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TU/e technische universiteit eindhoven

A suitable scaffold to mechanically condition tissue engineered blood vessels

Maria Stekelenburg, Robert v. Lith, Marcel C.M. Rutten, Carlijn V.C. Bouten, Frank P.T. Baaijens, Luc H.E.H. Snoeckx

Biomechanics and tissue-engineering, materials&technology

Introduction

Creating a small-diameter blood vessel substitute is one of the goals of tissue engineering. These substitutes could be used -among others- for coronary artery bypass surgery.
The challenge in this research area is to find the best combination of scaffold material, cells, seeding- and culture procedures. The properties of the tissue-engineered blood vessel can be influenced by mechanical and biochemical conditioning during culture.

Objective

Finding a scaffold with good mechanical properties and cell ingrowth suitable for mechanical conditioning of blood vessel constructs.

Methods

Figure 1 shows a simple experimental set-up that will be used to condition blood vessel constructs mechanically. The tubular constructs are connected to the set-up and can be exposed to shear stress by flowing culture medium through the tube, and/or circumferential stretch by applying a pressure over the tube.

Figure 1: *Bioreactor in which a shear stress and strain can be applied to tubular constructs*

Scaffolds

Electrospun polycaprolactone (PCL) is used as a scaffold material. As the pores in this scaffold are too small for cell penetration, a new electrospin-method was developed. PCL is sequentially electrospun in layers, alternating with polyethylene oxide (PEO), after which the PEO is washed out in water.

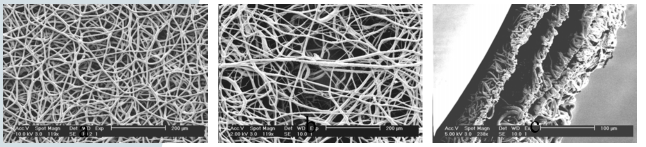

Figure 2: *Electospun PCL (a) and PCL(PEO) (b,c)*

Results

Figure 2 shows scanning electron microscope (SEM) images of the electrospun PCL and PCL(PEO) scaffold. The latter has larger pores (b) and, depending on the layer thickness of the PEO, a clear layered structure (c).

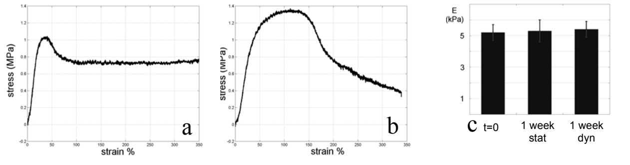

Figure 3: *Stress-strain curve of PCL (a) and PCL(PEO) scaffold (b) and the resulting Young's moduli (c) under static (PBS, 37°C) and dynamic (PBS, 37°C, 7.5 % strain) culture conditions after 1 week*

Uniaxial tensile tests of the tubes show approximately identical mechanical behavior of the PCL and PCL(PEO) tubes for strains up to 20% (figure 3a,b), i.e. in the range of mechanical conditioning, E=4.7 and 4MPa respectively. Figure 3c shows that the scaffolds keep their mechanical properties under (mechanical) culture conditions.

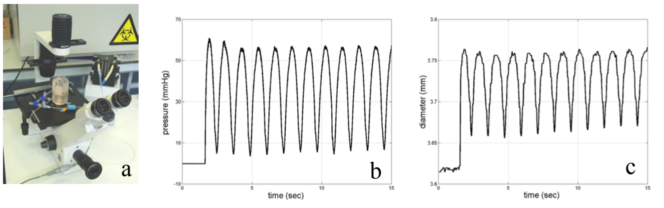

Figure 4: *The bioreactor on top of a microscope (a) to measure the relationship between pressure (b) and strain(c).*

The bioreactor with the tubular construct is placed on an inverted microscope to visualize the straining of the tube. At the same time the pressure inside the tube is measured. Figure 4 shows the pressure (b) and strain (c) measurement for a PCL tube. At a pressure of 60 mmHg the strain is approximately 5%.

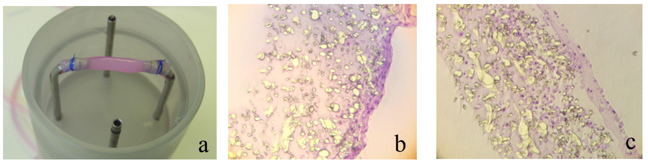

Figure 5: *Histology of cells in PCL and PCL(PEO) scaffold*

A fibrin gel with cells is applied to the constructs. Figure 5 shows the histological results for the PCL (b) and the PCL(PEO) (c) scaffold. The latter is more open and therefore the cells have penetrated deeper into the scaffold

Conclusions

Electrospun PCL has good mechanical properties for a scaffold material although cell ingrowth is a problem. With the newly developed PCL(PEO) scaffold the cell ingrowth is improved making this scaffold suitable for tissue engineered blood vessel construct, able to withstand mechanical conditioning.