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Endothelial/Smooth Muscle Cells Growth into Nonwoven Fiber Vascular Grafts

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Introduction: Coronary artery and peripheral vascular diseases is the leading cause of death in Canada (1 in 3), with 80% of Canadians having at least 1 risk factor for cardiovascular diseases a nd 10% more than 3 risks or more[1]. These figures stand for all Western countries. The s tandard surgical interv ention for small dia meter vessels is currently autologous vein (saphenous) bypass grafting when available and , for larger diameter (6 mm and more), synthetic grafts made of woven polyethylene terephthalate (PET) fibers (Dacron ™) or expanded polytetrafluoroethylene (ePTFE) characterized by a low compliance . The co mpliance mismatch between the graft and ar tery contributed to myointimal hyperplasia, particularly at anas tomotic sites[2], as a reason of hemodynamic flow perturbations , and thrombosis is a common problem. An urgent need thus exists for patent, compatible tissue engineered small -diameter (2 -6 mm) vascular grafts, to which endothelial cells (EC) can adhere, form an anti -thrombogenic luminal surface, exhibit vasoactive prop erties and improve patency. In this study, novel nonwoven PET fiber structures for vascular scaffolds obtained from the melt blowing process[3] are s tudied. Their nonwoven structure will allow for mechanical compliance adj ustment through fiber diameter and l ayout as well as porosity control , in contrast to woven Dacron structures. EC and smooth muscle cells (SMC) were seeded in the structures and their growth and attachment observed.

Mate rials and Methods : Nonwoven structures were obtai ned from melt blowing a s reported elsewhere [3] and used as disks. These disks were pre -wetted w ith cell media or with 0.5% gelatin and seeded (10^6 cells) with human brain EC (HBEC) and aortic SMC (AoSMC). Cells were allowed to grow for 6 days at 37°C in humidified atmosphere . They were then washed twice with warm HBSS, incubated with 10µg/ml CFDA (fluorescent probes) at 37° C for 45 min and washed again. Fluorescence of cells grown on the structures and on the bottom of the w ell (after removing the disks) was measured using a c ytofluorimeter reader. EC and AoSMC proliferation rates were determined from fluorescence measurements . Mechanical testing o f structures was performed to assess compliance , stre ngth (as a n indicator of burst pressure) and s train at break. Ribbons of structures (10 mm wide with effective length of 5 0 mm) were tested in uniax ial tension at a strain rate of 0.2 min^{-1}. Res ults are compared to properties of commercial vascular grafts (Hemashield ™, Boston Scientific) obtained in similar conditions.

Results and Discus sion: SEM of the nonwoven fibrous structure, well below the 20 µm range, is shown in Fig. 1. The fluorescence measured from HBEC and AoSMC proliferation for various periods of time are reported in Fig. 2. The fibrous structure tested allowed attachment and growth of types of cells . While HBEC surprisingly grew with similar efficacy on uncoated and gelatin-coated structures, AoSMC growth tended to be even significantly higher (20 -50%) for the non-coated fibrous structure as compared to the gelatin -coated structure. HBEC tended also to follow fiber alignment.

Fig. 1 Planar image of nonwoven PET fiber structure .

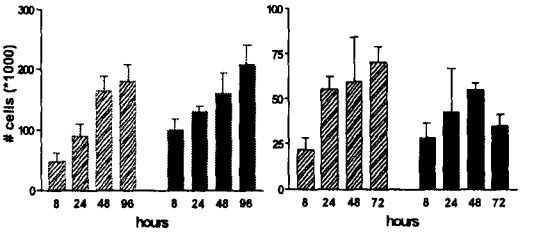

Fig. 2 Proliferation rates of HBEC (left) and AoSMC (right) grown on either uncoa ted (dashed) or gelatin - coated (full) structure. Bars represent m ean of cells ± std. dev. of 2 experiments performed in triplicates.

The compliance, strength and s train at break are shown in Table 1 . Results are compared with thoracic aorta properties (pig)[4], corrected for width and length . Results indicate that compliance of the nonwoven structure is within the same order of magnitude as the aorta compliance; while commercial grafts compliance is one order of magnitude lower. The load and strain at b reak values show a similar trend of too high properties for the commerc ial graft.

Table 1. Mechanical properties (8 tests, std dev 5%)

Material	Compliance $x10^{-3}$ (m/N)	Load at break (N)	Strain at break (mm/mm)
Nonwoven	1.1	8.6	38
Commercial	0.11	240	117
Aorta (pig)[4]	3.5-5.0	2.0-5.0	≈70

Conclusions: Nonwoven PET fibrous structures with tightly controlled porosity and fiber diameter present promising characteristics for vas cular graft fabrication such as good EC/SMC attachment and proliferation following fiber ali gnment, high compliance and deformation range similar to pig aorta values, contrasting with low compliance commercial grafts.

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