Title: Influence of Nitric Oxide Release on Bacterial Adhesion and Tissue-Implant Viability

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Abstract

The biological significance and benefit of nitric oxide (NO) releasing coatings for biomaterials is investigated by examining the resistance to bacterial adhesion and the implant host response. For this, numerous sol-gel films have been developed that act as a source of NO. Organosilanes containing two or three amines (aminosilanes) reacted with isobutyltrimethoxysilane form stable, translucent sol-gel coatings capable of releasing nitric oxide (NO) after exposure to a NO atmosphere. The NO release can be tuned by varying the amount and type of aminosilane. A decrease in *Pseudomonas aeruginosa* adhesion is observed with an increase in NO release up to a 95% decrease in cell coverage. The benefit of NO-releasing sol-gels as orthopedic coatings is examined with bacterial adhesion at medical-grade stainless steel. The *in vitro* adhesion of *P. aeruginosa*, *Staphylococcus aureus*, and *Staphylococcus epidermidis* under ambient and physiological temperatures decreases up to 80% in the presence of a NO. The relationship between NO flux and bacterial adhesion is determined by coating NO-releasing sol-gels with a polymer film to provide a control surface for monitoring bacterial adhesion. A 5-35% decrease in NO flux is observed after coating sol-gel films with 1030 μm of poly(vinyl chloride). A relationship between the resistance toward *P. aeruginosa* adhesion and NO release is discovered over surface fluxes of 0-30 pmol $s^{-1}cm^{-2}$. The host response to NO-releasing sol-gel is examined *in vitro* with L929 mouse fibroblasts to assess cytotoxicity and subcutaneous implantation in rats to examine the tissue response. Excessive levels of NO release from sol-gels produced cytotoxic effect on fibroblasts *in vitro*. Contrary, the *in vivo* implantation results suggest that NO-releasing sol-gels coatings reduce dense collagen deposition and are not necrotic. The inhibition of bacterial adhesion and stimulation of subcutaneous tissue growth demonstrate the potential advantages of integrating sol-gel based NO release into the designs of current implantable medical devices and biosensors.