

A Review on Artificial Organic Tissue

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Abstract: A new area for research in regenerative medicine called tissue engineering aims to address the issue of end-stage organ failure. Nonetheless, a vascular supply is necessary for complex tissues and organs in order to ensure graft survival and enable bio artificial organ function. Here, we created methods to decellularize porcine small bowl segments and use allogeneic porcine endothelial progenitor cells to repopulate the remaining veins and arterial tubular structures within these matrices. Quantitative 2-[18F] fluoro-2'-desoxy-glucose (FDG) positron emission tomography (PET) and the ensuing immune histological work up were used to characterize cellular adherence and vitality. Insulin-dependent absorption of FDG was mainly seen in the area of the former vascular structures in the generated matrices. A group of assisting techniques known as "bio artificial organ manufacturing technologies" can be applied to the production of human organs using bionic principles. Significant advancements in the creation of various organ manufacturing technologies have been made during the past ten years. The organ manufacturing technologies can be categorized into three main groups based on the level of automation: fully automated; (partially automated; and hand worked (or handmade). Each group has pros and cons for the production of bio artificial organs. Utilizing paired multinozzle three-dimensional printing techniques to automatically assemble human cells and other biomaterials to create unique organ substitutes for failing or defective organs in humans is one of the most promising bio artificial organs manufacturing technologies. This is the first review of modern technologies for manufacturing bio artificial the organs. Patients with ischemia, burn injuries, peripheral artery disease, and cardiovascular disease could benefit from our understanding of and control over the development and differentiation of the human blood vessels. Autologous vessel grafting from patients is a common clinical treatment for vascular related diseases. However, autologous vascular grafting is limited and frequently damaged by disease. Vascular research is making major advances thanks to a tissue engineering approach. The goal of tissue engineering is to replace, improve, or repair biological tissue function in a predictable and controlled way using a multidisciplinary approach.

Keywords: artificial organ, tissue engineering, 3D bio print.

1. Introduction

An artificial organ is a device or tissue created by humans that is inserted or integrated into a human body and connections with living tissue to replicate or replace a natural organ. Particular functions in order to facilitate the patient's easiest possible return to a normal life. Artificial organs could include, for instance, artificial joints and replacement bones used in the replacement of the hip [1].

According to the definition, the gadget cannot be forever linked to a stationary power source or other stationary resources like chemical extraction units or filters. Therefore, a dialysis machine is not an artificial organ, even though it Is an incredibly effective and essential life support system that nearly entirely replaces the functions of a kidney. There are numerous therapeutic uses for the capacity to form, maintain, and control the human vascular system. For the purpose of treating peripheral vascular disease, heart attack, ischemia, and wound repair, scientists have tried to utilize this capacity]. In conditions like ischemic and tissue-engineered constructs, it is necessary to promote vascular growth and repair. Vascular repair is particularly necessary in cardiovascular diseases because lack of oxygen causes cell damage and death in ischemic tissue. In the United States, cardiovascular disease was ranked as the primary cause of death in 2010 and as the leading cause of death worldwide in 2004. It continues to deplete the economy's health-care resources to the cost of billions of dollars, along with other vascular diseases [2], [3].

The development and clinical application of bio artificial organs are precluded by the absence of transplant blood flow. We created methods for producing bio artificial human tissue that naturally exhibits circulation. In order to assess tissue viability following transplantation and blood vessels network thrombogenicity, the tissue was implanted clinically as a proof of concept. Restoring damaged tissue's functionality or replacing a malfunctioning organ is made possible by tissue engineering. Extracellular matrix proteins, growth factors, cells, and biophysical stimuli are frequently used in tissue engineering techniques to repair damaged tissue and create new tissue with a functioning vascular network. Nevertheless, the creation of a stable, well-distributed, and network of connections is still difficult. Moreover, other crucial problems that need to be resolved are anastomoses with host vascular structure during implantation and the long-term viability of the new blood vessel in vivo [4].

In order to address the absence of tissues and organs for transplantation therapy, tissue engineering was first created as an alternative therapy for the treatment of tissue loss or endstage organ failure. It is an example of a biology-driven methodology that combines material technology and biotechnology to engineer biological tissues [3]. Although that has been a lot of advancement in recent years, maintaining the construct's survival both in vitro—during the tissue's

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cultivation and formation and in vivo during implantation remains a significant challenge in the field of developing thick, complex tissues. Since the host's vascularization is insufficient to feed the implant, the construct needs to be vascularized as soon as possible in vivo to ensure its survival and eventual integration [5], [6].

2. Developed Bio Printing

Bio printing is a collection of additive manufacturing (AM) techniques which allow the two-dimensional creation of living tissues and organs through the selective distribution of cells and growth factors, or their combinations. The data acquisition of magnetic resonance imaging (MRI) or computed tomography, or CT of the affected tissue or organ to be manufactured usually initiates the bio printing process workflow. By dispensing cells, hydrogels, or a combination of these, methods for bio printing have been developed and adapted over the last ten years to manufacture tissues or organs. Due to their low cost, pressure assisted systems are the most widely used class of bio printing technique [16].

- Significantly improving the patient's capacity for selfcare (a prosthetic limb, for example).
- Enhancing social interaction (e.g., cochlear implant) in the individual in need.
- Samples of man-made organs.

Example: Heart, kidney, liver, lungs, ovarian cysts, pancreas, heart.

Heart: Restoring damaged tissue's functionality or replacing a malfunctioning organ is made possible by tissue engineering. Extracellular matrix proteins, growth factors, cells, and physical stimuli are frequently used in tissue engineering techniques to repair damaged tissue and create new tissue with a functioning vascular network. Nevertheless, the creation of a stable, well-distributed, and network of connections is still difficult. In addition, other crucial problems that need to be resolved are anastomoses with host vascular tissue during implantation and the long-term viability of the new blood vessel in vivo. Three types of cell sources are available for tissue engineering: pluripotent stem cells (PSCs), adult progenitor and stem cells, and somatic cells. Vascular tissue engineering employs a wide variety of cell types within these categories. In a nutshell, mesenchymal stem cells, PSCs, progenitor cells of endothelial cells (EPCs), ECs, and small and medium-sized are some prevalent cell sources used for vascular constructs [7], [8].

When there is a problem with the heart, its valves, or a different field of the circulatory system, artificial organs related to cardiovascular disease are implanted. The artificial heart is usually used to replace the natural heart permanently or to provide a temporary solution until a heart transplant is possible [9].

Patients with serious coronary artery disease or end-stage heart failure undergo heart transplantation. The most popular method involves implanting a functioning heart—known as an allograft into the patient after the person donating has recently passed away. In the event that heart transplantation is not possible, the artificial heart is usually used to replace the natural heart for good or to provide a temporary solution [19]. A different cardiovascular device that can be implanted is an artificial pacemaker, which is able to completely bypass the natural living cardiac pacemaker when required, augment it periodically (defibrillator mode), or both. Ventricular assist devices, which function as mechanical circulatory devices and can either partially or totally substituted Regenerative medicine approaches that generate entire organs are necessary to offer a transplant of organs substitute. Integrating completely functional vascular structures into the designed construct is a major issue. We created three-dimensional human blood vessels in vitro as a basic approach towards vascularized tissue engineering. In line with the earlier study, once hMSCs were coimplanted with endothelial cells, they established into and performed as pericytes. The primary difficulty in tissue engineering vascular grafts, a new kind of regenerative medicine, is correctly integrating the construct with the host tissue. In light of the long-term functional result and biological and chemical interactions with the host, it is imperative to evaluate the safety of the tissue construct. The immunological response of the tissue created construct is mostly determined by the two components, namely the cell and the scaffold employed [16], [11].



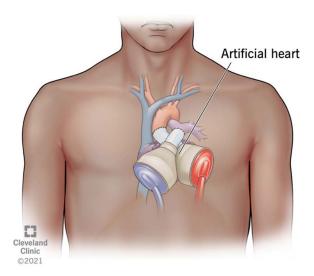


Fig. 1. Artificial heart [27]

Kidney:

The kidneys are intricate organs that constantly filter blood while preserving waste elimination and homeostasis. Hormones like erythropoietin, rennin, and calcium are produced by the kidneys [10].

When someone has advanced renal disease, a kidney transplant is the process of replacing one kidney with another organ. Dead donor kidney transplants are usually divided as Living-donor kidney transplants can be more classified as nonrelated (living-unrelated) or closely linked (living-related) transplants based on whether a biological relationship exists. For decades, efforts have been made to construct a wearable artificial kidney (WAK) that would enable longer and more frequent dialysis sessions; however, the project has failed nearly entirely due to unsolvable technical issues. An already published (10-17) small WAK (Figure 1) meant for continuous wear was examined both in vivo as well as in vitro. This first prototype weighed ten pounds in total. A commercially available, battery-operated micro pump (ambIT, Sorenson, Salt Lake City, UT) is used to anticoagulant blood drawn from a double lumen catheter (red) using heparin from a reservoir (white). The blood is then circulated through the blood channel of the WAK pump (grey) and into the dialyzer (AN-69 0.6 m². Hoopla, France). The twin channel catheter's (blue) vein side receives the returned blood. After an ambIT pump infuses a solution comprising magnesium, calcium, and potassium from another reservoir (black), clean the dialysate (green) enters the dialyzer. Changes to your text are indicated by orange highlights, and you may make more edits by clicking on words and changing them to synonyms. A second ambIT pump extracts a pre-amount of the yellow wasted dialysate into a collection bag. The remaining dialysate is passed through a sequence of yellow sorbent canisters, which are designed and constructed in our lab and include activated charcoal, zirconium phosphate, hydrous zirconium dioxide and urease. A brown reservoir solution containing sodium bicarbonate is infused into the dialysate using an ambIT pump.

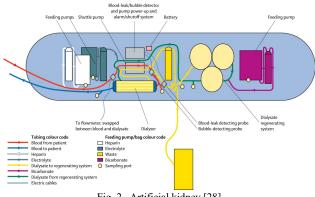


Fig. 2. Artificial kidney [28]

Lungs: Lung transplants may enhance the quality lifestyle and prolong life expectancy for end-stage pulmonary patients, although there are certain risks involved.) The patient's preoperative preparation takes about an hour. It takes four to eight hours to complete a single lung transplant, and between six and twelve hours to complete an additional lung transplant. A record of previous chest surgery could make things more difficult and take more time [18].

Artificial lungs show great potential for achievement in the near future, with some of them operating at nearly full capacity. Extracorporeal membrane oxygen (ECMO), a type of medical device being created by Ann Arbour company MC3, can be used to take significant load of native lungs and heart [14].

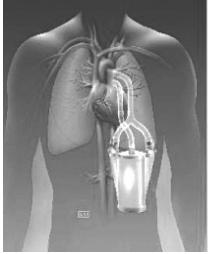
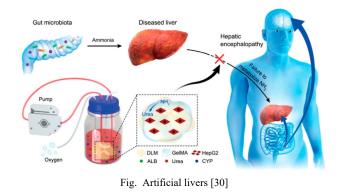


Fig. 3. Artificial lungs [29]

Liver: With a mean weight of 1.4 kg, the liver is the largest organ in the human body. It is made up of a small left lobe and a large right lobe divided by a band of connecting tissue. The metabolism of proteins, fats, and carbohydrates is also mediated by the liver. The process of transplantation involves using a healthy liver allograft to replace a diseased liver. An orthotropic technique is being used. Approved course of treatment for liver disease in its last phase. Today, a transplanted liver is a widely is available [18]. Recognized course of treatment for acute liver failure and end-stage liver disease. The purpose of an artificial liver is to serve as a network of support, permitting the patient's liver to regenerate in the event of liver failure or to maintain liver function until a transplant to replicate the liver's functions, an artificial liver needs a biological component. Although ALF patients are very sick, they can recover through liver regeneration. Extracorporeal liver support could help these individuals. Since portal Hypertension is often the predominant feature of CLF, patients with the condition are more difficult to treat because extracorporeal devices do not alleviate it. Extracorporeal liver support is still needed, however it's less necessary since that [19], [22].



Skin: Skin it is thought that British soldier Walter Yeo was the first to benefit from plastic surgery. Presented in 1917 by Sir Harold Gillies. Recent technologies, such as Avital Medical's autologous spray-on the epidermis other organs. As a result, the creation of well-characterized and genetically

controlled skin models may have significant effects on manufacturers, customers, regulatory bodies, animal welfare organizations, and scientists in addition to doctors and scientists. Standard monolayer (2D) cell cultures do not mimic the physiological architecture of the skin because the cells which make up human skin tissue grow inside an ordered threedimensional (3D) matrix surrounded by cells that surround them [18].

This essential three-dimensional structure is provided by a number of human skin recombinant varieties, often known as artificial the skin, which have now been rebuilt in vitro. The use of these organotypic skin models for various purposes, including as alternatives to animal testing, is considered in this review. In humans, the skin makes up one-tenth of the entire weight, therefore any damage to this organ can have serious repercussions. Healing an injured area can be very hard following surgery, illness, or burns. Any appreciable loss of dermis tends to cause the skin to shrink and become distorted, leaving a scar. Sadly, skin can't just be transplanted like other organs; instead, alternative techniques like grafting or reconstructive surgery are needed. 1 and 2 Although healing by second intention is a popular wound management strategy, it frequently takes several weeks longer to heal and has an uncertain cosmetic outcome [22].

3. Materials and Method

Every day, the culture medium was exchanged, contractility was monitored, and the distribution and viability of the cells were examined under a microscope.

Histopathology: After getting taken out of their silicone wells, technicians were fixed at a pH of 7.4 in three percent formaldehyde.

Force measurement and electrical AMTs were mounted on a container after being cut into strips measuring 10 mm by 1.5 mm. Two Peltier additionally elements that were cooled by water were used to maintain a constant 37°C temperature inside the space.

Stretching the AMT pieces was made possible by the opposite holder's flexibility. Digital recordings of the AMT-based force generation were subsequently used for offline analysis. Grass SD-9 system electrocardiograms were employed to track spontaneous electrical function of AMTs.

Form, Experience, and Solidity:

Trepan blue, which staining of AMTs revealed cellular vitality of 80%–18% prior to 3-dimensional seeding. The collagen-cell mixture in culture continued to gel until day 2.

36 hours after casting, contractions began showing up, and in 87% of technicians, they peaked in frequency and power on day 4. Waves contractions were observed both macroscopically and microscopically within AMTs. Every day, the amount of contractions was recorded, and it varied from 40 to 220 beats per minute. Force measurement:

According to Kraft's and colleagues' instructions, AMTs were sliced into 10 mm by 1.5 mm strips and mounted on a chamber (Figure 1). AMT strips (n = 10) were adhered to the metal holding arms on either side of the chamber, which held culture medium, using History (Braun). Two Pettier elements

with cooling water were used to maintain a constant 37°C temperature within the chamber [18].

A. Advantages

3D printer artificial tissue scaffolds can be used as functional models to study the biological effects of cells with respect to mechanical forces (cell culture), where the cellular growth is affected by scaffold properties such as the surface area porosity typically 50–85% and pore size typically 200.

The goal of tissue engineering is to assemble functional constructs that restore, maintain, or improve damaged tissues or whole organs. Artificial skin and cartilage are examples of engineered tissues that have been approved by the FDA; however, currently they have limited use in human patients.

B. Disadvantages

The use of transplants is associated with immune rejection issues and a restricted supply. To prevent this, immunosuppressant medications are used, but they are expensive to execute require lifetime use, and have serious side effects.

C. Scope

In dentistry, tissue engineering is used. It is used in healing of the heart, brain, skeletal muscles, etc. In vitro meat preparation: synthetic meat.

4. Conclusion

In the field of artificial organs, numerous studies on the principal organ systems have been carried out. Artificial organs that are extracorporeal or surgically placed offer several advantages. The benefits of artificial tissues include the potential for mass production and a decreased risk of rejection of the organ for patients. Even though recent advancements in organ transplant technology have improved survival rates, there is still a waiting list because of the current reliance on human donors, which limits the amount of organs available

References

- Heike Mertisching, T. Horsten Welles, Michal Hofmann Engineering of a vascularized scaffold for artificial tissue and organ generation Biomaterials, volume 26, issue 33, November 2005, pp. 6610-6617.
- [2] J. R. Fuchs et al, Tissue Engineering: A 21st xentu solution to surgical reconstruction Ann Thorac surg 2001.
- [3] Jannat Serbo, Shoron Gerecht, Vascular tissue engineering Scaffold platforms to promote angiogenesis stem cell research and therapy, January 2013.
- [4] Mertisching, Heike, Schanz Hohonna, Generation and Transplantation of autologous vascularized bio artificial h.t. Clinical and Translational research, pp. 203-210, July 2009.
- [5] Md Sarker B. Chen and DJ Schreyer, Experimental approaches to vascularization with in tissue engineering constructs Biomaterials science polymer, volume 26, issue 12, July 2015, pp. 683-734.
- [6] Tamar Kaully, Keren Kaufman-francis, Ayelet Lesman Vascularization the conduitneering part B, volume 15, no 2, March 2009.
- [7] Bramfeld H, Sabra, Centis Scaffold vascularization-A challenge for Three-Dimensional Tissue Engineering, Bentham science publishers, volume 17, no. 33.
- [8] T. Takebe, N. Koike, K. Sekine, Generation of Functional Human vascular Network Transplantation proceeding, volume 44, pp. 1130-1133, May 2012.

- [9] Lyndar. Thomas, Leksmir, Prabha D. Nair, "Tissue Engineered vascular grafts preclinical aspects, International Journal of cardiology, vol. 167, issue 4, August 2013, pp. 091-1100.
- [10] Victor Gura, Alexaanders, Macy, Thomos A. Golper, Technical Break Through in the wearable Artificial kidney (WAK) pub med central, 1441-1448, 2009.
- [11] Mark Crawford, Creating valve Tissue using 3-D bioprinting Advanced manufacturing, May 2013.
- [12] Paul's Malchesky, "Artificial organs Artificial organs 2018 A year review 2019 International centre for Artificial organs and transplantation and wiley periodicals.
- [13] N. Bursac et al, Am phyisiol Cardiac muscle tissue engineering, August 1999.
- [14] Anna Aimar, Augusto Palermo, Bernardo, The role of 3-D printing in medical Applications, March 2019.
- [15] Ventolac, L medical application for 3D printing current and projected uses Pharmacy and theraputics 2014 39 (10)704-711.
- [16] RD Weiser, DA Mickel, Cons of a bioengineering cardiac gift Thoric cardiovascular surg, 119(2000)368-375.
- [17] Tuffs, A Munich surgeons perform world's first Transplantation of whole arms British medical Journal 2009-03-30
- [18] Aadesh Suresh Sose, Dhanashari Santhosh M. Bosale, "A review on artificial organic tissue androgens," IRJMETS, volume 4, issue 11, November 2022.

- [19] Wang X, Tuomi J, Mäkitie AA, Poloheimo K-S, Partanen J, Yliperttula M. The integrations of biomaterials and rapid prototyping techniques for intelligent manufacturing of complex organs in: Lazinica R, editor. Advances in Biomaterials Science and Applications in Biomedicine. Rijeka, Croatia: InTech; 2013;437–463.
- [20] Carla A, Brohem Laura B., Artificial skin in perspective concepts and application Pigment cell and melanoma research, volume 24, issue 1, pp. 35-50.
- [21] Wang X, Yan Y, Zhang R. Rapid prototyping as tool for manufacturing bioartificial livers. Trends Biotechnol. 2007;25(11):505–513.
- [22] Marcia Resmos. E Silva, New dressing incl tissue engineering living skin, volume 17, issue 6, pp. 715-723.
- [23] Wang X, Yan Y, Zhang R. Recent trends and challenges in complex organ manufacturing. Tissue Eng Part B Rev. 2010;16(2):189–197.
- [24] Norman L. Sussman James H. Kelly Artificial kidney clinical gastro entology and hepatology, volume 12, issue 9, pp. 1439-1442, Sept. 2014.
- [25] Wang X. Intelligent free form manufacturing of complex organs. Artif. Organs. 2012;36(11):951–961.
- [26] Liu L, Wang X. Creation of a vascular system for complex organ manufacturing. Int J Bioprinting, 1(1):77–86, 2015.
- [27] Total artificial heart, Cleveland clinic.
- [28] Artificial kidney region, AJKD BLOG official blog.