

# BIOMEDICAL ENGINEERING AND ADDITIVE MANUFACTURING

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**Abstract:** Additive manufacturing (AM) technologies have evolved significantly in recent decades, bringing new trends to production processes. The advantages compared to conventional technologies are numerous: production is simpler and faster, geometry can be adjusted more easily, the quality of finished parts is better, less material is wasted, and costs are lower. Because of the wide range of possibilities, the different AM processes and the materials that can be used, these technologies have found their place in many industries, not least in biomedical applications. Flexibility in geometric freedom, in particular, is important for the fabrication of biomedical devices. It is already known that AM technologies can improve and facilitate diagnostics through the fabrication of customized and in-demand parts, support consultation between physicians and patients, and thus provide the opportunity to develop individualized, patient-specific medicine. This review briefly outlines current applications and AM techniques present in the biomedical field.

**Keywords:** additive manufacturing, biomedical engineering, applications.

## 1. INTRODUCTION

Past decades were significant for the fast development of additive manufacturing (AM) technologies, revolutionary influencing new production trends [1]. These technologies are known also by other names, i.e., rapid prototyping, layered manufacturing, solid free-form, 3D printing. For years they were used in the industries primarily for prototypes production. The main advantage of AM technologies compared to standard ones is that parts can be produced easier, faster, with more precision and freedom in design, with customizable geometry and higher quality, easier maintenance and logistics, and all this at lower costs [2,3].

Principle of AM production is binding materials, usually layer upon layer, with a goal to make 3D objects from 3D model data, which is contrary to the standard manufacturing methods [4]. Possibilities of part production are vast, due to different materials which can be printed, from metals [5], ceramics [6],

to polymers [7], to even biological matters [8]. Because of that, the application in different industries is very diverse, and that's how AM found its way into automotive and aerospace industry [9], architecture [10], printed electronics [11], daily life products [12], biomedicine [13], science and education [14,15]. In past two decades, AM technologies found their application in medical and dentistry area, by manufacturing different implants, scaffolds, devices, etc.

Role of AM and 3D printing in the field of biomedical applications and sciences became essential, because it improve and facilitate diagnostics, help consultations between doctors and patients, and provides insight for surgeries and surgery planning [16]. Conclusion can be drawn that utilization of AM in medicine can lead to individualized patient-specific medicine [17].

3D printers are used nowadays for manufacturing the anatomical models, prosthesis and orthoses, implants, dental products, surgical guides and instruments [13,18]. Also, possibility to 3D print a

human tissue with advanced biomaterials and specific polymerization process became remarkable achievement, as well as the possibility to use the microfluidic approach for cell 3D printing. On the other hand, there are still many issues that should be considered and require special attention when it comes to contact with living organism, such as poor dimensional accuracy and surface properties, low strength, biocompatibility of tissues, and possible corrosion of implants [19]. For this reason, researchers and scientists are working rapidly to develop a wide range of biomaterials with specific properties and to widen the knowledge of other possibilities and details that can be improved in the application of AM technologies in various biomedical fields. Research that Zarrabeitia-Bilbao et al. conducted have shown that the most frequent study areas with biomedical engineering applications of AM technologies are: materials science and biomaterials, nanoscience and nanotechnology, cell tissue engineering, biophysics and radiology, nuclear medicine and medical imaging, polymer science in transplantation biotechnology, applied microbiology, cell biology [20].

Medical applications of AM technologies and 3D printing have expanded significantly in recent years, primarily due to shorter production times for customized products. Especially in medicine, the ability to take a specific and customized approach for each patient is of great importance. 3D printing methods differ in production methods, different materials, and their properties, which must be taken into account when choosing the most appropriate approach [21]. This paper aims to provide a brief overview of trends and research in biomedical applications of AM technologies.

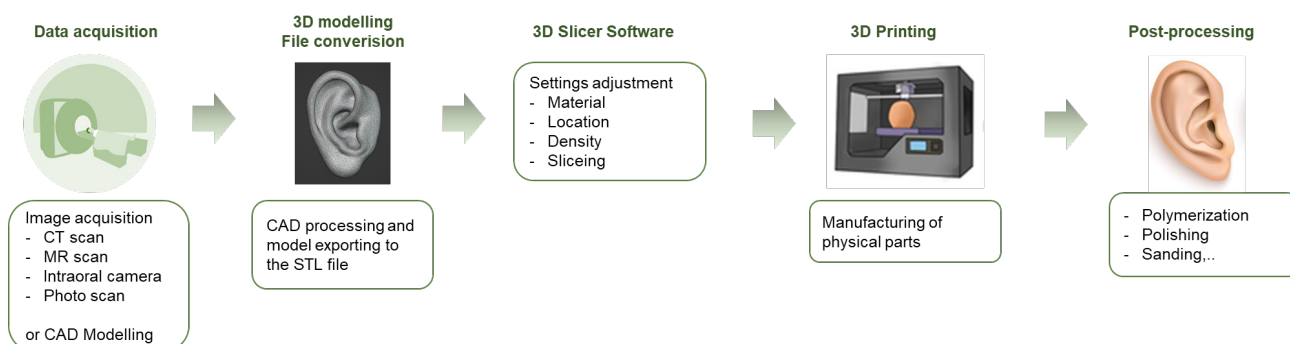
Depending on the selection of raw materials used, AM technologies can be divided into vat polymerization, solid material and powder material processes. However, the different material states lead to challenges in terms of residual stresses, surface properties, partial melting, voids, and micropores, which further complicates the achievement of good structural properties [22].

### 2.1. Vat photopolymerization

The process of photopolymerization is frequently used in AM technology in various processes to achieve high dimensional quality. This process is based on the principle of light-induced radical polymerization, in which liquid photopolymer resin solidifies in a chemical-physical reaction under the light of an appropriate wavelength [14]. There are several categories of vat photopolymerization processes based on the light source and polymerization mechanism, including stereolithography (SLA), digital light processing (DLP), continuous liquid interface (CLIP), and two-photon polymerization (2PP) [24]. Compared to other additive technologies, photopolymerization processes have higher accuracy of manufactured objects, which is certainly an advantage [25].

SLA and DLP offer higher resolution of printed parts on the order of ten micrometers in the XY direction. In SLA, a UV laser is used for selective photocrosslinking of thermoset polymer resins, while in DLP UV, a projector with a series of micromirrors or a digital light projection screen are used for the same purpose to crosslink the entire layer in one pass [26,27].

In addition, SLA and DLP offer the possibility to shorten the printing time by building up the ob-



**Figure 1.** Workflow of AM manufacturing process in biomedical engineering applications.

ject with a 100% infill density with a single exposure [28]. DLP is not a satisfactory solution when high transparency is required, as even commercial resins that are claimed to be transparent end up being difficult to see microscopically [29].

SLA is used in biomedical applications for the fabrication of patient-specific prostheses, dosage forms, drug-eluting devices, study models, surgical stents, plaster models, orthodontic devices (aligners and retainers), etc. [30-32]. DLP can be used for the production of medical devices and personalized medicines, as well as orthodontic plaster models [33].

## 2.2. Material extrusion

Thermoplastic filament material is wrapped around a spool, fed to the extruder where the material is heated and extruded layer by layer from a nozzle onto a build platform to create a 3D object [35]. One of the most important tasks in FDM 3D printing is to specify the properties of the filament so that it is printable [36]. Pharmaceutical applications use filaments that have drugs added to them, and the temperature of the filament melt must be kept low to avoid drug degradation. To produce the filament with incorporated drugs, the drug is melted and homogenized in the extruder together with the polymer and the appropriate additives, and then extruded through a die onto the build platform that forms the filament [37]. In addition to the mechanical properties of the filament, the rheological properties are also important, as they influence the melt index and the properties after extrusion (curing, cooling of the layers).

The application of the FDM process showed good results and high dimensional accuracy in printing medical models, drug delivery forms and devices, catheters, and wound dressings [38,39]. However, the limited availability of biodegradable thermoplastic filament materials, lower resolution of finished parts, and inability to use thermolabile drugs hinder wider application of this AM process [32].

## 2.3. Jet printing

3D inkjet printing, i.e., binder jetting and material jetting AM technologies use 3D printing mechanisms that behave similarly to paper jet printing. These are mainly powder-based processes in which layers of solid particles are bonded together with the

addition of a liquid printing material to produce a 3D model. In binder jetting, a liquid binder solution is sprayed onto the powder particles based on the CAD model, then the solution evaporates and binds the powder particles. Different types of powder materials can be used, including polymer, ceramic, glass, or metal powders [40].

On the other hand, in material jetting, thermoplastic or thermoset light-curing polymers are applied to the build platform in the form of molten droplets, followed by curing of the individual layers [41]. This process is mainly used for the creation of multicolor 3D surgical models [42]. Inkjet-based bioprinting of skin cells and nanoparticles in tissue engineering is under development and is also used in *in vivo* printing [43,44].

Inkjet systems have their advantages in the production of highly porous materials and can be used for the production of orally dispersible tablets [32]. In dentistry, the material jetting process is used for the production of study models, drilling and cutting templates, facial prostheses, and craniomaxillofacial implants [45].

## 2.4. Powder Bed Fusion

Selective laser sintering (SLS) is an AM process in which powdered materials are locally sintered and solidified layer by layer, with the laser beam controlled by a computer [13,46]. This process is used for the fabrication of complex shapes. The materials used for this technology are powdered ceramics, polymers, aluminum, and metals.

In selective laser melting (SLM), a laser is used to heat and completely melt the successive layers of the metal powder, unlike the sintered SLS powders [47]. Part of the powder is solidified, the unmelted part supports the structure, and after the process is completed, the remaining part of the powder is removed [46].

As for biomedical applications, SLS is used in the fabrication of medical implants, surgical instruments, study models, metal crowns, cutting and drilling templates [48-50]. Although the SLM process is a widely used metal AM process, there is still a lack of research on copper alloys and their antibacterial and antiviral behavior in the medical field. Also, the optimization of the pressure parameters is not yet at a satisfactory level [51].

### 3. BIOMEDICAL APPLICATIONS

Additive manufacturing have numerous applications throughout the field of biomedical engineering. Some of the areas where AM technologies are having high impact are:

- surgical planning and surgical tools,
- medical devices, orthopedics and prosthetics,
- pharmaceutical applications,
- dentistry,
- tissue engineering..

#### 3.1. Surgical planning and surgical tools

Challenging situations that may arise during surgical procedures are often unexpected and difficult to resolve. The use of simple models to simulate human anatomy and pathology has been known for centuries, usually in the form of clay and stone [52]. These organ models are an important part of modern medicine in various diagnostic and therapeutic approaches that represent the replication of a specific part of the patient's anatomy [25]. 3D printing with its result in the form of a printed organ model is an important way to obtain information about a specific organ of the patient during preoperative planning. The development of medical image acquisition and processing allowed a more detailed insight into the pathology of the patient's organs in a noninvasive way [53]. Medical imaging, i.e., MRI and CT scans, are known to be used for better visualization and surgical planning. The data obtained from these scans serve as 3D models of patient-specific pathology and enable further production of printed complex anatomies, especially in craniomaxillofacial, neurosurgery, and cardiac surgery [54]. This will allow surgeons to plan operations effectively and accurately, minimizing the risk of complications. AM technology also provides important guidance and tracking during surgery by providing a good overview of internal organs [46]. Printing difficult anatomical structures for training and surgical simulations is another important part of using AM techniques [23].

#### 3.2. Medical devices, orthopedics and prosthetics

Prostheses and implants must be compatible with the anatomy and needs of each individual patient, leading to problems with traditional manu-

facturing methods [13]. High-quality imaging techniques combined with AM technology have made it possible to create custom prostheses for people with disabilities of all types [55]. The fact that the design and fabrication of an orthopedic or prosthetic device begins with scanning the desired patient part provides engineers and researchers the opportunity to change the tuning in the design and fabrication of parts to fit the needs of the patient [22].

Veterinary orthopedics is also supported by AM technologies and is rapidly evolving. Bone models, animal-tailored implants, and surgical guides are commonly 3D printed, and further advances in this part of medicine are expected to create bone models, complex patient-specific implants, and surgical guides [56].

In addition to orthopedic and prosthetic devices, there are a variety of medical devices that are 3D printed, including eyeglass frames and contact lenses, hearing aids, and even assistive devices for people with disabilities [57-59].

#### 3.3. Pharmaceutical applications

Pharmaceutical applications of AM technologies are diverse and are changing the landscape of previously standardized pharmaceutical approaches [60]. Nowadays, it is possible to 3D print drugs in single doses as well as in multiple delayed and immediate release layers, allowing for different dosing profiles. This enables personalized treatments, while continuing the development of anatomy-specific complex drug delivery devices [61]. Among the biomimetic constructs produced for drug screening, 3D-printed drug release implants, ingestible tablets, and transdermal delivery systems are also being developed and used [32,57,62,63].

#### 3.4. Dentistry

The customization capabilities offered by AM technologies are an important factor in 3D printing applications in dentistry. Intraoral cameras and advanced 3D scanning capabilities enable the reconstruction of dental cavities and the printing of patient-specific dental implants and prostheses [64]. Visualization of treatment results is also possible, which facilitates the process. In dentistry, there are several areas where AM procedures are used, including orthodontics (oral and maxillofacial surgery),

orthodontics, prosthodontics and implantology, endodontics, and periodontics [65].

### 3.5. Tissue engineering

Tissue engineering as such is an interdisciplinary field in which life sciences, clinical medicine, biology, and engineering are intertwined [54]. The introduction of 3D printing in this field of research has enjoyed great popularity as it enables the production of artificial tissues or organs with controlled and mimicked biological characteristics of the original parts. The technology of 3D inkjet printing proved to be the most promising for using a wide range of bioinks to produce biomaterials, scaffolds with different properties, and different cell types [23]. The development of bone regeneration models using bone grafts is another popular area. Bone grafts are used to fill bone defects, but unfortunately the integration of the bone is not always successful due to the lack of uniform blood flow within the graft [57]. The future of tissue printing, or in other words bioprinting, is moving towards the creation of complete organs by enhancing them according to their specific impaired functions.

### 4. CONCLUSIONS

The revolutionary approach of AM technologies is based on their impact on production processes, capabilities and functioning, and in this way the impact on industry, society and people is significant. In biomedical engineering, AM technologies are developing rapidly and are already changing the medical product landscape. The customization of products, medical devices, dental devices, and drug delivery systems makes these technologies very attractive as they reduce time and cost while improving the success of the medical approach. The influence and importance of AM technologies in the biomedical field will increase in the future, even though they are well on their way.

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## БИОМЕДИЦИНСКО ИНЖЕЊЕРСТВО И АДТИВНЕ ТЕХНОЛОГИЈЕ

**Сажетак:** Технологије адитивне производње (АМ) значајно су еволуирале последњих деценија, доносећи нове трендове у производне процесе. Предности у поређењу са конвенционалним технологијама су бројне: производња је једноставнија и бржа, геометрија се лакше подешава, квалитет готових делова је бољи, мање се расипа материјал, а трошкови су нижи. Због широког спектра могућности, различитих АМ процеса и материјала који се могу користити, ове технологије су нашле своје место у многим индустријама, али значајно место имају и у биомедицинском пољу. Флексибилност и слобода у геометријском моделирању, посебно је важна за производњу биомедицинских уређаја. АМ технологије су доказале да је дијагностика олакшана и унапређена кроз израду прилагођених захтеваних делова, консултације између лекара и пацијената су олакшане, а тиме се пружа могућност развоја индивидуализованог, специфичног медицинског приступа сваком пацијенту понаособ. Овај преглед укратко описује тренутне примене и АМ процесе у области биомедицине.

**Кључне речи:** адитивне технологије, биомедицинско инжењерство, примена, области.

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