Influence of Stent surface microstructuring on endothelial cell migration and substrate thrombogenicity

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Background: Coronary stent implantation is currently one of the most performed coronary interventions, but requires a long-term therapy with anti-platelet agents to prevent stent thrombosis. Stents with microstructured surfaces should improve vascularisation, reduce thrombotic events and consequently shorten the length of anti-thrombotic therapy.

Methods: Differently designed, 2.5 μm high elevations or hollows were lithographically etched on silicon plates, subsequently coated with silicon carbide. As controls, smooth silicon plates, bare metal substrates, and cell culture plastic were used. The migration of human umbilical vein endothelial cell (HUVECs) was assessed in a modified barrier assay using cell culture inserts (n=10). Bi24h after cell seeding, inserts were removed and cell migration was monitored for 2, 20, 30, 40, 60, and 72 hours. Actin cytoskeleton was visualised with green phalloidin. Platelet concentrate or whole blood were incubated on the different surfaces in static and flow conditions to investigate surface thrombogenicity (n=10). For cell counting, P-selectin antibody conjugated with fluorescein was used. Images were taken with an incident light fluorescence microscope used for studies of non-transparent objects.

Results: Comparing different types of structured surfaces, improved endothelial cell migration over 24h was observed for 4.5 μm pillar-like structures, whereas smaller spiky structures (2 μm), hollows, and smooth surfaces (i.e. smooth silicon plates, bare metal substrates) had a negative effect on endothelial migration. Moreover, substrate specific interactions between the tested endothelial cells and the structure relief could be detected. The thrombogenicity assays under static and flow conditions performed using whole blood and platelet concentrate showed that the platelet adhesion was reduced on larger structures as compared to smaller sharp-edged structures, hollows, or the smooth surfaces.

Conclusions: Microstructured surfaces have strong influence on endothelial cell migration and platelet adhesion. These results open new possibilities to design stent surfaces which improve adherence and migration of endothelial cells, and inhibit thrombogenic processes.

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The Impact Of Triple Anti-Platelet Therapy For Endothelialization And Inflammatory Response At Overlapping Bioabsorbable Polymer Coated Drug-Eluting Stents In A Porcine Coronary Model

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Background: This study was conducted to evaluate the endothelialization and the inflammatory responses depending on the administration duration of triple anti-platelet therapy at overlapping bioabsorbable polymer coated biolimus-eluting stents (BESt) in a porcine coronary model.

Methods: We successfully deployed 36 overlapping BESts for the left anterior descending coronary and left circumflex artery or right coronary artery in 18 non-injured pigs. Total pigs were divided into 3 groups (12 overlapping stents of 6 pigs in each group) as follows: group I received aspirin 100mg and clopidogrel 75mg daily for 8 weeks, group II received aspirin 100mg and cilostazol 200mg daily for initial 4 weeks, group III received aspirin 100mg, clopidogrel 75mg, and cilostazol 200mg daily for 8 weeks. Follow-up coronary angiograms and histomorphometric and histopathologic analyses at overlapping and non-overlapping segments were performed respectively.

Results: Inflammation score was similar between overlapping and non-overlapping segments in all pigs (1.2±0.33 vs. 1.1±0.17, p=0.117). The neointima area (NA) and percent area stenosis (%AS) at overlapping segments were not significantly different among 3 groups. However, at non-overlapping segments, NA and %AS in group III were significantly smaller than those in group I (2.5±0.50 mm² vs. 1.8±0.43 mm², p=0.037; 48.9±12.85 % vs. 37.7±19.08 %, p=0.031).

Conclusions: Our study shows that BESt appears to be reliable on the inflammatory response at overlapping segments as well as non-overlapping segments. Long-term administration of cilostazol is more effective in reducing inflammation score compared to non-overlapping segments of BESts in a porcine coronary model.