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A Survey on Role of 3D Printing in Medical Field

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Abstract: *In the past, 3D printing was used mainly by major manufacturers that could afford expensive printers and materials. Over the years, 3D printing technology has evolved and become more affordable, making it a viable option for a wide variety of industries. Medical professionals, in particular, are beginning to use 3D printing to improve their practices and offer more customized and affordable healthcare options for their patients. Healthcare is one industry in which 3D printing has made a lasting impact. In 2018, the medical 3D printing market was valued at $973 million and is expected to grow to almost $3.7 billion by 2026. Medical applications for 3D printing are vast and will likely change the industry forever. The worldwide demand for the organ replacement or tissue regeneration is increasing steadily. The advancements in tissue engineering and regenerative medicine have made it possible to regenerate such damaged organs or tissues into functional organ or tissue with the help of 3D bioprinting. The main component of the 3D bioprinting is the bioink, which is crucial for the development of functional organs or tissue structures. The bioinks used in 3D printing technology require so many properties which are vital and need to be considered during the selection. Combination of different methods and enhancements in properties are required to develop more successful bioinks for the 3D printing of organs or tissue structures.*

Keywords: 3D Printing.

I. INTRODUCTION

3D printing or additive manufacturing (AM) is a process for making a 3D object of any shape from a 3D model or other electronic data sources through additive processes in which successive layers of material are laid down under computer controls. [1]Hideo Kodama of Nayoga Municipal Industrial Research Institute is generally regarded to have printed the first solid object from a digital design. However, the credit for the first 3D printer generally goes to Charles Hull, who in 1984 designed it while working for the company he founded, 3D Systems Corp. Charles a Hull was a pioneer of the solid imaging process known as stereolithography and the STL (stereolithographic) file format which is still the most widely used format used today in 3D printing. He is also regarded to have started commercial rapid prototyping that was concurrent with his development of 3D printing. He initially used photopolymers heated by ultraviolet light to achieve the melting and solidification effect. [2]Since 1984, when the first 3D printer was designed and realized by Charles W. Hull from 3D Systems Corp., the technology has evolved and these machines have become more and more useful, while their price points lowered, thus becoming more affordable.

II. 3D-BIOPRINTING

Bioprinting is a subcategory of additive manufacturing (AM), also known as three-dimensional (3D) printing. It is defined as the printing of structures using viable cells, biomaterials and biological molecules. Bioprinting must produce scaffolds with a suitable microarchitecture to provide Materials mechanical stability and promote cell in growth whilst also considering the impact of manufacture on cell viability; for instance, chemical cytotoxicity caused by the use of solvents or pressure-induced apoptotic effect produced during the extrusion of material. A significant benefit of bioprinting is that it prevents homogeneity issues that accompany post-fabrication cell seeding, as cell placement is included during fabrication.

The advantage of homogeneously distributed cell-laden scaffolds has been demonstrated by faster integration with the host tissue, lower risk of rejection and most importantly, uniform tissue growth in vivo. Conventional cell seeding techniques are either static or dynamic, and while the latter one results in better seeding efficiency and cell penetration into the scaffold, it is known affect cell morphology. Immediate vascularization of the implanted scaffolds is highly critical. With proper vascularization, the scaffolds are provided with an influx of oxygen/nutrients and an efflux of carbon dioxide/by-products; preventing core necrosis. Vascularization also supports the implants with remodelling .

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Bioprinting techniques have been employed to fabricate microvascular-like structures and have the potential to position endothelial cells within the 3D structures as a prevascularization step prior to implantation.

III. COMMON TYPES OF 3D BIOPRINTERS

Several kinds of additive manufacturing techniques have been developed for selective patterning of cells and biomaterials for fabrication of viable tissue constructs such as inkjet based 3D bioprinting (Cuiand Boland, 2009), extrusion based 3D bioprinting (Jones, 2012), laser assisted 3D bioprinting (Keriquel et al., 2017), and stereolithographic based 3D bioprinting (Dean et al., 2012) etc. Each of these 3D bioprinting techniques has been summarized in the following sections:

3.1 Inkjet Based 3D Bioprinting

This method employs the use of "bioink," which is simply a lowviscosity suspension biomaterial along with viable cells etc. that can be deposited over a "bio paper" such as hydrogel substrate, culture dish or a polymer construct etc. This AM technique is a non-contact printing technique, where the printing takes place in a digitally controlled pattern.

3.2 Extrusion Based 3D Bioprinting

Extrusion based bioprinting can be done by Direct ink writing (DIW) or pressure-assisted bioprinting methods as shown in Figure. Direct ink writing is a material extrusion process in which the apparatus continuously extrudes material out of the nozzle, generating 3D architectures layer-by-layer. Suitable materials for DIW should possess specific rheological properties, which enable easy printability. The material should be shear thinning to enable extrusion out of the printing nozzle. It should also possess a shear yield stress. To induce flow, a shear stress above the yield stress of the resin is applied. Subsequently, the shear stress is released, and the resin recovers its rigidity when placed on a substrate. Polymer resins are commonly blended with fillers, e.g., silica particles or nano clay to achieve desired rheological properties. The fillers induce shear thinning flow behavior and at optimal resin/filler compositions they can afford a material which possesses a shear yield stress.

3.2 Laser Assisted 3D Bioprinting or Laser Induced Forward Transfer

A pulsed laser beam is utilized in this process for deposition of bio-ink including cells onto a substrate. Utilization of laser for deposition of materials provides a non-contact direct writing process for 3D printing. As is visible in Figure, there are three key elements to Laser Assisted 3D Bioprinting : a pulsed laser source, a ribbon coated with bio-ink and a receiving substrate on which the bio-ink is to be deposited. UV lasers or near UV wavelength lasers with nanosecond pulse wavelength are used as the energy source. The laser serves to cause volatilization of the heat-sensitive bio-ink from the "ribbon."

IV. PROCESS METHODOLGY

With the ongoing progress in the development of organ printing technology there is a growing demand in digitized version of human anatomy or some sort of organ informatics. In this context great interest represent virtual human projects which allow to reconstruct virtual human organs. The first virtual human was funded by NIH and developed in USA several decades ago. Now there are Chinese, South Korean, Japanese virtual human projects. Most advanced attempts in building virtual human and logical extension of this concept have been recently made by group of committed researchers from UK and New Zealand.

SI . NO	PAPER PUBLISHED	REMARK	YEAR OF PUBLISHED
1	Current developments in 3D-bioprinting for tissue and organ regeneration	The use of 3D-bioprinting could potentially lead to personalised treatment for patients	2020
2	Organ Printing as an information Technology	The absence of optimal softwares eventually could be main part for further successful development.	2015

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3	The Role of 3D Printing in Medical Applications: A State of the Art	3D printing has introduced many advantages and possibilities in the medical field. Each specific case in which 3D printing has found application shown in this analysis is a demonstration of this.	2019

Table 1: Research Paper Published

The another very ambitious approach for application of information technology in the biomaterial science was named materiomics. There are already published several reviews and at least two books on this topic. The main promise of materiomics to develop high throughput screening assays for rapid testing and screening novel biomaterials. It could be potentially very important for development of bioprintable hydrogels and material for bioprintable solid scaffolds. In recent review it was written materiomics sets the stage for a transformative change in the approach to biomaterials research to enable the design of tailored and functional materials for a variety of properties in fields as diverse as tissue engineering, disease diagnosis and de novo materials design, by combining powerful computational modeling and screening with advanced experimental techniques.

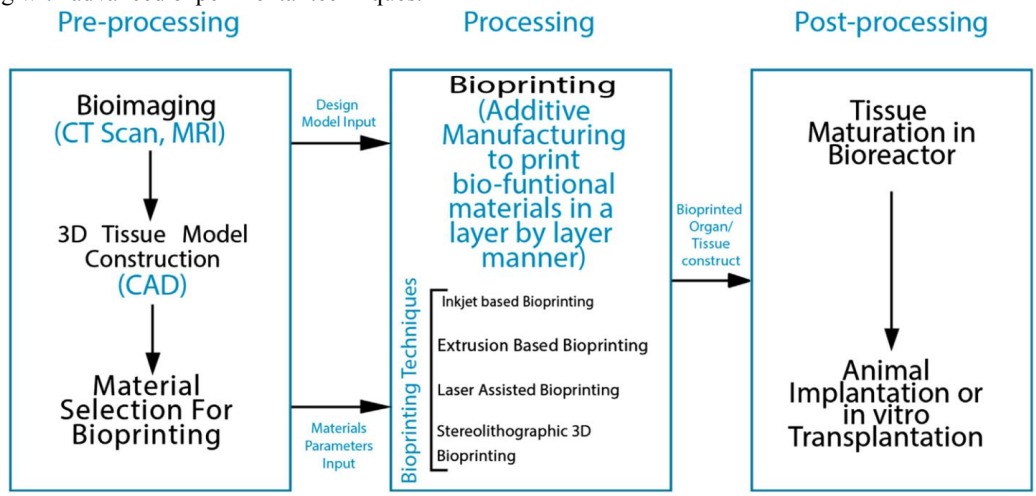

Fig 1: Flow-diagram for process of 3D Bioprinting

4.1 Organ Pre-Processing

Before building an organ, we must have a blueprint in the form of a computer-aided design of the designed organ. We might define this as computer compatible precise spatial information about the localization of cells in the 3D organ or, in other words, the "address" of each cellular or extracellular component of the tissue or organ that we want to built. There are several ways in which we can get the information about the anatomy, histological structure, composition and topology of human organs necessary for computer-aided design of printed organs. Recent progress in clinical bioimaging and ultrasound make it possible for us to discern the gross anatomical characteristics of organs even while they are still inside their owner. The advantage of this approach lies in its the capacity to demonstrate the patient's specific anatomical information as well that of his organs, not to mention the fact that we do not need to remove the individual's organ in order to examine it. However, resolution of this technique has not yet reached the histological and cellular level. More importantly, tissue composition and cell redistribution cannot be precisely identified as yet. In short, this method is not yet refined enough to be utilized in the process of organ printing. A second approach is based on computer-aided reconstruction of a histological section. This method provides a high level of resolution and information about the size and shape of the organ, as well as details about its composition. The problem inherent in this method lies in the fact that human organs are available for this sort of inspection only after death, and are hence subject to change and distortion. Other limitations of histological approach are that it is enormously labor-intensive, time consuming and is not patient specific. However, considering that organs have a polymeric structure and consist of repeating structural functional units, one can reconstruct only one typical organ unit and then assemble the whole organ in silico by adding a reconstructed unit based on the gross anatomical structure or by filling the available space.

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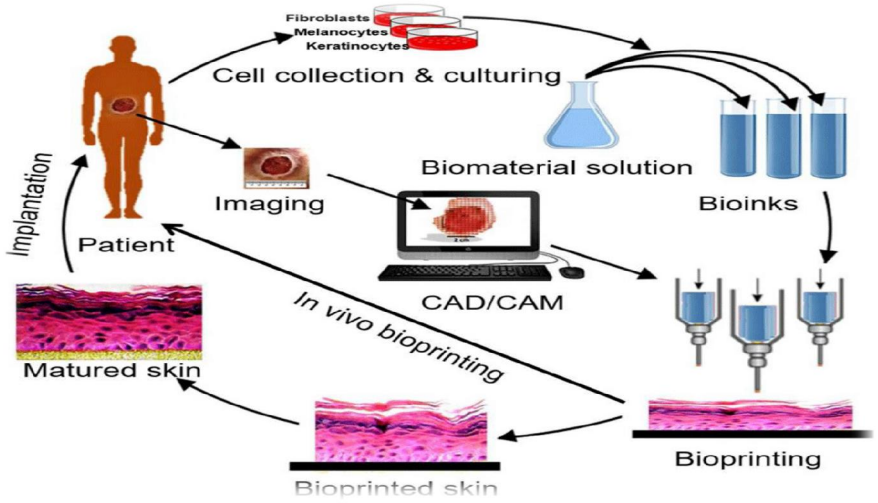

Fig 2: The process of 3d-bioprinting

4.2 Organ Printing: Processing

On of the most comprehensive approach to modeling organ printing technology and application of modern information technology tools is a development of virtual organ biofabrication line. The development of virtual organ biofabrication line is another interesting approach and logical and advanced way for industrial and clinical translation of emerging organ printing technology. Virtual organ biofabrication line must combine all possible visual information about machines, devices and processes through an interactive computer system capable to generate real-time animation and data and also and capable to provide a visit by virtual reality to the organ biofabrication plant as an avatar to visually, observe and virtually interact with all components of organ biofabrication line.

4.3 Organ Printing: Post-Processing:

Post-processing starts immediately after finishing bioprinting process (processing). The main task of designing post-processing is ensuring viability and survival of 3D bioprinted organ construct, fusion tissue spheroids into integrated constructs and its accelerated maturation. Modeling post-processing will enable non-destructive and noninvasive biomonitoring viability, integration and maturation of bioprinted organ constructs. Predictive mathematical modeling and computer simulation of tissue spheroids fusion in bioprinted construct is one of the most interesting problem which already attracted attention of several groups of researchers.

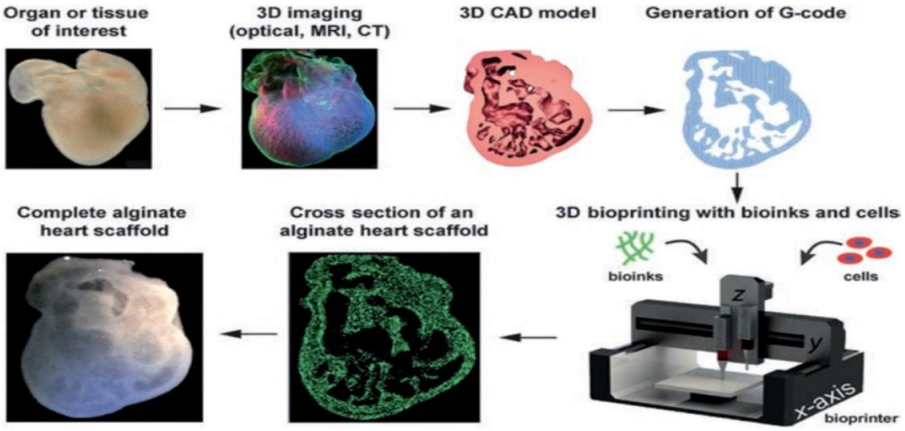

Fig 5.3. Three-dimensional bioprinting: spatial arrangement of cells, molecules, and growth factors within a confined 3D structure based on an alginate hydrogel bioink, using a computer-aided design for the production of tissues and whole organs.

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The initial step is a computer simulation and virtual representation of major biofabrication equipment such as cell sorters, robotic tissue spheroid biofabricator, robotic bioprinter and perfusion bioreactor. Second step is virtual placing biofabrication equipment into virtual building based according to logics of biofabrication process and restrictions imposed by related regulatory requirement. Finally, sequential steps of bioprocessing and organ bioassembly processes have been simulated on microlevel and seamlessly integrated with correspondent virtual biofabrication equipment. The resulted virtual biofabrication line should be additionally optimized and integrated. The virtual organ biofabrication line will be a needed step toward development of real organ biofabrication industrial plant. Thus, computer-aided design, computer simulation, mathematical modeling, virtual reality methods and informational technologies are essential tools for developing organ printing technologies and industrial scale biofabrication process engineering.

V. CONCLUSION

Additive manufacturing in the context of bioprinting offers a huge potential in the field of tissue and organ regeneration. It enables the fabrication of physiologically-relevant tissue with better and consistent functional outcomes in patients. Such techniques are advantageous over autografting or allografting considering autologous grafts cause unnecessary stress on the patient and there is an acute shortage of allograft donors. 3D bioprinting presents a unique opportunity in that it builds the tissue from bottom up and as such the risk of immunological graft rejection is not present all the while mitigating the issues related to donor scarcity. The use of 3D bioprinting could potentially lead to a personalized treatment for the patient which translates to better clinical outcomes as well as is aesthetically pleasing. However, despite all the advances that have been made in the field, there are still many challenges with regards to the biocompatibility and integration of the printed construct with the body.

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