

PHASE SHIFT MICROBUBBLE (SOLV, MVT-101, PSMB) REDUCES INFARCT SIZE IN A MVO PORCINE MODEL

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Introduction

Microvascular obstruction (MVO) is a common complication following successful percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI). Despite restoration of epicardial coronary blood flow, persistent obstruction of the myocardial microvasculature can limit tissue reperfusion, increase infarct size, impair cardiac function, and worsen long-term clinical outcomes. Ultrasound combined with intravenously administered microbubbles (MBs) has demonstrated the ability to enhance thrombus dissolution and improve microvascular perfusion; however, no FDA-approved microbubble therapy currently exists for this indication.

Microvascular Therapeutics (MVT) has developed novel nanoscale phase shift microbubbles (PSMB; Solv) and fibrin-targeted phase shift microbubbles (FTPSMB; Solv-2). These agents are approximately one-tenth the diameter of conventional microbubbles (150–300 nm versus 1–2 μm), allowing them to penetrate deeper into microthrombi where fibrin spacing is on the nanometer scale. Their small size also enables access to tissues beyond the vasculature and provides a platform for targeted intracellular therapeutic delivery. This study evaluated the ability of PSMBs to improve myocardial perfusion and cardiac function in a porcine model of MVO.

Purpose

The objective of this study was to evaluate the therapeutic efficacy of Phase Shift Microbubbles (PSMB) in improving myocardial perfusion and reducing microvascular obstruction in a porcine model of acute myocardial infarction using therapeutic ultrasound.

Support

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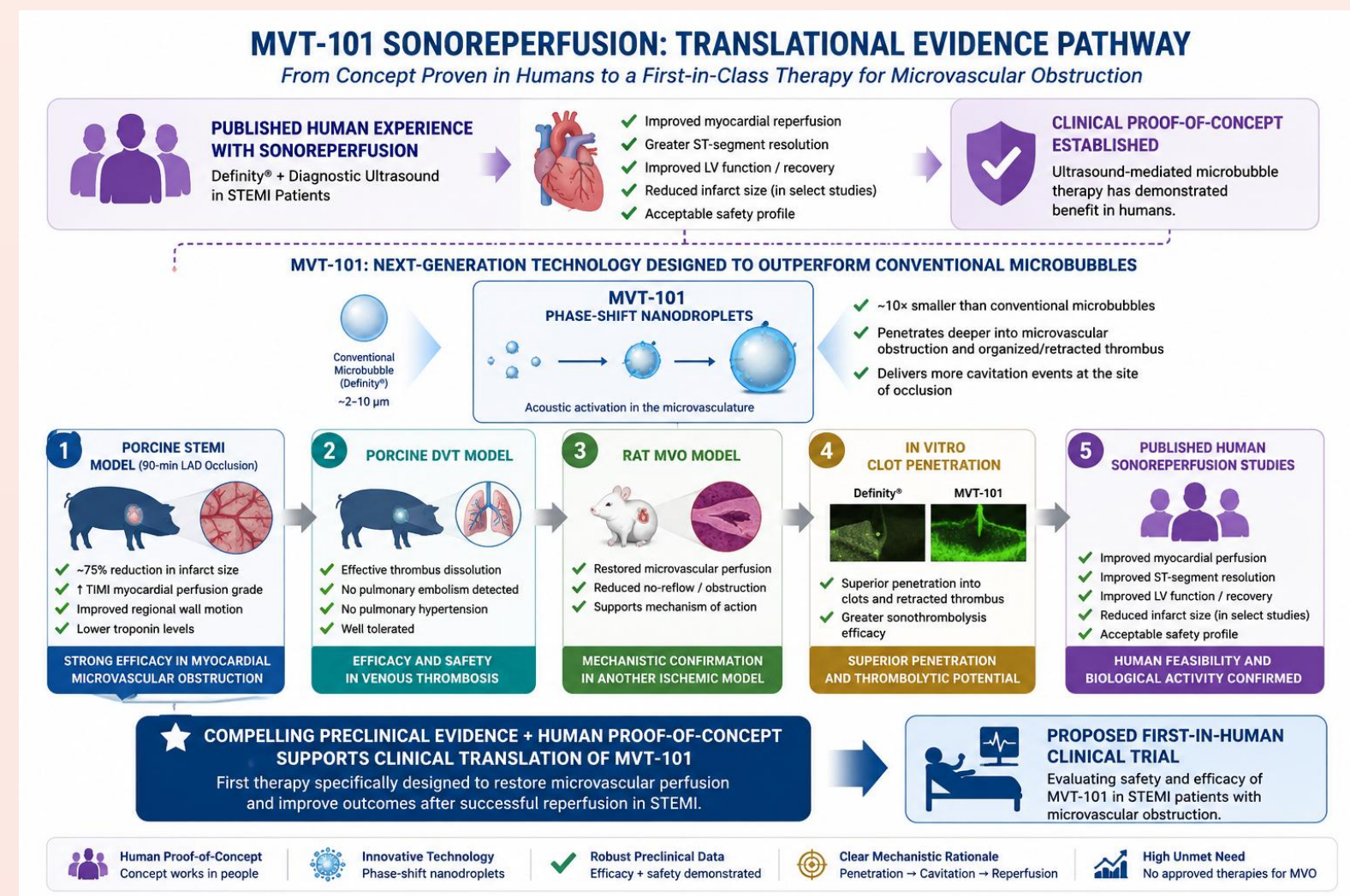


Figure 1: MVT-10 Sonoperfusion: Translation Evidence Pathway Flow chart showcasing the concept that was proven in humans to a First-in-Class Therapy for Microvascular Obstruction

Methods

PSMB Lipid Composition

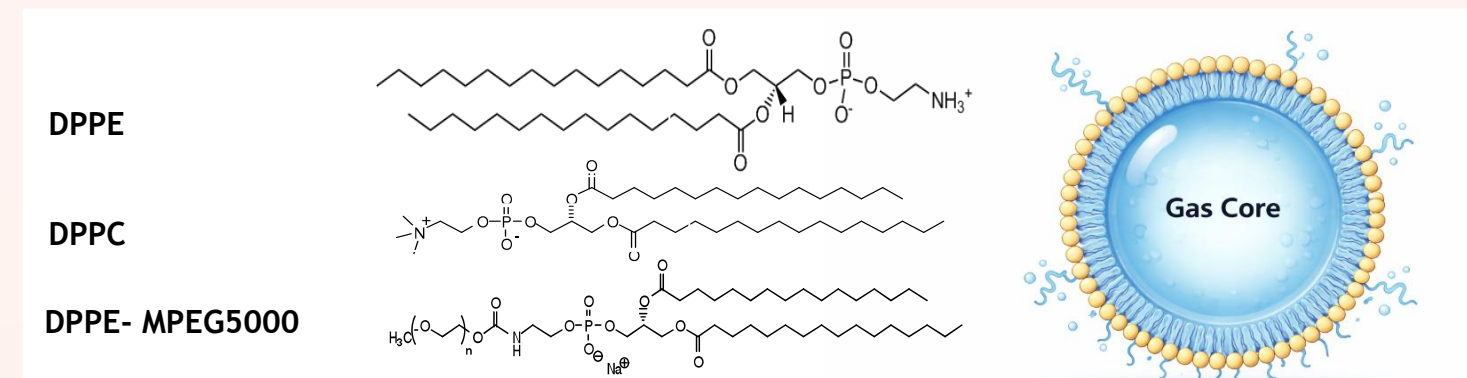
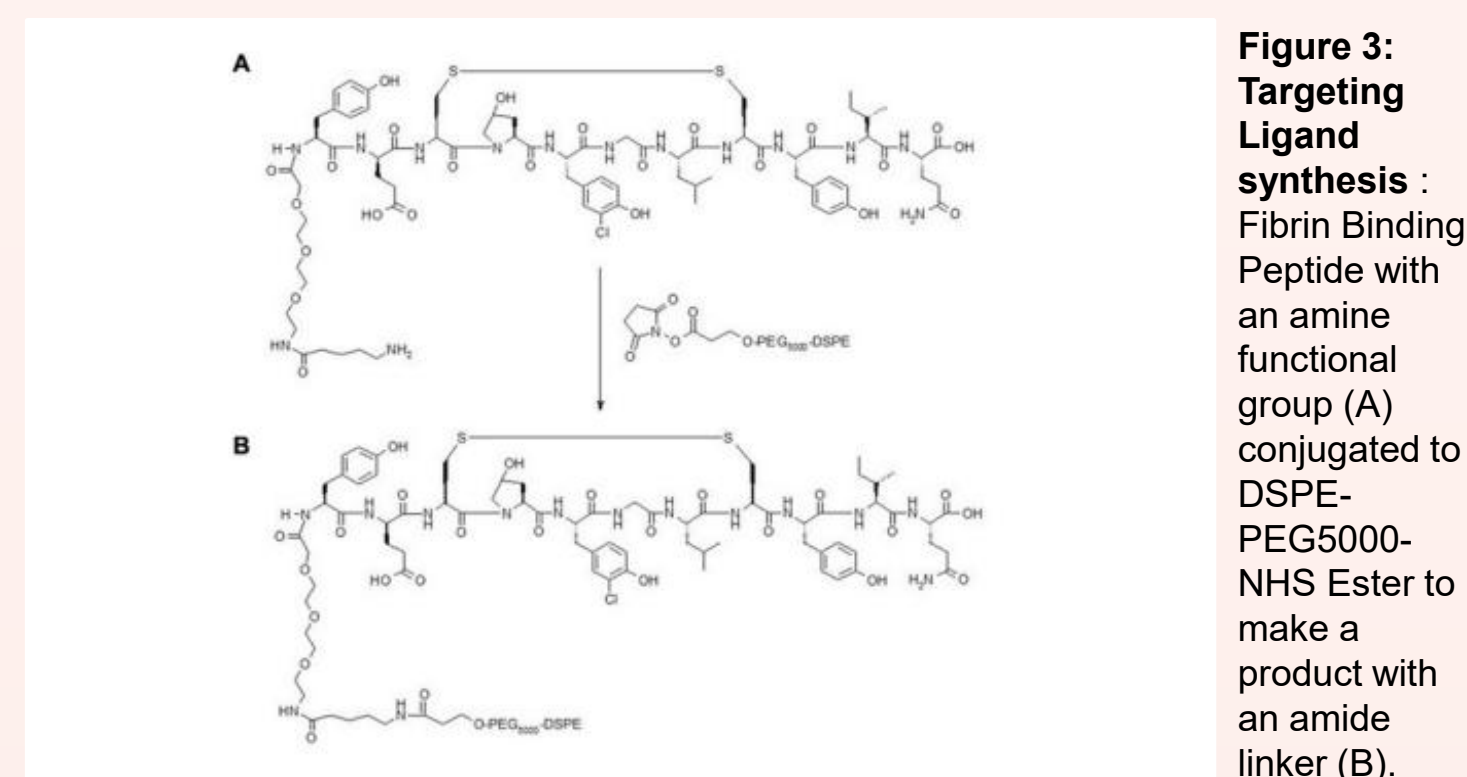


Figure 2: PSMB Lipid Composition. The lipid monolayer composing the PSMB (MVT-101) is made of 3 lipids, DPPE, DPPC, and DPPE-MPEG5000.



PSMB Characterization

Parameter	Specification	
Appearance	Cloudy to clear, colorless, slightly bubbly liquid that may include white foam	
Post Condensation Size Distribution <0.5 μm	0.5 μm - 10 μm * a 10 μm * Mean Diameter	Report
Post Condensation Size Distribution <0.5 μm	D10 (nm) D50 (nm) D90 (nm) EFF. D (nm) SPAN (nm)	Report
Pre-Activation Particle Size	D10 (nm) D50 (nm) D90 (nm) EFF. D (nm) SPAN (nm)	Report
Octafluoropropylene Content (Final Condensation)	Report	
pH	6.2 - 6.8	
Lipid Content	DPPE-MPEG-5K DPPC DPPE	0.243-0.365 (mg/mL) 0.321-0.481 (mg/mL) 0.036-0.054 (mg/mL)
Total Lipid	0.600-0.900 (mg/mL)	
Particulate Matter	≤ 3000 particles/mL, a 10 μm ≤ 300 particles/mL, a 25 μm	
Post Condensation Minimum Fill	1.0 - 1.6 mL for individual vials	
Sterility	0 CFU	
Endotoxin	≤ 8.33 EU/mL	

Table 1: Release Specifications for PSMB

- Dynamic Light Scattering (particle size distribution).
- GC-MS (gas content).
- pH
- Fill Volume
- HPLC (lipid content)

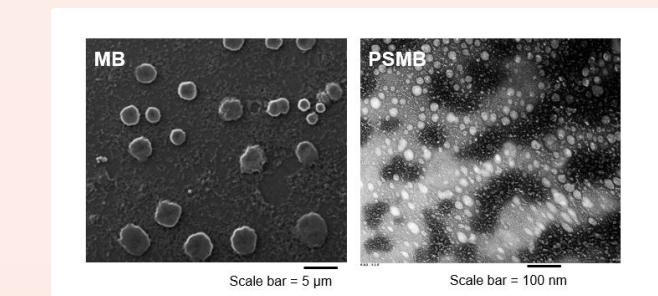
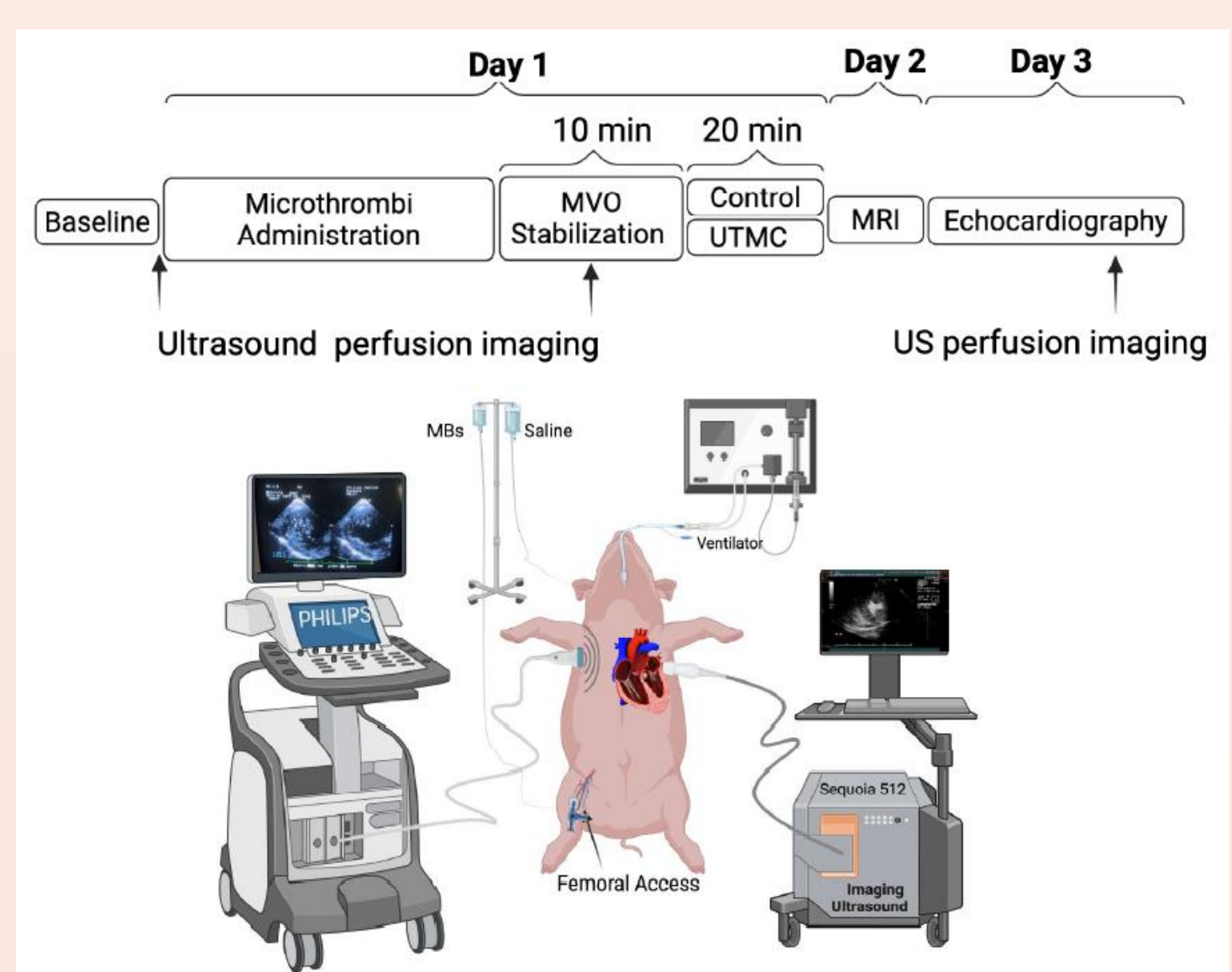


Figure 4: Transmission Electron Microscopy of Microbubbles and PSMB.

In Vivo Study Design



Results

PSMBs in a Model of MVO

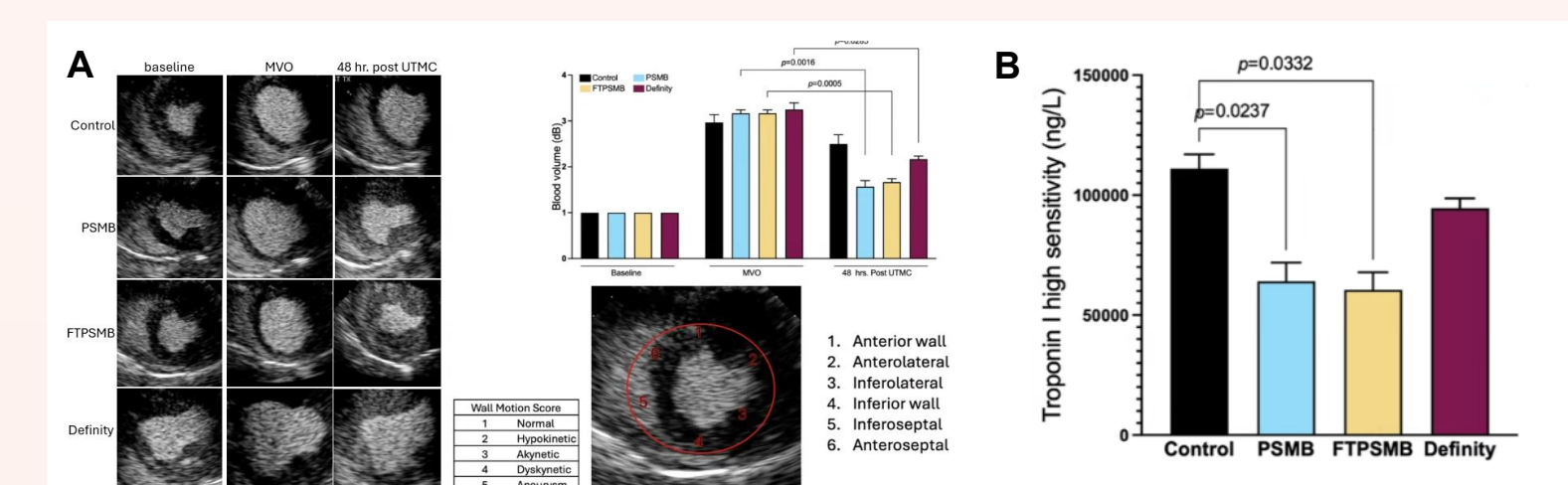


Figure 5: (A) Wall Motion Score Index in the left ventricle. (B) Troponin levels: There was no significance in the troponin levels post-treatment with Definity at day 3 (48 hours post MVO). There was a significant reduction of Troponin levels with PSMB or FT-PSMB.

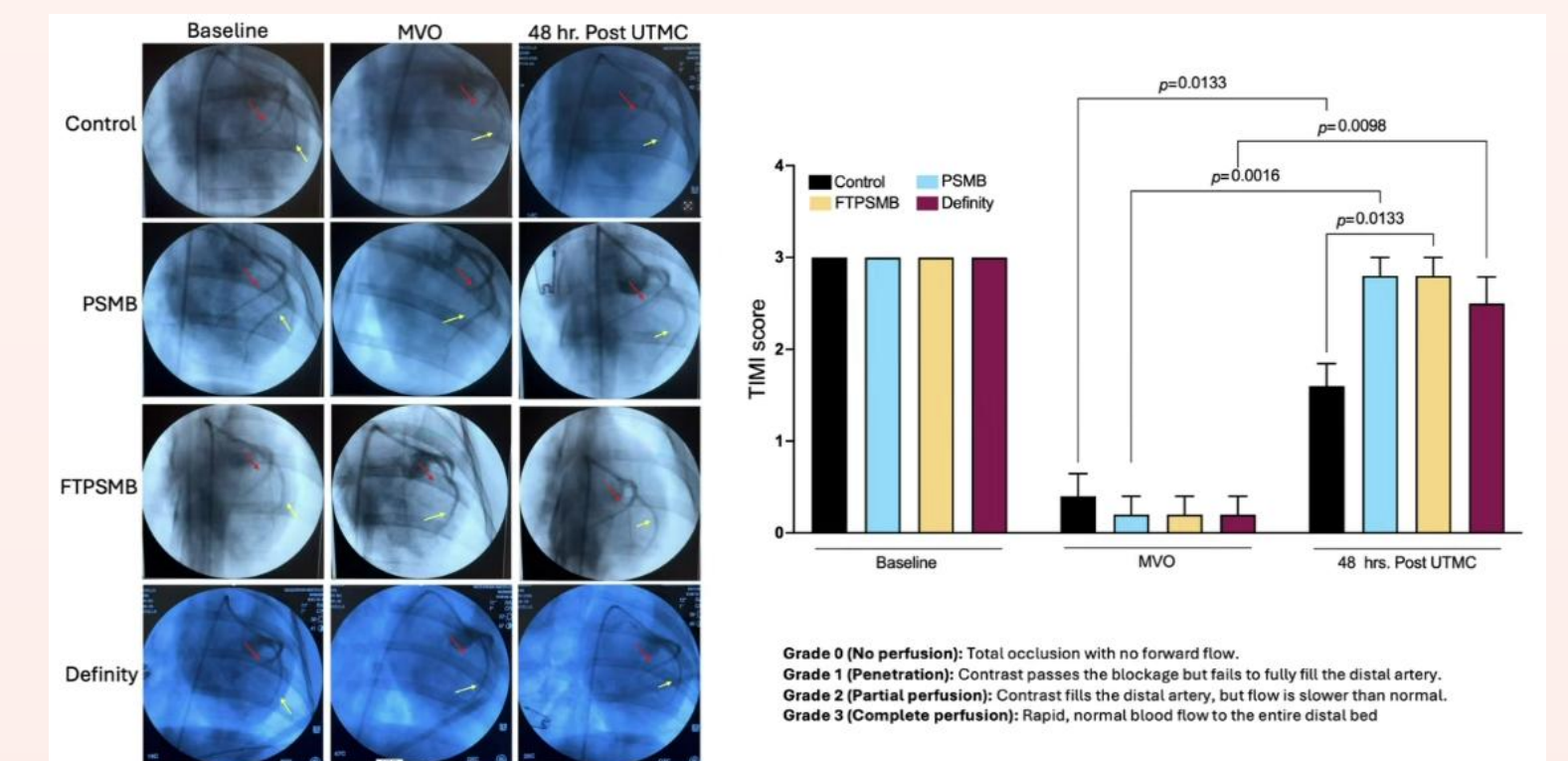


Figure 6: Thrombolysis in Myocardial Infarction (TIMI) Flow Grade: Epicardial vessel for TIMI Flow Grade. PSMB and MB are similar in TIMI (score of 3) but in the microvascular vasculature there is a difference because PSMB are smaller. Post-treatment the circumflex floor is improved as compared to control.

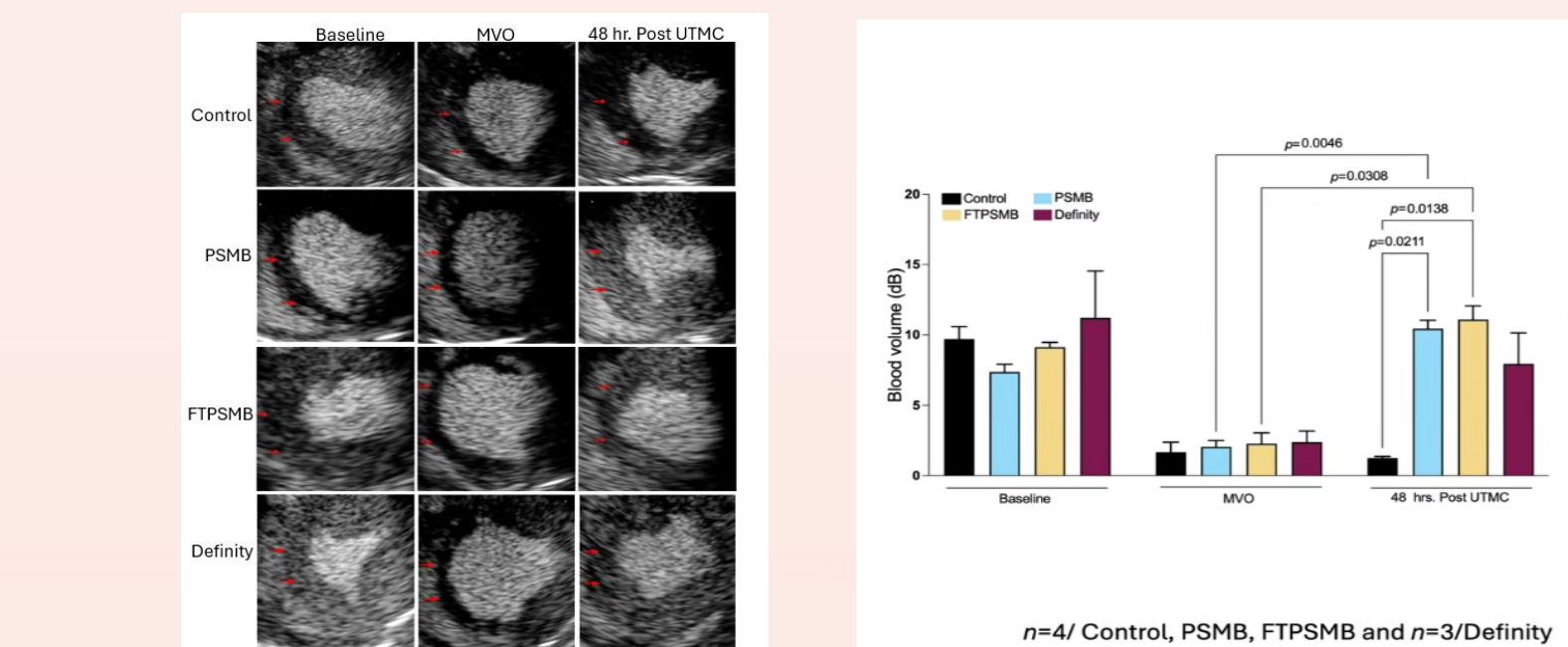


Figure 7: Total Blood Volume at Baseline, at MVO and at 48h post-MVO. n=5/control, PSMB, FT-PSMB; n=4/Definity

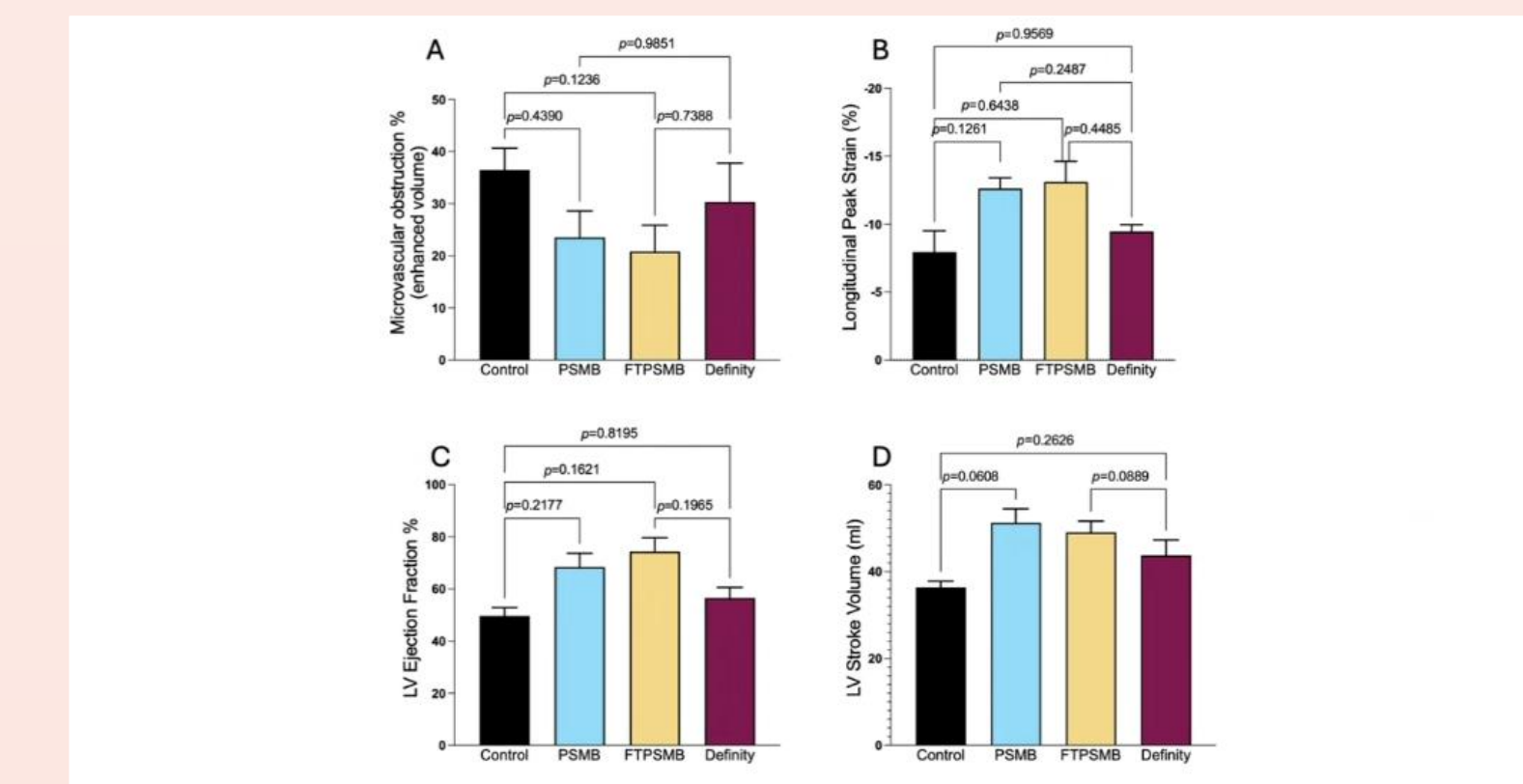


Figure 8: MRI parameters improved following PSMB and FT-PSMB treatment.

Results

Infarct Size Area Post MVO

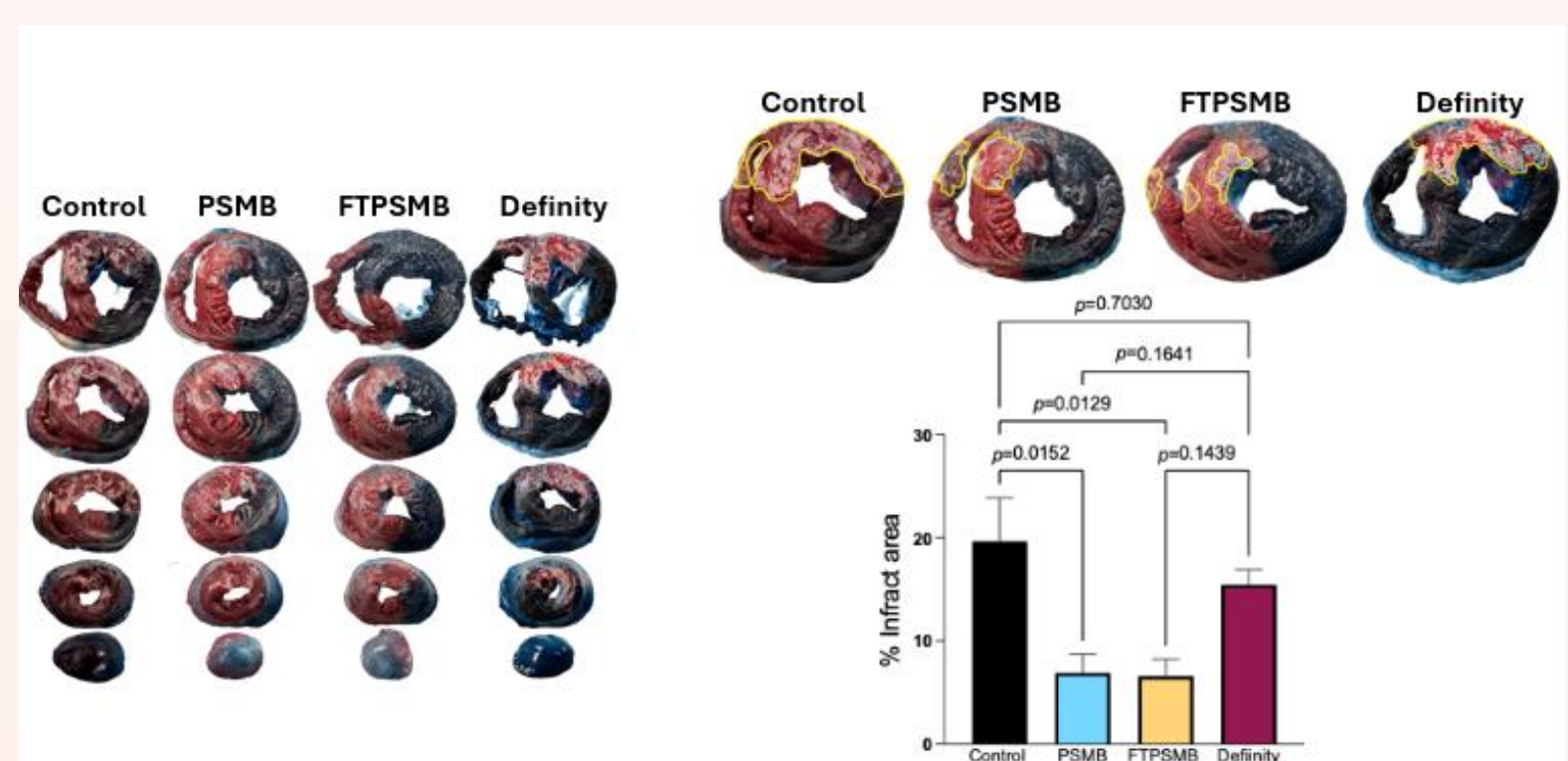


Figure 9: Infarct Size Area post MVO: Evans Blue and TTC (Triphenyltetrazolium chloride) staining are widely used techniques for Assessing myocardial infarction and tissue viability in research. The difference of the infarct area, as measured using TTC-Evans Blue staining, is statistically significant between the PSMB and FT-PSMB as compared to Control or Definity.

Parameters	Control	PSMB	Definity
Total Blood Volume#	2.0 ± 0.5	9 ± 1 (p=0.0191),*	5 ± 3 (not significant)
TIMI Flow Grade @48Hr	1.8 ± 0.1	2.9 ± 0.1 (p=0.0016),**	2.6 ± 0.2 (0.0098),*
Wall Motion Score Index#	3.0 ± 0.1	1.5 ± 0.1 (p=0.0016),**	2.1 ± 0.1 (p=0.0285),*
Troponin 1 (ng/L)	110000 ± 10000	65000 ± 10000 (p=0.0015),**	95000 ± 10000 (not significant)
Infarct Area (%)	20 ± 3	5 ± 1 (p=0.0224), *	18 ± 1 (not significant)

Table 2: Data Summary MVO Studies. #, comparisons are made to respective MVO (before and after treatment); * for p<0.05; ** for p<0.005

Conclusion

Ultrasound-mediated treatment with Phase Shift Microbubbles (PSMB) significantly improved myocardial microvascular perfusion following experimentally induced microvascular obstruction in a porcine model of acute myocardial infarction. Improved reperfusion was associated with enhanced cardiac function, favorable MRI findings, and a significant reduction in infarct size compared with control and conventional microbubbles. These findings support PSMBs as a promising image-guided therapeutic platform for the treatment of microvascular obstruction following PCI and warrant continued preclinical development toward clinical translation.

Future Work

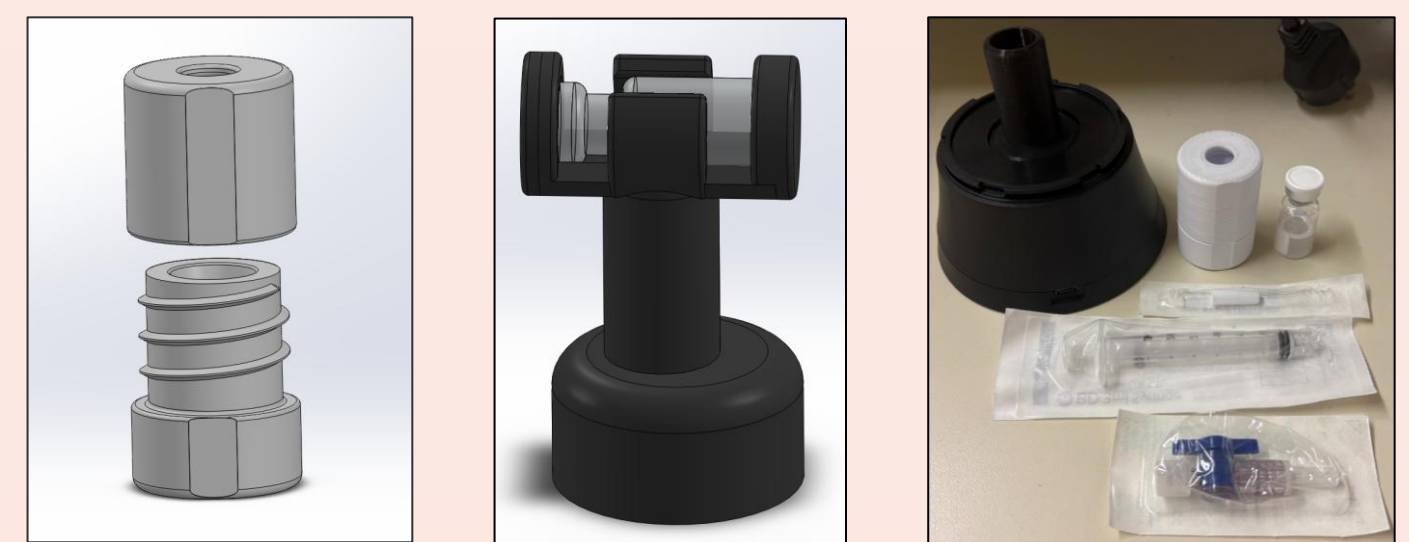


Figure 10: Manufacturing of PSMB. The developed NanoGenesis™ System (left) and portable battery-operated vortexing unit (adapter pictured in center and kit on right) enable production of Phase Shift Microbubbles (PSMB) outside of traditional pharmacy settings, expanding their potential use in combat environments, emergency medicine, and other resource-limited settings.