

[F-FC158] PTFE Grafts Coated with Cu(II)-Complex Polymer Coatings Generate Nitric Oxide: Potential for Reducing Arteriovenous Graft Stenosis and Thrombosis.

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Introduction: PTFE dialysis access grafts fail as a result of stenosis (due to neointimal hyperplasia) followed by thrombosis. Nitric oxide (NO) plays an important role in both these processes through its inhibitory effects on platelet adhesion and activation (prevents thrombosis) and smooth muscle cell migration and proliferation (prevents neointimal hyperplasia). NO is continuously produced by the endothelial cell lining of healthy blood vessels at an estimated flux of $\sim 1-4 \times 10^{-10} \text{ mol cm}^{-2} \text{ min}^{-1}$. The AIM of this study was to develop NO generating grafts for use in a pig model of arteriovenous (AV) graft stenosis. **Methods:** The inner surface of PTFE grafts were coated with 60% polyurethane/40% polyvinyl chloride, doped with 2 wt% Cu(II)-DTTCT. This is a lipophilic copper (Cu) containing ligand that generates NO from the reduction of endogenous S-nitrosothiols circulating in blood. This chemical reaction then provides further reducing equivalents that continuously regenerate the Cu sites. **Results:** Grafts coated with Cu(II)-DTTCT generated NO at a surface flux of $18 \times 10^{-10} \text{ mol cm}^{-2} \text{ min}^{-1}$, when tested in a standard solution containing 1mM S-nitrosoglutathione and 10mM glutathione as a reducing agent. Toxicity and pyrogenicity studies of aqueous and organic leachables from the Cu containing polymer coatings demonstrated no adverse effects. Preliminary *in vivo* results in a pig model of AV graft stenosis documented the release of NO by the coated grafts for 2 weeks post implantation. There was also reduction in the quantity of thrombus lining the Cu(II)-DTTCT grafts at 2-3 weeks post surgery in 2/4 animals. **Discussion:** We have developed NO releasing grafts using an innovative polymer technology that regenerates the copper containing ligand required for local NO release. Future clinical use of such grafts could reduce the very significant morbidity currently associated with PTFE dialysis access graft thrombosis.

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