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Experimental Study of the Antithrombogenic Behaviour of PEtU-PDMS Small Diameter Vascular Grafts

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Introduction

Cardiovascular diseases are increasing as the average age of elderly population continues to grow. For this reason coronary and peripheral vascular bypass grafting is performed more than 600,000 times annually in the United States and Europe. Autogenous saphenous vein is the conduit of choice for use as bypass graft both in peripheral and cardiac procedures, but it is not without significant constraints and complications.

Replacement of arteries with purely synthetic prosthesis, as expanded polytetrafluoroethylene (ePTFE) and polyethylene terephtalate (PET), leads to failure when small-diameter (less than 6 mm) or low-flow locations are concerned. This is due to thrombogenicity of the internal graft surface and intimal hyperplasia around anastomosis caused by a compliance mismatch between graft and native blood vessel.

In this study a silicone-based elastomeric material was processed to realise small diameter vascular grafts (5 mm). The innovative idea was to combine the excellent hemocompatibility of a particular reactive polydimethylsiloxane (PDMS) with the optimal physical-mechanical characteristic of an aromatic poly(ether)urethane (PEtU).

Materials and Methods

The PEtU-PDMS material synthesis containing 25% of PDMS was carried out at the *Laboratorio di Biomateriali*. Graft manufacturing is based on a physical principle applicable to polymer solutions known as phase inversion, through a peculiar instrument, named spray-machine. The grafts were realised with a high porous internal surface (120 μm average porous diameter), in fact it is well known the importance of grafts microstructure in inducing thrombus formation. 7 cm long PEtU-PDMS grafts have been interposed in the carotid artery of sheep as chronic experiments up to two years.

Two groups were evaluated. Group A (n = 4): proximal end-to-end and distal end-to-side anastomosis and 12 and 24 months time-points. Group B (n = 4): double end-to-side anastomosis with carotid resection and 6 and 9 months time-points. In Group B ePTFE grafts (5 mm) as reference were implanted in the controlateral carotid.

Graft patency was checked by a postoperative eco-doppler and once every fortnight thereafter.

At each time point, animals were sacrificed by barbiturate lethal injection and the grafts with the adjacent segments of carotid artery were explanted. Grafts were grossly examined and photographed, then samples for light microscopy (Hematoxylin & Eosin, Masson's trichrome and Von Kossa staining) and scanning electron microscopy (SEM) were opportunely fixed.

Results

Macroscopic observation. All the PEtU-PDMS grafts showed poor bleeding during implantation, no thrombus formation, no neointima hyperplasia and absence of calcification; only in the odd case there were signs of calcification. Two out of four ePTFE grafts were completely occluded by white and red thrombi and all were calcified. Nevertheless PEtU-PDMS grafts showed a significative dilatation and elongation respect to ePTFE grafts, particularly at later time-points.

Histological examination. PEtU-PDMS samples exhibited a fibrin infiltration, leading to herniate and dilate prosthesis wall independent from the prosthesis dilatation observed macroscopically.

Examination of the 24 months PEtU-PDMS samples showed that the material was degraded and some debris were surrounded by large foreign-body giant cells and active macrophages. The samples showed a replacement of the prosthesis by a fibroconnective wall with internal lining of endothelial cells and external sign of adventicial tissue formation. In some areas of a sample, signs of differentiated smooth muscle cells oriented longitudinally and circularly were observed in the neomedia tunica.

The ePTFE material was externally colonized by a dense fibrovascular tissue. At the external implant material interface there was a continuous line of macrophages and multinucleated giant cells. Tissue ingrowth within the implant material pores was observed in all of the explants with mineralized deposits associated with trabecular bone formation.

SEM analysis. The SEM analysis showed PEtU-PDMS prostheses endothelialization extending 2 cm beyond the anastomoses at 6-9 months of implantation – at these time points the medial segment was deprived of endothelial cells and occupied with a thin layer of thrombus elements. After 24 months, the PEtU-PDMS samples were lined by a normal and confluent endothelial cell layer.

Conclusion

These data suggested a biodegradable feature of the PEtU-PDMS graft as opposed to the ePTFE grafts. PEtU-PDMS graft showed clearly better patency and was less subjected to calcification than the ePTFE prosthesis. Moreover the obtained results concerning PEtU-PDMS graft are independent of implant technique used.

At present, implants of PEtU-PDMS graft inserted in a Nitinol® stent to prevent the circumferential dilatation are in progress in minipigs animal model. This composite grafts will have physiological characteristics of antithrombogenicity and tissue incorporation that are ideal prerequisites for obtaining functional small diameter vascular grafts.