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Applications of 3 Dimensional (3D) Printing in Biomedical Field

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ABSTRACT

Introduction: Three Dimensional (3D) printing was a daydream for various researchers and scientists. But now in today's era, this dream comes into reality. 3D printing is a rapidly growing technique in this era.

Objective: The objective of this review was to describe advanced applications of 3D printing in the biomedical field.

Methods: The methodology involves the critical review of the topic through different authentic scientific sources such as ScienceDirect, Pubmed, Google Scholar, etc. with the help of appropriate keywords.

Results: 3D system provide opportunities to medical and pharmaceutical industries to design more specific and authentic drug delivery system, high productivity of surgical and implants, more précised and personalized health care system and it is also helpful to save the life of people due to any organ failure or damage in case of any accidents or diseases. 3D printing is used to generate models, devices, surgical tools, delivery system, implants, and prostheses.

Conclusion: 3D printing has great potential for future use in the biomedical field. In future, 3D printing will bring a revolution in the health care system.

Key Words: 3 D printing, Bioprinters, Health care system, Pharmaceuticals, Prostheses, Implants

INTRODUCTION

3D printing is a new technology that is adopted by the industry in the last few years. The use of 3D printing is always like a dream in the case of a medical and health care system. However, now this dream of medical and health care society came true. 3D printing is the technology in which three dimensional solid objects can be created from a digital model. 3D printing has opened the doors and areas of people associated with the medical and health care system. Now, the medical, health care and pharmaceutical companies can able to produce more rapid manufacturing of products. The quality of the product should be more specified and can be easily monitored. This technology is expanding rapidly and is expected to bring revolution in the field of medical, pharmaceutical, and health care system ¹. The benefits of this technology are that it leads to an easy fabrication of tissue and bones, rapid creation of models and implants, high productivity of pharmaceutical products, more specificity in drug design, and manufacturing. The challenges which are

associated with 3D printing is that since it is very innovative and new technology so handling of such technology requires experts and the next challenge is that its compliance with the regulatory body ^{2,3,4}.

HISTORY OF 3D PRINTING

3D printing was invented by Charles Hull. He gave the name of "stereolithography," in the early 1980s. He was a graduate in engineering physics. Later, Hull formed a company that developed the 3D printer which is known as "stereolithography apparatus." In 1988, 3D Systems as were first commercially available which is known as SLA-250 ⁵.

However, 3D printing becomes a platform for medical society in the early 1990s. The first time, 3D printing is used in the field of pharmaceuticals where inkjet printing is used for binding of powders into the form of granules. Then the process is validated again and again till the desires shape and the

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quality of product are obtained. This research first happened in the 90s at Massachusetts Institute Technology by Sachs et al. ⁶ After that in 1989, another patent on 3D printing was filed by Scott Crump ^{7,8}. The first 3D printing drug is approved by FDA (Food and Drug Administration) in 2016 by a US-based pharmaceutical company named Aprecia Pharmaceuticals. Inkjet printing was used to develop Spritam (levetiracetam) tablets for oral use ⁷. The process of 3D printing is shown in Figure 1.

Earlier, 3D printing is utilizing in the fields of aerospace, mechanical engineering, automobile, etc. But, in recent years, the FDA motivates the use of 3D printing in the field of biomedical, pharmaceutical, and health care systems.

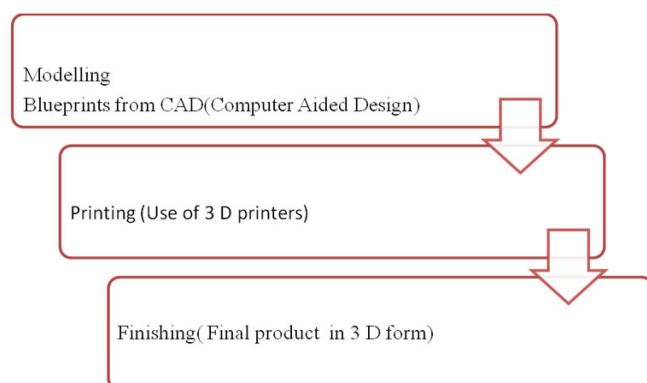


Figure 1: Process of 3D printing.

REGULATORY GUIDELINES

In the year 2017, US FDA released the guidelines on the technical aspects of using 3D printing in the biomedical field. The guidelines state that the validation of any steps and methods should be conducted to get a high level of assurance about the whole processes ⁸.

Documentation of each step should be done so that it can be as per the compliance of all processes. All the software used in the whole process should be checked, monitored, and validated regularly. Any deviation or change in any device, methods, and processes should be documented and validated. Any deviation in the system leads to revalidation again and again ^{9,10}.

The steps involved in 3D printing of any product are that the product is designed in a 3D dosage form. The design is converted to a machine-readable format which describes the 3D surface of the dosage form. The computer program divided these layers into different layers and then it is transfers layer by layer in machine ¹¹⁻¹³.

APPLICATIONS OF 3D PRINTING

3D printing finds application in the field of biomedical from 2000 onwards. For the first time, technology is used in the fabrication of dental implants. Recently, 3D printing is used in the fabrication of bones, skeletons, ears, jaws, blood ves-

sels, tissues, and organs as shown in Figure 2. The novel use of 3D printing involves tissue fabrication, implants, model fabrication, drug discovery, research, and designing of dosage forms¹⁴.

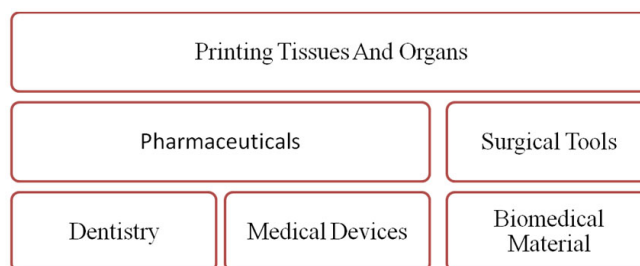


Figure 2: Applications of 3D Printing in various fields.

PRINTING TISSUES AND ORGANS

Tissue or organ failure is a major biomedical problem. The reasons for this problem include increased age, diseased states, road accidents, etc. Transplantation is not only expensive but there is also a deficiency of the organs to transplant. Further, it is very difficult to find the person who is ready to donate organs and secondly there would be the chances of tissue rejection. To avoid these problems associated with tissue and organ implants the technology of tissue engineering has been explored. Rather than using conventional tissue engineering, the 3D printing offers various advantages like appropriate cell placement, cell concentration and size control, control on speed. 3D printing can be used in organ printing ¹⁵. There are different 3D printing systems are used which includes laser-based, inkjet, extrusion-based but a part of all inkjet printing is used to produce organs and human tissues. Nowadays the researchers are using bio-printer to fabricate valves of the heart, joints, bones, spiral disk, and ear. Wang et al. produced artificial liver by depositing the different cells in hydrogels. For the fabrication of artificial liver, 3D bioprinting is used ¹⁶.

3D PRINTING IN PHARMACEUTICALS

The principle of 3D printing is also used in the case of drug delivery and dosage forms. The USFDA also promotes 3D printing in the development of dosage form and drug delivery. Spritam is first 3D printed pill which is produced a US-based pharmaceutical company Aprecia's by utilizing Zipdose Technology. The US-based pharmaceutical Aprecia uses Zipdose Technology for the formation of 3D printing of pill. The technology Zipdose is based on layering powder bed fusion method ^{17,18}.

Polypill: The concept of polypill is important for geriatric patients. As age is increasing the person may suffer from multiple diseases or disorders because with the increase in age the body functioning gets starts decreasing. So, there is a need for multiple drug therapy in such patients. Thus, a pa-

tient requires a dosage form with multiple numbers of Active pharmaceutical ingredients. On the very first time Khalid et al. use five different active pharmaceutical ingredients to form a 3 dosage form. The five different API's used in the study was pravastatin, atenolol, and ramipril, aspirin, and hydrochlorothiazide. The 3D extrusion printing was utilized in the manufacturing of polypill¹⁹.

TRANSDERMAL DELIVERY

Transdermal delivery is one of the important routes of drug delivery. This is because it offers advantages like it is a non-invasive route, it bypasses the first-pass metabolism and it is more convenient than other routes of drug administration^{20,21}.

Microneedles and transdermal patches are widely used to deliver the drugs by the transdermal route. Patches are used in transdermal drug delivery as it provides a continuous release of drug to the skin. Microneedles consist of a patch having needles like projections which are capable of penetration of drugs into the skin. In preparation of microneedles, inkjet printing is used for coating of the microneedles so that these microneedles release the drug in a controlled or sustain manner²².

DRUG-RELEASING IMPLANTS

Implants have the important and significant role in the drug delivery systems. The drug release implants are the implants that contain the biocompatible polymers in the implants and can control the release of drugs. The potential of 3D printed scaffolds for continuous drug delivery can be easily determined by conducting *in-vitro* studies. When the *in-vitro* studies conducted in 3D printed Scaffolds it shows equal effectiveness of drug release as the simple use of drugs. Thus, the 3D scaffolds can be used in the future for local drug delivery^{23,24}.

SURGICAL TOOLS

Computer-Aided Design is an effective tool in the present scenario for meeting the needs and demands of the operation theatre. The 3D printed tools can be effectively used for cuts and sutures. The 3D printed tools have advantages in terms of emergencies and it is more beneficial in developing countries because of its cost-effectiveness²⁵.

IMPLANTS AND PROSTHESES

3D printing is used in the fabrication of implants and artificial body parts such as limb, heart, breast implant. 3D implants are used in designing and fabrication of limbs, implants of dental, spiral and hip. The use of 3D printing in the field of Orthopedics opens the new door for the professionals working in this area. With the help of 3D printing, the implants and prostheses can be fabricated in time and also capable of meeting the customer's demand and acceptance²⁶.

ANATOMICAL MODELS

Nowadays the use of 3D printed anatomical models in the surgery and other medical studies has gained popularity. This is because these models are designed in such a way that they can be easily used to determine the whole structure and functioning of any body part. Further, the surgical models can be used in place of human cadavers because the use of human cadavers is costly and the availability of such cadavers requires special attention. Similarly, the neurological models, used by a neurosurgeon are useful in demonstrating the complex structure of the human brain²⁷. The 3D printed anatomical model of the human head and kit is shown in Figure 3.

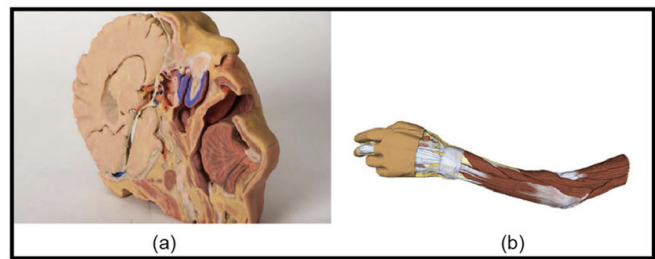


Figure 3: 3D printed human anatomical model kits, including (a) head and (b) arm, published by Monash University³⁴ (taken from open sources)

BIOMEDICAL MATERIAL IN 3D PRINTING

The use of biomedical material such as hard metals, polymers and ceramic materials are used to fabricate biomedical implants using 3dimensional technology. 3D metal implants are used in case of orthopaedics as well as in dental implants. These are having advantages over conventional implants. Since these new implants have better mechanical performance, safe, and more convenient to use²⁸.

EDUCATING THE PATIENTS

Patient care centre takes special care of patients in the health care system. The explanation of any condition to the patient by using a 2D CT Scan/ MRI is very difficult. So, to avoid to the difficulty of the patient to understand the 2-dimensional images (Figure 4), the 3-dimensional printing may help to increase the understanding of the patient about the 2-dimensional CT Scan/MRI²⁹.

APPLICATIONS OF 3D PRINTING IN DENTISTRY

3D printing is used by the combination of 3D CAM/CAD design and oral scanning the dental labs can easily fabricate dental crowns, models and a range of dental products. The main advantage of 3D printing is that it paces up the production of dental appliances productivity and production capacity^{29,30,35}.

3D MEDICAL DEVICES

The production of 3D medical devices is increasing in the present scenario. The devices include a *stethoscope*, *Multi-Sensory Perception Simulator* (SPSS) device produced by the Center for Hearing and Speech in Kajetany, Poland, or 3D printed lenses³¹⁻³².

FDA approved the 3-dimensional printed devices Fast Forward Bone Tether Plate which is helpful in foot surgery³³.

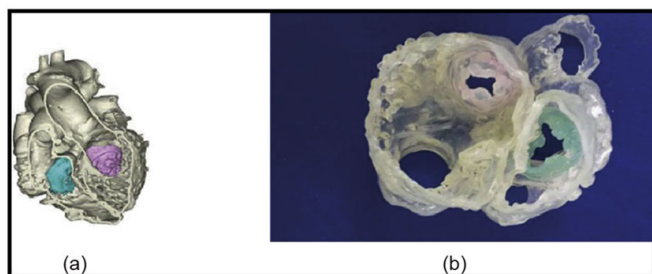


Figure 4: (a) CT scan and 3D echocardiography data model; (b) 3D printed cardiac module combining various medical imaging technologies³⁴(taken from open sources).

CONCLUSION

3D printing had made great progress in the biomedical field. 3D printing has various applications in the field of biomedical sciences. The 3D printing is used for printing organs and tissues, in pharmaceuticals, medical devices, surgical tools, implants and prostheses, anatomical models, dentistry, and educating the patients. It also leads to the growth of the personalized health care system. It offers various benefits in the fabrication of tissues, models, organs, and drug design in pharmaceuticals. The ongoing studies on 3D printers and the development of novel bioprinters will amplify the growth and development of 3D printing. In the future the 3D printing will revolutionalize the whole health care system, thus 3D printing has a bright future.

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Conflict of Interest

There is no conflict of interest among the authors.

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