Development of an electrospinning-based rapid prototyping for scaffold fabrication

Apinya Chanthakulchan, Pisut Koomsap and Kampanat Auyson
Department of Industrial and Manufacturing Engineering, Asian Institute of Technology, Pathumthani, Thailand, and
Pitt Supaphol
Petroleum and Petrochemical College, Chulalongkorn University, Bangkok, Thailand

Abstract

Purpose – This paper aims to present the development of an electrospinning-based rapid prototyping (ESRP) technique for the fabrication of patterned scaffolds from fine fiber.

Design/methodology/approach – This ESRP technique unifies rapid prototyping (RP) and electrospinning to obtain the ability of RP to create a controllable pattern and of electrospinning to create a continuous fine fiber. The technique follows RP process of fused deposition modeling, but instead of using extrusion process for fiber creation, electrospinning is applied to generate a continuous fiber from a liquid solution. A machine prototype has been constructed and used in the experiments to evaluate the technique.

Findings – Three different lay-down patterns: 0°/90°, 45°/135° and 45° twists were used in the experiments. According to the experimental results, stacks of patterned layers could be created with the ESRP technique, and the fabrication process was repeatable and reproducible. However, the existing machine vibration influenced the fiber size and the ability to control straightness and gap size. Also, incomplete solidification of the fibers prior to being deposited obstructed the control of layer thickness. Improvement on vibration suppression and fiber solidification will strengthen the capability of this ESRP technique.

Research limitations/implications – This research is currently limited to the introduction of the ESRP technique, to the development of the machine prototype, to the demonstration of its capability and to the evaluation of the structural properties of the fabricated patterned scaffolds. Further studies are required for better control of the patterned scaffolds and for investigation of mechanical and biological properties.

Originality/value – This unification of the two processes allows not only the fabrication of controllable patterned scaffolds but also the fabrication of both woven and non-woven layers of fibers to be done on one machine.

Keywords Layered manufacturing, Medical, Rapid prototyping, Scaffolds, Fiber

Paper type Research paper

1. Introduction

Tissue engineering (TE) has been introduced and has become a preferable alternative for healing patients from organ loss or damage (Yang *et al.*, 2002). TE is a process for biological substitute regeneration that is important for restoration, maintenance or improvement of functions for harvested tissues, implantations and prostheses (Yeong *et al.*, 2004). Normally, biological substitutes consist of cells, extracellular matrices made from cell secretions and biologic signals for simulating cell regeneration (Chua *et al.*, 2003). The cells are expanded from a small biopsy and seeded onto a carrier which accommodates and guides the growth of new cells (Chen *et al.*, 2002). The carrier is known as a scaffold which is a three–dimensional (3D) porous structure constructed for cell attachment, proliferation and differentiation (Tellis *et al.*, 2008).

For scaffolds to be applied, they must meet biological, structural and mechanical requirements. The biological properties depend on materials used. The material should be biocompatible to prevent the patients from inflammation and toxicity from the scaffolds (Chen *et al.*, 2002). For temporary scaffolds, biodegradability is another property to be concerned. The degradation rate should be suited with the cell growth rate (Yeong *et al.*, 2004). To support the cell growth and to guide the cell formation, sufficient space and contact area are needed. Porosity, which is space per whole volume ratio, should be high to contribute the space for cells to attach and regenerate in all directions (Chen *et al.*, 2002) while a large pore size accommodates and delivers the cells for tissue regeneration (Too *et al.*, 2002). For hard tissues, the porosity of the scaffolds should be at least 90 per cent, but, for soft tissues, the scaffolds should have porosity of 60-83.5 per cent (Yang *et al.*, 2001). The optimal pore size varies depending upon application. For example, it should be between 20-125 μm for skin regeneration, 45-150 μm for liver tissue regeneration and 100-400 μm for bone regeneration (Oh *et al.*, 2007). Besides, pore interconnectivity is needed for the exchange of nutrients and gas. It also allows the cells to

The current issue and full text archive of this journal is available on Emerald Insight at: **www.emeraldinsight.com/1355-2546.htm**

Rapid Prototyping Journal
21/3 (2015) 329–339
© Emerald Group Publishing Limited [ISSN 1355-2546]
[DOI 10.1108/RPJ-11-2013-0119]

Received 9 July 2013
Revised 22 November 2013
9 January 2014
Accepted 16 January 2014

penetrate into the scaffold structure. The high pore interconnectivity allows uniform cell distribution and cell flow (Chua *et al.*, 2003). Generally, the high porous microstructure scaffolds with interconnected pores and a large surface area are conductive to tissue ingrowths (Yoshimoto *et al.*, 2003). However, the large porosity inversely affects the mechanical property of the scaffolds (Zein *et al.*, 2002). Although the porosity should be high for sufficient space, the mechanical property is also concerned. The mechanics of the scaffold provide the strength that can maintain a structure in a 3D form during cell growth. In addition, the mechanical strength should be sufficient to protect the cells or new tissues from excessive loads, includes wound contraction forces (Tellis *et al.*, 2008).

Several techniques have been applied for scaffold fabrication. One of them is electrospinning that has been known for its capability to produce continuous fine fibers with diameters ranging from micrometers down to nanometers (Huang *et al.*, 2003; Mitchell *et al.*, 2011). A high direct current voltage power supply in kilovolt range is applied to draw a fiber from a polymer solution or polymer melt that is held in a metallic needle (Owida *et al.*, 2011). A positive line is connected to the metallic needle and a ground is connected to a collector plate or a rotating mandrel. The electric field formed between the needle and the collector plate creates an electrostatic force to the polymer solution. The polymer droplet at the needle tip is deformed into a Taylor cone when the electrostatic force is increased (Park *et al.*, 2008). When the force overcomes the surface tension of the polymer solution, the Taylor cone is elongated and the solution jets toward the collector plate. The jet comes out as a straight flight during a certain distance before it starts bending and becomes uncontrollable. During the flight, the solvent evaporates from the polymer solution and the jet is solidified (Shin *et al.*, 2001). The fiber is randomly deposited to form a non-woven fiber mat on the collector. Electrospun fibers have been used in various applications such as filtration, textile and medical (Yoon *et al.*, 2006; Deitzel *et al.*, 2001; Yang *et al.*, 2002), and more than 40 per cent of research publications on advanced applications of nanofibers are on tissue engineering (Thavasi *et al.*, 2008).

Similar to other conventional techniques (e.g. gas foaming, fiber bonding and solvent casting), electrospinning has inherent limitations in terms of the capability to control pore size and pore arrangement for a construction of internal channels within the scaffold (Lam *et al.*, 2002). This is due to the unstable flight trajectory of the fiber jet. To control the fiber deposition, the process should be modified to allow the fiber to reach the collector before it starts bending. This can be done by prolonging the straight part of the trajectory, or by shortening the distance between the needle tip and the collector to be within the straight part of the trajectory. For the first school of thought, researchers have attempted to align the fiber by controlling the speed and movement of the rotating mandrel collector (Edwards *et al.*, 2010), and by manipulating auxiliary electric fields to dampen the instability of the fiber jet (Deitzel *et al.*, 2001; Kim and Kim, 2006). Although the alignment can be controlled, the location of the fiber is still difficult to arrange and deposit on the desired positions.

The second school of thought is known as near-field electrospinning, in which the needle-collector distance is between one-half millimeter and three millimeters (Sun *et al.*, 2006). It has better control over the fiber deposition. However, because the flight distance is shortened, the solvent in the jet does not have enough time to fully evaporate (Chang *et al.*, 2008). As a result, the fiber will fuse with the previously deposited ones. Researchers have tried to increase the flight time (i.e. to extend the straight part) by lowering voltage and increasing viscoelasticity of the polymer solution (Bisht *et al.*, 2011).

Imperfections of the conventional techniques have encouraged the use of rapid prototyping (RP) technology in tissue engineering (Zein *et al.*, 2002; Rengier *et al.*, 2010). The potential advantages of RP for the fabrication of scaffolds include fewer design constraints, customization for specific patients, faster manufacturing speed, functionally graded materials, free of toxic solvents and controllable and reproducible porous structures (Zhou *et al.*, 2008). Several RP techniques have already been applied in the scaffold fabrication (Yeong *et al.*, 2004). Stereolithography apparatus (SLA), selective laser sintering (SLS), 3D printing (3DP) and fused deposition modeling (FDM) are the examples of commercial techniques applied. They have been used to create the scaffolds from various types of materials. For instance, SLA was reported for the scaffold fabrication from a resin-based poly(D,L-lactide) (PDLLA) (Melchels *et al.*, 2009), and SLS was reported for the scaffold fabrication from hydroxyapatite, poly-e-caprolactone (PCL) and polyetheretherketone (Mazzoli, 2013). Furthermore, these major RP techniques have also been used to make molds from negative profiles of the scaffolds for casting slurries of scaffolding materials to produce the structures indirectly. For example, researchers used SLA to create epoxy resin molds for making a titanium alloy hemi-knee joint and a porous bioceramic bone (He *et al.*, 2006). 3DP has been reported for making a mold for casting collagen scaffold (Sachlos *et al.*, 2003). Besides, researchers have also developed in-house RP techniques for this application such as low temperature deposition manufacturing (Xiong *et al.*, 2002), rapid freeze prototyping (Pham *et al.*, 2008) and selective vacuum manufacturing (Phattanaphibul *et al.*, 2012).

Among the techniques, FDM has a process closest to electrospinning. In the process, the material in solid filament form is fed into a liquefier to be melted into a semi-liquid state. The melt or soften material is extruded through a nozzle head that its movement is controlled to deposit the melt material to form a layer. FDM was reported to provide good control and reproducibility of the porosity and the microstructure of scaffolds (Too *et al.*, 2002). The scaffolds with predictable microstructure can be created by varying road width and road gap. If the road gap is increased, the porosity is increased, while the mechanical strength is decreased. The relationships of lay-down pattern, channel size, porosity and mechanical strength were studied from the scaffolds with 254-μm fiber size (Zein *et al.*, 2002). Similar to other RP techniques, FDM has been used to fabricate scaffolds from various biodegradable polymers and composites. For polymers, it was reported, for examples, for finding suitable structure and composition for biodegradable polymer scaffolds for cartilage

(Tanaka *et al.*, 2010), and for polymethylmethacrylate implantations (Espalin *et al.*, 2010). For composite, FDM was applied, for example, to fabricate controlled porosity composite scaffolds for bone tissue engineering (Kalita *et al.*, 2003). Several polypropylene (PP) – tricalcium phosphate (TCP) composite scaffolds were fabricated with different shapes, sizes and internal architectures. The study also reported that the low pore volume PP–TCP composite scaffolds could resist more compressive strength than the ones with the higher pore volume. Recently, researchers examined the use of soft elastomers and bioactive glass (BAG) in FDM (Korpela *et al.*, 2012). The study reported the printability of a PCL/BAG composite and a poly(L-lactide-co-ε-caprolactone) copolymer, and compared them with PCL and polylactide (PLA). Because the properties of material can be changed due to the high temperature, researchers proposed to modify FDM process to avoid the limitations. The melting process was replaced with dissolution process by adding the solvent instead (Yeong *et al.*, 2004). The system, however, required an additional process and the fiber was still limited by the nozzle size which was micro size.

This paper presents the development of an electrospinning-based rapid prototyping (ESRP) technique for fabrication of scaffolds with controllable patterns of fine fiber. It is an attempt to unify two potential processes to obtain the advantages of both processes: the capability to produce fine fiber of electrospinning and the capability to create a controllable pattern of RP. The next section includes the integration of electrospinning with RP techniques to achieve the two capabilities. Then an electrospinning-based RP is described in Section 3. Section 4 presents experiments conducted to evaluate the performance of an ESRP machine prototype before conclusions are addressed in the last section.

2. Integration of electrospinning and RP techniques

The importance of a nanostructured architecture has been recognized in scaffold fabrication that it can mimic the nanofiber structure of the natural extracellular matrix (Ma *et al.*, 2005). A combination of electrospinning and FDM was used to fabricate a tri-leaflet heart valve scaffold (Chen *et al.*, 2009). The heart valve ring graft was constructed from PCL by FDM, and the nanofibrous leaflets were created from thermoplastic polyurethane by electrospinning. These two parts were glued and sewed together to form the scaffold model. In this process, two techniques were used for different purposes. The ring need a controllable shape and feature that electrospinning cannot create. On the other hand, the leaflet needed more flexible shape and nanofiber size, so the electrospinning was used instead. Due to the unshaped scaffolds from electrospinning, FDM was used to create a tubular mold for coronary artery bypass graft (CABG) (Owida *et al.*, 2011). After the mold was produced, the electrospinning was used to fabricate the CABG scaffolds on FDM mold. The fiber diameter from electrospinning for CABG was less than 1 μm. Hybrid method using direct polymer melt deposition (DPMD) and electrospinning was also proposed to create dual-scale scaffolds (Park *et al.*, 2008). The electrospinning methods generated a nanofibrous mesh from PCL/collagen mixed solution and DPMD process created a PCL 3D structure with the diameter size about 400 μm. The nanofibrous mesh was inserted into the 3D structure to form the final scaffolds. The controllable shape and nanofibrous-inner scaffold with alternating layers could be fabricated. Another example is dual-scale scaffolds from PCL microfilaments and electrospun poly(lactic-co-glycolic acid) (PLGA) fibers (Mota *et al.*, 2011). FDM was used to create filaments in 0°/90° lay-down pattern with a diameter around 365 μm. The PLGA fibers with a diameter around 1 μm were collected on top of the PCL structures. The microfilament scaffolds with nanofibers on the top could be finished. According to these studies, the electrospinning and RP processes have been used to fabricate scaffolds separately. The electrospinning was used to create fine fiber while RP was used to achieve controllable shape.

3. Electrospinning-based rapid prototyping

The limitations of RP techniques to produce a small scale fiber and of electrospinning to control fiber deposition have motivated the development of an ESRP technique. This ESRP technique unifies rapid prototyping and electrospinning to obtain the ability of RP to create a controllable pattern and of electrospinning to create a continuous fine fiber. This technique follows RP process of FDM for a layer construction but instead of using extrusion process for fiber creation, electrospinning is applied to generate electrostatic force to draw a continuous fiber from a liquid solution. The fiber is laid down from a nozzle to a collector at predefined positions to create patterns layer by layer. The creation of lay-down patterns requires a relative movement between the nozzle and the collector which can be classified into three possibilities. The first one is all movements are assigned to the nozzle. Another possibility is all movements are assigned to the collector. Lastly, the movements are separated and assigned to both the nozzle and the collector. In case that all movements are assigned to one unit, the machine will have a complex structure, and the unit will be highly affected from the inertia and momentum. Due to the difficulties of assigning all movements to one single unit, the movements of the machine should be assigned to both the nozzle and the collector. For the nozzle movement, deflection can occur to the nozzle when it moves on horizontal plane with a fast speed, and the deflection has direct effect on the accuracy of the fiber deposition. On the other hand, the collector is not affected from the horizontal plane movement. In addition, the collector movement on the horizontal plane provides higher accuracy to control the locations of deposited fibers. Therefore, the horizontal plane movement should be assigned to the collector and the movement along z-axis is assigned to the nozzle.

Prior to the development of ESRP, experiments were conducted to investigate the possibility of applying RP concept with electrospinning process. Experimental apparatus was setup as illustrated in Figure 1. The range of appropriate voltages that produces continuous jet was determined at each standoff distance. Critical standoff distances for obtaining a straight jet were then identified, followed by the study on the effect of collector speed to the jet diameter. Afterward, scaffolds were fabricated by manual control layer by layer.

After experimental study was conducted, a prototype of ESRP was designed and constructed. The design and the