Biopolymer-Hydroxyapatite Matrix Composite Coatings for Stents

Q. Yang[1], M. Tsui[2], M. Lien[2], D. Smith[2], A.Rajtar[2], and T.Troczynski[1]
[1]Materials Engineering, The University of British Columbia, Vancouver, Canada
[2]MIV Therapeutics Inc. Vancouver, BC, Canada

Introduction: Coronary stents are small metallic mesh tubes used to keep coronary arteries open, usually following a balloon angioplasty. The primary advantage is that the stent implantation does not require open heart surgery, which significantly decreases the cost and risk of operations. However, a major limitation of metal (usually stainless steel or Co-Cr alloy) stent implants has been in-stent restenosis, which occurs in >20% of stented coronary arteries and often requires repeat intravascular procedures and/or surgery [1]. A drug eluting stent was developed to prevent in-stent restenosis. In general, the drugs are encapsulated into polymer matrix coating and slowly release by degradation of biopolymer and diffusion of drugs. Two drugs, rapamycin and paclitaxel, achieved significant efficacy in preventing restenosis and coated stents with these drugs have been approved for clinical use. Recently, a hydroxyapatite (HAp) coatings for sents was successfully developed. Animal testing shows that HAp is highly biocompatible and therefore appears as one of the best choices for stents [2]. HAp ultra-thin film (<0.5um) coatings survive very well the crimping-expansion of the stent and form an excellent, stable biocompatible film on stent surface. At the same time, the ultra-thin films provide little capacity for drug delivery. Thicker HAp coatings (>1um) provide sufficient capacity for drug delivery but may fail in crimping-expansion. In present research, a novel process for deposition of biopolymer-HAp composite coatings was developed to provide toughness and to overcome the intrinsic brittleness of thicker hydroxyapatite coatings for coronary stent applications.

Experimental Methods: The 316L stainless steel stents, provided by MIV Therapeutics Inc. were washed with alcohol in ultrasonic bath and dried in oven for 30 min. Porous HAp coatings were fabricated through Electro-Chemical Deposition (ECD). The electrolyte solution used for the electrochemically assisted precipitation of calcium phosphate consisted of 0.042 mol $Ca(NO_3)_2$ and 0.025 mol $NH_4H_2PO_4$ in distilled water. The pH of the solution was approximately 4.2, and the solution temperature was maintained at 65C. The ECD was carried out galvanostatically at a cathodic current density of 0.6mA/cm^2 for 0.5 - 10 min., the specimen was then rinsed with distilled water and air dried. Thickness of the coatings was in range of 0.5 – 2 um, porosity in the range 40 – 60vol%. The porous HAp coatings were impregnated with 3-10wt% PLGA solution. The extra solution on the coating surface was removed by spining. The weight of hydroxyapatite coating and biopolymer were measured with micro-balance (Sartorius ME5). The mechanical evaluation of coated stents was carried out by crimping the stents on balloon catheter and expanding the stent with hydraulic pump. The surface morphologies and microstructure were examined with SEM.

Results: The weight of HAp coatings on stents ranged from 15 to 30 ug and thickness from 0.5 to 1 um. The porous ECD-HAp coatings were damaged in crimping-expansion tests, Fig. 1A. However, the composite PLGA-HAp shows enhanced mechanical flexibility, i.e. enhanced strain to failure, strong interfacial bonding, and high fracture toughness, Fig. 1B.

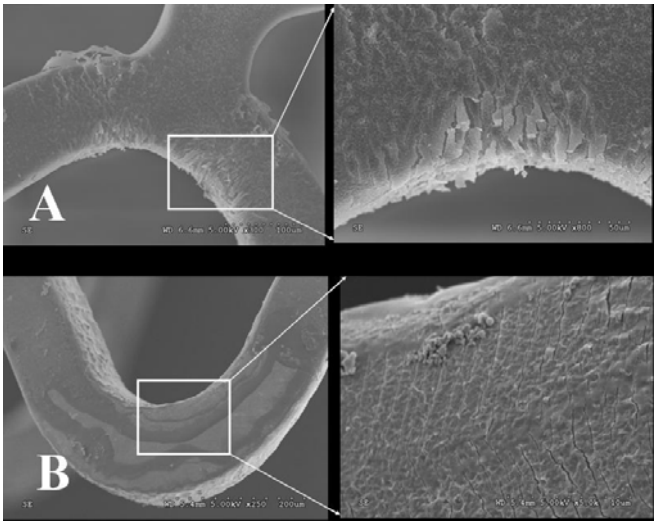

Fig. 1. SEM Morphologies of coated Stents after expansion test: (A) ECD-HAp coated stainless stent; (B) PLGA-HAp matrix composite coated stent.

Conclusions: PLGA-Hydroxyapatite matrix composites combine the reinforcing polymer phase with the ceramic matrix phase to create coatings with new and superior properties. The hydroxyapatite matrix provides a stable, biocompatible microporous framework with relatively high capacity for drug. The biopolymer filler provides toughness to overcome the intrinsic brittleness and lack of reliability of the ceramic. The novel composites combine the most desirable properties of bioceramics with those of biopolymers, to tailor properties such as strength and elasticity to meet the specific system requirements. The system was demonstrated to work well for the coronary stent coatings. The composite coating is extremely valuable for the stent applications because of the significant deformation of the stents during crimping and expansion.

References:

1. Holmes, et al. “State of the art in coronary intervention” Am. J. Cardiol. 91:50A–53A, 2003
2. G. Kaluza et al, ”Biocompatibility of Novel Ultrathin HAp Coating in Normal Porcine Coronary Arteries”, TCT Washington Oct. 2005

Acknowledgements: Authors sincerely thank IRAP, Canada for the financial support of the research project.