Advances and Trends in Tissue Engineering of Heart Valves

Y. S. Morsi
Swinburne University of Technology, Australia

C. S. Wong
Swinburne University of Technology, Australia

S. S. Patel
Swinburne University of Technology, Australia

INTRODUCTION

Improvements in health care and treatment of diseases have led to an increase in life expectancy in developed countries. However, this achievement has also inadvertently increased the prevalence of chronic illnesses such as cardiovascular disease, adding to the growing burden of health care cost globally. Unfortunately, this trend is expected to escalate in the foreseeable future. Cardiovascular disease remains one of the main problems in contemporary health care worldwide, accounting for approximately one third of the world's total death (Poole-Wilson, 2005). This article focuses on a subgroup of cardiovascular disease known as valvular heart disease whereby abnormalities or malfunctions of the heart valves are detected. It is estimated that 93,000 valvular surgeries were conducted in the United States in 2002 (American Stroke Association & American Heart Association, 2005) and valve replacement surgeries accounted for 75% of the surgery performed for valvular defects in Australia and, of that, 56% were for aortic valves (Davies & Senes, 2003).

BACKGROUND

Currently, there are two types of artificial heart valves used in valve replacement surgeries: mechanical and tissue valves. However, these prostheses are not without limitations. Mechanical valves are usually made from pyrolytic carbon attached to a PET-covered metal such as titanium frame. Although more durable than tissue valves, patients implanted with mechanical valves are subjected to long-term complications such as thromboembolism, leading to a life-time administration of anti-coagulant (Bloomfield, Wheatley, Prescott, & Miller, 1991; Oxenham et al., 2003). Alternatively, tissue valves created from biological tissues from human or animal (porcine or bovine) may be used. While tissue valves do not require long-term anticoagulants, they undergo progressive deterioration such as calcification and tearing of cusps, leading to structural failure (Hammermeister, Sethi, Henderson, Oprian, Kim, & Rahimtoola, 1993; Schoen & Levy, 2005). Moreover, these clinically used prostheses are incapable of growth or remodelling. Hence, extensive research and development is being conducted worldwide to explore the potential of an emerging field, Tissue Engineering (TE), as a solution for addressing the shortcomings of current prosthesis used in valve replacement surgeries.

TE is a multidisciplinary area that amalgamates the principles of engineering and biological sciences to create functional tissue which can be ultimately used to repair, regenerate, or replace diseased or damaged parts of the body. A general approach of TE involves utilising temporary porous three-dimensional (3D) scaffolds to: (i) define the complex anatomical shape of the tissue, (ii) guide the proliferation and differentiation of seeded cells, and (iii) provide mechanical support for the cells (Ang, Leong, & Chua, 2006; Yang, Leong, Du, & Chua, 2001). While conventional techniques such as solvent casting and particulate leaching can be used to manufacture scaffolds, their applications to create scaffolds for heart valves are largely restricted by their limitations such as lack of mechanical strength and use of toxic organic solvents (Ang et al., 2006; Sachlos &

Czernuszka, 2003). The creation of scaffolds for heart valves require specific characteristics and precision of the tissue to be captured and ideally these scaffolds should be tailored to individual patients.

RAPID PROTOTYPING TECHNOLOGIES

Recently, an increased interest has been generated for Rapid Prototyping (RP) techniques as powerful tools for fabrication of scaffolds. RP techniques may be able to address some of the limitations encountered in the conventional techniques. There are three types of RP techniques discussed in this article: fused deposition modeling (FDM), 3D printing, and bioprinting.

FDM is a material deposition process which uses a computer-aided design (CAD) model to generate 3D scaffolds (Masood, Singh, & Morsi, 2005). The scaffolds are generated through the extrusion of thin rods of molten polymer using a computer-controlled XYZ robotic dispenser (Figure 1). The layers of polymer are deposited in an interconnected manner, thus improving the mechanical stability of the scaffold. FDM enables complex yet accurate characteristics to be reconstructed from CT scans, which leads to the ability to create scaffolds customised to patients' needs. Scaffolds demonstrating the complex geometry of the aortic valve which incorporated the exact dimensions of the sinuses of Valsalva (required to preserve the flow characteristics of the valve) were successfully manufactured using FDM (Figure 2) (Morsi & Birchall, 2005). This technique offers a high degree of control over the shape, pore interconnectivity, and porosity of scaffolds as individual process parameters can be defined and improved (Ang et al., 2006). A high resolution of 250 μm can be achieved with the FDM. An added advantage of the FDM technique is that the process does not utilise toxic solvents and porogens for the manufacturing of scaffolds (Leong, Cheah, & Chua, 2003; Yang, Leong, Du, & Chua, 2002). The flexibility of this technique lends itself to produce scaffolds of varying designs and complexity, thus expanding its application to other areas of TE aside from heart valves.

The 3DP is a layered fabrication process whereby sliced 2D profile of a model determined by CAD file is transform to a STL file and printed on a fresh layer of powder via deposition of a suitable binder from the inkjet printhead (Figure 3). The powders used are natural polymers such as starch, dextran, and gelatin in conjunction with water-based binder so that the scaffolds can be used in medical applications, as toxic solvents can be omitted from the manufacturing process. The 2D profiles are then successively printed on freshly laid layers of powder until the entire scaffold is printed. These printed layers are held together through

Figure 1. Diagram demonstrating the fabrication process of FDM. The ABS filament is fed through the FDM head via the drive wheels and melted at the appropriate temperature in the liquefier. The polymeric fibres of 250 μm are then deposited layer by layer in an XYZ direction to produce a 3D scaffold.