



Epsin Mimetic Peptide

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Introduction



Coronary artery disease, a leading cause of death in the U.S., creates a critical need for effective grafts in small-diameter arteries (<4 mm). Maintaining graft patency is vital to prevent complications such as thrombosis, intimal hyperplasia, and aneurysmal-like dilation. Our goal is to develop a viable small artery graft that does not require pre-seeding with endothelial cells and instead releases peptides to promote healthy cell growth. To achieve this, we are synthesizing grafts from PCL with peptide-loaded microparticles embedded in a gelatin coating, designed to serve as scaffolds for endothelial cell deposition.

Hypothesis

Incorporating UPI peptide-loaded microparticles into a PCL-gelatin graft scaffold will improve endothelialization by enhancing VEGFR2 (vascular endothelial growth factor receptor-2, a key receptor that drives new blood vessel formation and endothelial cell survival) surface expression and reducing vascular inflammation.

Methods

- **Scaffold Fabrication:**
Polycaprolactone (PCL) dissolved in HFIP (hexafluoroisopropanol) → electrospun into fibrous grafts. PCL was chosen over collagen and fibrin for durability and controlled degradation.
- **Microparticle Loading:**
PLGA used to form microparticles with two viscosities (0.65, 0.21). Each batch was loaded with:
 1. UPI peptide
 2. Scramble peptide (control)
 3. No peptide (blank control)Particles were analyzed via SEM to confirm size and morphology.
- **Scaffold Coating:**
Microparticles suspended in gelatin, then coated onto PCL scaffolds. Gelatin was cross-linked to slow degradation and allow controlled peptide release.
- **Surgical Graft Implantation in Rats:**
 1. Rats were placed under general anesthesia for procedure.
 2. Sterile surgical tools were used to make an abdominal incision and normal saline was used to keep organs hydrated.
 3. Graft was placed using microsutures in the rat abdominal aorta.
 4. Rats were given a special diet and habitat following procedure to promote recovery.

Results

SEM confirmed consistent microparticle formation

Graft fabrication and coating were successful

Pending: in vivo data on graft patency, endothelialization, and peptide release

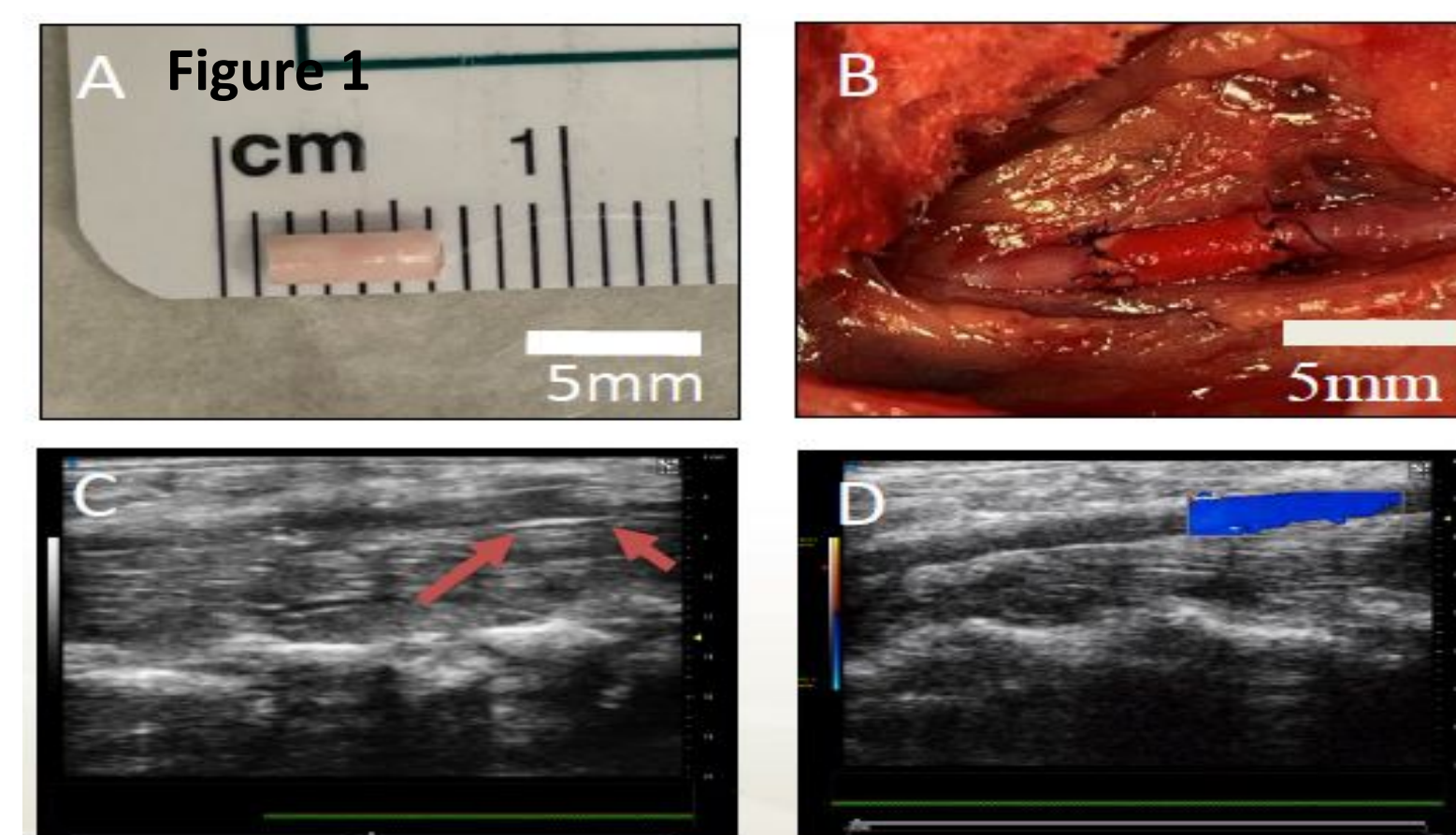


Figure 1: Successful graft implantation and ultrasound studies post-procedure

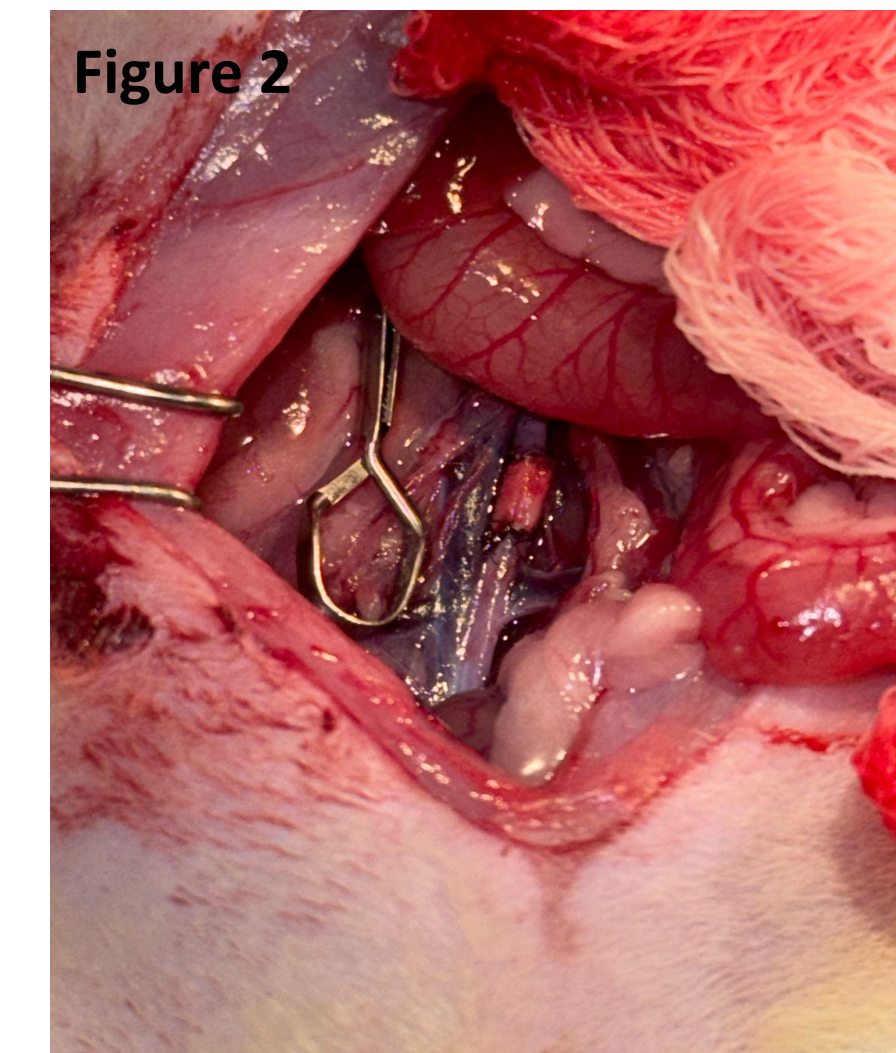


Figure 2: Successful graft with gelatin coating implantation.

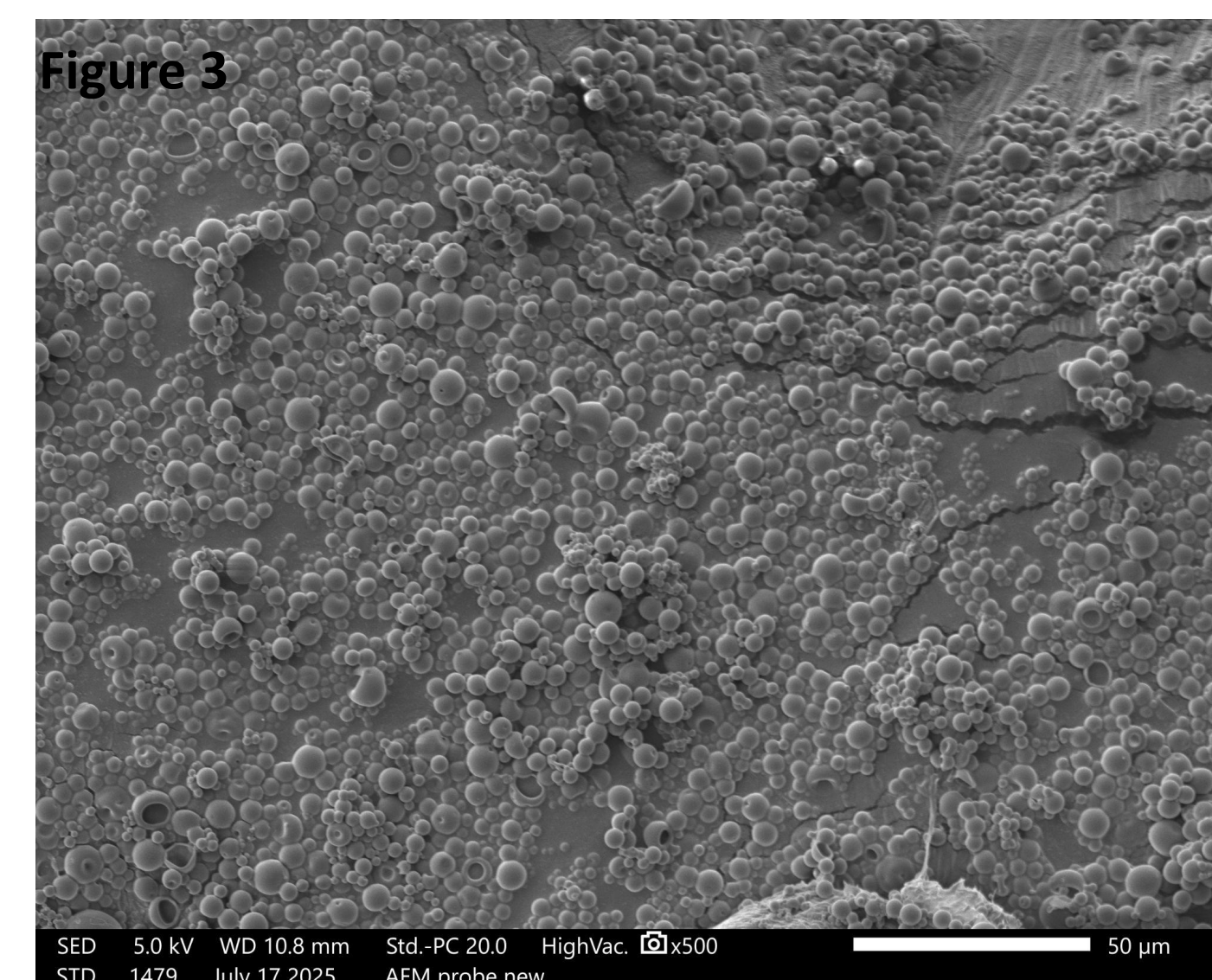


Figure 3: SEM imaging showing microparticle formation. This particular photo is from the UPI peptide batch.

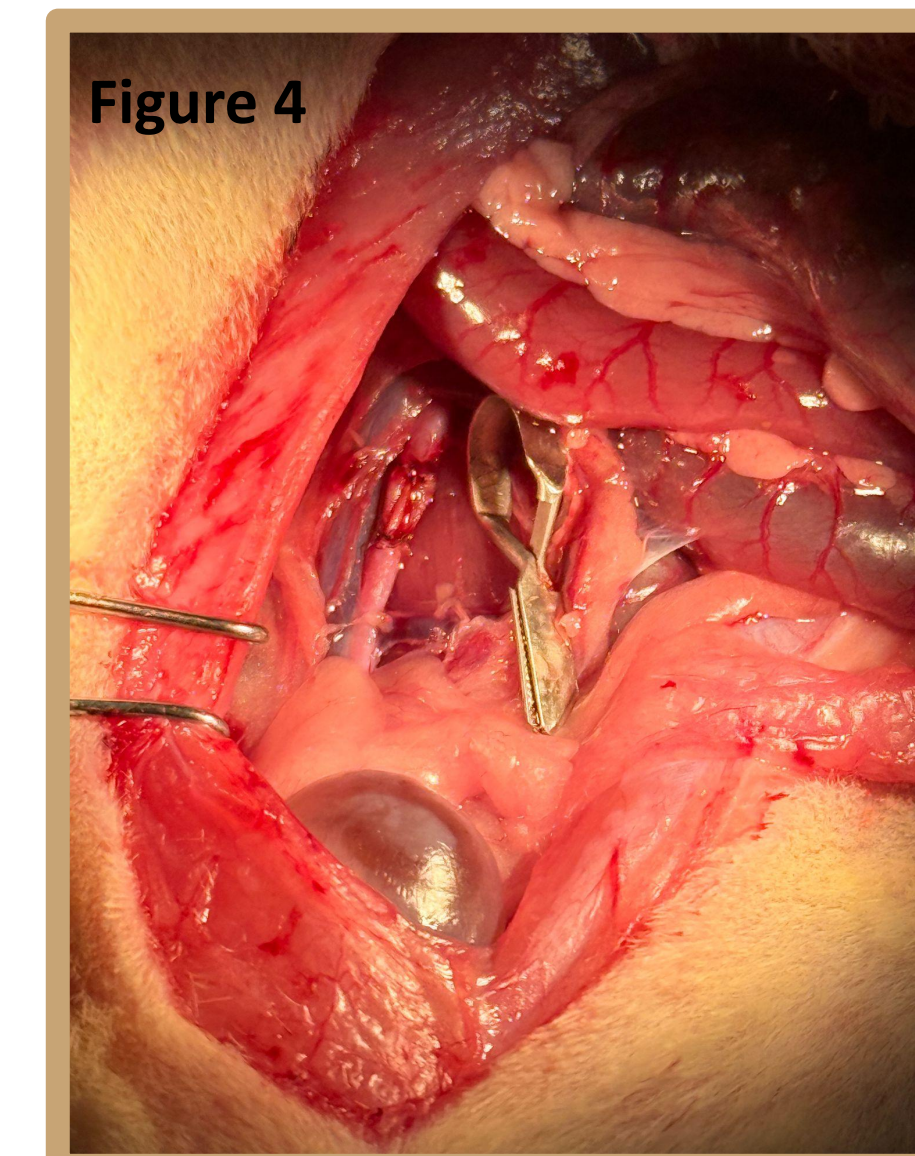


Figure 4: Successful graft with no coating implantation.

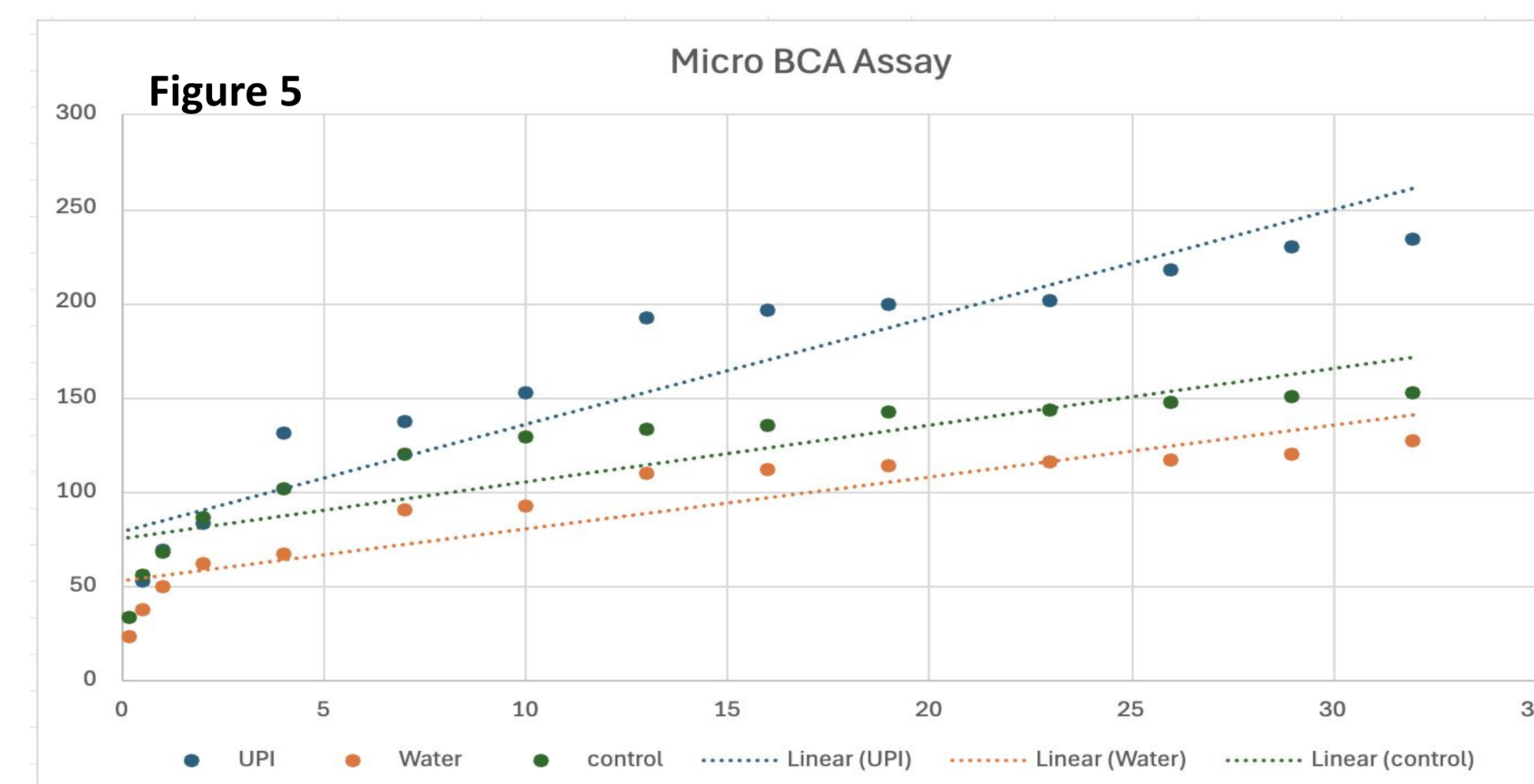


Figure 5: Graph demonstrating peptide release from grafts over an extended period of 32 days using Micro BCA assay.

Discussion/Summary/Conclusions

Scaffold fabrication was highly reproducible, with SEM imaging confirming consistent microparticle morphology across batches. Coating efficiency, however, was variable—only a subset of grafts demonstrated uniform gelatin-mediated retention, highlighting the need for optimization of the surface modification process. Preliminary release studies confirmed that the system achieved sustained peptide delivery, supporting the feasibility of this approach for vascular applications.

Surgical implantation of grafts into the rat abdominal aorta proved technically feasible but required significant microsurgical precision. The procedure demanded careful separation of the aorta from the vena cava, with anatomical variability and tissue fragility posing major challenges. Precise clamp placement between the renal vessels was critical, and graft integration required 16 microsutures to achieve stability. These factors contributed to a steep learning curve and variability in surgical outcomes, emphasizing the technical challenges inherent to this in vivo model.

Future studies will focus on evaluating graft patency, VEGFR2 expression, and inflammatory response to determine the therapeutic potential of the system while also working to standardize surgical outcomes in this technically demanding model.

References

1. Changizi et al. (2023) *Macromolecular Bioscience*, 23(9): e2300073
2. Shojaee & Bashur (2017) *Adv Healthcare Materials*, 6(12)

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