Progress in Processing and Evaluation of Hydroxyapatite Ultra-Thin Film Coatings for Coronary Stents

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Statement of Purpose: Restenosis, thrombosis, and inflammation are the problems associated with metallic stents in coronary arteries. The new generation of coated stents is expected to provide highly biocompatible interface, less thrombogenicity, and drug delivery capabilities. Unfortunately, many of the state-of-the art polymeric coatings have been associated with inflammation and other problems, especially in long-term contact with tissue. It has been known that hydroxyapatite (HAp), in addition to its excellent biocompatibility, is non-toxic, and does not induce allergic or inflammatory reactions, therefore making it a potential candidate as a coating on coronary stents. We have been exploring this potential for the last several years. The principal difficulty to overcome is the relative brittleness of pure HAp, as this is rather low-fracture toughness ceramic. We have been able to address these processing issues through manipulation of the coatings thickness, microstructure, and compositions, e.g. including composite coatings. This abstract reports on the advancements in the processing of the ultra-thin film (<0.5μm) HAp, and the results of several waves of porcine testing of HAp coated stents.

Methods: The ultra-thin films of HAp ceramics are deposited through sol-gel (SG) process reported previously [1] and heat treated at 400-500°C for up to 0.5hr. The heat treatment conditions determine the crystallinity of the film, e.g. the lower temperatures produce amorphous soluble films, whereas higher temperatures produce, denser crystalline stable films. In this work we evaluate the processing and in-vivo response of the stable crystalline ultra-thin films of HAp on stainless steel stents.

Results and Discussion: The resulting SG-HAp coatings are well bonded to the metallic surface of the stent (316L stainless steel), and thus provide long-term biocompatible surface of stents, even if covered with additional top-coat (e,g, soluble bio-polymer). Figure 1 illustrates the cross-section of the coating produced by focused-ion-beam (FIB) milling. The coating is uniform and rather dense (although ~20vol% of nano-pores do exist in this coating, they are too small to be resolved in this SEM micrograph). Additionally, such processed HAp films can also serve as a nucleation site for additional layers of functionally graded, thicker (~2.0 μm) coatings of HAp designed for drug delivery. These secondary layers of nanoporous HAp ceramic are specifically designated for drug encapsulation and controlled release. It is preferable that such nanoporous films are processed at room temperature, to achieve porosity in the range 20-50vol%. These porous HAp films are mechanically weaker than SG-HAp ultra-thin films, and therefore are typically combined with bio-polymer for improved mechanical performance and controlled drug release pattern [2]. For in-vivo tests in 10 Yucatan miniswine, 20 coronary arteries were randomized to receive HAp-coated 16mm Millennium Matrix stent or an identical bare metal stent, oversized to 110% of arterial diameter under IVUS guidance, followed up for 3 months. At termination, angiography and intravascular ultrasound were performed, followed by harvesting arteries for histology arteries for histology. The low amount of produced neointima in these two study stent types, Fig. 2, ranks with the best contemporary bare metal stents and some drug-eluting stents described in literature utilizing a similar experimental setting. The most important finding from this study is that the hydroxyapatite stent coating presents itself as uniquely biocompatible by comparison to polymeric stent coatings.

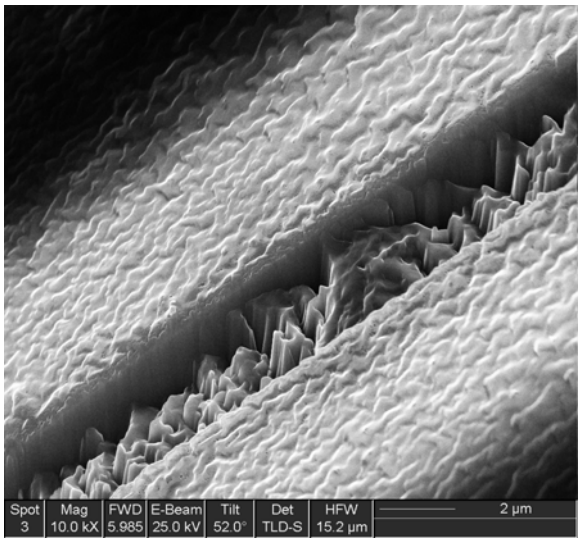

Fig.1. Focused-Ion-Beam (FIB) etched cross section of HAp coating deposited on 316L stainless steel stent

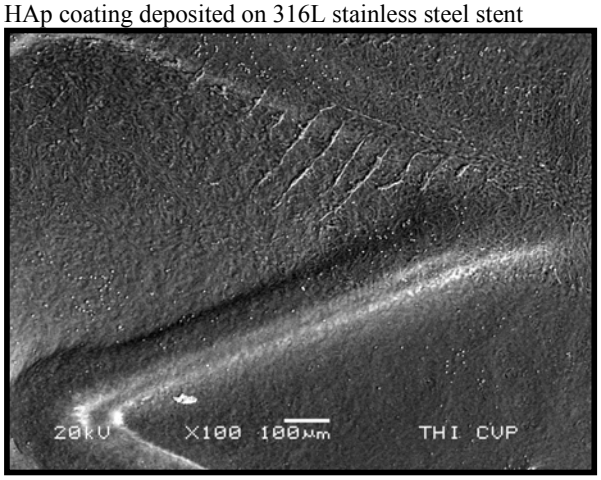

Fig.2. Neo-intima formation on HAp coated 316L stainless steel stent, explanted after 28 days.

Conclusions: The novel process for surface modification of metallic stents using hydroxyapatite is proposed. The initial processing and characterization results are extremely encouraging. The microporous ultra-thin HAp coating with a potential for drug elution shows promise of excellent long term biocompatibility and makes an attractive candidate for next-generation stent coating.

References:

1.T.Troczynski and D.Liu,"Novel Sol-Gel Hydroxyapatite Ceramic Coatings and Method of Making Same", US Patent No. 6,426,114 B1 Jul. 30, 2002

2. Q. Yang et al, "Biopolymer-Hydroxyapatite Matrix Composite Coatings for Stents", SFB Pittsburgh Apr 2006