3D Multi-layered Micro-fabricated Tissue Scaffolds of Biodegradable Polymers

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Statement of Purpose: Micro-fabrication technologies are presently of interest for tissue engineering since they can create complex micro-geometries resembling a natural tissue environment. However, most micro-fabricated scaffolds are two dimensional, and only very limited three-dimensional (3D) scaffolds have been constructed based on a layered fabrication approach [1] [2]. In order to construct such multiple layer tissue scaffolds with micro-structures in them, it is critical to have a proper bonding method which is biocompatible and preserves micro-structures during the process. Thus, we present a vapor bonding method which can create 3D multi-layered micro-fabricated tissue scaffolds of synthetic biodegradable polymers. Various micro-geometries are shaped in each layer by using a micro-molding method and then these layers are assembled and bonded together by the bonding method presented.

Methods: Synthetic biodegradable polymers, 85/15PLGA (85/15 poly(lactide-co-glycolide)), 35/65PCGA (35/65 poly(ε-caprolactone-co-glycolide)), PDO (poly-dioxanone), and Monocryl® in film form, whose thicknesses were 20-25μm, were donated by Ethicon, a Johnson & Johnson company. The polymer films were micro-molded to have various geometries: cavities, holes, and channels. Then, these micro-structured polymer layers were bonded together to form 3D multi-layered scaffolds. The bonding was performed by exposure of the micro-structured polymer layers to solvent vapors (Hexafluoroisopropanol $C_3H_2F_6O$, HFIP) in a bonding chamber, followed by a contact of two layers and purging of the solvent vapors from the chamber. Optimal operation parameters for biodegradable polymers such as a vapor pressure, dwell time, and contact pressure, were determined by observing the dissolution depths of the polymers exposed to solvent vapors. The observations were made by scanning electron microscope images (FEI XL30 Sirion model).

Results / Discussion: Optimization results of bonding parameters show the possibility of controlling the dissolution depth of biodegradable polymers on a sub-micron scale. Micro-structures from each biodegradable polymer had characteristic lengths of 20 μm and the SEM images of the samples under their optimal bonding conditions showed uniform dissolution depths smaller than a micro-meter without damaging micro-structures. Based on the optimized parameters, the layers of PDO and 35/65 PCGA were bonded together, as shown in Fig.1. The PDO samples contained 20μm size micro-cavities and were bonded at 40 torr of HFIP vapor pressure with full preservation of micro-cavities. The 35/65PCGA samples had various micro-structures such as cavities, holes, and channels. All the micro-geometries of 35/65PCGA had characteristic lengths of 20μm. 35/65PCGA multi-layer scaffolds, which were interconnected from one side to the other via 20-60μm holes, were created. The constructs had either same size holes or gradually enlarging holes across the layers. Another multi-layered scaffold of 35/65PCGA with 20μm channels is demonstrated for the possible application in nerve regeneration.

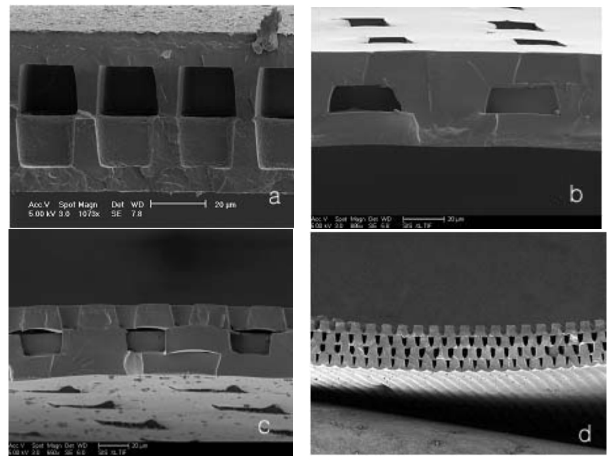

Figure 1 Micro-fabricated tissue scaffolds (a) 20μm cavities in PDO scaffold (b) Interconnected 35/65PCGA scaffold with 20μm holes (c) Gradient pores (20, 40, 60μm) in 35/65PCGA scaffold (d) 20μm channels in 35/65PCGA scaffold.

Conclusions: A method to create 3D micro-fabricated tissue scaffolds with synthetic biodegradable polymers was presented. The method was based on sub-micron dissolution of polymer surfaces by exposure to solvent vapors. It was demonstrated that control of sub-micron dissolution was feasible with four different types of biodegradable polymers. Full characterization to find optimal dissolution parameters was performed for the four biodegradable polymers. Various 3D scaffolds containing micro-structures such as cavities, holes, or channels were constructed by the combination of micro-molding and bonding methods. The examples include interconnected scaffolds and multi-layer channel scaffolds for guiding nerve regeneration.

References:

[1] J. T. Borenstein et al, "Living Three-dimensional Microfabricated Constructs for the Replication of Vital Organ Function", *Transducers '03 The 12th Int'l Conf. on Solid State Sensors, Actuators and Microsystems*, pp. 1754-1757, Boston, June 2003

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