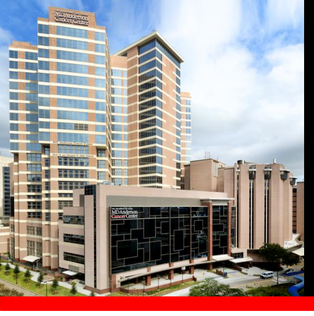

Tungsten nanoparticle and polymer blends as novel coating for raqiopaque resorbable inferior vena cava filters

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Background

Deep vein thrombosis (DVT) or pulmonary embolism (PE) affects about 900,000 individuals annually in the United States[1]. Currently, management is primarily through employment of anticoagulation therapy; however, placement of inferior vena cava filters (IVCFs) is recommended for patients with contraindications to anticoagulation. Absorbable IVCFs constructed with poly-p-dioxanone (PPDO) eliminate the need for filter retrieval. Radiolucency of PPDO-IVCFs can be improved with radio-enhancing nanoparticles (NPs).

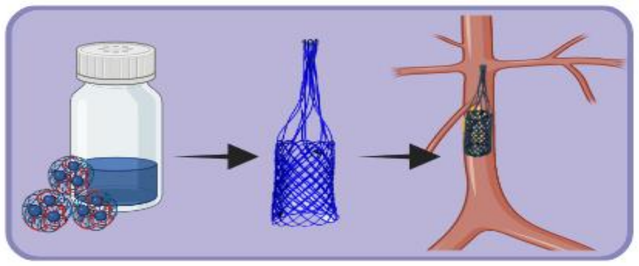

Fig. 1. Tungsten (W) NPs reinforced with polyhydroxybutyrate (PHB), polyvinylpyrrolidone (PVP) and polycaprolactone (PCL) polymer blends as a novel coating for commercially available PPDO IVC filters.

Methods

WNPs were synthesized by thermal decomposition of tungstic acid with oleic acid, oleylamine, and 1-octadecene as stabilizers under an Ar blanket. Physicochemical properties of collected WNPs were characterized by transmission/scanning electron microscopy (TEM/SEM), micro-computed tomography (CT), dynamic light scattering (DLS) and powder X-ray diffraction (XRD) patterns. PPDO sutures and IVC filters were coated with WNPs with PHB, PCL, and PVP using a wet-dipping technique.

In vitro cell viability and hemolysis assays were done using immortalized human vascular endothelial cells (EC-RF24) and erythrocytes from laboratory rats, respectively.

W+PHB and W+PHB+PCL+PVP IVCFs were deployed in separate pig models, monitored, and imaged using CT for 12 weeks. Post-mortem histology analyses were done to investigate possible systemic and local effects of WNP+polymer-embedded IVCFs.

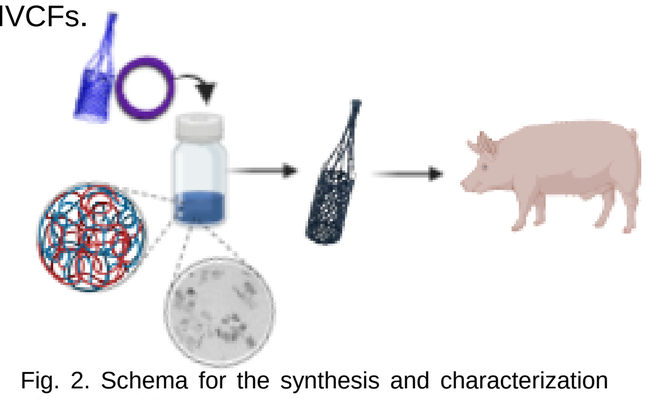

Fig. 2. Schema for the synthesis and characterization of WNP-IVCF and implantation in pigs.

Results

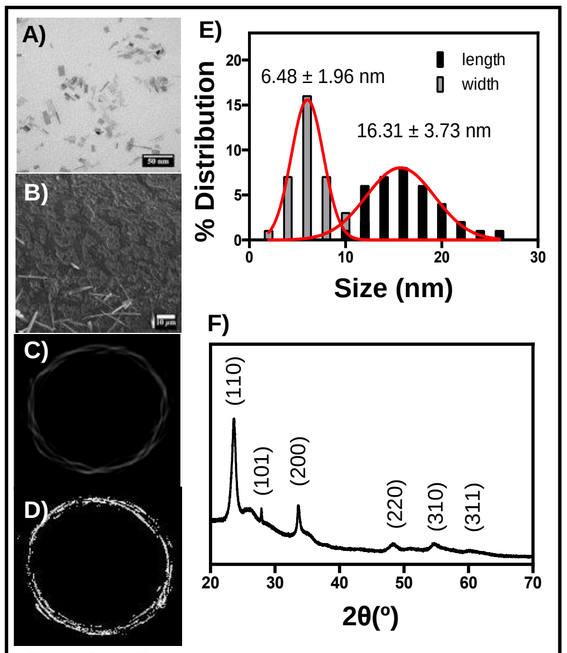

Fig. 3 Physicochemical characterization of WNPs. (A) TEM, (B) SEM, (C) X-ray, and (D) micro-CT images of WNP and WNP-coated sutures. (E) Distribution of the measured diameters from TEM. (F) XRD pattern of W.

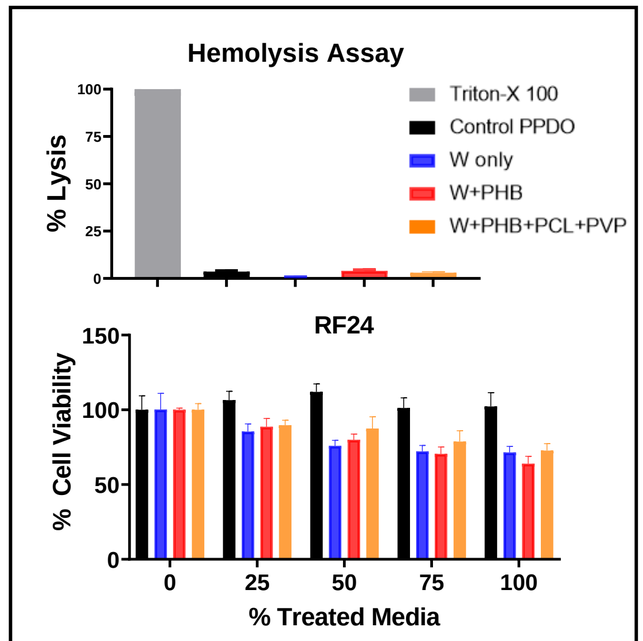

Fig. 4. (A) Hemocompatibility showing the % blood lysis after incubation with the untreated and treated PPDO sutures. (B) *In vitro* cell viability of EC-RF24 cells measured using alamarBlue assay after 24h incubation in varying ratios of treated cell culture media.

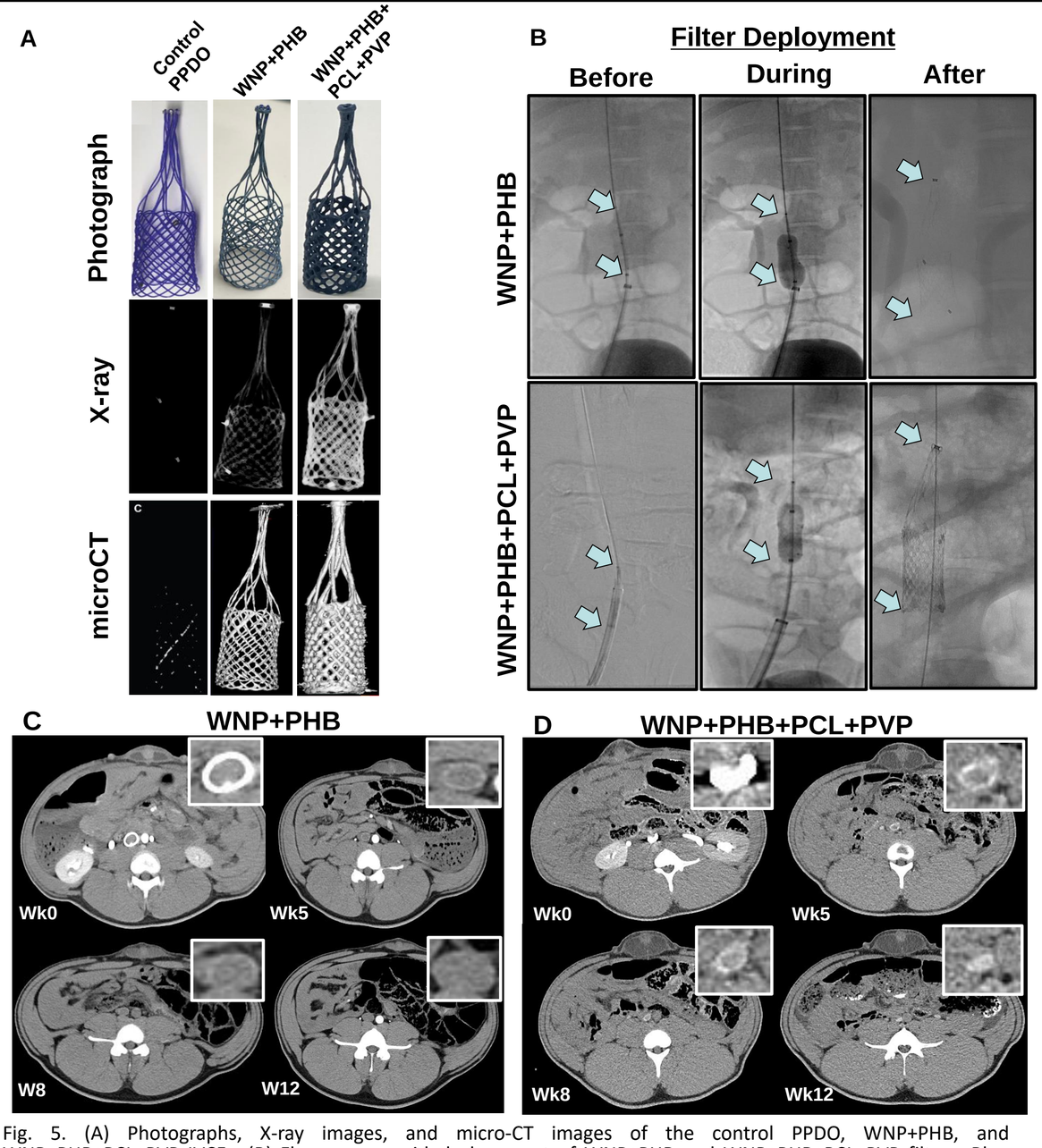

Fig. 5. (A) Photographs, X-ray images, and micro-CT images of the control PPDO, WNP+PHB, and WNP+PHB+PCL+PVP IVCFs. (B) Fluoroscopy-guided placement of WNP+PHB and WNP+PHB+PCL+PVP filters. Blue arrows indicate the tip and the bottom of the IVCF. (C-D) *In vivo* CT monitoring of WNP+PHB and WNP+PHB+PCL+PVP filters over a period of 12 weeks.

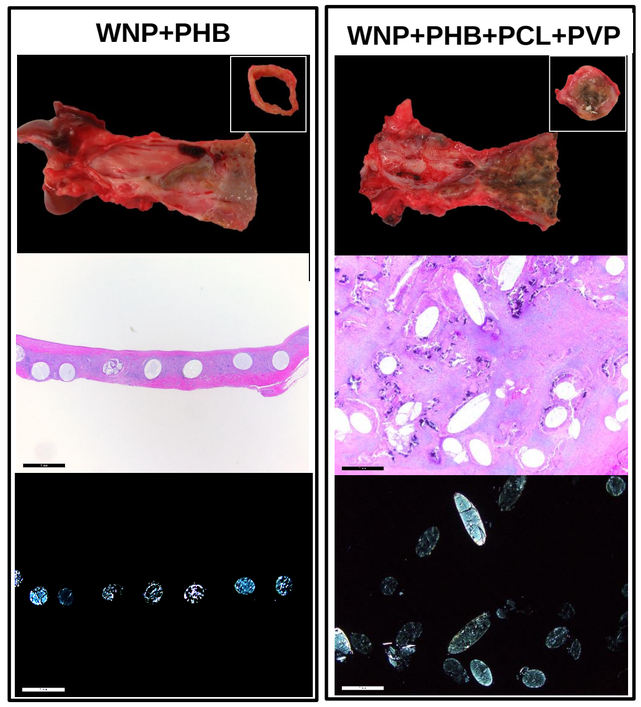

Fig. 6. Gross images from necropsy (top), H&E (middle), and polarized light histology (bottom) images of IVC-affected area of WNP+ PHB (left) and WNP+PHB+PCL+PVP (right) filters. Scale bar = 1mm

Conclusion

- *In vitro* cytotoxicity and hemolysis assay did not show any effects on W-IVCF.
- Bioresorbable IVCFs coated with WNPs and PHB+PCL+PVP reinforcement can be fully visualized in pigs under fluoroscopy and CT for real-time image-guided deployment and monitoring over time.
- Despite good visualization in fluoroscopy and CT from deployment until week 12, lumen of the WNP+PHB+PCL+PVP-coated IVCF pig did not seem to recover from initial inflammation as reflected by closed and necrotic lumen.

Future Direction

Although the addition of biocompatible polymers, PHB, PCL, and PVP enhanced the attachment of WNPs which resulted in increased radiopacity, localized inflammatory response was also observed in histology. Therefore, alternative polymers are currently being investigated to increase the surface roughness of PPDO and attachment of the nanoparticles. In addition, other high-Z nanoparticles, such as zirconium and gadolinium, are also being explored as potential radiopaque agents for IVCFs.

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Acknowledgements

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