International Journal of Recent Advances in Multidisciplinary Topics
Volume 3, Issue 4, April 2022
https://www.ijramt.com | ISSN (Online): 2582-7839



# 3D Bio-Printing in the Field of Cardiac Surgery, Bone and Ligament Surgery and Skin Surgery

Aadya Sinha[1*], Bimla Choudhary[2]
[1]Student, Neerja Modi School, Jaipur, India
[2]Teacher, Department of Biology, Neerja Modi School, Jaipur, India

***Abstract*: 3D bioprinting is a newly developed technology, the basic idea is to use a 3d printer which substitutes the 'ink' with specialized bioinks in hopes of being able to print fully functioning organs or parts of an organ. This technology combines multiple aspects of engineering, medicine and manufacturing to revolutionize medical treatments and help save patients from life threatening conditions and improve their overall quality of life. There are various clinical applications of 3D bioprinting in the field of Cardiac Surgery, Bone and Ligament Surgery and skin surgery. All of these subsections follow the same basic strategy but also involve slightly different techniques that are unique to them. The technology of 3D printing is very nuanced and convoluted making it susceptible to multiple ethical, legal and social issues regarding their use.**

***Keywords*: Bio printing, bone, ligaments, skin surgery.**

## 1. Introduction

The newly developed technology of 3D printing has infiltrated into the field of medicine. A 3D printer is a device that allows the user to print three dimensional objects, this idea follows the basic principle of creating and building, a basic design of the desired model is fed into the printer which slowly molds it by adding layers until the desired end product is achieved. Now, scientists are toying with different ways to use this basic principle and technology and use them in the field of medicine and treatment, the major goal is to modify the technology in such a way that it can print fully functioning, transplantable organs. This new idea, which is termed as 3d bioprinting will be of great use to the medical community and will be able to help a lot of people, the principle associated with bioprinting is the use of cells in place of the traditional ink of the printer and therefore the end product achieved would be a fully functioning organ. Currently, there are a plethora of people on the transplant list waiting for an organ transplant.

According to the website of the National Kidney Foundation, (https://www.kidney.org/news/newsroom/factsheets/Organ-Donation-and-Transplantation-Stats) the statistics regarding kidney transplant only are disheartening. Each day, 13 people die on the transplant list whilst waiting for an organ and every 14 minutes a new patient is added to the list and apart from just kidneys overall 121678 people are waiting for life saving transplant in the US alone and this number only increases as days pass.

Organ Procurement and Transplantation Network (OPTN) is an official U.S. government website managed by the Health Resources and Services Administration, U.S. Department of Health & Human Services and consists of all national data on the waitlisted candidates, organ donation and matching, and transplantation. This is very important in helping organ transplant institutions match waiting candidates with donated organs. Institutions also depend upon these databases to manage time-sensitive, life-critical data of all candidates, before and after their transplants.

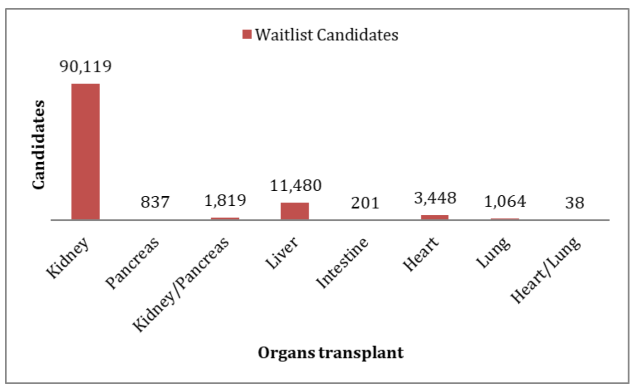


Fig. 1. Waiting list candidates as on 20th January, 2022
Source: Organ Procurement and Transplantation Network (OPTN data)

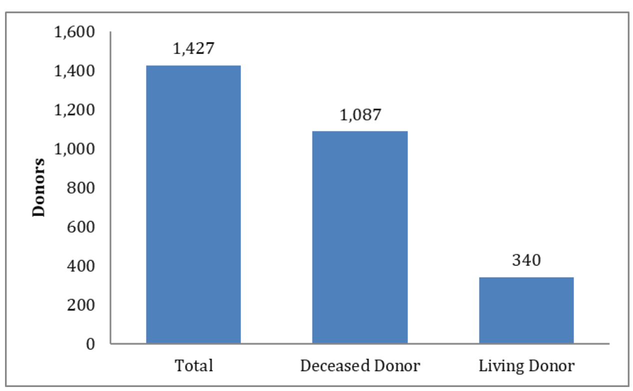


Fig. 2. Donors recovered - January 2022
Source: Organ Procurement and Transplantation Network

*Corresponding author: aadya10sinha@gmail.com

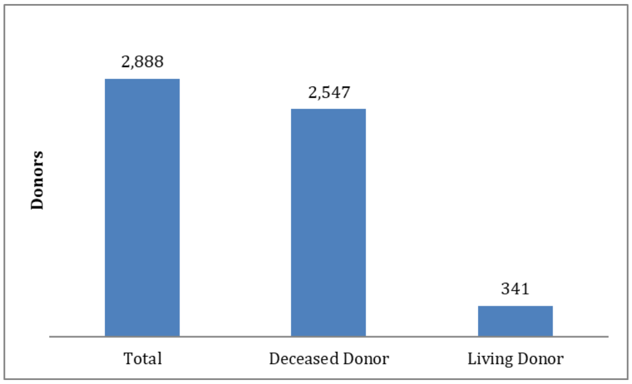


Fig. 3. Transplants performed - January 2022
Source: Organ Procurement and Transplantation Network (OPTN data)

3D bioprinting can be a great asset in this case, if the organs can be printed from the patient's own cells, then the long periods of wait and the uncertainty of the transplant list could be eliminated. This would improve the healthcare system, treatment plans and the overall quality of treatment that a patient is getting.

With a technology as vast and advanced as 3D bioprinting, it is only understandable that an idea like this would take a lot of time and modification before it can be well equipped for commercial use. Although, as of now we might be decades away from actually being able to print fully-functioning organs, many scientists have been successful in printing small allograft, valves and tissue by using 3D bioprinting.

Currently, there are a lot of clinical trials going on in different parts of the world regarding the use of this technology, multiple researchers and scientists are keeping a close eye on the technology and trying to find fixes to its shortcomings.

One shortcoming and fix for this is given in an article by BBC Future by the title 'Why Astronauts Are Printing Organs in Space' stated the pros of this technology and how this would be very beneficial for critically ill patients. The article gave a theory about how we might be able to put this technology to use, by using the patient's own cells and modifying them such that they could be used as the 'ink' of the printer and then the printer being able to produce fully functioning organs. According to the article, 3D bioprinting was particularly carried out in space to prevent the printing organs from collapsing in presence of gravity on the ground.

The attempts to create a bioprinter that could be used for medical purposes showed that the gravity of the earth posed a humongous restraint. This called for the need to try and use this technology in a possibly gravity free environment in order to cut down the complications that have arisen due to gravity.

### *A. Types of Bioinks*

There is a large variety of printers available that can be used for 3D bioprinting, this also leads to a large variety of printing techniques that can be used such as, ink-jet printing, laser-induced forward transfer, micro valve-based and extrusion-based bioprinting. The bioinks that form the basis of 3D bioprinting differ from printer to printer providing us with different results. For example, viscous bioinks work best with extrusion based bioprinting.

Hydro gels give us an aqueous environment and structural support, this makes cell survival and proliferation more efficient and therefore makes hydro gels a very preferable choice as a bioink. Many types of hydro gels such as collagen, alginate, gelatin, hyaluronic acid etc.

Using a blend of alginate and methylcellulose as a bioink retrieved good results such as easy extrusion, high printing fidelity and achieving scaffolds. To thoroughly examine bioinks, criteria such as proliferation, cell viability and growth of cells are judged. Other factors such as flow rate, printing speed and layer height are used to evaluate the printability of the ink; this gives a methodical idea about the efficacy, convenience, feasibility and quality of the ink.

The efficiency of a particular ink to be printed smoothly, accurately and without any complications is termed as printability, other parameters that help us evaluate the printability of an ink are; ratio of line width to nozzle diameter, number of layers that can be formed before the structure collapses, curvature of printed lines etc.

Despite the need of evaluating printability in order to help with the efficiency of ink, it cannot be denied that it is a tedious and time taking task. This is especially true for bioinks containing cells as once the bioink and cells are mixed together, there is no time for considerable testing because it puts the cell viability in jeopardy. Due to this, cells containing bioinks get printed at parameters that are not optimal for that particular ink which becomes a threat to printing fidelity. All of this can lead to slight discrepancies in the requisitioned structures; this is extremely dangerous because this means that there is a high probability that the smooth and precise functioning of the 3D printed tissue is compromised.

If the printed lines are too thin the overall structure would be fragile and therefore easily break, moreover if the lines are too thick it would hinder the efficiency of the structure. The consistency of the bioink also plays a crucial role in determining its overall functioning, the ink may become diluted when the cells are added leading to slight moderations. Therefore, evaluating the overall cell fidelity becomes a meticulous and tedious task as there are so many factors that impact it. Computer simulations are a good way to thoroughly evaluate bioinks while cutting down on time and cost.

*Clinical Applications of Bone and Cartilage:*

Cartilage is a flexible connecting tissue that can bend but does not tolerate stretching therefore injury to the cartilage is very common. Our current methods of dealing with these injuries have multiple shortcomings, lack in efficiency and are more of a short-term solution with limited longevity. The most common method of treating such injuries is the use of an osteoarticular allograft. Similar to organ transplant, an allograft is a tissue obtained from a donor and is transplanted into the recipient; this technique is used to deal with large defects and injuries. Although osteoarticular allograft provide very good outcomes with a little to no chance of rejection but, on the other hand it leads to an immense delay in treatment due to the considerable time it takes for a suitable match to be found. (Ji et al., 2017) Finding a flawlessly compatible match is a very integral part of allograft, the success rate here depends less on the skill of the surgeon to perform the surgery and more on whether a fitting and appropriate match is found. This leads to unpredictability, the waiting time to find a suitable match is at least a year if not more and takes a humongous toll on the patient's quality of life, causing the patient extreme discomfort, restriction and pain. Therefore, there is an imperative need for alternative options to surface in the coming years for better and faster treatments; 3D bioprinting is one of the up-and-coming methods that can prove to be efficient and feasible for such injuries/deformities. A 3D printer, which will use the patient's own cells and tissues to 'print' out grafts which can then be transplanted into the patient. This reduces the patient's waiting time from years to days to even hours and can give us vastly superior results that will be one step ahead of the traditional treatment plans. Such 3D printing grafts will require nuanced strategies and immense supervision in order to give us a nuanced result but will give us a speedy, structured and overall better treatment plan.

Commonly used bioinks for 3d printing are Gelatin and Hyluronic acid (HA), these have proved to be extremely efficient in cartilage regeneration but have also shown a few shortcomings as controlling its structure and biocompatibility remains a difficult complication to cope with. A bioink procured through hybridization of gelatin methacryloyl (GelMA) and glycidyl-methacrylated HA (GMHA) for material extrusion 3D printing of cartilage has been experimented with by mixing them in varying ratios and observing their results. This led us to the conclusion that a combination of 7 percentage GelMA and 5 percentage GMHA gave the best outcomes with desirable mechanical properties and printability.

### *B. 3D Printing in Cardio*

Congestive Heart Failure or CHF negatively impacts the pumping power of the heart due to fluid buildup causing the heart to work efficiently. According to CDC, heart failure was mentioned as the cause of death on about 379800 death certificates. Most cases of heart failure will require implantation of a pacemaker, transplant of one or more valves and / or arteries and in some alarming cases, it may even require a complete heart transplant.

Heart transplants are required when no other treatment has shown effective results and the patient's condition worsens. In a heart transplant, a fully functioning heart is taken from an organ donor and transplanted into the recipient's body. It is a risky surgery with a great possibility of rejection or infection. Getting on the waiting list is also a tedious task, a patient can only get on the list once he or she has been properly assessed and approved to be fit for a transplant by a transplant center.

For people who are ill suited for a heart transplant are given alternate treatments such as the Ventricular Assist Device (VAD). VAD is an artificial mechanical pump that is implanted in the skin and helps the heart with pumping blood, although this device is mostly used as a short-term treatment for people awaiting a transplant, nowadays, using the VAD as a long-term solution is becoming increasingly common.

Another artificial option is the mechanical heart, a mechanical heart is a man made pump that mimics the heart and can be used in cases of severe heart failure, just like the VAD, it is commonly used to span the gap of time while the patient is waiting for a transplant but is also used as a permanent cure in cases where it is not possible for a heart transplant to be done. Despite so many treatment plans being available in today's day and age, the need for an even more structured and systematic approach is required. The waiting period for a heart transplant is very long, patients often have to wait for years on end in order to find a suitable donor, and this often reduces their quality of life and also puts them at risk for serious complications with many people that often die while waiting for a transplant. Therefore, the need to further modernize such treatment plans is required, 3D Bioprinting can be extensively used in this fields as well, by using a 3d bioprinter with suitable inks a fully functioning heart or certain valves can be engineered out of a patient's own cells, this would lead to a faster and more efficient treatment.

Apart from that, 3D printing is also useful in preparing and planning out medical treatments and strategies. A recent study focused on developing a carefully engineered heart model with particular specificities to help in medical training. This study utilized the Flying bear P902 printer Flex Thermoplastic Polyurethane (TPU) filaments, both non transparent and transparent filaments were used by designing two separate trials (Yakof, Khairul Shah Affendy, et al.)

Besides 3D bioprinting having various clinical applications and promising future results, but as with any other up and coming technology it raises a lot of ethical and legal concerns.

Regulation and use of bioprinting have been defined as a problematic area by various government and legal institutions. 3D model designers, medical professionals, researchers, lawyers, members of the ethics committees need to work together and use their expertise in order to make 3d bioprinting a part of everyday clinical practice.

One of the major legal issues in 3d bioprinting is the responsibility of the quality of the product. If the finished bioprinted product isn't up to par in context to the quality, it can put the recipient's health and overall well-being in jeopardy, therefore it is extremely crucial to keep a close watch on the quality of the product as even miniscule inconsistencies in quality can prove to be a serious predicament. This leads to an array of questions that need to be addressed. Who should be held responsible for the quality of the product, the medical institution or the 3D bioprinting providers? How can the quality be kept in check? How can it be ensured whether the quality is adequate or not?

Another concern raised is the issue of intellectual property; this includes patents, design rights, research studies, trademarks etc.3D printing can be a solution to the problem of organ shortage but it may lead to a new problem of accessibility. This technology will be expensive and therefore only affordable to the rich people and the gap between the processing classes will widen.

### *C. Ethical Issues with 3D Bioprinting of Artificial Ovary*

The requirement of transplantation of artificially created reproductive organs like testes, ovaries or uteruses do not gain much attention as they are not viewed as fatal but improving and revolutionizing such transplants can drastically improve a person's quality of life. Although a number of treatment plans to preserve fertility such as embryos and acolytes exist, this is not the case for cancer patients in whom the cancer had metastasized to the ovary. In such cases, either the ovary needs to be removed or the harsh cancer treatment such as chemotherapy and radiotherapy destroys the organ beyond the possibility of restoration.

The development of such a technology that can produce transplantable artificial ovaries will help a vast number of patients, this can help them retain the endocrine function of the ovary and can allow them to give birth to biological offspring's. 3D printing in this case can be a very resourceful technology which can help produce a fully functional artificial ovary.

However, the use of 3D bioprinting to produce artificial reproductive organs raises a lot of ethical concerns.

The first thing here that we need to keep in mind is the risk-benefit ratio. Here, procedures like ovariectomy; chemotherapy and radiotherapy are nuanced and convoluted treatments but are needed to save the life of the patient and therefore, are considered important. The transplantation of an ovary however serves no function in saving the life of the patient and therefore is not deemed as a necessity or a priority. Another ethical issue that is raised is the safety of the patient and the offspring, the concern of whether the external influence or handling of ovarian follicles might result in genetic discrepancies in the egg which might have a direct impact on the health of the offspring. Also, several types of cancers are genetic therefore; there might be a risk of the transmission of the genetic variant from parent to offspring.

Another raised concern is the fact that the time taken from the removal of the ovary to the production of the artificial one could be very long and the patient might change their mind. The patient might get pressured into motherhood due to the use of such an expensive technology; voluntary transplant rejection in this case is a major issue.

Even though 3D bioprinting seems as the perfect solution for a vast range of medical problems on paper, its practical use is slightly more convoluted. There is no doubt that 3d bioprinting has multiple advantages but a major concern that is raised is the fact that it will only be of benefit to a particular community, namely the richer classes of the society. Therefore, the promising advantages that have been listed will not be the absolute medical game changer that we hope, bioprinted organs will be extremely expensive due to the cost of this technology, and this will make it unaffordable to a large chunk of the population who need it. This disrupts our hopes of cutting down on the number of people waiting on the transplant list for an organ.

Another major issue is the uncertainty of a new technology. As this technology is still being developed, there are a lot of things that we are still unsure of. Printing smaller structures such as skin grafts and parts of the heart valve is still easier but fully functioning organs such an entire kidney or hollow organs such as an ovary are more difficult and require extreme precision and a very developed technology. Even then, scientists aren't sure about the time duration it would take to be able to successfully print a fully functioning organ.

Another concern is the fact that the use of cells as the ink of a printer remains a clinical paradigm. As the technology is still being tested, we are still unsure of the complications that could occur, whether during printing or once the organ has been successfully transplanted, the risk of the patient developing a complication such as formation of teratomas or even worse cancer and problems with the implant such as dislodgement and migration remains a possibility and problem. Although 3D bioprinting has been proved effective as a short term treatment, we don't have enough research to prove that it is completely safe and efficient in the long run.

A major concern that is raised is the right to property and ownership of 3D printed organs.

## 2. Conclusion

3D BIO is a revolutionary technique in medical science which will make the organ transplantation much quicker and relatively safer than the procedures in practice at present. It however has to address many issues before it is adopted as a routine practice of treatment. Cost involved is one such aspect besides social, legal and other statutory regulations which the medical professionals may have to face in implementation. But in introduction of any change or new technology such teething problems are common features. With consistent efforts towards modification and refinement, 3D bio printing will be a normal procedure in organ transplantation replacing the age-old practice of manual surgery involving marathon waiting time apart from risk and physical suffering.

## References


[1] Kirillova, Anastasia, et al. "Bioethical and legal issues in 3D bioprinting." *International Journal of Bioprinting* 6.3 (2020).

[2] https://optn.transplant.hrsa.gov/data/

[3] Lee, Ji Seung, et al. "3D-printable photo curable bioink for cartilage regeneration of tonsil-derived mesenchymal stem cells." Additive Manufacturing 33 (2020): 101136.)

[4] Yakof, Khairul Shah Affendy, et al. "Development of 3D printed heart model for medical training." *Intelligent Manufacturing & Mechatronics*. Springer, Singapore, 2018.109-116.

[5] https://www.cdc.gov/heartdisease/heart_failure.htm

[6] https://optn.transplant.hrsa.gov/data/