Additive Manufacturing in Medical Field: An Overview of Bio printing

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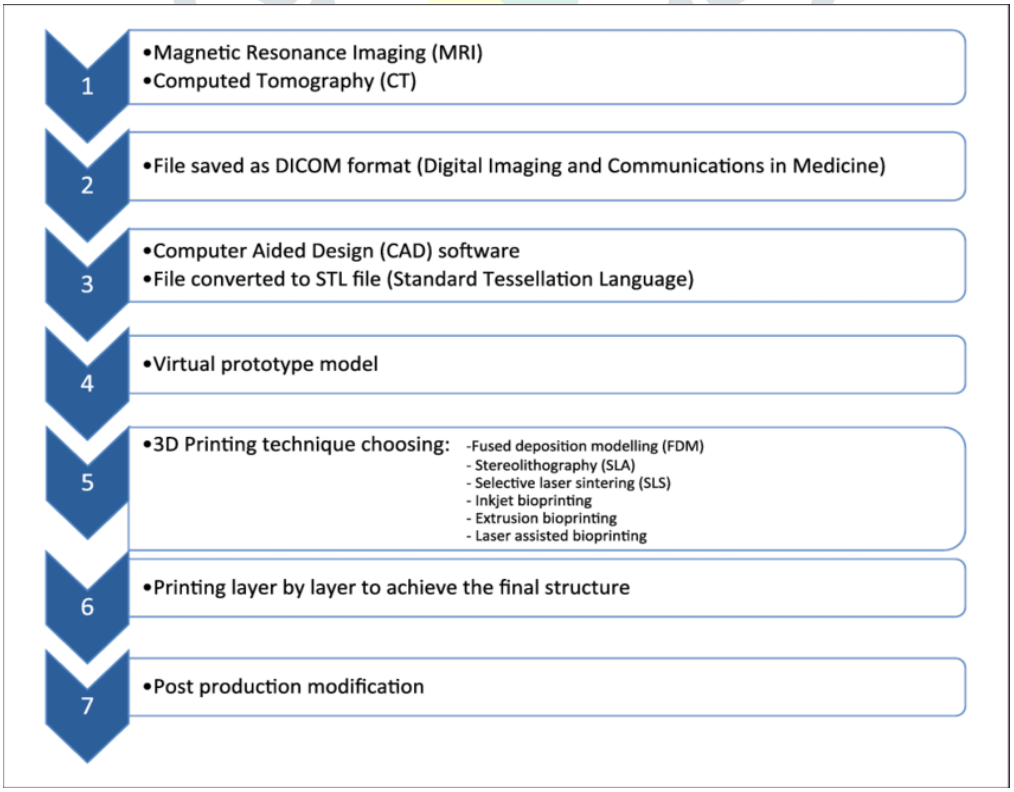
Abstract **- Three dimensional printing has remarkable potential as a fabrication method in creating scaffolds for tissue engineering. Recent advances in medical field have enabled 3D printing of biocompatible materials, cells and supporting components into complex 3D functional living tissues. 3D bioprinting 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 bioink 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, Bioink, Biomolecules.**

I. INTRODUCTION

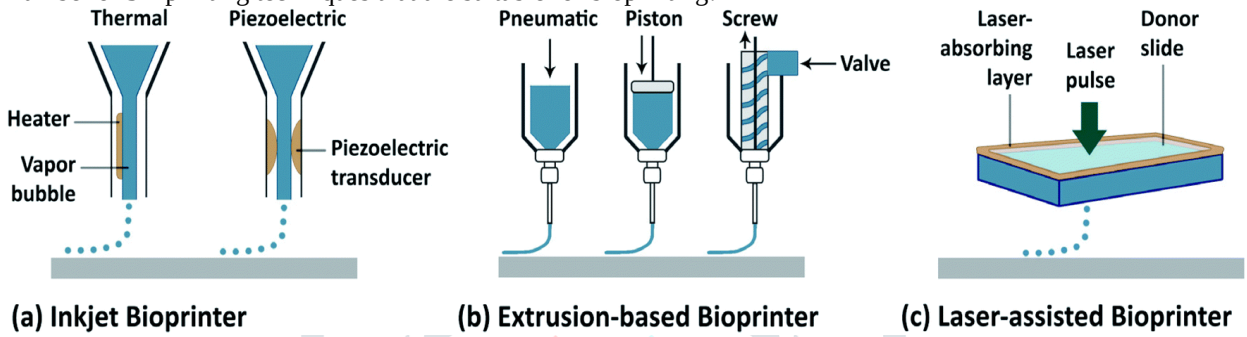
Tissue engineering is an integrative branch which is mainly focused on two major areas: (i) developing new technique to repair, regenerate, and replace damaged tissues and organs and (ii) creating in vitro tissue models to better understand tissue development, disease development, and to develop screen 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), stereo lithography (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 micro valve printing and inkjet printing.



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.

II. 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 3D bioprinting [5]

A. 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.

B. 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].

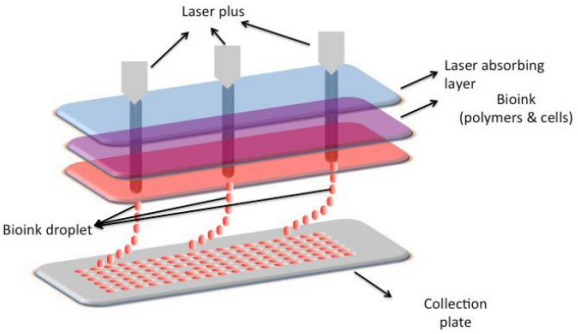
C. Properties of Biomaterials That Make Them Suitable for 3D Printing:

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

II. METHODOLOGY

A. Laser-assisted Bioprinting:

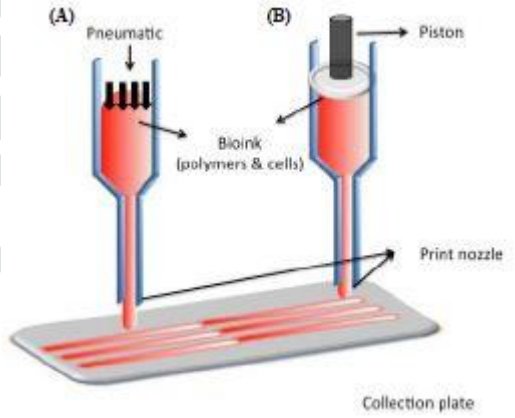
Laser-assisted bioprinting is based on the laser pulse to generate a high-pressure bubble between a solution and a piece of glass containing cells towards the collective substrate (Figure 5). It can produce micro cell-laden 3D constructs with a range of viscosities (1–300 mPa/s) of polymers in a high resolution [13]. The advantage of laser-assisted bioprinting in organ 3D bioprinting includes avoiding the problems of nozzle clogging with cells and/or polymeric biomaterials.



Schematic diagram of laser-assisted bioprinting

B. Extrusion-based Bioprinting:

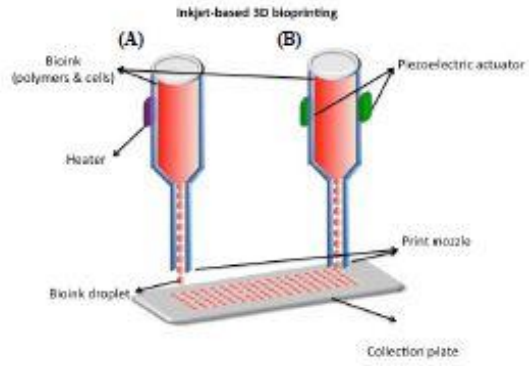
Extrusion-based bioprinting is a particular deposition process using fluidic polymeric solutions or hydrogels as bioink (Figure 4). The extrusion-based bioprinters are normally consisted of a three-axis automatic extrusion system equipped with a fluid-dispensing nozzle (or head) [14, 15]. During the extrusion processes, cell-laden bioink are deposited in cylindrical filaments under the control of a computer-aided designing (CAD) model. At present, it is the only technology that can produce large scale-up cell-laden constructs containing both micro-/macro physiological environments in a controllable manner. For extrusion-based bioprinting, the enabling 3D printers and biocompatible polymers are two major factors (*i.e.* elements) affecting the final 3D constructs.



Schematic diagram of extrusion-based bioprinting.

C. 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. Bioink 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

III. CONCLUSION

3D bioprinting has the robust capabilities to produce tissue/ organ structures with ease; however, it needs further enhancements in different areas such as bioink, 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.

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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