

# **FUTURE PERSPECTIVES OF BIOMEDICAL POLYMERS**

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# LUMINAL SURFACE MICROGEOMETRY AFFECTS THE PATENCY RATE OF POLYURETHANE BASED SMALL-DIAMETER VASCULAR GRAFTS

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## INTRODUCTION

From philosophical point of view biomaterial scientists have been divided on the strategies to develop newer synthetic surfaces for vascular grafts. Considerable effort has been spent on the development of a completely inert non-porous passive surface which would serve as a mere conduit with which blood would not interact. However, such a passive surface has not been found yet. The other philosophical approach is to produce grafts with textured or porous surface design to encourage a blood/surface response with subsequent development of a more efficacious graft/tissue complex. Wesolowski et al. <sup>1</sup>, reported that porous synthetic grafts are incorporated better into the surrounding tissue than impervious grafts. The tissue ingrowth induces an intima of fibroblasts, fibrin, and blood cells and, therefore, seems to improve patency rates. Golden et al. <sup>2</sup> studied the effect of varying porosity (between 10 and 90  $\mu\text{m}$  internodal distance) on the healing of 4.0 mm ID PTFE grafts. Although a drawback of this study is the limited series of animal implantation experiments, does appear to be an optimal porosity for PTFE grafts near 60  $\mu\text{m}$ , since 10 and 30  $\mu\text{m}$  fail to achieve luminal endothelial cell coverage, and 90  $\mu\text{m}$  grafts exhibit instability of the intima with focal endothelial cell loss. Regarding polyurethanes numerous techniques have been described to produce porous or filamentous small-diameter vascular grafts (SDVG) from these materials. However, these techniques as a final product all produce relatively porous, dry, hydrophobic graft materials which result inadequate to form a functional graft/tissue complex. The approach we used to fabricate porous polyurethanes grafts relies on a process which utilizes a spray technique associated to a phase-inversion effect of a polymer solution <sup>3</sup>. As a results of this unique material processing, membranes display a tridimensional, interconnected filamentous porous structure with hydrophilic properties. By varying some of the parameter of the "spraying, phase-inversion" technique the fine gel-like structure of the grafts can be widely varied, that is grafts can be fabricated with wall structure features different from those of the luminal surface.

## EXPERIMENTAL DESIGN

To understand the role played by what we call the "luminal surface microgeometry" (LSM) [the architecture of the graft surface which interacts with blood and cells] in affecting the patency rate of SDVG, two types of grafts (1.5 mm ID, 450  $\mu\text{m}$  wall thickness) were fabricated, using Cardiothane 51<sup>TM</sup> (Kontron Instruments Inc., Everett, MA), with either a skinned (SG) or a

porous (PG) luminal surface and a relatively porous wall structure. Because the luminal surface of the PG series resulted relatively compact and did not provide enough interfiber space, another series of grafts was fabricated with a luminal surface featuring higher interfiber spaces (near 110  $\mu\text{m}$ ) (HPG). SG, PG and part of the HPG series were implanted at "Brown University" (BU), Providence R.I., as infrarenal aorta replacements in male Sprague-Dawley rat. The results of these experiments have already been reported <sup>4</sup>. The remaining part of the HPG series (n=13) was implanted at "Beth Israel Hospital" (BIH), Boston MA, in the same animal model (weigh: 275-350 g; grafts length: 17-26). The results at BIH are summarized as follows:

## RESULTS and DISCUSSION

### Three months time point (7 grafts explanted):

- The patency rate was 92.3% (12/13) as judged by palpable femoral pulses and strong Doppler signals. One occluded graft revealed an associated infection. The other grafts (n=6) were patent with wide open anastomoses and complete endothelialization. There was no macroscopic evidence of intimal hyperplasia at the sites of either anastomosis or along the length of grafts luminal surface. The endothelium stained positive for Von Willebrand's factor.

### Six months time point (1 graft explanted):

- All remaining 6 grafts were patent at this time period. One graft was explanted and examined. There were no significant macro or microscopic differences between this graft and the ones retrieved 3 months after implantation.

### Ten months time point (5 grafts explanted):

- All the remaining 5 grafts were patent at this time period. There were no significant macro or microscopic differences between these grafts and the ones retrieved 3 and 6 months after implantation. There was no evidence of aneurysms formation or material biodegradation.

The results obtained with the HPG series implanted at BIH validate the observation previously done at BU that LSM appears to be the main determinant of grafts patency and completeness of the healing process. The patency rate at BIH was 92.3%, better than 73% obtained at BU.

## CONCLUSION

In relatively porous wall SDVG made from polyurethane materials endothelialization is a function of the LSM. It appears to be an optimum of surface architecture that seems to provide synthetic receptor sites that encourage a neointima that restructures over time as a result of natural biological mechanisms. This observation is under testing in larger animal models.

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