

Current Perspectives on Printing Technology for Biomedical Applications

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Editorial

Bioprinting is an innovative and essential technology that has created a revolutionary impact on both medical and pharmaceutical sciences and gained considerable interest worldwide. The term “Bioprinting” refers to the contemporaneous printing of living cells and biomaterials (via execution of various bioink printing methods) in a stipulated layer-by-layer stacking pattern in predefined locations using a computer-assisted design program (CAD) and manufacturing (CAM) blueprints process for the fabrication of biocompatible constructs [1]. It has wide implications in the field of biomedicine and pharmaceuticals such as regenerative medicine, tissue and organ fabrication, designing implants, pharmaceutical research: high throughput drug screening and drug delivery, creating anatomical models and constructing customized prosthetics, toxicology, transplantation and cancer research [2]. Apart from these benefits, the major issue of 3D-bioprinting is the static and inert nature of 3D printed biomaterial or constructs. 4D-bioprinting is a novel technique where the fourth dimension, “time”, is integrated along with 3D-bioprinting [3]. Using 4D-bioprinting, the fabricated material can change their shape and/or function on-demand and over time, which may have great advantage for developing scaffolds that only become active when they encounter particular environments [4].

Rapidly growing scientific studies tend to explain the wide application of 3D-bioprinting in understanding dynamics of bone tissue, liver, lung, cartilage, cardiac, pancreatic, skin and neural tissue engineering because of its potential to fabricate anatomically correct organs thereby mimicking the patient-specific tissue constructs [5]. It is therefore noteworthy to highlight here a few studies to understand the emerging concept of 3D-bioprinting in biomedical applications. Endothelial progenitor and multipotent stromal cells are co-bioprinted on heterocellular tissue constructs (made up of matrigel and alginate hydrogels) in well-defined and spatially controlled fashion. The construct was then implanted into mice *in vivo* and the incorporated osteoinductive biphasic calcium phosphate microparticles and growth factors tend to induce differentiation of multipotent stromal cell into osteogenic lineage thereby facilitating bone formation [6]. Similarly, human induced pluripotent stem cells (hiPSCs) are bioprinted, stimulated and differentiated into hepatocytes for mini-liver generation [7]. Phamduy et al. [8] established an unprecedented *ex vivo* model which biomimics an actual microvascular network system that implements time-lapse elucidation of cell dynamics during cancer angiogenesis. In this study, Laser-direct-write technology has been used to deposit MDA-MB-231/MCF-7 breast cancer cells and fibroblasts into spatially-defined locations on cultured rat mesenteric tissue to study cell migration within microvascular networks [8]. In drug discovery, recent attempts in 3D *in vitro* systems enhance the ability to evaluate the drug efficacy and toxicity, hastening its translation into clinics. Bioprinting has also been widely used to create 3D tissue models for anticancer drug development studies. Cell-laden temperature controlled bioprinting of biocompatible constructs made up of matrigel and collagen placed on top of prefabricated poly-dimethyl-siloxane substrates were incorporated into microfluidics device to study prodrug, amifostine conversion and radioprotection in hepatocytes and improve the solubility and targeting effects of drug for liver disorders [9].

The major challenge in tissue engineering is the vascularization that has to be tackled when engineering functional tissue, which can be achieved with the aid of 4D-bioprinting technology. For instance, multiple cell types such as mesenchymal stem cells, fibroblast and endothelial cells were patterned onto hydrogels through a layer-by-layer 4D-bioprinting system. The cell migration and aggregation process results in vasculature formation which was confirmed by endothelial-specific gene expression [10]. Recently, soybean oil epoxidized acrylate was used as an ink for fabricating 3D-bioprinted biomedical scaffolds to elucidate biocompatibility and cytocompatibility with human bone marrow mesenchymal stem cells. The 3D-bioprinted scaffolds also tend to exert potent shape memory effects, thus facilitating 4D functionality and highlight the importance of renewable plant oils for biomedical scaffold development and 3D fabrication methods [11].

More recently, some of the bioprinting findings have started to showcase their benefits for the health care. Two researchers at the University of Toronto have developed the ‘PrintAlive’ bioprinter that creates skin-like “living bandage” (mixture of biopolymer, human keratinocytes and fibroblast) for severe burn treatment and this technique could move to preclinical trials to revolutionize skin regeneration studies [12]. Bioprinting has also been adopted by University College London to create 3D printed ears for implantation in children with severe ear disfigurements [13]. With the aid of 3D-bioprinting technology, an Indian oral cancer patient was able to replace a section of his upper jaw, removed after undergoing tumor surgery, with a new set of teeth [14]. In the near future, we hope that increased research and interest in bioprinting due to clinical, commercial, and industrial applications enhance its development and energizes the scientific community to perform better and achieve breakthrough innovations in this field.

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