Microstructural and Functional Analysis of Polymeric Composite Materials for Near Infrared Imaging

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Statement of Purpose: Catheters offer a variety of uses in the clinical setting, including the delivery of chemical agents (such as drugs and imaging dyes), nutrients and blood to patients (1). Peripherally inserted central catheters (PICCs) are widely used in neonatal and pediatric intensive care units. However, the long-term placement of PICCs increases the likelihood of migration of the catheter from the target location, resulting in adverse effects to the patient. To determine and monitor catheter location, clinicians utilize X-ray imaging. Despite X-ray being the gold standard, neonates are particularly at an increased risk from prolonged radiation exposure, including proclivity to develop lymphoma and other forms of cancer later in life (2). Thus, there is a clear need for catheters that can be imaged without ionizing radiation using materials with high translational and commercial potential. We hypothesize that catheters can be constructed with a near-infrared sensitive agent, IRDye 800CW, and imaged without modifying the microstructural and functional integrity of the PICC. The objective of this study is to demonstrate fluorescent-polymer composites as improved PICC materials, which we anticipate will provide physicians with a safe and effective substitute to X-ray imaging (3).

Methods: Medical grade thermoplastic polyurethane (TPU) was provided as a gift from Bayer Medical. IRDye 800CW is a fluorescent agent that has successfully undergone FDA approved toxicity studies in animal models, and currently used for IRB cancer imaging studies. IRDye 800CW was mixed with TPU at 0.025 wt%, pressed into thin films, sectioned, and extruded using a Haake Twin Screw Minilab compounder. Extruded tubes with and without dye were tested for mechanical properties, surface characterization, dye stability, and contrast enhancement and distribution. Contrast enhancement was determined using a LI-COR NIR Imaging System while placing tissue equivalent materials over extruded tubes up to depth of 3 cm. TPU tubes without dye were used as controls.

Results: Successful extrusion of hollow tubes of TPU with and without the dye was achieved. Fluorescence scans of TPU Composite (dye added) tubes show substantially greater intensity compared to plain TPU that does not contain the dye (Fig.1-left). Additionally, the fluorescence profile intensities for the TPU Composite tubes pervade the entire length of the sections, suggesting that adequate incorporation of the dye occurs following extrusion. Quantitatively, there is a decrease in fluorescence intensity as the depth increases, but the signal is still visible at 3 cm (Fig. 1-right).

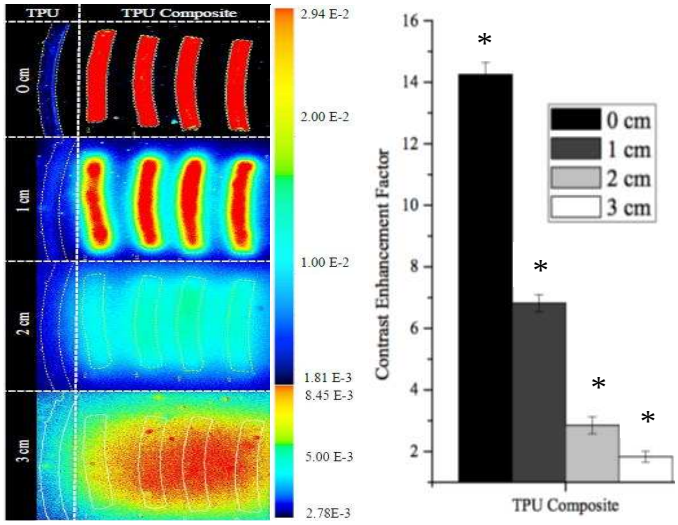

Figure 1. Fluorescent intensity scans (left) and contrast enhancement factor (right) of TPU Composites. Samples were imaged at an excitation wavelength of 778 nm. 0, 1, 2, 3 cm correspond to the thickness of tissue equivalent covering the samples. The fluorescence intensity decreases as a function of depth, though signal is still observed at 3 cm. All values are statistically different ($p<0.5$). Error bars represent standard deviation (n=4).

Conclusions: Results suggest the incorporation of 0.025 wt% IRDye 800CW with medical grade TPU can be successfully extruded and imaged, confirming presence and conservation of dye function. Addition of the dye does not significantly affect the surface or mechanical properties of the TPU, but allows for catheter imaging at depths up to 3 cm. This proof of concept study shows that near infrared enhanced catheters may provide a potentially attractive alternative to the use of ionizing radiation for PICC line monitoring. Furthermore, the use of materials that are already approved (or undergoing approval) in medical applications indicates strong translational and commercial potential.

References: **1.** (McCay AS, et al. PICC Placement in the Neonate. N. Engl. J. Med. 2014;370(11)) **2.** (Hall EJ. Radiation biology for pediatric radiologists. Ped. Radiol. 2009;39(1):57-64). **3**. (Systems and Methods for Optically Guided Placement and Monitoring of Medical Implants. U.S. Patent Application No: 14/493,137. 2014-09-22).