Bloodcompatibilty of Slipskin® and ptfe coated guidewires

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Statement of Purpose: PTCA (percutaneous transluminal coronary angioplasty) procedure starts with the penetration of a coronary stenosis with a guidewire. The outer surface of the guidewire is of great interest for biomaterials science. The surface must be smooth (lubricious) and blood compatible. Lubricity is needed to prevent damaging the vessel wall, which could lead to coagulation during or after the PTCA procedure. Many commercial guidewires are coated with PTFE (poly(tetrafluoroethylene)) which has an excellent lubricity but a moderate bloodcompatiblity.[1] Hydrophilic slippery-when-wet coatings provide an alternative to PTFE coatings.[2] One example is the Slipskin® copolymer, which is built from N-vinyl pyrrolidinone and butylmethacrylate.[2] Incorporation of heparin into the coatings can improve the bloodcompatibility of these guidewires. Here we compare 5 different guidewire coatings: (*i*) Slipskin®; (*ii*) Slipskin® mixed with sodium heparin (Slipskin®-NaHep); (*iii*) Slipskin® mixed with benzalkonium heparin (Slipskin®-HBAK); (*iv*) PTFE; (*v*) PTFE-HBAK. Heparin release, heparin exposure, thrombin generation under flow, whole blood contact, platelet adhesion, cell contact and cytotoxicity were measured

Methods: Heparin release was measured over a time period of 24 h in phosphate buffer (10 cm guidewire which was cut into 20 small parts, in 10 mL) at 37 °C. Samples were withdrawn and heparin was measured using a specific chromogenic substrate which measures the thrombin residual activity.[3] The exposed heparin was measured using the toluidine blue method.[3] Thrombin generation under flow was performed by flowing whole blood through the guidewires. Thrombin concentrations were measured as described before.[3] The guidewires were exposed to whole blood in a static experiment for 1 h and photographed. Platelet adhesion was examined by incubation with platelet rich plasma (PRP) for 45 min and the number of adhered platelet were measured by a lactate dehydrogenase (LDH) assay. In order to assess possible cytotoxicity of the coils, a cell contact assay and a MTT experiment were performed. Sterile guidewires were washed with sterile PBS buffer, incubated with 3T3 mouse fibroblast cells, and left for 3 days. Guidewires were examined with light microscopy. Extracts of the guidewires were used for the MTT assay.

Results/Discussion: The release experiments showed that heparin release from the PTFE-HBAK coil is slower than from the Slipskin®-NaHep coil. No heparin release is measured from the Slipskin® guidewire which was loaded with HBAK. However, more heparin is exposed on the Slipskin-HBAK coils than on the other guidewires. This is in line with the fact that NaHep is much better soluble in aqueous solutions as compared to HBAK. The thrombin generation experiments showed that blood compatibility of the guidewires can be improved by incorporation of heparin (see figure 1).

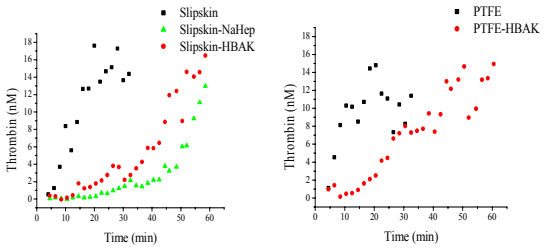

Figure 1. Thrombin generation curves.

For Slipskin®, the lagtime (onset of thrombin formation, thombin concentration > 2 nM) increases from 8 min to 22 min upon mixing with HBAK and to even 40 min upon mixing with NaHep. For PTFE the lagtime increases from 7 min to 18 min upon mixing with HBAK. A pronounced effect of heparin was also found upon incubation of the 5 different wires/coatings in full

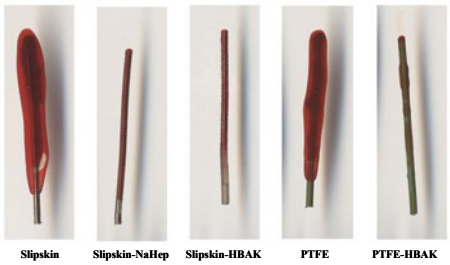

Figure 2. Guidewires exposed to whole blood.

blood (see figure 2). Large clots are found in the absence of heparin (Slipskin® and PTFE). Platelet adhesion decreased in the order: PTFE > Slipskin® > ≈ Slipskin®-NaHep > PTFE-HBAK > Slipskin®-HBAK. The MTT cytotoxicity assay showed that the guidewires loaded with HBAK are cytotoxic. Cell contact experiments are still ongoing.

Conclusion

It can be concluded that the bloodcompatibility of guidewires can be improved by incorporation of heparin. This study shows that guidewires coated with Slipskin® in which NaHep is incorporated have the best bloodcompatiblity. The MTT experiment shows that incorporation of HBAK leads to cytotoxic materials.

1) **References:** Gobeil F, et al. Can J Cardiol 2002;18:263-269.
2) Hanssen JHL et al. 1999;48:820-828.
3) Aldenhoff et al. Biomaterials 2004;25(16):3125-33.