

Design and Development of an Heparin Bonded Vascular Graft

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Although saphenous vein remains the material of choice for vascular reconstruction, fem-popliteal grafts composed of polyester have gained in popularity due to the similar rates of occlusion and ease of use. Despite these advantages, there is continuing concern over the nevertheless high rates of occlusion, for both native and synthetic grafts which significantly contributes to the greater than 30% failure rate experienced within one year. As these failures often lead to limb loss and other serious complications, the availability of a non-thrombogenic graft or one with reduced thrombogenicity would have significant clinical impact and could serve to reduce the incidence of thrombosis related complications.

Polymeric biomaterial surfaces such as polyester and PTFE are intrinsically thrombogenic. Grafts composed of these materials can be surface modified in order to reduce this inherent thrombogenicity. Heparin treatment of the surfaces of a number of medical devices such as catheters, heart valves, stents and bypass circuitry has successfully been used as a means of reducing surface thrombogenicity.

In 1991, InterVascular, developed the concept of adding unfractionated high molecular weight heparin to the inner lumen of a graft through a stable bonding process. It was believed that this modification of the graft surface could significantly reduce its thrombogenicity and potentially improve graft performance and clinical outcome. Heparin is coupled to the InterGard Heparin surface using tri-dodecylammonium chloride (TDMAC) which forms an insoluble complex with heparin and in turn binds with high affinity to the polyester flow surface through its long hydrophobic tails. The heparinized graft is then coated with collagen which acts as a barrier to prevent rapid release of the heparin from the graft surface. A series of studies was performed to evaluate the safety and efficacy of the InterGard heparin coated graft. Animal studies were performed to confirm that no bleeding complications and good healing characteristics were associated with the use of the heparin bonded graft.

In addition, complete ISO 10993 biocompatibility tests were performed to assure that safety and biocompatibility requirements were met. Bench studies were conducted to evaluate the retention of heparin on the InterGard heparin graft in a simulated model of circulation using physiological flow rates and pressures. In these studies, heparin levels remained constant for 7 days in the InterGard heparin collagen coated graft but declined dramatically in the non-collagen coated graft demonstrating that the stable bonding process of ionic coupling to TDMAC followed by hydrophobic interaction with polyester immobilizes the heparin to the graft. Furthermore, the collagen coating helps retain the heparin complex preventing its premature release. Additional studies were performed which demonstrated that the heparin-collagen coating dramatically reduces the deposition of fibrin (a measure of thrombogenicity) relative to uncoated polyester grafts. These studies coupled with ongoing promising clinical data continue to support the safety, utility and clinical benefits associated with the InterGard Heparin graft.