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3D PRINTING IN OPHTHALMOLOGY: FROM MEDICAL IMPLANT TO PERSONALIZED MEDICINE

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Abstract
Accurate modeling of anatomical features is made possible by three-dimensional printing, which has found widespread use in the medical field. Orbital models were among its first applications in eye care, used for surgical planning and training. This has now allowed for the creation of custom-fit prosthesis in oculoplastic surgery. It has developed to include the manufacturing of medical equipment, surgical instruments, eyeglasses, and delivery systems for radiation and medication. Many institutions 3D-printed their own eye protection during the COVID-19 epidemic due to increasing demand for personal protective equipment and supply chain difficulties. The most common procedure carried out globally is cataract surgery.for instance, magnetic resonance imaging.

Keywords: 3D printing; corneal transplant; Drug delivery; Orbital implant.

Introduction

The first three-dimensional (3D) printer was invented in the 1980s by Charles W. Hull using the stereo lithography (SLA) technique (1). 3D printing (3DP) was then described as a process of layering materials on top of each other to create certain objects (2). Hence, 3DP is also part of the additive manufacturing (AM) technology. The stereo lithography printing technique was introduced to biomedical applications a few decades ago, which inspired new printing techniques to emerge and had been constantly improved upon to suit different unmet clinical needs. This new range of techniques is identified based on its layering methods and the specific materials that could be used during the printing process (3,4). The cost of AM is very expensive when it comes to large scale production. However, the 3DP technology is highly cost-effective in smaller scale production.

1.1 History of 3D printing:

In 1981, Hideo Kodama at the Nagoya Municipal Industrial Research Institute, Japan, described a technique to create 3D objects under ultraviolet rays using photo curable polymers by an additive method, but he did not finish the patent application. In 1984, Charles W. Hull invented, and in 1986 then obtained the patent for, the stereolithography apparatus (SLA). Subsequently he founded 3D Systems and produced the first commercial SLA printer in 1988, this being the first printer type used in the medical field. In 1989, two novel printers were patented: Carl Deckard patented Selective Laser Sintering (SLS), and S. Scott Crump patented Fused Deposition Modeling (12).

1.2 The Production process of 3D Printing:

Conceptually, in medicine, the production of 3D printed models involves image acquisition, image post processing, and rapid prototyping.61 Image acquisition is usually carried out using a digital imaging platform to delineate the anatomy from a patient, most commonly by computed tomography (CT) or magnetic resonance imaging (MRI). Subsequently, the acquired images are converted and modified to stereo lithographic digital models using segmentation software and putter aided design (CAD) software. Based on the obtained digital models, appropriate 3D printers are employed to print the desired tangible and physical objects by different additive methods (3) a schematic diagram of the 3D printing process

2. Common 3D Printing:

Of the various 3D printing technologies that exist, the 5 most accessible and widely used printer types will be discussed. The main differences among them are the underlying additive techniques, sources of raw material, cost, and accuracy. Different types of 3D printers and their applications are summarized. In terms of the additive techniques and raw materials, FDM is based on extruding small beads of thermoplastic materials bonded to the layer underneath. Both SLA and Multijet modeling (MJM) are using photopolymers, whereas SLA is actively using an ultraviolet laser, and MJM is using a piezo-based print head under ultraviolet exposure. In contrast, SLS and direct metal laser sintering (DMLS) are power based, where SLS utilizes small particles of metals, plastics, thermoplastic or ceramics that are used by power-based laser. DMLS uses metal alloys exclusively. In terms of cost, FDM is the lowest, while the cost of DMLS is the highest among these printers, in terms of accuracy; SLA is generally regarded to produce the most accurate products. For generalizability, SLS and MJM have a wider range of medical applications, including prostheses, tissue implants, surgical guides, anatomical models, and surgical instruments as shown in below (4).

2.1 3.D Printing IN Ophthalmology:

3D printing applications in ophthalmology are not concept usually different from those in other fields of medicine. Nevertheless, the accessibility of the inner eye and particularly the anterior segment, coupled with the immune privileged status of the eye, and the multitude of tools available for diagnosing and identifying various ocular conditions, turn the eye into a fertile ground for the implementation of 3D novel printing solutions(5). Advancements in biocompatible materials and the use of auto logo us stem cells enhance implant adaptability and reduce the risk of rejection as well as irritation caused by the implanted material. . The following is a summary application of 3D printing in ophthalmology Studies of 3D bio printing in ophthalmology.

2.2 Role of 3D Printing in Medical Field:

Every year, 3D printing offers more and more applications in the healthcare field helping to save and improve lives in ways never imagined up to now. In fact, the 3D printing has been used in a wide range of healthcare settings including, but not limited to cardiothoracic surgery , cardiology ,Gastroenterology neurosurgery , oral and maxillofacial surgery ,ophthalmology , otolaryngology , orthopedic surgery , plastic surgery , podiatry , pulmonologist , radiation oncology , transplant surgery , urology and vascular surgery (6).

Table: 1 Types of 3D technologies

Tissues	Studies	3D printing techniques
Cornea	• Corneal tissue bioprinting	• Laser-assisted bioprinting/ pneumatic 3D extrusion bioprinting
	• Contact lenses	• Digital light printing
	• Drug releasing patches	• Hydrogel-based bioink
Glaucoma	• Drug-eluting implants, e.g. contact lenses	• Fusion deposition modelling and hot melt extrusion
	• Minimally invasive glaucoma surgery (MIGS) devices	• Projection micro stereolithography
Retina	• Macular buckle	• CAD software 3D printing
	• Retinal model	• Inkjet bioprint
Orbit	• Orbital implants	• Computer-simulated rapid prototyping (RP) models
Lids	• Adjustable eyelid crutches	• 3D printing
	• Drug-loaded punctal plugs	• Digital light processing (DLP) 3D printing

3. Application of 3D.

Printing in other disciplines

3D printing has been utilised in Medicine since very early in the evolution of the field. Dentistry and orthopedics are the two disciplines with the most use of 3D printing technologies.39, 55 Studies and reports of 3D printing applications have also been published in head and neck surgery,22 plastic surgery,11 cardiac surgery,30, 37, 45, 67 and gastrointestinal surgery.77 In this section the applications of 3D printing in dentistry, orthopedics, and head and neck surgery are introduced.[23]

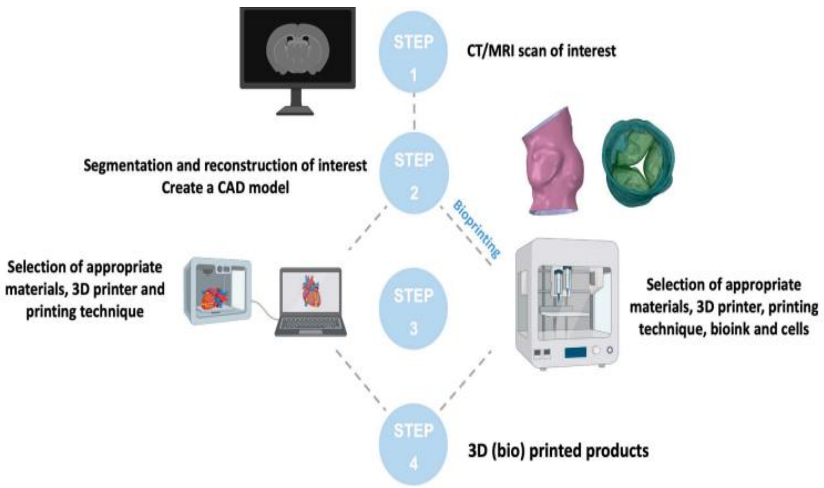

Figure : 1

4. Standardization of 3D Printing

A 3D-printed product is produced through image acquisition, image post-processing and rapid prototyping; each process plays an important role in the quality of the final product. Currently, there is no consensus on the standard of 3D-printed products, limiting the generalizability of the process(6). In order to improve the quality and consistency the 3D printed product, a standard operating protocol (SOP) for medical uses is necessary and would best written by experts who have multidisciplinary knowledge of the 3D printing process chain. The SOP should include

(1) Image acquisition protocol for 3D modeling;

(2) Image post-processing protocol for generating medical images to 3D model;

(3) Product manufactures protocol for 3D printing techniques, that is, which printer(s) should be used for a specific product;

(4) Quality assessment to ensure the safety of 3D printed product for medical use

5. Cost of 3D Printing

The global market for 3D printing was estimated to exceed US $6 billion in 2019,24 while the worldwide imprinting market was estimated to reach US $1.82 billion by 2022.26(7) Examples of the cost of 3D printed models are shown in below table.

Discipline	Item	Cost
Ophthalmology	Ocular foreign body simulator[40]	US$580
	Anatomical orbital model[B]	≤ €300
	Artificial eye/ prosthesis[H]	US$40 (student's prototype) US$4000
Orthopedics	Glenohumeral model[69]	US$150
	Adult pelvis[69]	US$1,100
	Prosthetic hand[82]	US$50 (materials cost only) US$4000 (fully assembled hand)
	Prosthetic hand[74]	US$500
	Bone reduction clamp for hand fractures[11]	US$75 (FDM) US$1200 (DMLS)
Cardiology	Pulmonary artery[45]	US$100
	Pulmonary artery with flexibility and ability for catheter insertion[45]	US$700
	Internal carotid artery (commercial version)[53]	US$250 (disposable component) US$4000 (reusable component)
	Cardiac structures[67]	€200 - €400
Otolaryngology[76]	Septoplasty/ Rhinoplasty surgical simulator (single use)	CAN$186
	Skull base surgery trainer	US$900
	Endoscopic endonasal skull base drilling	US$500 (materials cost only)
	Laryngeal simulators	US$2.08-6.97
DNA printing[12] (predicted costs)	Protein	US$500
	Human genome	US$2.2 billion
	Plasmid	US$5000
	Bacterial genome	US$1.5 million
	Yeast genome	US$4.2 million

€ = Euro

Table: 2

Currently, the cost of 3D printing is one of the obstacles to its widespread use in medical field. The cost of 3D printed product usually is assumed to be cheaper than the convention product because of low-cost hardware. However, this is not the only expense in 3D printing industry (11). The total cost of 3D printing should also account for software (design and post processing), regulatory cost for medical device, and labor cost (design, operation, training, maintenance, and engineering). Among these, design accounts for the largest part of the cost because only experienced designers can create medical-grade 3D printed products

7. Patent Expiration:

As 3D printing technology has been available for more than 30 years, some of the patents have expired. The U.S. Patent and Trademark Office (USPTO) sets the current patent term at 20 years from the patent application date. Currently, over 12,000 patents are linked to 3D printing, and many of them are related variously to methods, processes, systems, software and designs. Expiration of some of the key original 3D printing patents has paved the way for cheaper manufacture and broader development. Since 2002, about 225 3D printing patents have expired, of which 16 were related to the 3D printing process, including FDM, SLS and SLA. Hence, the earlier 3D printing technologies are more affordable for individuals. Owing to advancing technology and reducing prices, domestic 3D printers are now available in the United States for less than US $1000.24 unfortunately; many of these printers are only capable of producing small products, limiting their widespread use (10).

8. Quality Assurance of 3d Printed Models:

Quality assurance (QA) is a series of error prevention means to provide sufficient confidence for a product through systematic measurement and processes monitoring. It has been developed to ensure the quality of medical treatments for decades (12). With the increasing popularity of medical 3D printing, there is growing demand for extending quality assurance and control to 3D printed devices. In general, model quality is evaluated by measuring the degree of reliability, maintainability, and sustainability. Researchers assessed the accuracy of 3D printed models using different measuring methods including

9. Challenges of 3D Printing in Ophthalmology:

Despite the potential successes of 3D printing in ophthalmic practice, some limitations of this emerging technology must be addressed so that adoption and wider applications in ophthalmology can be realized.

10 .Ethical challenges:

With the development of 3D printing, ethical concerns have been raised about the commercialization of human organs, similar to cloning technology. There have even been some religious objections to the technology(12).49 For example; it is debatable whether 3D printers can be used to print a mutated organ capable of longevity. Some are also concerned that this technology is for only for the wealthy, raising the possibility that disparity in healthcare may be widened, especially if objects that are 3D printed are commercialized at high cost. Another ethical issue centers on intellectual property.

11. Quality of Printed Models:

In general, the quality of a model can be assessed in terms of accuracy, durability, and user satisfaction. For accuracy and durability, impact factors generally include medical images of patients, types of 3D printer, printing parameters, and the properties of raw material. For example, if the segmentation process of 3D printing is performed manually, the proficiency of technicians may affect the reliability of the 3D printed product. Furthermore, some anatomical structures such as they cannot be 3D printed accurately as current imaging technology cannot capture the details of the vessels. With regard to 3D printers, models printed by FDM are relatively cost-effective, but exhibit lower resolution and more surface roughness. Compared with SLS and SLA that only produce uncolored models, MJM can produce multi-color models and simulate the texture of both hard and soft tissues using different biomaterials. The selection of biomaterials is important in deciding how best to create 3D- printed object in different ophthalmic cases.

Retina:

The retina is a complex tissue made of different cellular layers that detects and converts light signals into electrical signals, which are then transmitted to the brain. Photoreceptors, known as rods and cones, are responsible for the photo transduction. The retinal pigment epithelium (RPE) is a monolayer found between the retina and the choroid. The RPE provides growth factors and plays an important role in nutrient transport and of the photoreceptors. Any damage to the retinal layers can lead to diseases, such as age-related macular degeneration (AMD) and retinitis pigments (RP) (13). These diseases are caused by photoreceptor deterioration that leads to RPE atrophy.

Retina Educational Models:

Traditionally used models such as Navarro's schematic eye have inspired the creation of 3Dprinted models for research and training.

Model eyes have been printed to assess the funds viewing range of various lenses as well as the quality of wide-angle imaging and OCT instruments. Model eyes have also been printed for retinal laser training [19, 20].

Conclusion:

The development of 3DP technology has made it possible for us to make customized medical items, something that is not possible with traditional manufacturing methods. 3DP's flexibility and adaptability will improve the future of therapeutic fields like orthopedics and dentistry. The medical research community is encouraged to consistently provide advanced treatment and acquire patients' trust by the promising discoveries of 3DP in ophthalmology. Though 3DP in the field of ophthalmology is still largely unexplored, it has the unquestionable potential to offer ground-breaking treatments for a wide range of eye conditions. Modern medicine has taken a breakthrough step with the introduction of 3D bio printing as a fresh technique. The development of bionics in 3D printing may be able to address the scarcity of corneal transplants while also fostering improved tissue regeneration. Furthermore, the individualization of AM manufacturing is ensured by the ever improving 3DP procedures designed for drug administration systems and ophthalmic devices. More research is needed to fully understand the function of 3DP in the medical area given the difficulties and barriers associated with biomedical 3DP manufacturing.visualizing.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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