Fabrication and Characterization of Medical Grade Polymer Contrast Agent Composites for Near Infrared In-Situ Imaging

André Stevenson[a], Laura Reese[b], Neel Sanghvi[c] , Raj Shekhar[c], Lissett R. Bickford[b,d], Abby R Whittington[a,b,e]
[a]Department of Materials Science and Engineering, Virginia Tech, Collegiate Square, Suite 302 Blacksburg, VA 24061
[b]School of Biomedical Engineering and Sciences, Virginia Tech, ICTAS Blacksburg, VA 24061
[c]The Children's National Medical Center, 111 Michigan Ave NW #200 Washington, DC 20310
[d]Department of Mechanical Engineering, Virginia Tech, Randolph Hall Blacksburg, VA 24061
[e]Department of Chemical Engineering, Virginia Tech, Randolph Hall, Blacksburg, VA 24061

Statement of Purpose: Peripherally-inserted central catheters (PICCs) are essential thin, pliable polymeric medical devices that deliver medications, nutrients, and fluids to neonates[1]. PICCs can remain inserted for weeks and even months before removal[1]. During this time, the natural movement and growth of the child may displace the PICC causing serious complications. X-ray imaging is the gold standard in verifying catheter tip position[2]. However, the associated high cost, negative health risks to newborns following exposure, and the inability to frequently inspect catheter position raise concerns about the current approach. We hypothesize that catheters can be constructed from a polymeric composite with optical contrast materials that can then be visualized using near-infrared (NIR) fluorescence, forgoing the need of ionizing radiation. The objective of this study was to design and characterize novel optical polymer composites that can ultimately be used as PICCs. These composites would allow for the early detection of a migrating tip to be corrected before adverse side effects could occur.

Methods: Medical grade polyurethane (PU) was provided as a gift from Bayer Medical. IR Dye800CW infrared dye is a non-reactive fluorescent agent that has successfully undergone FDA approved toxicity studies in animal models, and currently used for IRB studies for cancer detection imaging[3]. IR Dye800CW was mixed with PU at 0.01 wt% and extruded using an annular die (Solid Concepts Inc, Austin, Texas) and Haake Twin Screw Minilab compound extruder. Extruded tubes with and without dye were tested for dye retention and contrast enhancement, distribution, mechanical properties, and surface characterization. PU tubes without contrast agent were used as controls.

Results: Successful extrusion of hollow tubes of PU without and with the dye was achieved. Initial imaging of the composite tube samples revealed an intense orange fluorescent profile due to the addition of IR Dye800CW (Fig. 1A). The control sample appears white in color due to the absence of dye (Fig. 1A). Over short times (less than 3 days) greater than 98% of the dye was retained in the extruded tube's polymer matrix (Fig. 1B). In addition, scanning electron and atomic force microscopy analysis show tubes composed of IR Dye800CW have smoother surface features. Smoother surfaces are desirable for ease of catheter insertion.

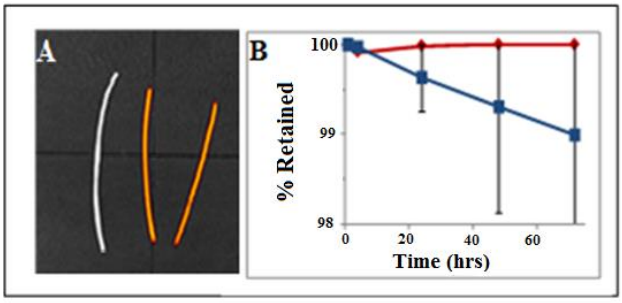

Figure 1. PU tubes were imaged for fluorescence visualization (1A) where the first tube acts as control without dye and was white in color. The second and third tubes contain 0.01 wt% IR Dye800CW and appear fluorescent with orange hue (1A). Retention without (▲) and with (◆) 0.01 wt% IR Dye800CW was determined by absorbance at 800 nm by UV-VIS Spectrophotometry (1B). Standard deviation bars represent three composite samples (n=3).

Conclusions: Preliminary results suggest the incorporation of a NIR fluorescent dye at only 0.01 wt% with medical grade PU can be successfully extruded and imaged confirming presence and intensity of dye. The intensity images suggest IR Dye800CW remained stable in the polymer matrix during extrusion. Furthermore, the retention of the dye in the polymer matrix over time suggests that composite materials can be visualized in situ without significant loss of contrast agent. Future work will include mechanical testing and gathering a numerical approximation of fluorescent intensity at physiologically relevant depths using pixel data from Image J software.

References: **1.** "Central Venous Access Catheters (CVACs)." *Minimally Invasive Surgical Solutions*. NikaLabs, 2012. Web. 31 Jan. 2014. **2.** Pettit J. *NANN*. 2007;2:1-71. **3.** *Clinical Trials.gov*. National Institutes of Health, n.d. Web. 31 Jan. 2014.

Acknowledgements: This research was made possible by a Virginia Tech Carilion Research Institute and Children's National Medical Center joint research grant. In addition, the Interdisciplinary Graduate Education Program Fellowship in Regenerative Medicine served as student support (A Stevenson).