Superior *in vivo* biocompatibility of a hydrophilic polymer coated prosthetic vascular graft

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Introduction

Over the past decades the necessity for synthetic small diameter vascular prostheses has increased steadily. These vascular grafts often fail because of thrombotic complications or inflammation.[1] The underlying problem is lack of endothelialization of the blood contacting surface, which is hard to achieve *in situ*. Formation of a functional endothelial cell layer on the luminal surface is required for proper control of haemostatis and prevention of inflammation. In previous studies we have demonstrated that high density lipoprotein (HDL) adsorption to hydrophilic blood-contacting surfaces strongly increased endothelialization and improves blood-compatibility *in vitro*.[2] Here we report on the *in vivo* performance of synthetic vascular grafts, coated with a hydrophilic polymer. The grafts were implanted in the carotid artery of goats. First the *in vivo* adsorption of plasma proteins and HDL to the blood-contacting surface was studied. Then the luminal surfaces were assessed for the presence of endothelial cells, leukocytes, platelets and thrombus. The adsorption of HDL to the luminal surface of our vascular graft prototype is expected to stimulate endothelialization *in vivo* and to increase the patency rate when compared to hydrophobic control surfaces.

Methods

The synthetic vascular graft had a hydrophilic polymer coating, consisting of 90 mol% N-vinyl-pyrrolidinone (NVP) and 10 mol% n-butylmethacrylate (BMA).[3] Grafts with an inner diameter of 4 mm and length of 5 cm were implanted as interposition grafts into the carotid arteries of goats. As comparison, vascular grafts with a hydrophobic coating of NVP/BMA 10/90 were used.[2]

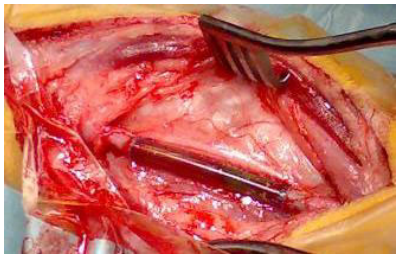

Figure 1. Vascular prosthesis as interposition graft into the carotid artery of a goat.

The grafts were explanted after 3 and 28 days, and assessed for protein adsorption and endothelialization respectively using western blotting and scanning electron microscopy (SEM).

Results and Discussion

Adsorption of HDL *in vivo* was demonstrated to exclusively occur on hydrophilic surfaces. Hydrophobic surfaces adsorbed increased amounts of fibrinogen and albumin and no detectable amounts of HDL. Retrieval after 28 days showed that all hydrophilic grafts were patent, while 2 hydrophobic grafts (of 6 in total) were occluded. Careful observation of the hydrophilic luminal surface demonstrated a cell layer with typical cobblestone morphology (fig 2, left). Additionally, the hydrophobic graft surfaces demonstrated increased numbers of leukocytes and more thrombus coverage. The identity of the endothelial cells on the hydrophilic surfaces was confirmed in an experiment using specific monoclonal antibodies for endothelial specific markers.

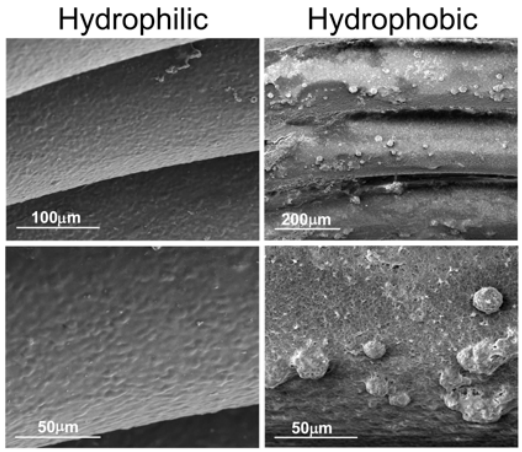

Figure 2. SEM image of the luminal surface of the vascular prosthesis after explantation.

Conclusions

Hydrophilic coatings preferentially adsorbed HDL *in vivo* under blood-flow conditions. The polymer-HDL surface seems to be a good substratum for endothelialization *in vivo*. Our data indicate that hydrophilic polymer coatings are good candidates for long-term blood contacting devices like small synthetic vascular prostheses since they induce *in situ* coverage with an endothelial cell layer that prevents thrombus formation and leukocyte adhesion.

References:

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