Nonfouling Polyurethane Coatings on Stents to Improve Blood Compatibility

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Introduction: Surfaces with the ultralow fibrinogen (Fg) adsorption (Γ_{Fg}) of less than 10 ng/cm^2 required to substantially reduce platelet adhesion [1] are good candidates for improving blood compatibility of cardiovascular devices. Such surfaces might be particularly useful in reducing late stent thrombosis observed for drug eluting stents that reduce stenosis [2, 3]. Polyurethanes (PUs) have excellent mechanical properties, and have been widely used in pacemakers and other blood-contact devices for this reason. But Γ_{Fg} on PUs is normally far above the ultralow value. A series of novel polyethylene glycol segmented linear PU block copolymers (PEG-PUs) were developed to meet the criteria of ultralow Γ_{Fg} [4]. The ability of these PUs to function as stent coatings that resist delamination and reduce protein adsorption and platelet adhesion was investigated in this study.

Materials and Methods: Two PEG-PUs, PU-82 and PU-84, were synthesized with PEGs of molecular weight 1000 and 2000 Da, respectively. We used the standard three-step solution addition polymerization, including isocyanate prepolymerization, diol chain-extension, and gradual approach to stoichiometry, as previously described [3]. PU-82 and PU-84 contain 42 or 58 wt% of PEG units, respectively. Biospan®, a PU from Polymer Technology Group, served as a control. NIR Ranger stents from Boston Scientific (316L stainless steel, 2.5 cm long, unexpanded diameter 1.5 mm) were used. To improve PU adhesion, the stents were treated in nitrogen plasma for 1 min. The stents were then coated by dipping 20 times in 0.1% PU solutions in N,N-dimethylacetamide. Fg and von Willebrand factor (vWf) adsorption from human blood plasma to the stents was measured using ^{125}I proteins [3, 4]. Platelet adhesion was done in an agitated platelet suspension [5].

Results and Discussion: SEM results showed that smooth and uniform stent coatings were achieved for all PUs, and no cracks or ruptures were observed after stent expansion to 2.75 mm or 4.5 mm in diameter, or after soaking in PBS buffer at 37°C (data not shown). These results show that PU-82 and PU-84 are feasible stent coatings. Fig. 1 shows the effects of PU coatings on protein adsorption to the stents. Γ_{Fg} on PUs exhibited a Vroman effect, i.e. the maximal Γ_{Fg} occurred in 0.1% plasma instead of 100% plasma. In contrast with Γ_{Fg}, the adsorption of vWf (Γ_{vWf}) increased with plasma concentration without showing a Vroman effect. However, under all conditions, PU-82 and PU-84 coatings had greatly reduced Γ_{Fg} and Γ_{vWf} compared with bare metal or Biospan® coated stents. PEG-PU coatings also markedly reduced platelet adhesion as shown in Fig. 2. The stent coated with PU-82 had no significant platelet adhesion and no evidence of platelet aggregates (Figure 2c & 2d). Uncoated stents not only had more platelets (Fig. 2a), but platelet aggregates were also observed (Fig. 2b). The above results showed that PEG-PUs can be successfully used to coat stents that exhibit greatly reduced protein adsorption and platelet adhesion. We therefore would expect these stents to show improved blood compatibility *in vivo* as Γ_{Fg} and Γ_{vWf} and platelet adhesion are major mediators of clotting events. In work not shown here, we also found that antiplatelet drug (dipyridamole) could be incorporated into the PU coated stents and was released in a controlled rate that could be used to further improve the thromboresistance of stents.

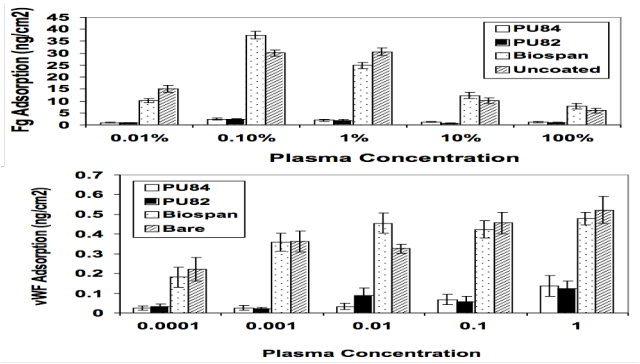

Figure 1. Γ_{Fg} and Γ_{vWf} on bare or PU coated stents after two hours at 37°C in plasma diluted to various extents.

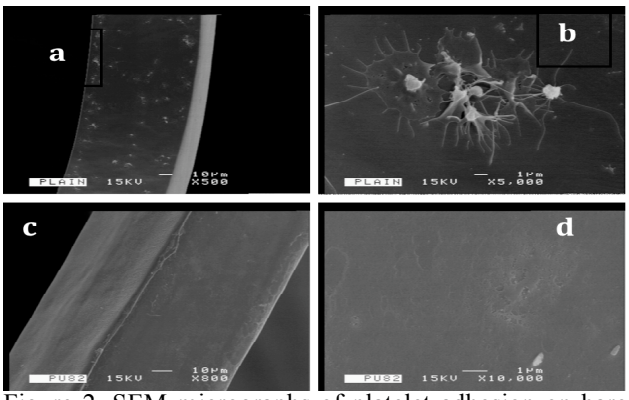

Figure 2. SEM micrographs of platelet adhesion on bare metal stent (a) (b), and on PU-82 coated stent (c) (d).

Conclusions: PEG-PUs greatly reduced protein adsorption and platelet adhesion and could withstand stress during stent expansion. They are promising polymer coatings for stents and may also resist oxidative degradation due to the inability of macrophages to adhere.

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