Integrated Biological Coating (IBC) for Renal Dialysis Catheters

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Statement of Purpose: Catheters that possess mechanisms to fight thrombosis complications would greatly extend the period between catheter replacements and therefore benefit patients. An integrated biological coating (IBC) process that used passivation, anticoagulation, and fibrinolytic mechanisms was developed. The non-fouling property of base coating comprised of polyethylene oxide (PEO) provides basic defense to repel all proteins from reaching the surface so as not to trigger complications. Modified heparin compound with improved anticoagulation activity scavenges thrombin formation and so prevents clot formation. If a fibrin clot should form on a surface, fibrinolytic agent will ultimately lyse the clot. Both the inside and outside catheter surfaces were successfully coated using Spire's proprietary technology, the Ion-Core process, that exploits electron energy to activate polymeric surfaces of complicated geometry,.

Methods: Double lumen, split tip catheters (Spire Biomedical) were treated, both inside and outside, at first using the Ion-Core process developed by Spire. The catheters were then coated with base coating, antithrombotic and fibrinolytic agents. Coating uniformity was evaluated using Coumassie stain in a mixture of alcohol (25% v/v), acetic acid (15% v/v), and water (60% v/v) for 40 min. Activities of modified heparin compound was evaluated using customized anti-Xa assay using the amidolytic method with a chromogenic substrate according to Teien et al.[1] The assay started by incubating the sample surface with an excess of AT. Excess FXa was then added. A subsample of solution was removed and residual FXa measured by reacting with the chromogenic substrate, CBS 31.39 (Diagnostica Stago), and p-nitroaniline was detected using optical absorbance at 405 nm after addition of acetic acid. The heparin equivalent activity was obtained from a calibration curve generated using a series of solutions of known heparin concentration. Fibrinolytic agents on the surface were estimated using a customized Elisa protocol using monoclonal antibody against the agent. In vitro bovine whole blood evaluation of coated catheters was performed at the Utah Artificial Heart Institute in Salt Lake City. The test circuit consisted of 12.5 mm I.D. PVC tubing (outer loop to mimic the vein) into which the 3 catheters were inserted and sealed. Blood flow in the outer loop was 2-2.5 L/min and the inner loop was 200-300 ml/min. A pressure gauge was placed in the inner loop. A pressure difference of 150 mmHg indicated occlusion.

Results / Discussion: The photo (Fig. 1 left) showed the hydrophilic effects after Ion-Core activation. The activated polyurethane tubing in water showed the meniscus at 0.9 cm higher than liquid's surface while untreated tubing showed meniscus 0.3 cm below. The photo (Fig. 1 right) showed catheters before and after coating. The catheter at the top of the figure was not coated. The catheter in the middle of the figure was coated but not stained. The catheter at the bottom of the figure was coated and stained. The uncoated catheter did not have significant stain under the investigated condition. From the figure, it is clearly seen that the coating was uniformly applied to the targeted surface.

Fig. 1. Surface properties of catheter tubing at different stages of coating. The left photo indicates the effects of Ion-Core activation. The right photo reflects the effects of biological coating with Coumassie stain.

Activities of biological agents were evaluated. Parameters that influence coating density were investigated. Currently, the coating method was able to control the amount of biological agents on the surface. Currently, the coating technique is able to give heparin with activity as high as 91 ± 9.0 (SD) pmol/ cm^2 on coated surfaces. The fibrinolytic agent on the surface was estimated to be 22~26 IU/ cm^2 in density.

In vitro bovine blood tests indicated that uncoated catheters as well as catheters with Ion-Core activation only clotted faster (Fig. 2, left) than catheters coated with IBC technology. Uncoated catheters also showed significant amount of blood clots on surface at the end of the experiment.

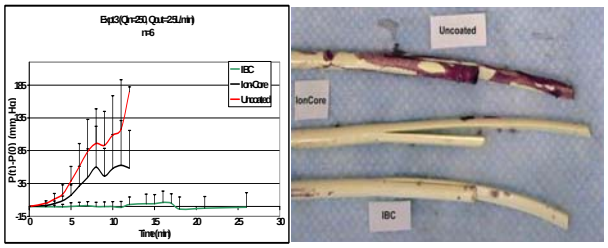

Fig. 2. In vitro evaluation results of polyurethane catheters before and after IBC coating. The chart at the left indicates the pressure change during the course of the in vitro experiment. The photo at the right reveals the status of the catheter at the end of the experiment.

Conclusions: Combination of Ion-Core activation of polymeric surface with biological coating provided uniform biological coating on surface. In vitro bovine blood test showed significant improvements to catheters coated using the IBC technology.

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