Rapid Fabrication and Characterization of Pediatric Nitric Oxide (NO) Releasing Catheter

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Introduction: Intravascular (IV) catheters used in clinical practice can activate platelets, leading to thrombus formation and stagnation of blood flow. Currently, there are 500,000 admissions to neonatal intensive care units each year. Most of these babies require management through central venous, umbilical venous, or umbilical artery for the administration of parental nutrition, chemotherapy, blood products, fluids and life-saving medications. Thrombus formation is a challenge due to complications in patient populations, medical device failure, increase in insurance costs, and the inconvenience of having to remove and interchange the catheter. Recent studies using hand-casted nitric oxide releasing catheters in adult male New Zealand rabbits showed enhanced patency compared to controls. The aim of this research was to fabricate silicone catheters using an automated spin-casting platform to ensure uniform wall thickness, reproducibility and rapid wall composition modification for long-term NO release.

Materials and methods: A spin casting method was used to cast silicone resin into hollow cylinder shapes. A casting die into which the polymer resin was dispensed was driven by a high rpm motor. Centrifugal forces acting on the resin creates an axial hollow core at 2600 to 3600 rpm while 70^{o}C heat was applied to the control volume of the casting die for 20 minutes. This was followed by a 5 minute cool down. NO releasing catheter can be rapidly casted either by incorporating diazeniumdiolated dimethyl-1,6-hexadiamine (DMHD-N_2O_2) NO donor into polydimethylsiloxane (PDMS) resin and casting or casting only PDMS first followed by top-coating the catheter lumen with DMHD- N_2O_2 PDMS mixture. The former was used in this study and the effect of polylacticglycolic acid (PLGA) effect on NO release kinetics was analyzed. NO release from the catheters were measured using a GE 280i Nitric Oxide analyzer while samples were submerged in phosphate buffer saline (PBS) (pH 7.34, 37 ^{o}C) for one hour.

Results and Discussion: Catheters fabricated measured 4.9 ± 0.7 cm long with 0.11 ± 0.01 cm outer diameter and 0.07 ± 0.01 cm inner diameter. The wall thickness measured 0.02 ± 0.003 cm. The composition of NO releasing catheters all had 3.4% of DMHD- N_2O_2 with either 0.1 g or 0.05 g or 0.01 g of PLGA. Three samples were analyzed for each catheter group containing the above PLGA additive. As shown in Figure 1, the level of NO flux was a function of PLGA amount and time. Catheters with higher PLGA content released higher NO levels within the measurement timeframe. The representative release profile shows 0.01 x 10^{-10} mol/min/cm^2 peak flux for 0.1g PLGA catheter compared to 0.005 x 10^{-10} mol/min/cm^2 for 0.05 g PLGA catheter.

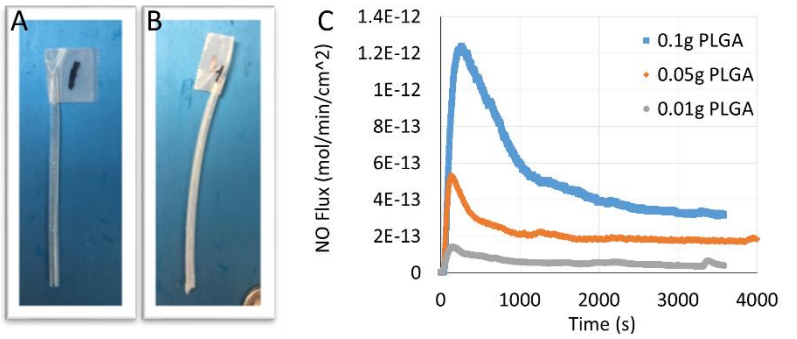

Figure 1: Control catheter A) and nitric oxide releasing catheter B) and one hour nitric oxide flux profiles of catheters modified with either 0.1 g, 0.05 g or 0.01 g of PLGA C).

Conclusions: The spin-casting platform provided an easy-to-use method to rapidly fabricate silicone catheter with different material compositions. Catheters generally had uniform wall thickness, but however misalignment of the casting die can lead to small variations in wall thickness. It was observed that the PLGA content had an effect on the amount of NO released within the measurement timeframe. Further studies are needed to modulate NO release from catheters by optimizing the material composition. Ultimately a long-term NO releasing catheter can limit complications such as blood coagulation and bacterial colonization associated with indwelling catheters.

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