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Biomedical applications of additive manufacturing: Present and future

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Abstract

Three dimensional printing (3DP) or additive manufacturing (AM) of medical devices and scaffolds for tissue engineering, regenerative medicine, ex-vivo tissues and drug delivery is of intense interest in recent years. A few medical devices namely, ZipDose®, Pharmacoprinting, powder bed fusion, HPAM™, bio-printer and inkjet printer received FDA clearance while several biomedical applications are being developed. This paper reviews influence of type of AM method and process parameters on the surface topography, geometrical features, mechanical properties, biocompatibility, in vitro, and in vivo performance of diverse orthopedic applications. Attempts have been made to identify gaps, suggest ideas for future developments, and to emphasis the need of standardization.

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Keywords

Additive manufacturing, Biomaterials, Characteristics, Orthopedic implants, Standards.

1. Introduction

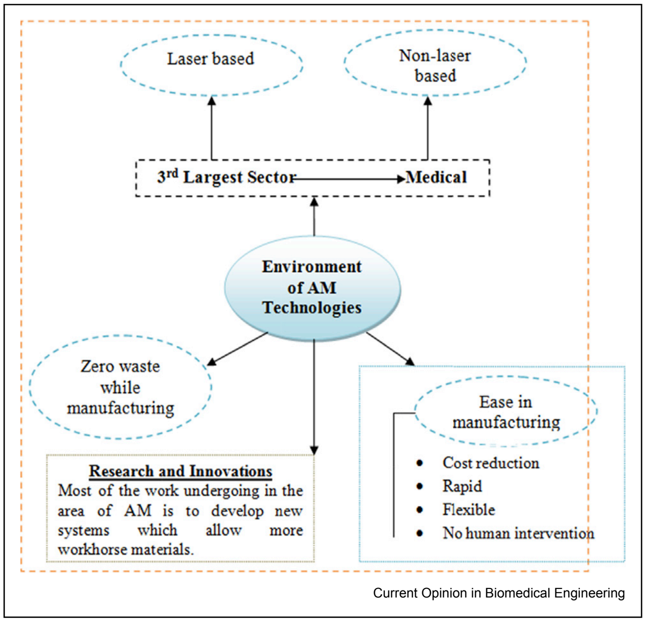
ASTM-F42 Committee defined the additive manufacturing (AM) as *a process of joining materials to make objects from 3D model data, usually layer on layer*, opposite to conventional manufacturing technologies [1]. These technologies utilize an unconstrained environment, as highlighted in Figure 1.

AM researchers are developing a wide range of biocompatible feedstock material and processing systems for medical devices, like hip, knee or articular cartilage joints. The various biomaterials and their applications in biomedical engineering (refer Table 1). Table 2 summarized some of such applications.

The working principle, except the processing of feedstock, is same and the process (specifically in the task of implant development) starts from collection of the work starts with capturing the internal medical data of a patient through are the Computed Tomography (CT) and the Magnetic Resonance Imaging (MRI) technologies [7]. Then the collected images are converted into computer aided design (CAD) model via Digital Imaging and Communications in Medicine (DICOM) directory. The finalized CAD model should be simulated through MIMICS or 3D doctor software for visualizing the fitment [8]. A standardized procedure is available for generating the required *Standard Triangulation Language* (STL) format of implants [9]. After this, as per the requirements of the implant in-terms of desirable quality characteristics the input variables such as slice/layer thickness, printing speed, printing temperature, orientation, raster angle, air gap, contours, environmental temperature/conditions, type of input current, types of laser and its parameters, workhorse material, environmental factors, etc., can be selected on the basis of literature survey or personal experience. Figure 2 shows the schematic of converting human specific data into physical part via AM. The process starts from CT scan data and eventually completes after preliminary surgical verifications.

Issues such as: poor surface characteristics, poor dimensional accuracy, low strength, bio-compatibility, microstructure issues, corrosion of the implants, etc., need the research attentions. It is inevitable that some of the factors critical to the implementation of AM technologies are also important to the adoption of other manufacturing technologies [10]. Particularly, it is of big interest to study the effect of processing parameters on biocompatibility/cell culture analysis as the finally produced structure is liable to alter its properties as the processing conditions change, due to the variation in the material, geometry and integrity of the layers while fabrication task. No matter if the variations analyzed will be limited, but the improvements accomplished would always be supposed to have significations. Moreover, the standard test standards, often come into play while the test and analysis, may not be able to give realistic information because of its differentiation, from the customized orthopedic or tissue, in-terms of geometrical features. Hence, it is highly important to test and

Figure 1



Environment of AM *(Courtesy: ref.* [1–6]*)*.

simulate the laboratory results on the same part which is going to serve. Ducom Instrumentation has already developed apparatus for tribological testing of as-real geometry of the implants. In this review article, the influence of various process parameters on characteristics of orthopedic implant has been reviewed in Section 2, and the information provided will help for the development of required standards as discussed in Section 3.

Table 1

FDA cleared 3D printed biomedical applications.

Material	Application
CP-Ti	Screw and abutment
Ti-6A1-4V	Artificial valve, Stent, Bone fixation
Ti-6Al-7Nb	Crowns, Knee joint, Hip joint
Ti-5Al-2.5Fe	Spinal implant
Ti-15 Zr-4Nb-2Ta-0.2Pd	Crown, Bridges, Dentures, Implants
Ti-29Nb-13Ta-4.6Zr	Crown, Bridges, Dentures, Implants
83%–87%Ti-13%–17%Zr (Roxolid)	Crown, Bridges, Dentures
316L	Knee joint, Hip joint, Surgical tools, Screw
Co-Cr-Mo, Co-Ni-Cr-Mo	Artificial valve, Plates, Bolts, Crowns, Knee joint, Hip joint
NiTi	Catheters, stents
PMMA, PE, PEEK	Dental bridges, articular cartilage, Hip joint femoral surface, Knee Joint bearing surface, Scaffolds
$SiO_2/CaO/Na_2O/P_2O_5$	Bones, Dental implants, orthopedic implants
Zirconia	Porous implants, Dental implants
Al_2O_3	Dental implants
$Ca_5(PO_4)_3(OH)$	Implant coating material

Information gathered by online search.

2. AM based biomedical implants: examples of manufacturing strategies for orthopedics

In this section, we have reviewed the various characteristics of AM based orthopedic implants to highlight the importance of from process parametric study for obtaining better service life, safety, workability and convenience of patient after implantation. All the upcoming characteristics are important to get qualified during pre-surgical verifications after the fabrication of the implant, as highlighted in Figure 2.

2.1. Surface characterization

Implant surface characteristics plays an important role in the osteointegration like: macroscopic, microscopic and nano-metric characteristics [12]. It has been found that the reaction of osteogenic cells to different surfaces was increased on rough surfaces [13], and as compared to smooth surfaces the textured implants surfaces exhibit more surface area for integrating [14] as observed in in-vivo investigations [15]. However, fine surface finish has also been reported as better in case of hip joint applications [16], as fine contact between artificial implant and natural bone structure will help in smooth motion. However in actual, it is not yet standardized that how much rough or fine surface is required for different implants. The authors are believed that for non functional implants, one should prefer textured surfaces and such surfaces are easy to obtain with AM technologies due to the presence of staircase effect [17]. But when the implant is functional such that it has relative motion, then the mating surface should be as fine as possible as roughness could have effect on increased wear [18]. Some of the researchers have used chemical etching [19], mechanically [20] or combinations [21] for improving the surface finish of the titanium implants, however their effects on the chemical composition of the implant material, geometrical scale (to nano level) and other mechanical properties are required to study. Table 3 gives a detail of processing parameter(s) of AM process for surface roughness of produced implants.

2.2. Geometrical characterization

- Dimensional

Developments of exact shape, size and minute geometrical textures on artificial biomedical implants are essentially important for their proper functionality [39,40]. However, it is difficult to produce on an appropriate material and earlier was done by hand crafting from the surgeon [41]. Conventional CNC