In vitro Assessment of HydroPICC Resistance to Tip Occlusion

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Central venous access devices (CVADs) are necessary components for the effective delivery of medical treatment to patients in critical care settings. Catheter-related thrombosis is one of the most common causes of device failure with overall thrombotic complications rates as high as 18%.[1] Catheters used for vascular access are commonly prepared from thermoplastic polyurethanes (TPUs) or silicones that provide flexibility, durability, and strength;[2] however, these polymeric materials are hydrophobic and therefore susceptible to non-specific protein adsorption.[3] Significant research has been conducted to improve the protein resistance of polymeric biomaterials by using coatings, films, and direct surface modification as well as bulk modification with surface modifying additives;[4] however, these modifications are often transient and are not durable solutions for protein resistance in long-term vascular implants, masking the underlying issue.

The HydroPICC™ Technology

Access Vascular, Inc.'s HydroPICC™ device is constructed of a proprietary combination of biocompatible polymers to create a high-strength hydrogel material. Hydrogels inherently possess low interfacial tension, which has been shown to resist thrombus adhesion. For decades, the medical device industry has focused on grafting hydrogels or hydrophilic polymers to surfaces of more durable biomaterials in an effort to decrease their thrombogenicity. Access Vascular, Inc. has engineered a solution to this problem by developing a unique hydrogel composition that combines the superior mechanical properties of TPUs with the intrinsically low thrombogenicity of hydrogels into a single bulk material.

Assessment of Thrombotic Occlusion *in vitro*

Quantification of the thromboresistance of the HydroPICC material was evaluated in a 2-Phase *in vitro* blood loop model. Resistance to thrombotic occlusion was assessed by Thrombodyne, Inc. (Salt Lake City, UT), using an established *in vitro* blood flow loop model.[5] N=6 HydroPICC devices were hydrated in sterile saline for approximately 24 hours prior to testing along with TPU samples comprising of N=6 PowerPICC devices (Bard Access Systems, Inc.). Fresh bovine blood was collected by cardiac puncture and heparin was added to achieve a 0.75 U/mL concentration. Catheter samples were inserted into the blood flow loop of 1/4 inch (6.4 mm) inner diameter polyvinyl chloride tubing for approximately 120 minutes (Phase 1: Flow). Blood was maintained at 37 °C and continuously metered at 200 mL/min through the loop using a peristaltic pump for the duration of testing to simulate physiological blood flow across the device. Separately, $CaCl_2$ and minimal heparin were mixed into fresh citrated bovine blood and aliquoted into separate vials. After the flow phase, the devices were removed from the heparinized blood circuit and the distal tips of the catheter samples were inserted into the recalcified blood vials and incubated at 37 °C until a clot formed (Phase 2: Stasis). At the end of the clot formation phase, the devices were removed from the vials and gently rinsed with saline to remove any loose

blood, taking care not to remove adherent thrombus. To assess luminal patency, a 4-way stopcock was attached to the luer hub of each catheter with a pressure gauge attached to one port and a syringe with saline to the other port; then pressure was applied to the syringe in an attempt to flush the saline through the lumen and the maximum infusion pressure was recorded.
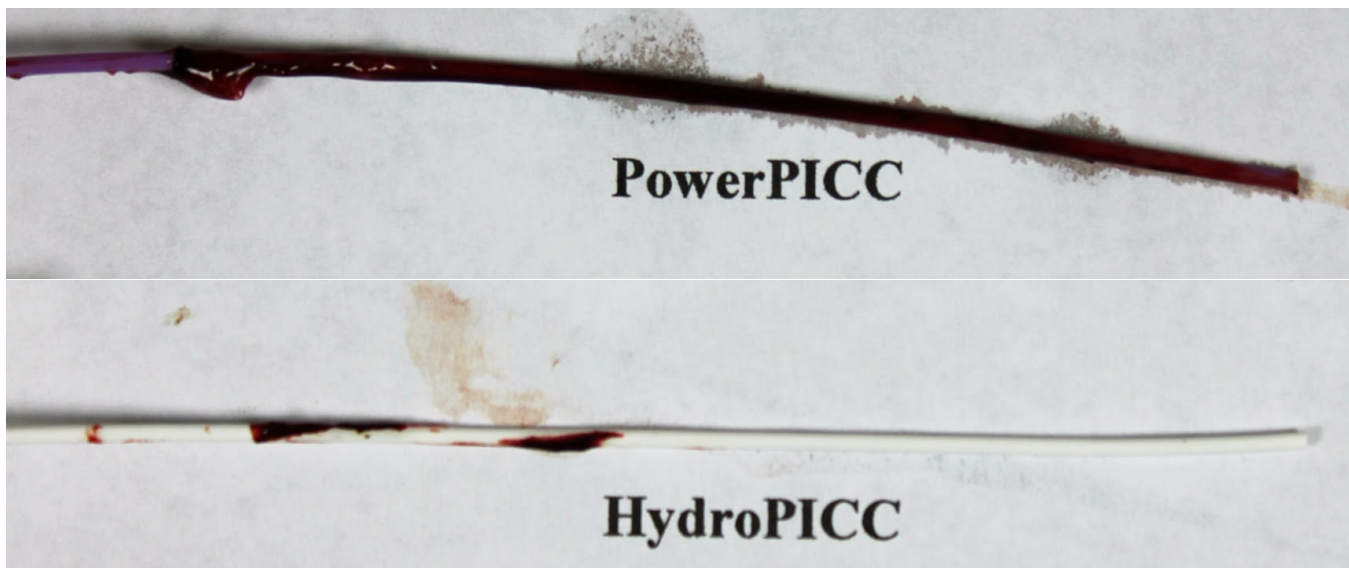
Figure 1. Representative optical image of thrombus accumulation on PowerPICC polyurethane (top) and Access Vascular HydroPICC (bottom) catheters after removal and rinsing from *in vitro* blood loop.

The 2-Phase *in vitro* blood loop model provides a valuable assessment of device resistance to thrombotic occlusion. The hematological parameters (*e.g.*, hemodynamics, anticoagulation) in this *in vitro* model are more controlled than in *in vivo* models, thus enabling direct semi-quantitative evaluation of thrombogenicity. Extraneous dynamic parameters (*e.g.*, vessel geometry, animal physiology, activity, variable hemostasis and homeostasis, and infection) that can confound *in vivo* assessments can be eliminated in the *in vitro* blood loop model. This allows the thromboresistance evaluation to be focused on the device surface properties/chemistry, with other parameters remaining relatively constant. A representative optical image of a set of paired samples after exposure to the 2-Phase *in vitro* blood loop model are shown in **Figure 1**, qualitatively indicating a significant amount of thrombus accumulation on the TPU sample, while the HydroPICC device exhibited only a minimal amount of thrombus accumulation. A box plot of the mean ± standard deviation of the maximum infusion pressure for the TPU control samples as compared with the HydroPICC device is shown in **Figure 2**. The HydroPICC devices exhibited, on average, 67% lower maximum infusion pressures when compared to PowerPICC. Furthermore, typical pressures for venous infusion devices in adults is ~150 mm Hg;[6] therefore, a device requiring an infusion pressure greater than 150 mm Hg could be considered occluded. All PowerPICC devices (n=6) were characterized as occluded as a result of exposure to the 2-Phase blood loop model, while none of the HydroPICC devices (n=5) were characterized as occluded.
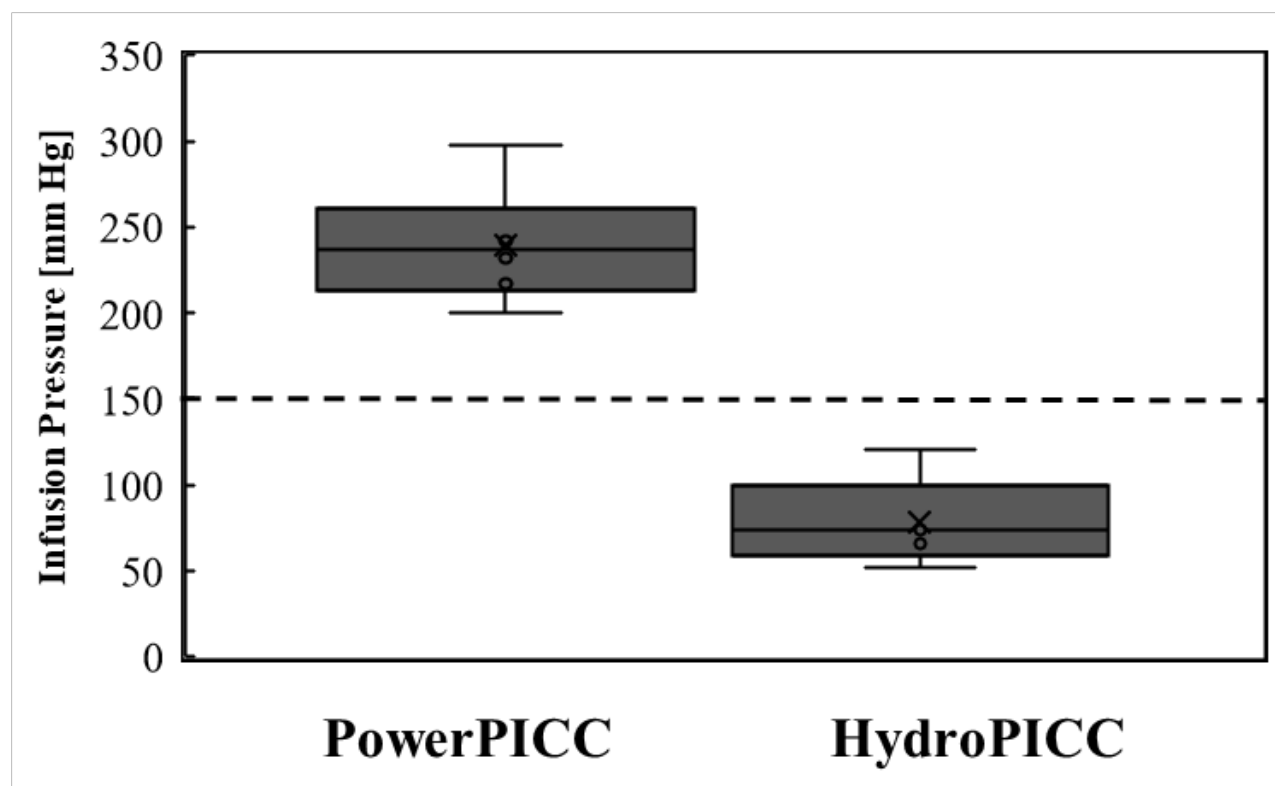
Figure 2. Maximum infusion pressure of PowerPICC and HydroPICC devices after exposure to the 2-Phase *in vitro* blood loop. Dashed line indicates typical patient infusion pressure (150 mm Hg).

Conclusions

Catheter-related thrombotic occlusions are one of the most common causes of CVAD failure. The HydroPICC technology represents a new method to reduce catheter-related thrombus accumulation by fabricating catheters from an inherently non-thrombogenic bulk hydrogel. Resistance to thrombotic occlusion of the HydroPICC technology was evaluated in a 2-Phase *in vitro* blood loop model, with results showing that the HydroPICC device exhibited a complete (100%) reduction in thrombotic occlusion rate when compared to a conventional TPU (PowerPICC) catheter. Based on the *in vitro* testing in this report, the HydroPICC technology is shown to be a viable class of thromboresistant hydrogels to replace conventional polyurethanes and silicones in vascular access and other blood-contacting medical device applications.

Note:
Data on file at Access Vascular[7]. Reduction of thrombus accumulation was evaluated using in vitro and in vivo models. Pre-clinical in vitro/in vivo evaluations do not necessarily predict clinical performance with respect to thrombus formation.

No correlation between in vitro/in vivo testing methods and clinical outcomes have currently been ascertained.

References

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