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3D Bioprinting: Printing To Biomedical Applications

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ABSTRACT

3D printing is a process of making a physical object from a three dimensional digital model, typically by laying down successive thin layers of a bio ink. In healthcare, 3D printing technique is used for various procedures such as the development of implants, tissue replacements, skin replacementsand prosthetics. Other than this, it finds its use in creating replicas of bones, organs, blood vessels and also for planning out critical surgeries by creating a duplicate of the diseased organ. Considering its versatile use, 3D bioprinting is an upcoming province. The surgeon uses Computed Tomography (CT) images to produce a simulated 3D anatomy model from a sequence of two-dimensional images. This gives the surgeon an edge by converting the details found in CT images in a more comprehensive format. Today's era demands a personalized approach to everything including medical treatments which can be made possible with the help of Bioprinting. 3D printed models play a key role in the entire surgical programme, from preparation to reduction of reoperation rates and training of the aspiring surgeons. This technology also saves a tremendous amount of time and money. This technology needs to be explored for its limitless possibilities and innovation in the medical industry. Challenges and the future of 3D bioprinting This technique is in its early stages, we need a lot of research and improvement as to make its functioning smooth and accurate. It can change the face of medicine and medical industry. Overall, 3D bio printing is a rapidly evolving field of research with immense challenges, but tremendous potential to revolutionize modern medicine and healthcare

KEY WORDS: 3D BIOPRINTING, HEALTHCARE, TECHNOLOGY AND COMPUTED TOMOGRAPHY.

INTRODUCTION

3D bio-printing is a form of additive manufacturing that uses cells and other biocompatible materials in the form of ink. These are known as bioinks, which are used to print living structures in a layer-by-layer manner imitating the behavior of natural living systems. First thing to do in 3D printing is to create a digital model. Then, there are various ways or methods to proceed, like the Stereolithography Apparatus printing (SLA), Extrusion based, Droplet based or Laser based Bioprinting. To print the biological conduits, further we need to supply the bioinks(raw materials) which can be in the form of a suspension of living cells, or even stem cells which can differentiate into the desired target cells.

After performing all these processes, which require a few hours, we get the desired product. Bioprinting is a pretty new technology, and has a huge potential to benefit industries like medicine and cosmetics. A tremendous amount of research is needed in this area through which we can use a variety of biomaterials as bioinks to improve the quality and functionality of the product. Apart from organ printing, bioprinting is also being used to fabricate in-vitro tissue models for drug screening, disease modeling, and several other in-vitro applications (Dey M, 2020).

The introduction of minimally invasive approaches such as laparoscopic surgery and more recently, robotics, has

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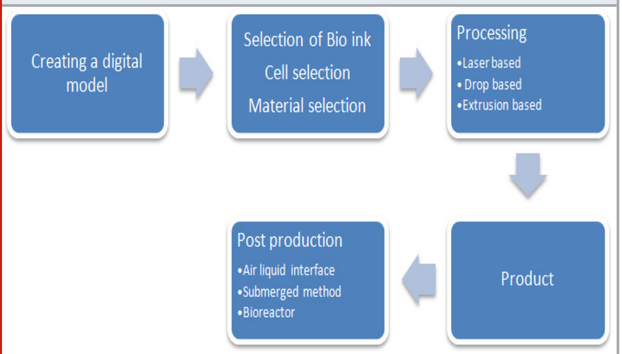
fully transformed surgeon's interventional approach. In order to prepare not only the different phases of the intervention, but also the access to surgical equipment, a better understanding of the specific anatomy is needed. As a result, surgeons must have access to facilities that enable them to thoroughly examine the clinical condition. Furthermore, in the fields of orthopedics and traumatology, it is possible to enable the surgeon to practice the operation on a 3D printed model before performing it, such as inserting screws or plates or checking the drilling route (F. Langlotz and E. Keeve 2003).

Figure 1



DISCUSSION

3D printing was invented by Charles Hull in the mid-1980. For medical professionals, 3D printing can create remarkable advancements in the treatment procedures. 3D printing techniques are used in various fields such as engineering, manufacturing, education, art, and medicine as well. It is a major upcoming technology, with a lot of potential for further research. We have also seen the rise of 3D printing in medicine related areas in the ongoing pandemic. Engineers have manufactured dozens of PPE kits, face shields and medical equipments with the use of 3D printers. With the prevalence of bioprinting there will be a shift from the generalized and rigid form of treatment to a more customized and patient-specific approach (MarijaVukicevic, et al 2017).

Bioprinting focuses on the individual care instead of developing a universal treatment set up for all patients. Customized drugs are dear, though it will increase the inequality between the wealthy and poor. Since 3D printing is a personal treatment, the overall public assumes that it should forestall the folks with monetary problems from receiving care. However, bioprinting improves universal access to aid which would in turn bring down the time and cost of treatment. For instance, prosthetic limbs and associated orthopedic surgeries can be done in an economical manner. Patients wouldn't need to wait for months for his or her turn, which would ultimately decrease the expense. The bioprinter could also be customized to manufacture bone replacements and turn out custom-made prosthetic limbs quickly. Presently in the United States the Transplant list states that about 115,000 people are awaiting a transplant, which can take nearly two years to obtain, while nearly 2 million people have lost a limb.

There is an enormous shortage and inaccessibility of donor organs, it is estimated that 900,000 deaths each year can be prevented by fabricating engineered organs. People who were antecedently excluded from these medical advancements can currently have access to them. Though the production and setting up of this industry requires massive amounts of workload and monetary investments, later on it can reduce the cost of treatment significantly. According to the National Foundation for Transplants, a standard kidney transplant, on an average, costs upwards of $300,000, whereas the cost of a 3D bioprinter is as little as $10,000 and costs are expected to reduce further as the technology evolves over the coming years. In a developing country like India, this can prove to be a great boon.

The roots of bioprinting have already penetrated in India. One big company has already started in Bengaluru, Karnataka. It aims to create a paradigm shift in pharmaceuticals, cosmetic and clinical research and development. We can use bioprinting to create cells, stem cells, tissues, implants, prosthetics, drugs, medical tools, equipment and lastly even an organ. Time is also a crucial factor in bioprinting. Printing a conduit may require several hours, excluding the earlier process of collecting of base requirements like the bioinks and creating a digital model whereas it can reduce several hours of a complicated surgery by enabling the clinicians to plan out the procedure by creating bioprinted replicas of the patient, this helps especially while dealing with the tumors. The clinicians create a digital model with the help of existing CT / MRI scans and then print the model so as to study and approach the tumor. Eventually, we can also use the patient's cells itself to avoid rejection. The prevalence of 3D bioprinting can be revolutionary (Heinrich MA, et al 2019).

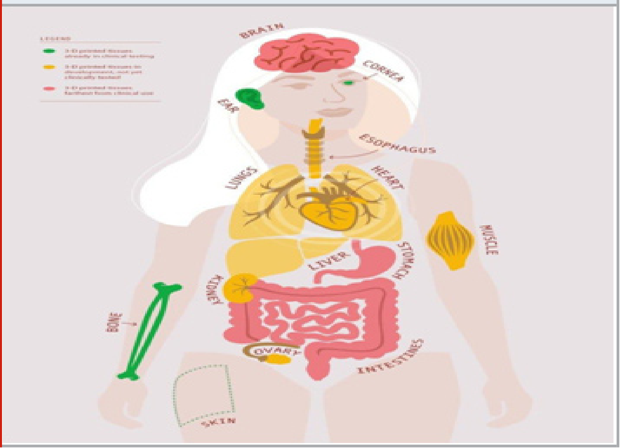
Present clinical procedure, however, is mostly used as critical support for preoperative preparations for diagnostic photographs such as CT and MRI or, in some cases, simulations or 3D reconstructions. 3D printed templates are helpful in order to provide the surgeon with informative details and to enhance the surgical planning. It can help to explain the procedures to new surgeons and patients by using printed models which have similar bio-mechanical properties. It can also be helpful for the testing of procedures on patient-specific (PS) anatomy. It is important to note that the applications of 3D bioprinting are not limited to organ printing. It also holds great promise in less explored avenues, such as using scaffolds for drug delivery, studying disease mechanisms, or creating personalized medicines (Gu Z, et al 2020).

Bioprinting may be used to improve human strength, speed, or endurance. For instance, bioprinting may be used to manufacture enhanced bones and replace regular human bones that are stronger and more flexible. The 3D printer may also be used to improve muscle strength by making them more "resilient" and less prone to fatigue. The lung functioning may also be increased by replacing it with an artificial lung that can maximize oxygen efficiency in the blood. Bioprinting could build a culture free of disease and imperfection, which would have a risky yet incredible effect on civilization.

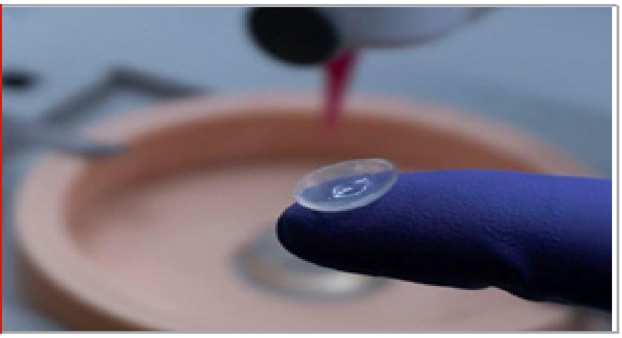
Furthermore, with the 'organ-on-chip' bioprinting technique, 3D bioprinted organs may eliminate the need for animal drug testing. An organ-on-chip is essentially a computer chip with cells from a specific tissue implanted in it. One chip can be used to represent the lungs, and another could be used to represent the kidneys, and so on. These chips can be attached to activate the body as a whole, allowing drug treatments to be tested on the whole body before going through clinical trials (Papalkar, Parag et al 2019).

Applications of 3D Printing6: If we see some of the applications where 3D printing is currently in use;thedetails are as follows.

Figure 2



Ophthalmology (Ruiz-Alonso S, et al 2021): The cornea plays a very vital role in formation of the image. If the cornea gets damaged we may not be able to see or we may see blurry images. Prospectively, with the help of the 3D bioprinting we will be able to replace a patient's cornea with a new and efficient one composed of their own stem cell (if the condition is not derived from diseases) and if damaged by disease, donated cells can be used to bio print new corneas.



Otolaryngology (Jeong HJ, et al 2020): The field of Otolaryngology encompasses care for the ears, nose and throat. Otolaryngologists remedy issues with hearing, speech, swallowing, sleeping, breading, sinuses and head and neck cancers. For instance, the trachea which sits anteriorly to the esophagus and carries air to the lungs, can become narrowed from cancer radiation treatments and reduce breathing rates in a condition known as tracheal stenosis, replacing a radiated trachea with a bio printed one can aid in re-establishing normal breathing patterns. Damaging of the hair cilia that lines the interior of the ear can cause detrimental hearing loss. As hair cilia cannot be replaced, a bioprinted ear can provide both the structural and functional framework for the ear to pick up vibrations and translate this into auditory code. There have been instances where the hair follicles have been created by using 3D bioprinting, however, the studies are still in progress.

Cardiovascular system (Cui H, et al 2018): Harm to the blood vessel caused by infection or injury poses a significant risk of disease and death. While synthetic vascular grafts have been marketed successfully for clinical use, currently only large diameter vessels (>6 mm) are readily available. However, the trials for substitutes of small vessels (<6 mm) are progressing and they face major clinical problems globally.

A 3D Printed Heart (Source: Carnegie Mellon University): Cardiovascular diseases, ranging from arrhythmias to cardiomyopathy. When exacerbated to end stage heart failure, can only be remedied by conducting heart transplantations. However, the potential prospects of heart transplantations are often mitigated by the coalescing of long waiting lists and limited organ donors. Recently, a heart was bioprinted with a cardiac cell bio ink. To create the bio ink, omental tissue was taken and decellularized. The decellularized tissue was then translated into stem cells, which were then mixed with a hydrogel to create cardiac cells. The blood vessels of the heart utilize a bio ink of cardiac and endothelial cells. Though anatomically and biochemically resembling a heart, the bioprinted heart does not contain any physiological ability. With the integration of physiological properties, the 3D bioprinted heart will be able to treat an array of cardiovascular diseases.

Hepatology (Cui H, et al 2018): In vitro liver tissue models can currently be created using recently developed 3D bioprinting technology. Liver functions were established after seven days differentiation in vitro, and later transplanted into mice. The findings showed a robust proof of concept, demonstrating that a model of liver tissues had in vivo hepatic functions and alleviated liver failure after transplantation, implying that 3D bioprinting could be used to produce human liver tissues as substitute transplantation donors for the treatment of liver diseases.

Dermatology (Pantermehl S et al 2021): Burns continue to be the world's leading source of trauma. More than 11 million people worldwide and 1 million people in the U.S. need medical attention for burns every year. Although split thickness autographs remain the gold standard treating method for dealing with serious injuries, sufficient coverage depends on the availability of safe skin donors. The production of dermal replacements has resulted in improved longevity and full-thickness injury closure.Moreover, excellent outcomes have been noted in rapid wound protection, which has accelerated health treatments, including manual cell seeding and cell spraying. In addition, the development and direct supply of skin cells to particular places can be achieved by bioprinting—typically using Inkjet printers. A new, motive bioprinter device that deposits skin cells directly into thickness wounds has been approved in a proofs of concept study released in Scientific Reports in 2019.

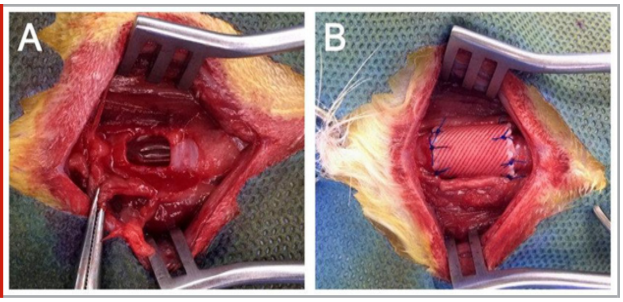
Respiratory System (Yu J, et al 2020): An infant patient with a rare respiratory disease known as tracheobronchomalacia (TBM) was given a tracheal splint that was created using 3D printing which proved to be successful. We can bioprinttrachea- stem cells derived from the bone marrow and respiratory epithelial cells are used as the composition for bio ink. The bio ink is filled into the printer's cartridge and then released from the nozzle in an orientation akin to the trachea. The stem cells mature into chondrocytes (cartilage cells), which aid in the formation of the trachea. A bioprinted trachea was successfully implanted into a rabbit recently, demonstrating the development of cartilage from stem cells. This bioprinting of a trachea should be extended to humans, where we can bioprint tracheas for patients with severe stenosis (narrowing of the trachea) or cancers (tumors) within the trachea. Under any scenario, it's critical to remove the whole trachea and replace it with a new one, perhaps bioprinted.

Application of 3D bioprinted artificial trachea. (A) Approximately 10 × 10-mm half-pipe shaped tracheal defect on the ventral part of the trachea. (B) The defect was replaced with 3D bioprinted artificial trachea and sutured with 5-0 absorbable suture material.

Orthopedics (Genova T et al 2020): As already stated, 3D printing technology is commonly used to produce bone models used in complicated orthopaedic cases in pre-operational preparation. For instance, a surgeon will print a 3D model of a complex joint reconstruction, know the potential challenges and prepare accordingly. Still, for doctors and researchers it is very helpful to use 3D replicas of bone fractures in trauma cases for preliminary treatment.

The development of surgical guides is also helpful in 3D printing. These guides may be used to take accurate bone cuts intraoperatively. This procedure reduces the operation time and has broad consequences for the patient, the surgeon and the hospital. The time and effectiveness of the procedure can be increased and the patient can see better results. Cases such as complex defects can be handled more effectively by means of precise, directly fitting 3D printed guidance models.

This technology is useful in reducing costs (in relation to operational time and intraoperative bleeding) and enhancing accuracy and reducing surgical and postoperative risks. Another benefit of orthopaedic 3D printing is to provide a patient a greater and clearer understanding of what is performed in the operation room, as the surgeon can readily demonstrate. For patient training 3D printed models are helpful, as patients themselves can understand their concern and steps to correct the problem are taken.

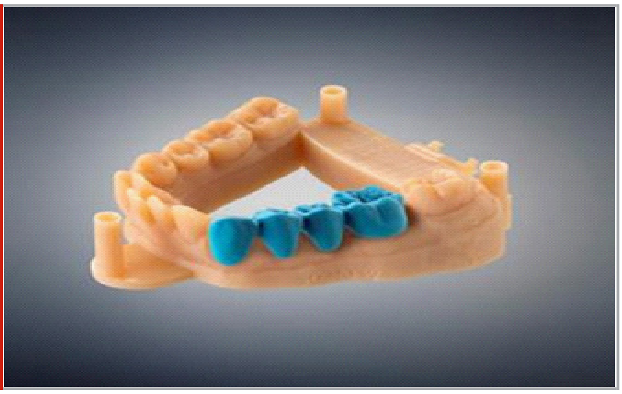


Dentistry

3D printing has some of the major applications in dentistry: It can be used to replace or patch the chipped tooth. The dentist uses a small optical device to scan the patient's teeth. The representation of the teeth and gums that are stored as a digital file created in three dimension. The dentist will plan the tooth fix digitally and print the finished result on a 3D printer. Also, for creating an orthodontic model. The current system involves making the patient bite on gooey, uncomfortable clay so that it can harden into an original form model for braces or Invisalign treatments. With the use of 3D printing technology they can create an accurate digital model eliminating the errors owing to the clay model.

The same process can be used to fabricate the various digital implants such as crowns, bridges, caps, dentures and lastly to construct surgical tools.

Each patient's fact reflects high costs for the addition and operation of a dental laboratory. A single crown will easily cost a patient $2,000 or more using standard technology. If 3D printers reduce operating costs by 80%, dentists can pass the savings to their patients. Manual modelling requires time and 3D printing makes it possible to print several conduits simultaneously. The accuracy of 3D printers is also increased when digital images are converted into physical structures with 16 micron layers being printed top-on-side. Both dentists and patients prosper from increased processing capability and more reliable end outcomes.



CONCLUSION

In today's technologically driven world, new advancements are sprouting up enormously. Also, with rise of the pandemic we are sensitized with the importance of technology. The answer is yes, 3D printing organs is not a fiction anymore, the starting process is practically difficult, but end result will be a boon. This technique is in its early stages, we need a lot of research and improvement as to make its functioning smooth and accurate. It can change the face of medicine and medical industry.

Even though 3D bio printing is advancing at a commendable rate with researchers trying to develop new printing modalities as well as improve existing modalities, there still remains a multitude of challenges that need to be overcome. This is a field of research which requires synchronized efforts form the experts from various fields such as IT, Biology, Bio chemistry, etc.Overall, 3D bio printing is a rapidly evolving field of research with immense challenges, but tremendous potential to revolutionize modern medicine and healthcare.

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