Ultra-thin non-polymeric coatings for DES

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Statement of Purpose:
Although earlier generation DES made significant contribution in addressing issues arising from stent implantation; they still remain far from perfect. For example hypersisitivity/inflammation reaction to the polymer matrix is being pondered as a possible cause to late stent thrombosis. However; attempts to produce polymer-free DES have proved to be a significant challenge. Poor mechanical durability and lack of efficacy have been two of the major challenges faced by polymer-free systems. This work has intended to develop a polymer-free resorbable coating for DES application which meets the mechanical durability requirements while maintaining at least the same level of efficacy as those of the earlier generation polymer-based DES coatings. This has become possible by development of a microporous hydroxyapatite coating that can act as a reservoir for the polymer-free drug formulation. The HAp coating protects the folmulation from mechanical damage while regulating drug release.

Methods:
Metallic stents (stainless steel or cobalt chromium alloy) were coated with microporous HAp using an electrodeposition technique. HAp-coated stents were further coated with an oil-based sirolimus formulation with the dose of 3μg/mm. The morphology, thickness and mechanical durability of the HAp coated and sirolimus coated stents were examined using scanning electron microscopy. The safety and preclinical efficacy of the HAp and sirolimus-eluting HAp were evaluated in a porcine coronary model. In order to evaluate clinical efficacy of the sirolimus-eluting HAp; 15 patients with single *de novo* lesion located in native coronary arteries with 3.0-3.5mm diameter and ≤14mm in length were consecutively enrolled. Primary endpoints were 30 days MACE (safety), and in-stent late lumen loss at 4 and 9 months. Serial angiography and intravascular ultrasound (IVUS) were obtained at index procedure and 4 and 9 months follow-up.

Results:
Scanning electron microscopy shows a coating thickness of 0.6μm (Fig 1). Preclinical testing on the polymer-free coating proves the mechanical durability and biocompatibility of the coating. Baseline characteristics included mean age of 63 years, 33% women, and 16% diabetics. LAD was the prevalent target vessel (56%). Reference diameter was 3.20±0.26mm, lesion length was 13.33±1.66mm, and %DS was 73.3±8.7.. Sirolimus eluting stent was successfully implanted in 100% of lesions with final TIMI 3 flow obtained in all cases. Control angio and IVUS at 4month confirm the efficacy with a late loss in stent: 0.295mm and the mid term safety. The 9 month follow-up data will be presented at the meeting.

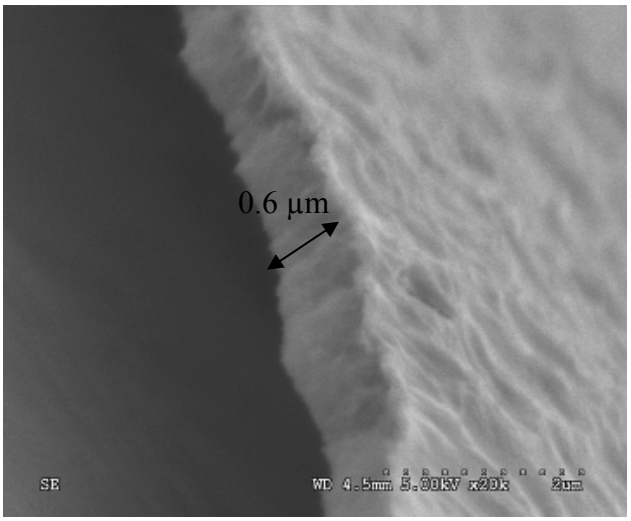

Figure 1 Scanning electron micrograph of the cross section of sirolimus eluting hydroxyapatite coating.

Conclusions:
A submicron hydroxyapatite coating has been coated on metallic stents. The HAp coating is capable of carrying drug. The sirolimus carrying HAp coating has shown efficacy and safety in the first human experience with a drug dose up to 50% lower than the currently available DES. The results of this work suggest that it is possible to have an ultra thin coating on the surface of the stent that is capable of effectively delivering the drug to the arterial tissue.