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Original Research Article

3D PRINTING: A REVIEW

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Abstract: This review article is a summary of organ and tissue showing 3D printing. Processing 3D of appropriate shape, structure and size is the most difficult and challenging job for tissue engineering Tissue organ printer is being presented by us which is exclusively designed for constructing similar shapes and sizes, which is possible by using biodegradable polymers while printing cell-laden hydrogels. The right shape of the tissue can be attained and it is possible by representing clinical imaging data as computer model of the anatomical defect and also to interpret the model into various programs that are used to control the movement of the printer nozzles. The incorporation of micro channels into the tissue constructs facilitated diffusion of nutrients to printed cells, and as a result it overcomes the diffusion limit of 100-200 µm for cell survival in engineered tissues. We demonstrated the ability of ITOP by making mandible and calvarial bones, cartilages and skeletal muscles. The ITOP can be used in future in developing or making of more complex tissues and organs of solid nature.

Keywords: Bioprinter, biomimicry, biocells, tissues, organs, bioprinting techniques

Introduction: During 1400 AD woodblock printing and subs sequent evolution of industrial scale printing press took place which helped in quick reproduction of images, information dissemination and text. Advancement in printing technology took place in past few decades from 2D to 3D and this advancement was more complex and difficult to happen. Quick prototyping could be possible due to the evolution of 3D printing and initially used by manufacturing companies to make similar structures of various electrical components and other objects. In incorporation to the applications in the manufacturing and consumer sectors, 3D printing can transform science and education surely.

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Materials & Methods: There are three basic approaches of 3D bioprinting and are as

follows: 1) Biomimicry 2) autonomous self-assembly and 3) mini-tissue building blocks Which are described below?

Biomimicry as name shows that biomimicry is ispired by biologically inspired engineering and can be used in:

1) Researches – pertaining to material
2) Cultures Methods for cells, and
3) Nanotechnology

The use of 3D bioprinting is producing of similar reproductions of cells, tissues and organs. This can be possible through reproduction of particular cellular functional components of tissues, for example, mimicking the branching patterns of the vascular tree or manufacturing physiologically accurate biomaterial types and gradients. For this approach to succeed, the cloning of biological tissues on the micro scale is very important.

Autonomous self-assembly: Second perspective to clone biological tissues is to use embryonic organ development as a guide. The initial components of cells of a growing tissue manufactures his own ECM components, appropriate cell signal and deemed organization and patterning to yield the expected biologic micro-architecture and function.

A 'scaffold-free' type of this approach uses self-assembling of cellular spheroids that undergo fusion and cellular organization to mimic developing tissues. Autonomous self-assembly relies on the cell as a primary driver of histogenesis, directing the composition, localization, functional and structural properties of the tissue.

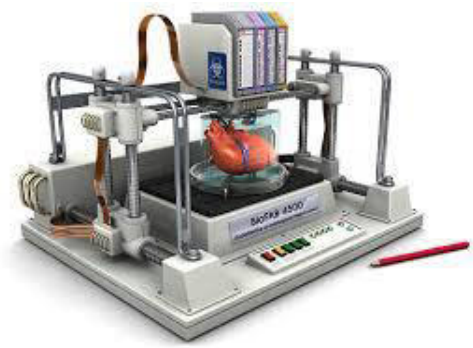


Figure 1: Bioprinting Machine (ref: http://win-health.org/3d-printing-sirris-takes-a-step-further-with-its-bioprinting-project/)

Mini-tissues: The concept of mini-tissues is relevant to both of the above strategies for 3D bioprinting. A 'scaffold-free' type of this perspective used in self fabricating of cellular spheroids which undergoes fusion and cellular organization to mimic development tissues. Independent fabricating of cells relies on the cell as a primary driver of histogenesis, directing the composition, localization, functional and structural properties of the tissue. Tissues and/or organs contain small and useful building blocks or mini tissues. The definition of mini tissue can be understood as that they are the little useful components of tissues, Example: Kidney nephrons, by the process of self fabricating these nephrons can be merged into biggest form. There are two major policies: self fabricating cell spheres (similar to mini-tissues) are assembled into a macro-tissue using biologically inspired design and organization.

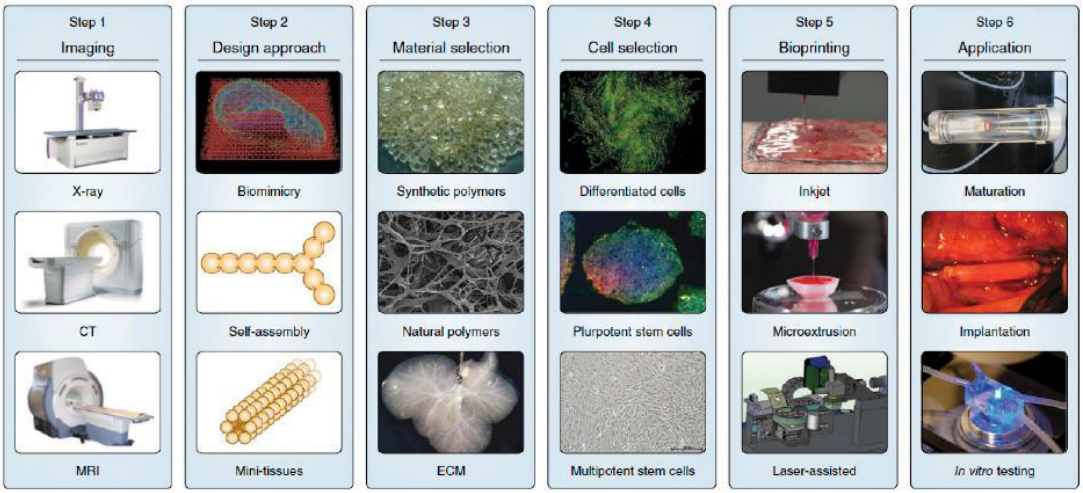


Figure 2: Damaged tissue 3D Bioprinting

A typical process for printing 3D tissues. Imagining of the damaged tissue and its environment can be used to guide the design of bioprinted tissues. Biomimicry, self fabrication of tissues and small tissues building blocks is designed and this approaches used in single combination. Choosing materials and cell source is essential and specific for the tissue and function. The material can be synthetic rubber or natural polymers and decellularized ECM. Cell sources may be allogeneic or autologous

These components have to combine with systems of bioprinting such as inkjet, micro extrusion or laser printers. Before process of transplanting few tissues need maturation period in bioreactor. Digital design is required essentially to reproduce the difficult, diverse architecture of useful tissues and organs are a comprehensive understanding of the composition and organization of its component.

Imaging and digital design: Medical envision automation is an indispensable tool used by tissue engineers to provide information of 3D structure and functioning on cellular, tissue, organ and organism levels. These technologies include most noninvasive imaging modalities, the most frequent being computed tomography and MRI. Computer-aided design and computer-aided fabricating tools and mathematical modeling are also used to collect and digitize the complex tomographic and architectural information for tissues.

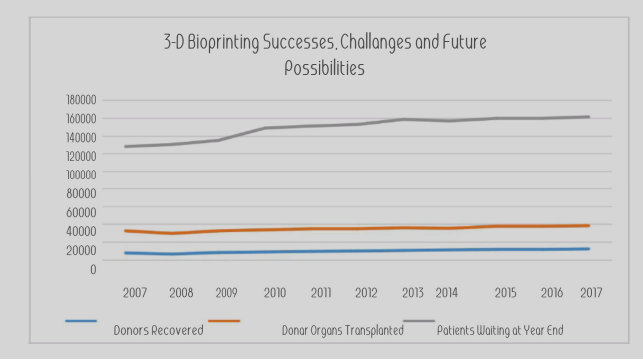
Tissue bioprinting strategies: The most important automation technique is used for deposition and patterning of biological matters is inkjet, micro extrusion, and laser assisted printing. Medical visualization automation is a useful aspect used by tissue experts while engineering for issuing facts related 3 dimensional structures and functioning on cells, tissues, organs and organism levels. These technologies include most noninvasive imaging modalities, the most famous being computed tomography and MRI. Different features of those technologies shall consider as one of the most important factors in 3D bioprinting, which are surface resolution, cell viability and the biological materials used for printing.

Inkjet bioprinting: Inkjet printers which are also referred as drop-on-demand printers are the most frequently used type of printer both non biological and biological applications. A controlled volume of liquid is delivered to predefined locations.

The inkjet printer for the first time was being used for applications of bioprinting and it was an upgraded version of 2Dimensional ink-based printers. Biological material and electronically controlled elevators were used to replace the ink in the cartridge and the paper respectively. Now, inkjet based bioprinters are used for printing purposes biological materials at faster rate, increasing resolution, precision and speed.

Inkjet printers use thermal forces to eject drops of liquid on the substrate, which can support or form part of the final construct. Many inkjet printers contain a piezoelectric crystal that creates a wave inside the print head that break the liquid into droplets at regular intervals. Applying a voltage to a piezoelectric material tends a rapid change in shape, which in generates the pressure needed to eject drops from the nozzle.

Acoustic radiation force used by other inkjet printers linked with ultrasound field for throwing out droplets of liquid from air-liquid interface.



Graph: 1 3-D Bioprinting Successes, Challenges and Future Possibilities

Micro extrusion bioprinting: The Microextrusion bioprinting is the most frequent and affordable and nonbiological 3Dimensional

printers use microextrusion. Microextrusion bioprinter usually made of a temperature-controlled material-handling and allocating system and stage, with one or both capable of movement along the x, y and z axes, a fiberoptic light source that illuminate the deposition area and for photo initiator activation, a video camera for x-y-z command and to control, and solo unit of piezoelectric humidifier . A few systems use multiple print heads to facilitate the serial ejection of several materials without retooling.

Nearly 29,999 3Dimensional printing machines are being sold worldwide every year, and academic institutions are increasingly purchasing and applying this technology in tissue and organ engineering research. Industrial printers are costlier but have better resolution, speed, spatial controllable in nature and more flexibility in the material.

Laser-assisted bioprinting: Laser-assisted bioprinting is built on the principle of laser-induced forward transfer. Initially evolved to move metals, laser-induced forward transfer technology which has been successfully applied to biological material, such as peptides, DNA and cells.–Although this is less common than inkjet or microextrusion bioprinting, LAB is increasingly being used for tissue- and organ-engineering applications.

A typical LAB device made up of a pulsuating laser beam focusing system, a 'ribbon' that has a donor transport support made from glass that is covered with a laser-energy-soak up layer e.g., gold or titanium and a coating of biological material The purpose of laboratory is effected by numerous factors, including the laser fluency (energy delivered per unit area), the surface tension, the wet ability of the substrate, the air gap between the ribbon and the substrate, and the thickness and viscosity of the biological layer. Because LAB is nozzle-free, the clogging problem with cells or matters that plague rest bioprinting automations is ignored.

LAB is more suited between range of viscosities (1–300 mPa/s) and with minimal effect able to print mammalian cells on cell viability and functions. LAB can deposit cells at a density of up to 108 cells/ml with microscale resolution of a single cell per drop using a laser pulse repetition rate of 5 kHz, with speeds p to 1,600 mm/s.

Materials and scaffolds: Deposition of metals, ceramics and thermoplastic polymers were the applications where 3dimensional printing was being used initially in non biological forms. As the 3dimensional printing is a challenging job it takes a great difficulty while finding right material and process to achieve desired results.

Materials which are currently used for the purpose of medicine regeneration for restoring and regenerating are predominantly based on either natural polymers including alginate, gelatin, collagen, chitosan, fibrin and hyaluronic acid, often isolated from animal or human tissues or synthetic molecules such as polyethylene glycol; There is benefits of natural polymers for 3Dimesional bioprinting and other tissue engineering applications are their similarities to human ECM, and their inherent bioactivity. The advantage of synthetic polymers is that they can be tailored with specific physical properties to suit particular applications.

Challenges faced for using synthetic polymers can include poor biocompatibility, toxic degradation products and loss of mechanical properties during degradation. Even so, synthetic hydrogels, which are both hydrophilic and absorbent, is attractive for 3D bioprinting regenerative-medicine applications owing to the ease of controlling their physical properties during synthesis.

Printability: A crucial property of a suitable matter is that it can be rightly and precisely deposited with the desired spatial and control. Some types of bioprinting technology, such as inkjet, have limitations over material viscosity, whereas others, such as microextrusion, may require the matters for having specific crosslinking mechanisms or shear-thinning properties.

Processing parameters, such as nozzle gauge, discover the shear stress to which cells are exposed as well as the time needed for the matter to be deposited to form a 3D structure. For example, inkjet printing needs matter with a quick crosslinking time to facilitate the coating of a complex 3D structure. Microextrusion, however, can be incorporate highly viscous matters to manage a 3D structure and shape after deposition, with final crosslinking occurring after fabrication.

During the printing process materials with either low thermal conductivity or the capacity to protect the cells during delivery may increase cell viability and function after printing. Although post printing cell viability may range markedly which is based on printer specifications, material properties, resolution and cell types, inkjet bioprinting studies usually quotes cell viabilities in surplus of 85%, microextrusion printing studies report viability ranges of 39–79%.

Biocompatibility: With the emergence of tissue engineering, the goal for biocompatibility has been changed from requiring an implanted matter to coexist with the endogenous tissue without eliciting any unwanted local or systemic effects in the host to implanted materials can be expected to passively allow or actively produce desired effects in the host118.

Biocompatibility in bioprinting can include the expectation of a mobile and controllable contribution to the biological and functional components of the construct. This could include interaction between endogenous tissues and/or the immune system, supporting appropriate cellular activity and facilitation of molecular or mechanical signaling systems, all of which are essential for successful transplantation and function.

Degradation kinetics and by-products: As a material scaffold degrades, the embedded cells can secrete proteases and subsequently produces ECM proteins that define the new tissue. The deterioration kinetics of the materials must be understood and controlled. There are various aspects of degradation which shall be considered. The first is the capacity of cells to control degradation rates, ideally match the range of degradation with the capacity of cells to replace the materials with their own ECM proteins.

This is highly challenging because materials with suitable functional and mechanical attributes for a given tissue may not match the capacity of the cellular components to replace the material upon degradation. Degradation byproducts are also very important because they often define the biocompatibility of any degradable material.

Structural and mechanical properties: If a material is important for the maintenance of a 3D framework printing, in resisting or fabricating specific forces or as an anchoring point for mechanical leverage, then maintenance of these properties is also essential for continued function of the construct. Materials must be carefully selected based on the required mechanical properties of the construct, and different structural requirements will be needed for diverse tissue types ranging from skin and liver to bone. One approach to reduce this restriction is the utility of sacrificial matters which can give the required shape and mechanical belongings over a given period of time.

At the time of printing the sacrificial material may be used so to allow cross linking occurring in the constructor and it can be incorporated into the construct and functions until the matter produced endogenously can carry out this function sufficiently. For designing of matter with specific and appropriate shape one should take special care in this approach. Also potential foreign body responses or toxic degradation shall be avoided. Recently the importance of biomimicry for biocompatility has been studied.

Material biomimicry: These biomimetic components into bioprint construction are able to have an effective and active role while proliferation, functions and attachments. Materials are largely influenced on attachment

of cells and this truth is well known by everyone. The above principles can be useful in controlling the proliferation of cell and different cells in a scaffold

The addition of surface ligands to a material can rise cell attachment and proliferation on the matters substrate. Cell attachment can be affected by the presence of nanoscale features such as ridges, steps and may be grooves. The 3Dimensional environment in a tissue engineered construct can influence cell shape and affect the differentiation process.

Cell sources: Correct functioning of the fabricated construct can be achieved through choosing cell for tissue organ printing. Organs are comprised through various tissues and tissues are comprised through various cells with specific and important biological actions and functions which are recapitulated in the tissues. The type of cell, and functions of it determines the support it can provide.

Current choices to print cells may involve either the deposition of many primary cell types into patterns that faithfully represent the native tissue cells that can proliferate and differentiate into required cell types. Cells which are chosen for printing should closely mimic the physiological state of cells in vivo and are expected to maintain their in vivo functions under optimized conditions.

Result & Discussion: Many of the challenges which are faced by the 3Dimensional bioprinting field relate to specific technical, material and cellular aspects of the bioprinting process . Although the area is at an initial phase, in creating different tissues at human scale that are approaching the functionality needed for transplantation successfully. Technological challenges may consist the requirement for risen resolution, speed and similarity with biologically applicable matters.

As we proceed away from the revision of preexisting automation and can begin to design 3Dimensional bioprinters to manage particular biological components, the range of compatible materials can be extended, and methods to deposit materials and cells with increasing precision and specificity can be developed. The pace of invention can be grown to produce constructs of clinically applicable structure.

One method to attain this would be to start miniature functional tissue blocks that could be scaled up to a clinically applicable structure by using a macro-scaffold to join blocks. Commercialization may require scalable automated robotic automation that incorporates each of the components of the biofabrication production line88. This may not only include just the bioprinting device but also the fabrication of matters, tissues and cells and other supporting components.

Conclusion: Since the last many months, researchers not only have demonstrated proofs of concept examples of different bioprinting technologies, but also have showed that how can 3D bioprinting can make difference in the future of tissue engineering which is ranging from manufacture of organ and tissue constructs for functional regeneration to appropriate models to pharmacological testing.

The 3D cell-embedding volumes of biomaterials can be generated by bioprinting could serve as biomimetic builds with required composition, structure, and architecture to make sure better cell viability and more importantly support the functionality of the tissues, asdemonstrated by numerous studies where tissues such as vasculature, heart, liver, cartilage.

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