Nitric Oxide Releasing Catheter Disinfection Device

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Statement of Purpose: The paucity in strong antibiotics and rise in antibiotic resistance in the microorganisms requires development of alternative antimicrobial approaches to prevent device related infections. Nitric oxide (NO) release from *S*-nitrosothiol (RSNO) donor loaded polymers can be enhanced using metal, heat, or light as catalysts.[1] This work establishes practical use of RSNO incorporated medical grade silicone rubber (SR) polymer in combination with light-emitting side glow fiber optic to develop simple, biocompatible, and anti-infective **d**isposable **c**atheter **d**isinfection **i**nsert (DCDI). The physiological levels of NO release from the insert can be photoinitiated using a simple mobile phone application that can both prevent bacterial adhesion and disinfect the surface of indwelling catheters.

Methods: To generate a NO-releasing insert, a polymer tubing was first prepared by impregnating commercial silicone tubing with *S*-nitrosothiol-*N*-acetyl-penicillamine (SNAP).[2] The SNAP impregnated SR tubing was then mounted on a side glowing fiber optic to light up the full length of SNAP tubing using a Bluetooth operated light source. The amount of SNAP impregnated and diffused in the presence and absence of light and stability with various sterilization methods was investigated using various characterization techniques. The photocatalytic ability of light from the insert was validated using chemiluminescent nitric oxide analyzer in the presence of red, green, blue and white light. The ability to tightly regulate the NO release levels from the insert was confirmed at different nominal light intensities ranging from 0 – 100%. The antibacterial properties of insert were evaluated using a 4 h bacterial adhesion method against two clinical pathogens: *S. aureus* and *E. coli*. The insert was also studied for its ability to disinfect an S. aureus infected catheter in a challenging *in vitro* catheter infection model which strongly represents the end-use clinical application of the DCDI device. Finally, the biocompatibility of the insert was tested towards NIH 3T3 mouse fibroblast cells over 24 h.

Results: The characterization of DCDI using UV-vis spectroscopy revealed about 5 wt% of SNAP impregnated into SR polymer. DCDI demonstrated excellent compatibility with ethylene oxide and UV light sterilization; two clinically relevant sterilization techniques. The NO release kinetics in the dark (absence of light) and with different wavelengths of light and intensities (0 – 100%) revealed maximum catalysis of NO from SNAP in the presence of white light (combination of red, blue, and green) at 100% light intensity (**Fig 1**). The control of NO release via modulation of light in DCDI device can be used to prevent catheter infections or inserted within an infected catheter to eradicate the colonized bacteria.

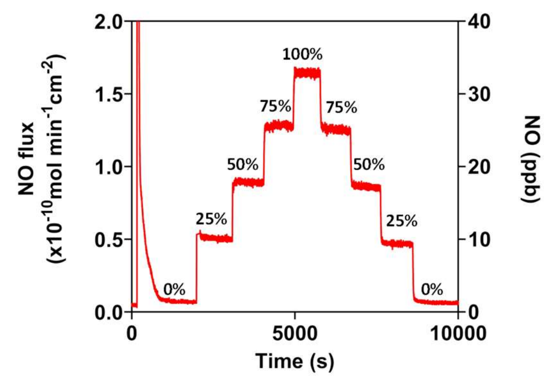

Fig. 1. Nitric oxide (NO) release from DCDI in the absence and presence of light ranging from 0 - 100% intensity at 37 °C. NO release can be controlled real-time using a smartphone application.

Exposure of DCDI to *S. aureus* and *E. coli* led to >99% reduction in viable bacterial adhesion on the surface of DCDI with just 4 h of exposure ($p < 0.05$) compared to unmodified SR. With the dual-active interface of SNAP and light, the DCDI was also able to disinfect an infected catheter by eliminating more than 97% bacteria in a *S. aureus* infected *in vitro* catheter model.

Conclusions: The light induced NO releasing DCDI device can be used to enhance the lifetime of the indwelling catheter by both disinfecting the catheter surface *in situ* and preventing the impending infections. The therapeutic levels released from NO releasing from DCDI can be the next effective biocompatible solution for catheter related blood-stream infections.

References:

1. Yang, T.; *et al. Advanced Science* **2018,** *5* (6), 1701043.

2. Wo, Y.; *et al. ACS Biomater. Sci. Eng.* **2017,** *3* (3), 349-359.