Available online at www.sciencedirect.com

ScienceDirect

Procedia Manufacturing 12 (2017) 113 – 119

Procedia MANUFACTURING

International Conference on Sustainable and Intelligent Manufacturing, RESIM 2016, 14-17 December 2016, Leiria, Portugal

Development of heterogeneous structures with Polycaprolactone-Alginate using a new 3D printing system – BioMED$_{\beta eta}$: design and processing

Biscaia S.[a], Dabrowska E.[b], Tojeira A.[a], Horta J.[a], Carreira P.[a], Morouço P.[a], Mateus A.[a], Alves N.[a,*]

[a]*Centre for Rapid and Sustainable Product Development, Polytechnic Institute of Leiria, portugal*
[b]*Warsaw University of technology*

Abstract

Direct Digital Manufacturing of implantable biomedical devices is the strategy for designing and constructing three dimensional (3D) structures. DDM (i.e., biomanufacturing) technologies have been widely used to construct complex 3D structures (scaffolds), where chemicals, biomaterials, and cells are deposited in a layer-by-layer fashion. These technologies control size, microarchitecture and pores interconnectivity in scaffolds, essential to transporting oxygen and nutrients for cell survival. As the Tissue engineering field progresses, new types of printers have been designed to accomplish functional engineered tissue constructs. However, the availability of innovative 3D biomanufacturing technologies for hard tissue and organ engineering is scarce and with several equipment limitations. In this work, a new biomanufacturing system, BioMED$_{\beta eta}$, composed of three different fabrication modules (thermoplastic micro-extrusion, multi-head deposition of hydrogels and electrospinning) was used to fabricate (3D) scaffolds using layer-by-layer alternated deposition of polycaprolactone and alginate hydrogel. The BioMED$_{\beta eta}$ system demonstrates the possibility of obtaining scaffolds with well-defined architecture, using both natural and synthetic polymers. Nevertheless, there are still parameters to optimize related with the design of 3D constructs and materials processing.

Peer-review under responsibility of the scientific committee of the International Conference on Sustainable and Intelligent Manufacturing

Keywords: Tissue engineering, Biomanufacturing, Bioprinting, Micro-extrusion, Heterogenous scaffolds

* Corresponding author. Tel.: +351-244-569441; fax: +351-244-569444.
E-mail address: nuno.alves@ipleiria.pt

Peer-review under responsibility of the scientific committee of the International Conference on Sustainable and Intelligent Manufacturing
doi:10.1016/j.promfg.2017.08.015

1. Introduction

Tissue engineering (TE) aims to build functional tissue or organ substitutes, through tissue regeneration or total substitution using a patient's autologous cells. This strategy includes the use of support structures to guide tissue formation. Research has been focused on the development of scaffolds which provides biomechanical support for cell adhesion, proliferation and differentiation. Such constructs are biocompatible devices, with controlled biodegradability rate and high porosity and pore interconnectivity to promote proper tissue vascularization [1-5]. Recent studies have underlined the development of heterogeneous 3D structures as one of the most promising TE strategies. However, heterogeneous tridimensional scaffold development is significantly dependent on diversified biomanufacturing systems and technologies.

3D Bioprinting is a DDM technique designed to tri-dimensionally pattern deposition of cell-laden systems (e.g. hydrogels) using additive manufacturing (layer-by-layer) construction principles to obtain functional tissues such heart tissue, blood vessels, heart valve, trachea, etc.) [6]. Apart from the simplicity of the concept, bioprinting is extremely dependent on precise position cell-carrying systems, availability of printable biomaterials at low temperatures, cell sources and growth factors. Bioprinting can be subdivided in extrusion-based biopriting (EBB), inkjet, and laser based –technologies: extrusion consists of solid-freeform fabrication based on continuous dispensing of cell aggregates, cell loaded biomaterials, micro-carrier, etc. EBB technologies are generally superior in deposition volume, cell density and printing speed. In opposition, commercially available extrusion-based bioprinters have very limited resolution (~100μm) compromising the cell patterning and organization [7]. Inkjet technology consists on drop-on-demand (non-contacting) system with varying droplet sizes determined by temperature, frequency of pressure pulses and ink rheological properties. Individual droplets are ejected in consequence of thermal (thermal bioprinting), piezoelectric (piezoelectric bioprinting) or electrostatics (electrostatic bioprinting) actuation which surpasses the ink surface tension [8]. Lastly, laser based-technologies (LaBP) involve cell transfer from a "cell solution" which sublimates under exposure to a pulsed laser releasing the underlying biological substances. This process provides a higher resolution and great cell viability [9].

A melt-extrusion-based technique, i.e., Fused Deposition Modelling (FDM), deposits thermoplastics filaments, with diameters ranging from 100 to 500μm, through an extrusion nozzle heated to a temperature higher than the polymer's melting temperature. The liquefied polymer is drawn onto a platform it solidifies culminating with scaffolds with increased mechanical properties suitable for hard tissue applications (i.e. bone) [10]. A significant drawback of melt-extrusion techniques relate to the inability of cell to survive or biomolecules to retain normal activity in consequence of high temperature of the systems; however it has been proved that FDM scaffold are beneficial in mechanically supporting the cells avoiding structure collapse while tissue is forming [11].

Smaller polymer fibers with typical diameters of 5-30μm are made using electrospinning processes: melt or solution-based. Melt electrospinning consists in ejecting liquefied polymer from a spinneret by application of a high potential difference applied between its orifice and the collector. The polymer melt fibres are then solidified at the base of the collector with random alignment. As alternative, solution-based electrospinning allow the use of polymers which do not withstand high temperatures, but a solvent instead [12].

Because native tissues present heterogeneous characteristics, heterogeneous scaffold fabrication implies the combination of multiple techniques to obtain different scales of microstructure and properties. Multi-head systems have been studied to obtain heterogeneous structures, particularly, by combining biodegradable thermoplastics and hydrogels materials [13-16]. However, such apparatus present limitations regarding their bulk dimensions, limited possibility of techniques and materials combination, reduced control over the geometric and structural tri-dimensional parameters, complex operating system, etc.

BioMED$_{\beta eta}$ equipment allows combination of different biomaterials for construction of functionally graded scaffolds with well-defined architectures using a wider range of materials and three different biomanufacturing techniques: micro-extrusion system, a multi-head hydrogel dispensing system and electrospinning modules. This work aims to study and validate the BioMED$_{\beta eta}$ equipment as a new biomanufacturing system for construction of heterogeneous tridimensional scaffolds. Due to the complexity of the validation process, this report will only focus on the development of heterogeneous scaffolds by combination of micro-extrusion (thermoplastic) and multi-head dispensing (hydrogels) techniques.