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An Overview of Inkjet Bioprinting

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Abstract

Three dimensional printing has remarkable potential as a fabrication method in creating scaffolds for tissue engineering. Recent advances in medical field have enabled 3D printing of biocompatible materials, cells and supporting components into complex 3D functional living tissues. 3D bioprinting is being applied to regenerative medicine to address the necessity for tissues and organs suitable for transplantation. 3D bioprinting involves creating scaffolds layer-by-layer by depositing a bioink which is a mixture of cells, biocompatible polymers and biomolecules. The major component of the 3D bioprinting is the bioink, which is crucial for the development of functional organs or tissue structures. The bio-inks used in 3D bioprinting technology require so many properties which are essential and need to be considered during the selection. The bio-ink maintains a stable cell suspension, preventing the settling and aggregation of cells that usually impedes cell printing, whilst meeting the stringent fluid property requirements needed to enable printing even from many-nozzle commercial inkjet print heads.

Keywords**:** *Additive Manufacturing, Scaffolds, 3D Bioprinting, Tissue Engineering, Bio-inks, Biomolecules.*

Introduction

Tissue engineering is an integrative branch which is mainly focused on two major areas: (i) developing new technique to repair, regenerate, and replace damaged tissues and organs and (ii) creating in vitro tissue models to better understand tissue development, disease development, and to develop screen drugs. Among the currently used 3D printing technologies like fused deposition modeling (FDM), direct ink writing (DIW), inkjet bioprinting, selective laser sintering (SLS), direct metal laser sintering(DMLS), stereolithography (SLA) and laser-induced forward transfer (LIFT), the DIW and inkjet bioprinting are always preferred for 3D printing of living cells [1]. The suite of bioprinting techniques that allow the controlled deposition of living cells has expanded to include extrusion printing and laser printing, as well as drop-on-demand approaches like microvalve printing and inkjet printing.

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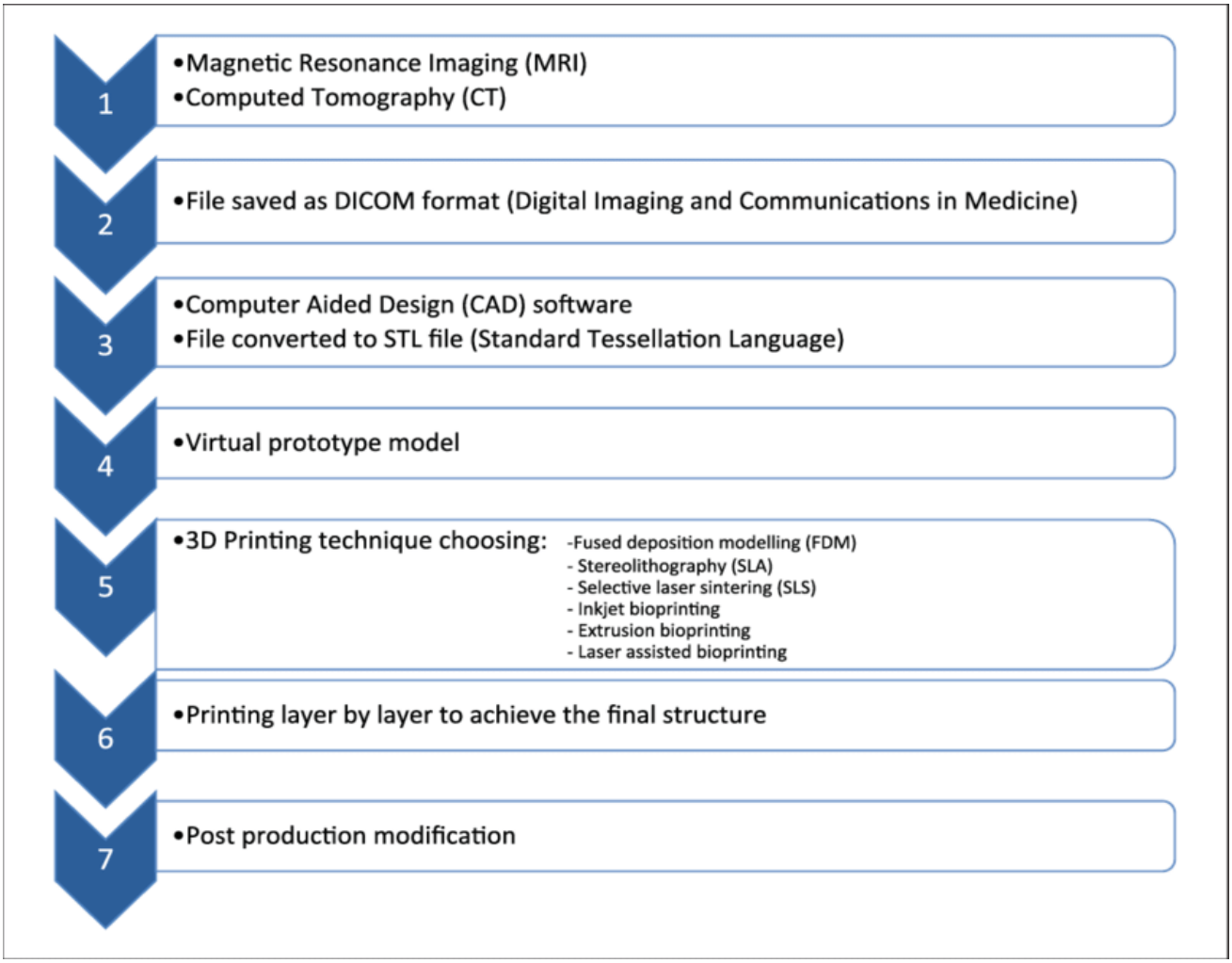

The choice of the biomaterial is dependent on the target tissue. In recent research, much focus was towards engineering biodegradable biomaterials. Depending on the chemical composition, biomaterials are classified into ceramics, polymers, and composites. The ceramics class of biomaterials has major components of inorganic metal compounds and/or calcium salts [2,3]. These biomaterials have been primarily used in orthodental applications. Polymers are used in soft tissue engineering because of their equivalency with connective tissues. The composite class of biomaterials is blends of ceramics and polymers. These several composites have applications in orthopedic and dental TE. In the continuing quest to engineer functional tissues and organs, bioprinting could allow the fabrication of multi-cellular constructs where cell-cell and cell-material interactions mimic the physiological environment and where cellular responses to stimuli are more reflective than that found in vivo. Drop-on-demand techniques are attractive due to their relative simplicity and capability for precise non-contact deposition, yet have been hindered by some critical limitations [4]. Cell settling and aggregation within printer reservoirs restricts the working of nozzles and leads to non-uniform cell distribution. Inkjet printing provides additional challenges as the ink must fulfill stringent fluid property requirements such as viscosity and surface tension for efficient deposition.

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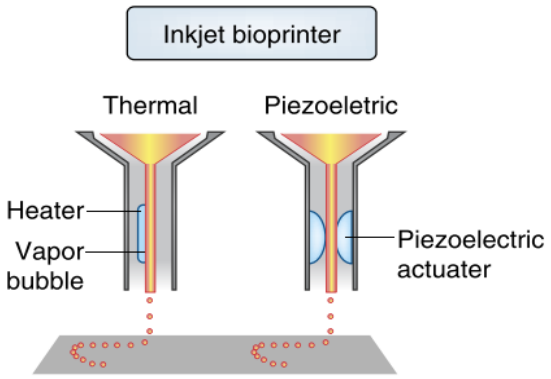
Theory

3D bioprinting process should be relatively mild and cell friendly as it is required to allow cell printing. This requirement limits the number of 3D printing techniques that are suitable for bioprinting.



Processes involved in Inkjet bioprinting [5]

Requirements of bioink for 3D bioprinting:

For developing tissue/organ structures, two important categories of bioink materials are used in 3D bioprinting. One of this is the cell-scaffold based approach and the other one is a scaffold-free cell-based approach. In the first method, the bioink consists of biomaterial and live cells, which are printed to develop 3D tissue structures. Here, the biodegradation of scaffold biomaterial takes place, and the encapsulated live cells grow and occupy the space to form predesigned tissue structures [6]. But, in the scaffold-free cell-based method, the living cells are printed directly in a process which resembles the normal embryonic growth.

Need for Scaffolds and Tissue Engineering:

Tissue engineering offers an alternative method to resolve the issue of ever increasing need for organ transplants. Data from the Organ Procurement and Transplant Network (OPTN) indicates that as of January 2018, over 115,000 patients needed organ transplant, while only 34,769 transplants were performed [7]. Using approaches from TE and RM, the gap between the number of patients awaiting transplants and donors available can be filled. In degenerative diseases affecting organs, such as the kidneys, liver, pancreas, and heart, the organs fail completely and organ transplant from another human is the only available treatment one can get. Patients may or may not have the time to wait until they receive an organ donation, leading to death of 20 patients every. The aim of TE is to create functional organs from patients' own cells [8].

Properties of Biomaterials That Make Them Suitable for 3D Printing:

The principle of bioprinting is that the biomaterial which is in the form of liquid, is printed layer by layer until the whole object is fabricated. Immediately after the biomaterial in liquid form leaves the print head, the biomaterial is solidified to retain the shape [9]. This method of converting from sol to gel is the key for a biomaterial to be adapted in bioprinting. Polymers and composites are most widely used because they can be polymerized using various methods, rendering them "3D-printable". Factors that are important to make biomaterials suitable for 3D printing processes are rheological properties and the

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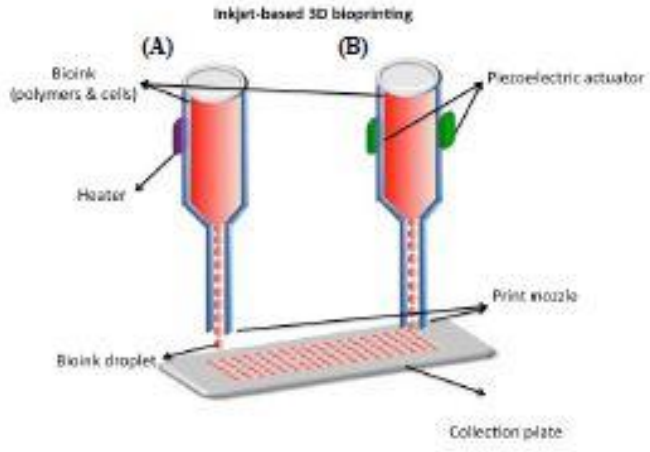
method of crosslinking [10-12]. These properties are, again, dependent on the method of bioprinting, i.e., requirements for bioinks used in inkjet printing are different from extrusion-based bioprinting.

Methodology

Inkjet-based Bioprinting:

Inkjet-based bioprinting initially employed a commercial printer to spray cells (Figure 3). Inkjet bioprinters, known as droplet-based bioprinters, use thermal or acoustic force to eject liquid drops onto a substrate and build constructs layer-by-layer. In thermal inkjet bioprinting, "bioink" droplets are generated by electrically heating the print head to force cells in the liquid drops out of nozzle by increasing pressure. Bioinks made of cells, scaffold materials and growth factors can be deposited accurately through controlling the droplet size and deposition rate. During the inkjet bioprinting process, the heating temperature can reach approximate 300 ^{0}C [17, 18].



Schematic diagram of inkjet-based bioprinting

Since the early twentieth century, inkjet bioprinting technology has experienced rapidly development. It is the earliest use of biological printing technology. It adopts non-contact printing technology using ink (cells or biological materials) to realize organ fabrication based on the digital models of tissues and organs in computer. The technology could be mainly divided into two types: thermal inkjet printing and piezoelectric inkjet printing. Thermal inkjet printing technology mainly uses heating element to spray droplets. The element is used to heat the adjacent area of ink rapidly, so that the ink in the pressure cavity will be gasified into bubbles. The pressure generated from gasification makes a part of the droplet overcome surface tension and be squeezed out of the extrusion nozzle; when voltage is released, bioink cools quickly and returns back into the pressure chamber [19]. The droplets can be squeezed continuously by applying and releasing voltage repeatedly. Piezoelectric inkjet printing technology mainly uses piezoelectric materials to spray droplets. When voltage is applied on both ends of the piezoelectric element, piezoelectric element bends and droplet near the nozzle is squeezed out. When voltage is released, the piezoelectric element restores back to its original shape. In this way it can achieve continuous extrusion drops through applying and releasing voltage repeatedly. Cui et al. used inkjet printing technology to repair articular cartilage of human body, which was proved to be potential to lead tissue to regenerate efficiently [20]. The system was by means of controlling the process parameters such as cell concentration, volume and precision of droplet, nozzle diameter and average diameter of printing

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cells to print cells and biological materials. Weiss et al. developed an inkjet printing platform with multi-nozzles to manufacture composite structures. A variety of growth factors, such as fibrinogen and thrombin, together with cells were printed precisely into cell skull defect of mice [21]. They showed the feasibility of *in-situ* printing; however, due to the complexity of this process, it was not suitable for practical use. Inkjet printing technology has been applied earlier so it is relatively mature, and its main advantages include: (1) Similar to color printing, inkjet printing can integrate multiple nozzles to synchronously print cells, growth factors, biological materials together and is capable of building heterogeneous tissues and organs; (2) inkjet printing is a non-contact way of bio-fabrication. Nozzles and the culture medium are separate, so possible cross-contamination in the printing process can be prevented. It can be printed on solid, hydrogels and liquid interfaces. And there is no additional requirement for printing graphic smoothness, which is advantageous to the *in situ* print; (3) inkjet printing is in high speed and high efficiency, which is beneficial to solve the organ printing-related problems such as longer production time and biological activity decline, and is suitable for large parts manufacturing; (4) the droplet volume is small, similar to a single body cell size, so that precise operation can be realized to the individual cell. Although there are many research achievements with inkjet printing technology, still there are some limitations: (1)Because the nozzle diameter is too small, the cells are more likely to precipitate and accumulate, which limits the printing density (<5×106 cells/ml); (2) during the thermal printing process the nozzle is heated to a very high temperature, so it would be harmful to cells, and at the same time the existence of shear stress would also reduce the cellular activities; (3) the fusion between droplets is not easy, and the shape of the droplets cannot be accurately controlled. The structural integrity of printing is also a problem need to be solved when using inkjet printing [22].

Conclusion

3D bioprinting has the robust capabilities to produce tissue/ organ structures with ease; however, it needs further enhancements in different areas such as bio-inks, commercialization of the 3D printed products, etc.

This method can facilitate to develop more complex patient specific 3D structures for urgent medical needs. It has numerous advantages like design flexibility, printing modes, use of specific cell lines, control of biodegradation and mechanical properties, etc.

The development of ideal bioink is still in progress and owing to the significant contributions from around the world, it may be possible to use this technology for commercial applications in the future.

Natural biopolymers have good biocompatibility, but usually perform poorer at mechanical properties, which make it achieve the required formability as a single printed material. By contrast, synthetic biopolymers generally have good formability with poor biocompatibility.

1) Bioprinting literature has grown exceptionally fast and developed concomitantly on several topics, including biomedical engineering. Recent fronts had emerged through the last decade, such as “hydrogels” and “stem cells”.

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References

1) Daniel Medeiros, Biomedical Engineering, University of Rhode Island BME 281 First Presentation,October 6, 2015 *Journal of fundamental of biomaterials.*
2) Ravichandran. R , Sundarrajan. S, Venugopal. J. R, Mukharjee. S, Ramakrishna. S, Advances in Polymeric Systems for Tissue Engineering and biomedical Applications. Macromol. Biosci A Journal of Function Biomater.
3) Adrien Naveau and Rawen Smirani "A Bibliometric Study to Assess Bioprinting Evolution", 2017
4) Wei D, Yin L, 1995, The situation and problems of human organs transplant technology in china. Journal of Chinese Medical Ethics, 6: 31–34.
5) Mehmet Rezmi Dokmeei " Bioinks For 3D bioprinting: An overview" Journal of Biomaterials Science.
6) Committee F42 on Additive Manufacturing Technologies. Terminology for Additive Manufacturing Technologies; ASTM International: West Conshohocken, PA, USA, 2012.
7) Veysi Malkoc "Challenges and the future of 3D bioprinting", 2018
8) Fan Liu, Chen Liu and Qiuhong Chen "Progress in organ 3D bioprinting", 2018
9) Shen Ji and Murat Guvendiren "Recent Advances in Bioink Design for 3D Bioprinting of Tissues and Organs", 2017
10) Kim J D, Choi J S, Kim B S, 2010, piezoelectric inkjet printing of polymers: Stem cell patterning on polymer substrates.
11) Donald McCallum Gordon G. Wallace "Bio-ink for on-demand printing of living cells", 2013
12) Janarthanan Gopinathan and Insup Noh "Recent trends in bioinks for 3D printing", 2018
13) Colina M, Serra P. Fernandez-Pradas j M, 2005,DNA deposition through laser induced forward transfer. Biosens Bioelectron.
14) Zhang T, Yan Y. Wang X, 2007, Three Dimensional gelatin and gelatin/hyaluronan hydrogel structures for medical regeneration, International Journal of Bioact Compat Polym.
15) Shengfa Wanga, Lichao Zhou "Lightweight of Artificial Bone Models Utilizing Porous Structures and 3D Printing", 2017
16) Bin Zhang and Yichen Luo, "3D bioprinting: an emerging technology full of opportunities and Challenges", 2018
17) Udayabhanu Jammalamadaka and Karthik Tappa, "Recent Advances in Biomaterials for 3D Printing and Tissue Engineering", 2018
18) Phillippi J A, Miller E, Weiss L, 2008, Microenvironments engineered by inkjet bioprinting spatially direct adult stem cells towards muscles and bone like subpopulations. Stem Cells 26(1).
19) Boland T, Xu T, Damon B, Cui X, 2006, "Application of inkjet printing to tissue engineering".
20) Biotechnol J
21) Calvert P, 2007 Printing cells. Science 318(5848):208–209
22) Sumerel J, Lewis J, Doraiswamy A, Deravi LF, Sewell SL, Gerdon AE, Wright DW, Narayan RJ, 2006, "Piezoelectric ink jet processing of materials for medical and biological applications". Biotechnol. J.
23) Chen FM, Lin LY, Zhang J et al, 2016, "Single-cell analysis using drop-on-demand inkjet printing and probe electrospray ionization mass spectrometry".

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