3D BIOPRINTING OF ORGANS AND TISSUES - a current status.

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ABSTRACT: *Three Dimensional bioprinting is a kind of digital and additive manufacturing which involves incorporation of techniques from various fields. The main prerequisites for printing with living cells are the tissue growing capacity,biological working of the implants and also the cells viability .There is an increasing demand for assemblage of biologically pertinent materials with an optimum goal of reproducing multicellular tissues and organs .Further development of bio organ fabrication will be useful for organ printing technology .For accurate printing of mimic organ structure, hydrogels are used. Bio-printing system based on stereo lithography is a low cost beneficial technology for microscale cell pattern. It is an overview of recent technology advances in 3D printing and also concepts related with bioprinting activity. Tomographic and architectural information of tissues are collected by Computer Aided Designing (CAD). It is an alternative method, instead of replacing organs and tissues from donor. It is a technology where engineering meets biology.*

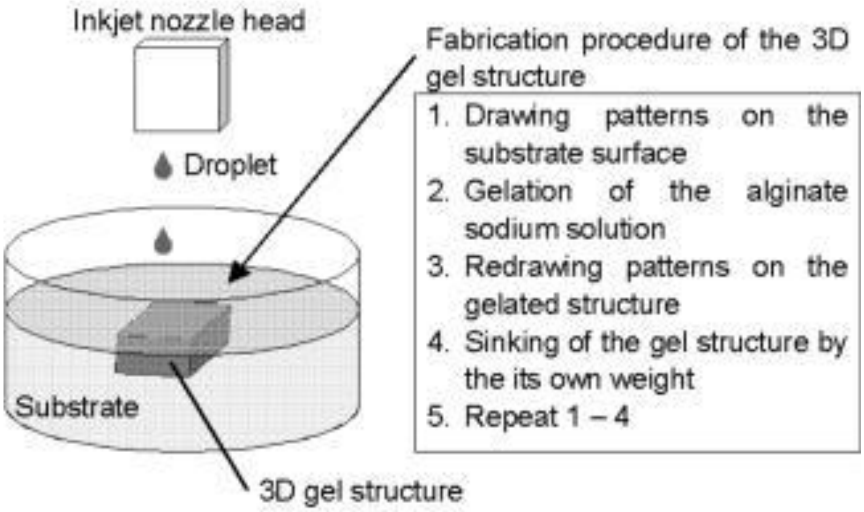
Key Words: *Additive manufacturing, CAD, bio-organ fabrication, hydrogel.*

INTRODUCTION

Recent inventions facilitate the cells and biomaterial components into a multiplex functional living cells which is a three dimensional one [1] .Scaffolds self-assemble during fabrication. This tissue engineering technique is expeditious and has an ability of being scaled [2] .During cellular construction, the greatest challenge is to produce the appropriate shape, size and also the suitable structural integrity. Hydrogels helps in achieving the mechanical stability [3] .In three dimensions - Bio ink is known as creating heterogeneous structures by exactly co-printing several materials [4]. Sorting of cells and fusion of tissues are the morphogenetic principles for self -assemblage of multicellular unit. It is necessary to equip micro environmental cues for successful attempt [5]. The living materials are tissue spheroids and micro tissues that are enclosed with definite properties, biological materials and limited composition. Under the tissue engineering field, robotic bio-fabrication is enhanced by organ printing [6] The bio-printing technology meet the current challenges like vascularization, cell distribution ,high resolution ,innervation, cell deposition .Patterning the cell at micrometer scale is used in biomedical engineering [7]. Thermoplastic polymer provides mechanical stiffness that can be tailored for extensive range of hydrogels. For improved clinical output, well organized implants having characteristics almost identical to native tissues are chosen [8]. 3D micromoulding involves photocross linkable hydrogel construction with many features related to architecture which is fabricated with microchannel networks. GelMA hydrogels are used for demonstration to check the functionality based on cell-laden tissue, vascular networks [9]. For excellent bioprinting, pluronic F127 is used [10] . Different jet based technology also used for printing live cells [11]. For the past few years the field which is based on regenerative medicine has been progressed to a very great extend. In contrast, 3Dbioprinting separates native tissues and engineered tissues which are made artificially [12]. Recently for drug discovery organ-on-chip has been introduced which shows only limited fabrication method .It mimic the exact working conditions of the organs [13]. Comparing with traditional tissue engineering this 3D technique is flexible and they often sophisticate .3D scaffolds which are porous are implanted after printing .It is useful in vitro regenerative research [14]. Prototyping technology helps in forming the 3D structures undisturbed with gelatin hydrogel and hepatocytes .The mixture of about 30 layers like gelatin, hepatocytes were overayed into a spacial structure. This helps in performing biological functions [15] .Bio-ink based on nano-cellulose is used for printing cartilage structures like chondrocytes, sheep meniscus and human ear. These were 3D printed using CT and MRI images as an engineering design [16]. Fabrication of solid freeform technology involves alginate scaffolds which are encapsulated with endothelial cells. The resolution for deposition is 10 μm and minimum velocity is 100 μm [17]. Though there are many natural polymers available to develop gelatin and hyaluronic acid yet photocrosslinkable bio inks are used. Hydrogels and biological tissues interaction helps in promoting the regeneration of tissue complexity [18].Collagen type I plays a major role in promoting the tissue formation, maturation and cell-cell adherence [19].This 3D bioprinting creates a demand on medical devices and also in tissue scaffolding . There is a lot of demand focused on the production of the reality 3D living tissue of humans [20].

TYPES OF 3D-BIOPRINTING TECHNOLOGY- 3D-printing technology is an emerging one which helps in testing, fundamental areas, clinical practice and also in drug delivery [21].

INKJET BASED BIOPRINTING- By ejecting tiny ink drops, inkjet printers produces high resolution. When a heat is produced living cells easily gets damaged. In order to avoid the damage, electrostatically operated inkjet system is used. Technology based on microseeding where living cells are seeded has many potential uses [22]. Bio-fabrication of 3D inkjet has been used for intricated functional tissues [23].For the gel construction, ejection of sodium alginate from inkjet nozzle occurs. Living cells are used as a material for 3D gel formation [24].



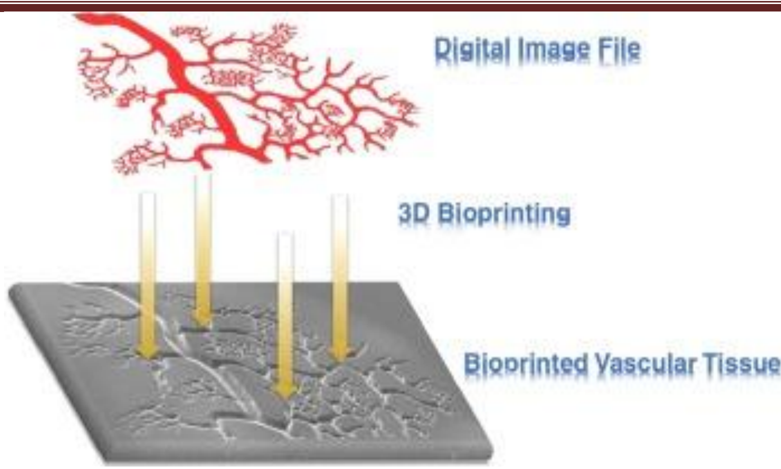
3D GEL STRUCTURE [24]

LASER-ASSISTED BIOPRINTING- It acts as a promising technology. Laser cell bioprinting should be elucidated carefully since it causes cell death [25]. The main aim of this bioprinting is assemblage of human osteoprogenitors [HOPs] and nanohydroxapatite [nHA]. It can be adapted for the bio-fabrication of 3D materials. Quartz ribbon is focused by infrared laser allowing the consecutive of 3D printing [26]. This is similar to computer aided designing (CAD) blue printing which helps in understanding the features of cells [27]. In Laser-assisted forward process, cells attain its original phenotype [28].

EXTRUSION BASED BIOPRINTING- In this type, structure of biomaterial can be made. Structure of cell-laden can be printed [29]. For 3D production, co-axial extrusion needle is incorporated using cell-laden having low viscosity. For controlling the bio-ink deposition; extrusion structure is connected to a microfluidic appliance [30]. Using rheology, the ink solution of extrusion printability is found. There is a need for extrusion printing for the construction of Alginate-Gel [31]. Extruded filament helps in creating the 3D structure due to its increase in the rigidity [32].

3D BIOPRINTED FUNCTIONAL TISSUES AND ORGANS (REGENERATION)

Stem cells should be isolated and differentiated into specific cells. Bio ink with blood vessels, specific organ cells is transferred into the printer [33]. Complex shape ear can be printed using cell –laden hydrogel and poly-caprolactone. This process regenerate fat tissue and auricular cartilage [34]. The muscle tendon unit fabrication involves IOP system for deposition of various components .This system helps to form integrated tissue with mechanical and biological characteristics [35]. Pluripotent stem cells are bioprinted which is based on valves. It's secretion of albumin and the morphology characters are similar to hepatocytes. This development may be used for personalized medicine and drug development which is animal free [36]. Bone can be printed by FDM method. It was 3D printed into a scaffold which is encapsulated by MSC hydrogel [37]. NT2 cells are 3D printed and cells start adhering. After culturing it extends neuritis [38]. Vascular tissues are 3D printed by bio plotting. It shows an excellent viability of cells [39]. Diagrammatic representation of functional tissue is given below.



FUNCTIONAL BIOMATERIAL FOR TISSUE ENGINEERING [40].

APPLICATIONS – Extrusion based printing deposit cells and materials easily [31].It can be used for discovering the drugs, research and also in toxicology [1]. In a single step process soft actuators can be manufactured [41]. F127 helps to template microscopic and macroscopic structure which can be enhanced with many rheological characteristics providing a stage for tissue engineering [42]. Hydrogels have high permeability of metabolism [43]. Among many polymers; modification of polymers like polyvinylalcohol, poly carbonates and poly ethylene glycol is enough to convert biomimetics to fabricate the hydrogel [44]. The agreeable side –effect of 3D bio printing is bio printed mammalian cells can be used for gene delivery as well as for drug delivery [45].

LIMITATIONS- 3D printable biomaterial availability is in demand [46]. In extrusion printing shear stress may lead to cell death. In laser based bio printing use of ultraviolet rays causes negative impact on cells. Slow printing may not be suitable in case of rapid fabrication. Material selection for bio-ink should be in liquid state with accurate viscosity which is a drawback for inkjet based bio printing [47]. Manual deposition of 3D printed skin may lead to shrinking and unable to retain its shape [48]. The cost of 3D printer for higher resolution is high [49]. Complicated structure of organs in the human body requires development to fabricate merchantable bio printed organs and remarkable research is needed [50].

CONCLUSION AND FUTURE PERSPECTIVES – This reviews about the standpoint to develop 3D organ and tissue. 3D bio printing is a future challenge for building solid organs and complex tissues. Instead of restoring the organs from the giver, patient own particular living cells that is which part is going to get replaced can be taken and grown in laboratory and replaced again to that particular patient. In case of bio printing of structures, organs or tissues it is digitally scanned and printed layer by layer three dimensionally. The major advantage is the body accepts the replaced thing because its resemblance will be the same and there is no chance of rejection since it is made up of patient's own cells. It acts as a next frontier in medicine where some complicated tissues and organs devices should be developed. Enhancement over the limitations will definitely result in gain for better fabrication.

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