Bonding of biodegradable polymers for micro-fluidic tissue scaffolds

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Statement of Purpose:

Biodegradable polymer scaffolds for tissue engineering require highly interconnected and controlled geometry of microstructures in order to guide cell growth and to achieve sufficient supply of nutrients and oxygen [1,2,3]. Implantable controlled drug delivery devices are another example that require precisely micro structured polymer constructs in order to program the desired device release rates [4]. In response to these demands we introduced a solvent vapor bonding technology that allows assembling micro-structured polymer constructs avoiding damage to the surface structure. This bonding method is compatible with various synthetic biodegradable polymers without modifying their properties. Based on this technology a variety of micro-structures such as micro-channels, cavities, and pores were fabricated into three-dimensional tissue scaffolds. Cell culturing study of human coronary artery endothelial cells (HCAEC) on bonded multi-layer scaffolds was conducted in order to demonstrate the biocompatibility of the fabrication and bonding processes.

Methods and Materials

50/50 poly (DL-lactide-co-glycolide) (50/50PLGA) was purchased from Absorbable Polymer Technologies, Inc. 85/15PLGA and poly (p-dioxanone) (PDO) were donated by Ethicon, Johnson & Johnson Company.
Bonding of two micro-structured polymer surfaces is obtained by physical entanglement among loosened polymer chains on both the surfaces. The polymer chains are disentangled by solvent vapor absorption at the polymer surface. The investigations were carried out in a customized micro bonding station. HFIP (Hexafluorosoisopropanol, 1,1,1,3,3,3-hexafluoro-2-propanol, VWR International) was used as a solvent. Human coronary artery endothelial cells (HCAEC) were obtained from Cambrex (Walkersville, NJ). Endothelial cell basal medium and additives were purchased as EGM-2 MV endothelial medium kit (Cambrex, Walkersville, NJ).

Results and Discussion:

The depth of polymer dissolution was controlled by altering the vapor pressure (p_g) of HFIP solvent. Vapor solvation of the polymer surface is required to enable physical entanglement of polymer chains which is a fundamental part of forming a solid bond between polymer films. However, micro-structural damage should be avoided. According to these constraints and in combination with bonding strength measurements, the optimal pg for the HFIP bonding of micro-structured PDO layers was 5.33kPa. Optimized pg values was found for 35/65PCGA, 85/15PLGA, and Monocryl®.

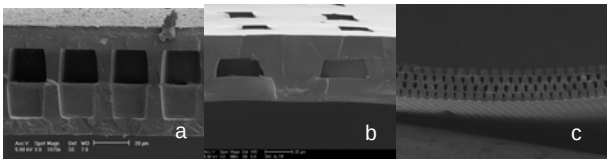

Fig. 1: Micro-bonded tissue scaffolds. (a) PDO scaffold (b) interconnected 35/65PCGA three-layer scaffold (c) 35/65PCGA four layer scaffold.

Two PDO layers containing micro-cavities (20μm size) were bonded together (Fig. 1.a). Seamless bonding between two layers was achieved uniformly without damage to the micro-cavities in both layers. A 35/65PCGA scaffold with more than two layers was fabricated showing that multiple exposures to solvent vapors did not affect micro-structures in all the layers (Fig. 1. b,c).
HCAE cells were cultured on single and double layered micro-fabricated scaffolds made of 35/65PCGA along with a control sample of unprocessed material. The HCAE cells on the bonded scaffolds attached well to the polymer surface and showed good viability after two days of culture, indicating the fabrication and bonding processes are biocompatible and that little or no toxic HFIP resides in the bonded structures which was also confirmed by gas chromatography measurements.

Conclusions:

A vapor solvent bonding technology for micro-fabrication of three-dimensional biodegradable polymer scaffolds has been developed. The technology highlights high resolution bonding of interconnecting micro-structures and of micro-structured polymer layers. Construction of complex micro-fluidic structures within and across the layers of multi-layered scaffolds was demonstrated. The biocompatibility of the presented method was confirmed by culturing human coronary artery endothelial cells on the constructed scaffolds.
Micro-patterned polymers having feature down to 100 nm to can be bonded without damage to these structures..
Using this bonding technique the fabrication of hybrid scaffolds that incorporate mitogenic factors are currently under investigation.

References:

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