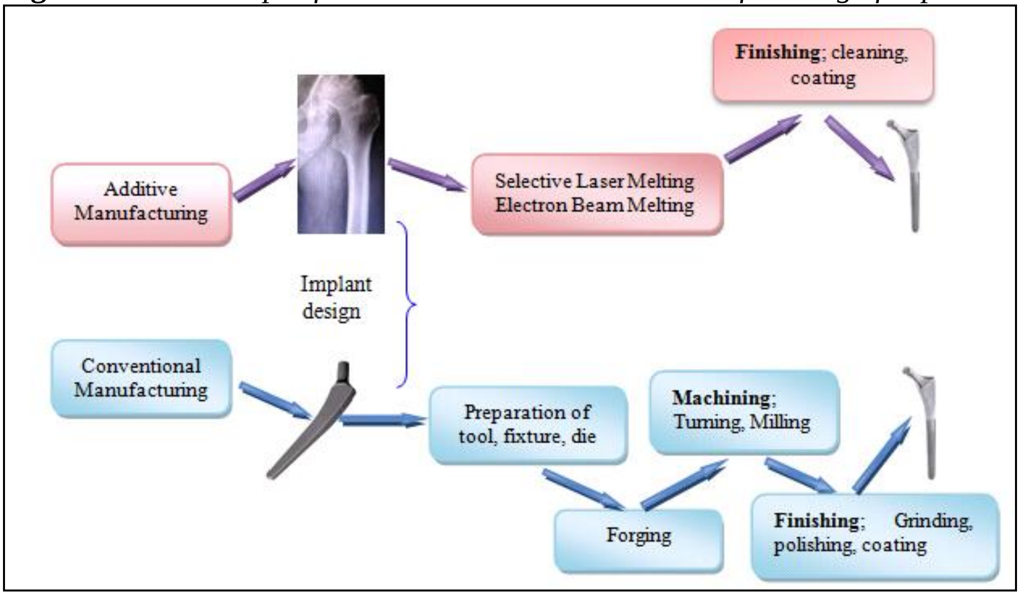


*Source:*Tunchel et al., 2016.

Electron Beam Melting (EBM)

Electron beam melting (EBM) is another powder bed fusion AM method that uses high-energy electron beam to melt and fuse the metal powder. A focused electron beam scans the top layer of the powder and melts the powder particles (Gebhardt, 2011). The process resembles SLM process but there are some distinct differences between SLM and EBM. EBM is applied under vacuum atmosphere while SLM is under inert gas atmosphere. Moreover SLM uses laser, EBM uses electron beam. EBM uses conductive materials and it is faster than SLM method. It is thought that EBM would revolutionize the metal implant manufacturing sector (Sing et al., 2015). EBM method makes possible to manufacture complex shaped, monolithic, custom-based implants. With conventional manufacturing methods, the prosthesis is produced in standard dimensions and specifications. But with AM methods it is possible to produce implants in special dimensions according to the patient's own specifications determined by using MRI or CT data(Thompson, 2017).Besides, EBM gives opportunity for manufacturing porous hip and knee implants that serve bone cell ingrowths and optimal stress shielding (Murr et al., 2012). For manufacturing hip implant parts such as press fit and cemented implants, EBM technology is a cost efficient manufacturing method especially in mass production. EBM method provides opportunity to obtain solid or porous parts of the implant in same manufacturing process step. It eliminates expensive secondary processes such as bioactive porous coating and makes possible to optimize pore geometry, pore size, relative density and roughness for improving primary fit and osssointegration of bone implant interface (Arcam AB, 2017). A comparison of conventional and additive manufacturing of an orthopedic implant can be seen Figure 2.

Figure 2.*Process Steps of Additive and Conventional Manufacturing of Hip Stem*



Source: Dutta and Froes, 2016;Bandyopadhyay and Bose, 2016;Bandyopadhyay et al., 2015.

Response of each material to the AM processes may be different so experimental studies must be done for each material type to optimize process parameters and to define product properties. For these reasons, Liu et al. studied about EBM method to find if it is suitable for clinical implant applications of Ti-6Al-4V. They reported that there were significant differences in bending strength, bending stiffness and hardness of the EBM manufactured samples, than control samples which were manufactured by conventional methods and EBM is a promising AM method for titanium implant manufacturing (Liu et al., 2014).

Advantages and Limitations of Additive Manufacturing

Conventional manufacturing of orthopedic implants contains difficult and expensive steps such as casting, forging, machining, surface finishing and coating operations. Each of these steps requires expensive machines, tools, dies and fixtures. Therefore, it is very difficult to manufacture patient-specific implant because of the high costs. The production type in conventional methods must be batch or mass production. AM technology provides possibility for manufacturing custom based implants without any fixtures, dies and tools but just with CAD data of the implant and 3D printing machine (Bandyopadhyay et al., 2015; Tetsworth et al., 2017). Elimination of the expensive tools from manufacturing process decreases costs and enable to job production.

AM technology provides opportunity to use different material combinations and functionally graded structures for obtaining excellent material properties. AM methods incorporated in modern manufacturing systems and they are concerned as being the most suitable technology for cyber-physical production systems. Moreover AM processes are environment friendly, reduces wastage of material and save energy (Sing et al., 2015; Rüßmann et al., 2015; Lasi et al., 2014).

However, there are some challenges waiting for to be solved about implant manufacturing. The variety of materials and strength of final products are insufficient. Biomaterials and biocompatible nano additives must be developed for any 3D printers. The used file formats such as STL and AMF (additive manufacturing file format-suggested by ASTM) of AM methods do not contain product manufacturing information (Sagbas and Bulutsuz, 2017). This restricts the obtaining desired dimensional accuracy and reproducibility. Also for achieving desired surface quality, post-processing activities are needed (Gibson et al., 2015; Bandyopadhyay and Bose, 2016).

For future development of the AM technology usage in orthopedic implant manufacturing, researches are focused on producing complex final net shaped implants that mimics human anatomy and ready to be placed directly in patient body. Investigating new materials such as polymer, metal, ceramic and composite structures of these materials group are one of the most developing areas of AM technology. Software also being improved for converting patient imaging data more accurately to the AM system and producing orthopedic, dental and other biomedical implants in desired dimensional and surface quality with resolutions below 10 microns for a part greater than 1 cm in size. Moreover, manufacturing of porous structures from biocompatible artificial materials, living cells, genes and proteins are the main future trends of AM technology in biomedical application area (Petrovic et al., 2012;Hollister and Bergman, 2004).

Conclusions

Additive manufacturing technology is promising novel area that will change implant manufacturing industry. It is well known that AM technology has not been an alternative manufacturing method for fabrication of final products but it continuously improves and will take place of many conventional manufacturing methods in near future. It provides opportunity for manufacturing prosthesis by using 3D imaging data of the diseased bone, without fixtures, tool and dies. Research is continuing to overcome limitations such as lack of different material types, standardizations, dimensional accuracy, resolution, etc. of AM technology. Moreover, medical manufacturing companies make high investments to AM machines and they plan to manufacture all the medical implants by AM methods.

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