Journal of Science: Advanced Materials and Devices 1 (2016) 1–17

Contents lists available at ScienceDirect

Journal of Science: Advanced Materials and Devices

journal homepage: www.elsevier.com/locate/jsamd

Review article

Three-dimensional printing of biological matters

Ahmed Munaz [a], Raja K. Vadivelu [b], James St. John [b], Matthew Barton [c], Harshad Kamble [a], Nam-Trung Nguyen [a, *]

[a] Queensland Micro- and Nanotechnology Centre, Griffith University, Brisbane, QLD, 4111, Australia
[b] Eskitis Institute for Drug Discovery, Griffith University, Brisbane, QLD, 4111, Australia
[c] Centre for Musculoskeletal Research, Menzies Health Institute Queensland, Griffith University, Brisbane, QLD, 4111, Australia

ARTICLE INFO

Article history:
Received 3 April 2016
Accepted 6 April 2016
Available online 19 April 2016

Keywords:
3D bio-printing
3D positioning system
Bio-ink
Hydrogel
3D scaffolds
Organ construction

ABSTRACT

Three-dimensional (3D) printing of human tissues and organ has been an exciting research topic in the past three decades. However, existing technological and biological challenges still require a significant amount of research. The present review highlights these challenges and discusses their potential solutions such as mapping and converting a human organ onto a 3D virtual design, synchronizing the virtual design with the printing hardware. Moreover, the paper discusses in details recent advances in formulating bio-inks and challenges in tissue construction with or without scaffold. Next, the paper reviews fusion processes effecting vascular cells and tissues. Finally, the paper deliberates the feasibility of organ printing with state-of-the-art technologies.

1. Introduction

The invention of the printing press changed the course of human history. The disruptive technology of printing text and images impacted society globally, acting as media for education, religion, politics, language, and culture [1]. Since then, a number of innovations further enhanced the printing technologies. For example, the introduction of dot matrix printers revolutionized the consumer market, where a computer linked to a printer as its peripheral device allowed desktop publishing and on-demand printing, reducing cost and time. The advent of the Internet introduced further an advancement, which allows documents to be available anywhere and printed just by the click of the mouse. Personalised printing made education, scientific research and arts more accessible to the broad population. Table 1 lists the major milestones in the history of printing technology. Although Charles Hull first introduced in the late 1980 three-dimensional (3D) printing through the so-called stereo lithography technology, its significance only started to materialise at the turn of the 21st century [2,3]. This versatile printing technology allows the fabrication of a wide range of 3D objects, from electric components to biological implants, through layer-by-layer patterning with ultraviolet (UV) exposure of photoresist films [4].

A 3D printer can also dispense biological materials making bio-printing possible. Generally, bio-printing can be achieved with layer-by-layer positioning of biomaterials as well as living cells. The precise spatial control of the functional materials allows for the fabrication of 3D tissue structures such as skin, cartilage, tendon, cardiac muscle, and bone. The process starts with the selection of the corresponding cells for the tissue [5]. Next, a viable bio-ink material is prepared from a suitable cell carrier and media. Finally, the cells are printed for subsequent culture into the required dimensions. The several approaches of 3D bio-printing are biomimicry, autonomous self-assembly and mini-tissue building blocks [6]. In contrast to conventional 3D printing, 3D bio-printing is more complex in terms of the selection of materials, cell types, growth/differentiation factors, and sensitivity of the living cells construction.

A typical 3D bio-printing process consists of the pre-processing, processing and post-processing stages. Pre-processing consists of the formation of an organ blueprint from a clinical bio-imaging system (i.e. MRI) and the conversion of this information into a direct instruction software of the standard template library (STL) for the printing hardware, which includes but is not limited to a series of integrated tools such as automated robotic tools, 3D positioning systems with printing head, ink reservoir, nozzle

* Corresponding author.
E-mail address: nam-trung.nguyen@griffith.edu.au (N.-T. Nguyen).
Peer review under responsibility of Vietnam National University, Hanoi.

http://dx.doi.org/10.1016/j.jsamd.2016.04.001

Table 1
Major milestones of the history of printing technology.

Milestone	Year (CE)	Details
Book printing	200	Woodblock printing used in China.
	1040	Letters rearranged for each page in movable typing.
	1440	Printing press introduced by Johannes Gutenberg.
	1884	Introduction of hot metal type setting.
	1907	George C. Beidler invented the Photostat machine.
Desktop printing	1968	Dot matrix printing invented by Digital Equipment Corporation.
	1970	Inkjet printing produced by Epson, Hewlett-Packard, Cannon.
	1979	Laser printer developed by HP for desktop.
3D printing	1984	3D printing invented by Charles Hull called stereo-lithography.
	1991	Word's first fused deposition modelling (FDM) invented by stratasys that uses plastic and an extruder to make 3D model.
	1992	Selective laser sintering machine (SLS) invented by DTM using power with laser to print the 3D model.
	2000	3D ink jet printer and multi-colour printer produced. Following year, desktop 3D printer introduced.
	2009	Commercial 3D printer available to market.

systems, video cameras, fiberoptic light sources, temperature controllers, piezo electric humidifiers, and integrated controlling software.

The processing stage is the actual printing session of the bio-ink using the bio-printers. The processing stage includes bio-ink preparation, clinical cell sorters (e.g. Celution, Cytori therapeutics), cell propagation bioreactors (e.g. Aastrom Bioscience), and cell differentiators to construct the desired biological structures.

The post-processing stage comprises the necessary procedures to transform the printed construct into a functional tissue engineered organ, suitable for surgical implantations. The post-processing stage may also include perfusion bioreactors, cell encapsulators and a set of bio-monitoring systems [7]. Each of these auxiliary machines has their own important roles for scaling up bio-printing. For example, cell encapsulators and bioreactors are essential to restrict undesirable fusion processes after the construction. Mironov et al. proposed a bio-reactor that is believed to maintain fragile tissue construct with sufficient time for post processing of tissue fusion, maturation and remodelling [8].

2. Technological considerations

The main technological challenges of 3D bio-printing are (i) the 3D positioning process, (ii) the formulation of a bio-ink and (iii) the dispensing system.

2.1. Three-dimensional positioning

Precise positioning of the print head plays a crucial role for the additive layer-by-layer construction of a 3D object. The positioning system is sometimes referred to as the bio-assembly tool (BAT) that utilizes computer aided design/manufacturing (CAD/CAM) software to precisely deposit various 3D heterogeneous cells [9]. BAT generally consists of multiple printing heads that can travel in a XY plane and adding through the Z axis for the printed layer [10]. A number of sensors are necessary to detect the thickness of each printed layer, and to adjust the print head for the next layer. Control software allows for the synchronization of these printing heads in the 3D space. The software may also consist of a number of text files or scripts for organizing the movement of the BAT and controlling the speed, air pressure as well as temperature. The 3D platform should be able to stop at various points during the printing process to change the bio-ink if necessary. Fig. 1 illustrates a typical 3D positioning system incorporating a print head and a printing bed.

For mapping a human organ, an X-ray, magnetic resonance imaging (MRI) or computed tomography (CT) scan can be converted to a bio-computer aided design (Bio-CAD) [11,12]. Surgical navigation software such as Stryker (Kalamazoo, United States), MedCAD (Dallas, United states) are some of the commercially available Bio-CAD packages. The Bio-CAD software visualizes 3D anatomic structures, differentiates heterogeneous tissue types, measures and differentiates vascular and nerve tissues and generates the desired computational tissue model [13]. A specialized software such as Rhinoceros 4.0 (real time simulation integrated with MATLAB/Simulink) can modify this bio-CAD design in extremely detailed slices with contour boundary paths that then can be synchronized with the 3D positioning system [13–16]. The software consists of a console and a master. The console analyses the 3D model, renders it onto a series of commands to be sent to the positioning stage. The master controls the positioning coordinates of the print head.

Surface mapping observes the printing status of each layer and decides the time to begin the construction of the next layer. The waiting time may vary from material to material, depending on its concentration and its thickness. For instance, Song et al. utilized a prototype system consisting of stepper motors for each X, Y, and Z axis movement and another axis for dispensing materials with a syringe. The positioning system had a precision of approximately 0.05 μm along the X and Y axis and of 0.125 μm in the Z axis. The optimum speed for depositing the material is typically between 1 and 10 mm/s. The software transferred the CAD model to a layered process path in Extensible Markup Language (XML) that directly controls the positioning system [17].

One of the most common problems of additive printing is the accumulation of errors that is associated with the printing height. This problem poses a big challenge to the construction of a large number of layers [18]. The accumulative errors eventually lead to an unsuccessful attempt for the 3D construct. However, for better

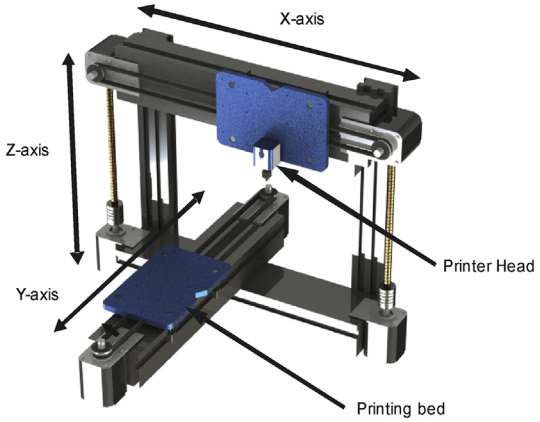

Fig. 1. Schematic of a 3D positioning system incorporating a print head and printing bed system.