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An Insight Into 3D Bioprinting and its Potential to Combat Various Diseases

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Abstract

The existence of various organs in the human body and their ability to synchronise with one another in order to perform diverse functions is essential for the proper functioning of the body. However, these organs may get affected by various diseases caused due to pathogens and mutations or may even get affected by hereditary diseases. Many of these diseases damage the organs and they may even be fatal to the person. In such cases it becomes essential to transplant healthy organs into the affected individual. These organs can be transplanted from a donor, but this process has its own drawbacks. For this purpose, the novel approach involving the 3D bioprinting of organs for transplantation have paved the way to overcome the drawbacks. Three dimensional organs can be developed by allowing the 3D bioprinter to deposit layers of cells on scaffolds to develop tissues and eventually the organs. It is necessary to ensure that the scaffold is capable of providing the right microenvironment and therefore supporting the type of tissue being cultured to develop the organ. Another important factor is the proper vascularisation of the organ being developed so that it can be efficiently supplied with blood containing nutrients for its proper growth. Keeping these factors in mind 3D bioprinting is constantly evolving as an efficient process of producing organs for transplantation in patients with severe diseases. This review gives a better understanding of the process of 3D bioprinting and its importance in the modern world.

Keywords: Biomaterials, Tissue Engineering, 3D Printing, Cell Culture.

1. Introduction

All organisms found in the present world have originated from single cells. These single cells combined to form tissues which in turn led to the development of organs and organ systems in living beings. For the proper functioning of the organism every organ of the body plays an equally important and diverse role. The brain is the most important organ which coordinates the function of the other organs while the proper functioning of the other organs results in the proper nourishment of the brain. Blood is the body fluid found in human beings which supplies nutrients obtained through digestion to the brain and all other parts of the body. The heart is responsible for the pumping of the blood throughout the body. Blood also carries oxygen produced by the lungs without which energy cannot be produced in the body efficiently. Organs such as the kidney play an important role in filtering out waste products from blood. Another important organ is the liver which apart from its role in digestion to produce nutrients for all other organs is also responsible for the detoxification of the body. There are many more organs present in the human body which perform various essential functions required for the proper maintenance of the body. The most important point to be understood from the function of the organs is the interconnectivity between each organ in the body. Organs are susceptible to various diseases caused by pathogens. If a single organ is affected by any disease it would affect every other organ in the body due to the interconnectivity between the organs and this would lead to a disruption in the balance maintained by the body.

2. Common Diseases of some body organs

Each and every organ of our body can be affected due to several pathogens, due to heredity or mutation. Organs of the different systems of human body can be affected by various disorders. Diseases of the digestive system involve many organs such as Intestine, Stomach, Liver, Gallbladder, and Pancreas and include diseases like 'Acid reflux of stomach' which is also called as Gastroesophageal reflux disease (GERD), Chronic diarrhoea, Constipation, Ulcers, Haemorrhoids, Hepatitis of liver, Liver cancer etc. [1] Also, if the respiratory system of our body is affected then it can cause some chronic diseases of heart and lungs like Asthma, Chronic Obstructive Pulmonary Disease (COPD), Bronchitis, Lung cancer, Cystic fibrosis, Pneumonia, Emphysema and Heart valve disease, Cardiac failure, Arrhythmia. Throat cancer is also a respiratory disease. When different blood cells are affected, they cause Iron deficiency anaemia, Thalassemia, Leukaemia or Blood cancer, Sickle cell anaemia, Lymphoma, Multiple myeloma, Myelodyplastic syndrome, Thrombocytopenia or low platelet count like common diseases. Nephrosis, Kidney stone, Diabetes, Glomerulonephritis (inflammation of glomeruli), Hydronephrosis and Pancreatic diseases like Acute pancreatitis, Reptic ulcer, Acute cholecystitis are some common disorders of our urinary system. The major part of our body is the nervous system. In the introduction, it was told that all the corresponding organs and their functions are directly connected to the brain. So, the disorders of the brain functions can also cause critical problems to the other organs of the system. There are some vital diseases of central nervous system. Those are commonly Brain cancer, Epilepsy, Multiple sclerosis, Alzheimer's, Parkinson's, Huntington's diseases. Autoimmune diseases such as Rheumatoid arthritis are the common disorders of peripheral nervous system while on the other hand, Botulism, Muscular dystrophy, Fibromyalgia, Tendonitis, Rhabdomyolysis are some muscle disorders. [2-7] Other than these common problems, various body parts can be affected individually like ears, eyes, reproductive systems, thyroid etc. So, among all of these chronic diseases majority them are harmful and sometimes fatal. In order to cure some of those fatal diseases of specific organs, new and stress-free body organs are needed to be implanted to the patient's body. However, there are some criteria needed for the donor organs like they should be susceptible and compatible to the donor body but all the time these criteria cannot be fulfilled. So, to get rid of this problem new age scientists have come up with the ideas of artificial implants instead of donor body parts, which are specially customized for patients. The process to make these bio-models is called 3D bioprinting. It is used to generate accurate replicas of patient's body part.

3. 3D Printing

Bioprinting uses 3D printers to fabricate a three-dimensional structure of biological materials, from cells, tissues to organs. The printing technology started from two-dimensional (2D) printing which has advanced to the modern day three-dimensional (3D) printing in which materials are distributed through precise layer-by-layer positioning to form the desired 3D structure. It is a manufacturing process in which the desired materials are fabricated by joining or depositing materials—such as plastic, metal, ceramics, powders, liquids, and even living cells—in layers to produce a 3D object, this process is often known as additive manufacturing (AM) or rapid prototyping (RP). The purpose of 3D printing is to perform biomimicry by mimicking the tissues and organs which can be later transplanted in the human body. There are numerous printing processes, which vary in its usage with respect to its speed, resolution and materials. [8-9]

3D bioprinting is done based on 3 main categories: biomimicry, autonomous self-assembly and mini-tissue building blocks. Biomimicry can be achieved by reproducing specific cellular functional components of tissue. There are various factors which play a pivotal role in synthesis of a biomaterial scaffold like the supporting cells, microniche, various growth factors and extracellular matrix as well as the biological forces. Autonomous self-assembly uses embryonic organ development as a guide. A developing tissue produces its own ECM components, along with various signal transduction pathways and patterning to yield its desired biological micro-environment. This process mainly relies on the cell as the primary driver of histogenesis, directing towards the composition, locali-zation, functional and structural properties of the tissue. Mini-tissue building blocks are the smallest structural and functional unit of a tissue. Mini-tissues can be fabricated and assembled to form larger constructs by designing or self-assembly or a combination of both. There are two ways for self-assembly synthesis: firstly, self-assembling cell spheres, which are similar to mini-tissues are assembled into a macro-tissue using biomimicry and secondly, high-resolution reproductions of a tissue unit are designed with high-accuracy and then allowed to self-assemble into a functional macro-tissue. The 3D printed scaffold is then transplanted, or in some cases after a period of *in vitro* maturation, is reserved for *in vitro* analysis. [10]

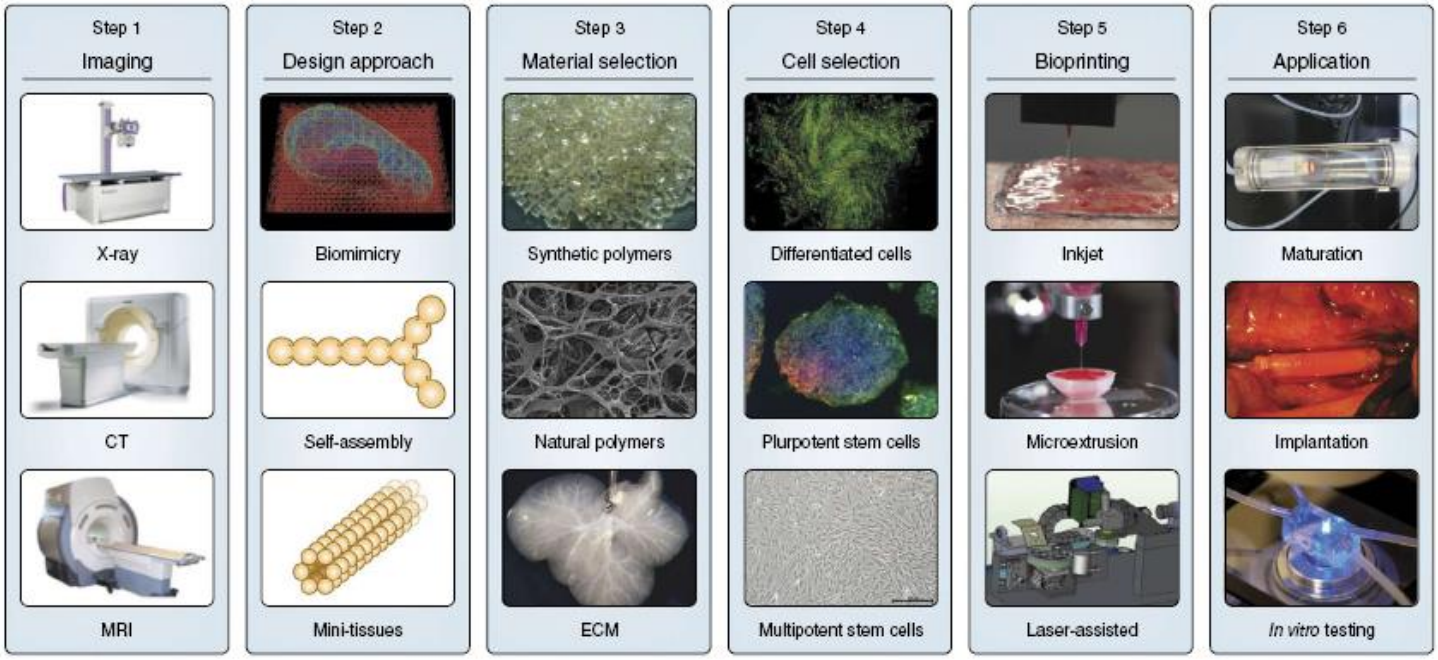

Fig 1: A typical process for bioprinting 3D tissues. [10]

Further research on the mentioned processes and different strategies is required to print a complex 3D biological structure with multiple functional, structural and mechanical components while maintaining all the different properties.

4. Determining factors of 3D bioprinted composite scaffolds in organogenesis

The process of 3D bioprinting comprises of precise deposition of cells, growth factors and construction of scaffolds to make tissue models. The formation of organs requires appropriate intercellular signalling. Certain surface parameters of scaffolds such as topography, stiffness and porosity play important roles in transducing signals [11]. Proper adhesion to substrate generates signals regulating several features including migration, proliferation, and differentiation. The stiffness of substrate regulates effects on cell lineage specification by exerting mechanical forces at focal adhesions [12]. For better longevity and functionality of printed architectures, vascularization must be studied further. In general, the ability to create multilayered tissues, preservation of cellular functions has been demonstrated as progression in bioprinting of muscular hollow organs [13]. The excitable, contractile phenotype of smooth muscle cells must also be addressed [14]. The death of cells residing at the core of scaffolds is caused due to the insufficient oxygen transport in scaffolds. [15]. Major cause of cell death due to the absence of oxygen is associated with improper vascularisation [16]. This signifies the importance of parameters such as pore size, shape, and interconnectivity in the 3D scaffold, which regulates the growth of new blood vessels and oxygen transportation in the limit of the diffusion length of oxygen [17]. Bioprinting of more physiologically relevant organ implants is needed to facilitate the manufacturing of transplantable functional replicas of organs. However, to print efficient 3D constructs with functional transplantable properties requires higher mechanical strength of hydrogels which is lacking in various outputs. Hence, blending of various techniques is essential.

5. Conclusion

The 3D bioprinting technology has entrusted the field of regenerative medicine with immense possibilities. Various biopolymers used in hydrogel assembly have shown the potential in eliminating drawbacks such as immunogenicity, lack of biodegradability. However, it still has its limitations. It is a rising trend to combine multiple 3D printing techniques together to fabricate a single model. Application of electric, magnetic fields during printing process can assist in the precise orientation, alignment, distribution and assembly of functional nanoparticles within the 3D printed models. The future of 3D bioprinting lies in the development of a more robust bioink that can match the biological and physical properties of the tissue and allow the printing of cells with maximum viability. The use of sacrificial bioinks may result in fabrication of blood vessels and can help in mimicking the host specific tissue architecture. Additionally, computer aided designs can be used to print *in vitro* models. Since its inception 3D bioprinting has made promising progress in overcoming tissue engineering challenges. The technology has proved itself to be worthy of further research. Further multidisciplinary expertise is needed to answer its entire clinical potential.

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