A Comparison of Thrombus Dissolution Efficacy With Single and Multiple-Cycle Histotripsy Pulses In Vitro

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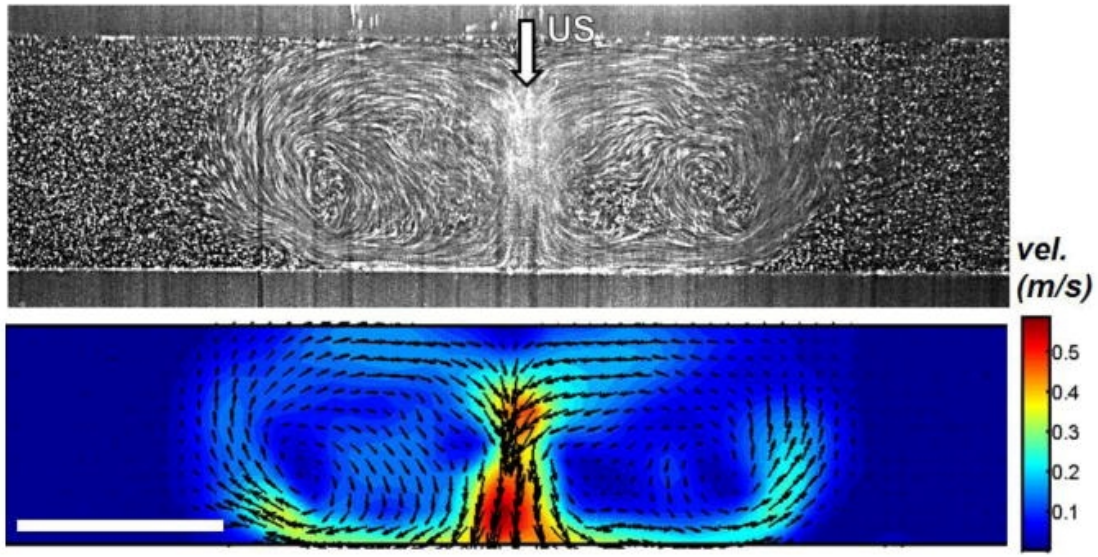
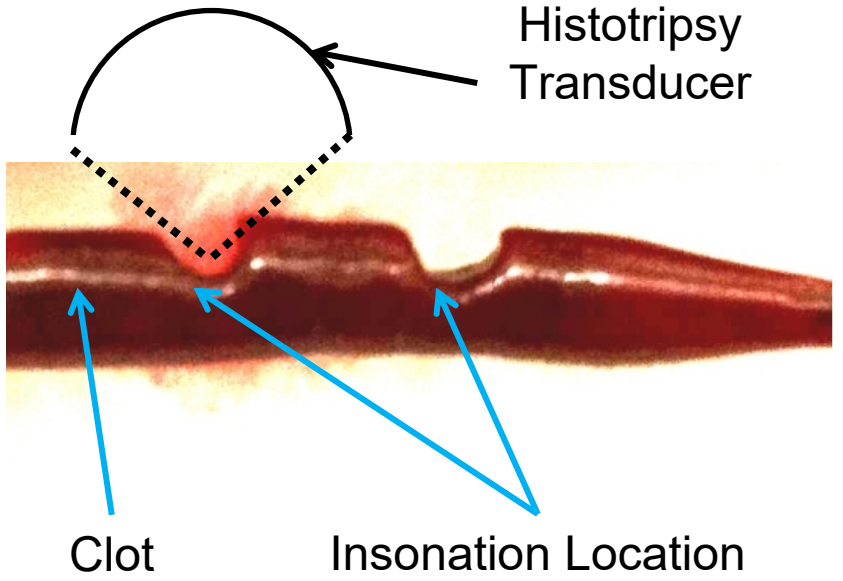
THE UNIVERSITY OF CHICAGO

Motivation: Chronic Deep Vein Thrombosis

- DVT is a burden on the public health
- Need treatment for thrombolytic resistant clots[1]
- Histotripsy enhances thrombolytics in non-responsive clot model[2]

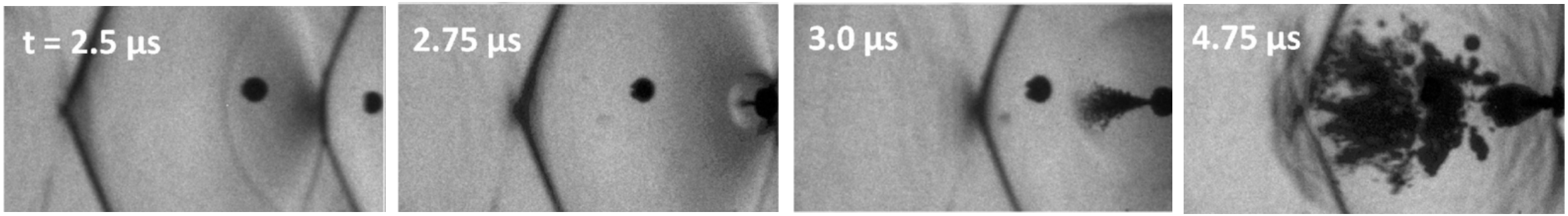


Maxwell et al. *Phys. Med. Biol.* 2014



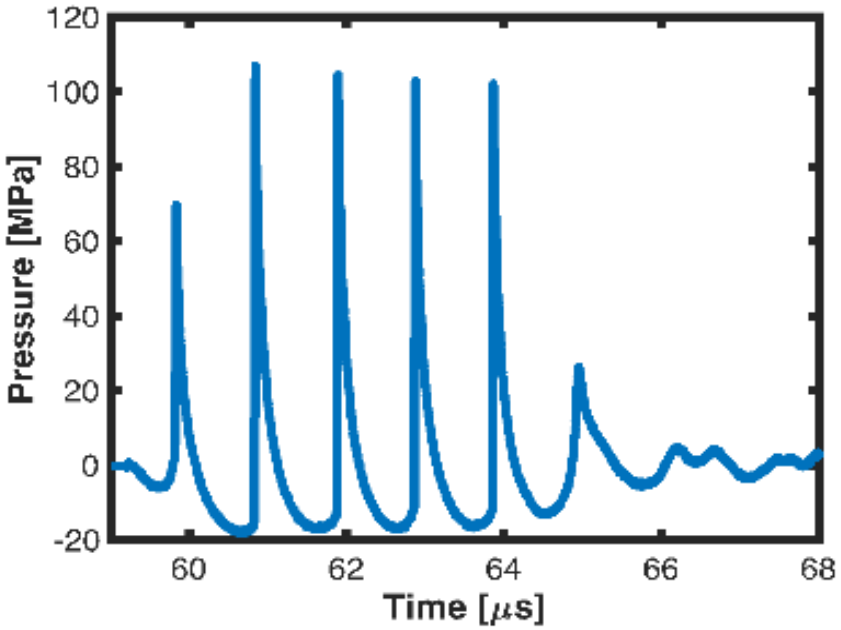
1 Augustinos *Circulation* 2004
2 Bader *Phys. Med. Biol.* 2016

Histotripsy: Shock Scattering Cavitation



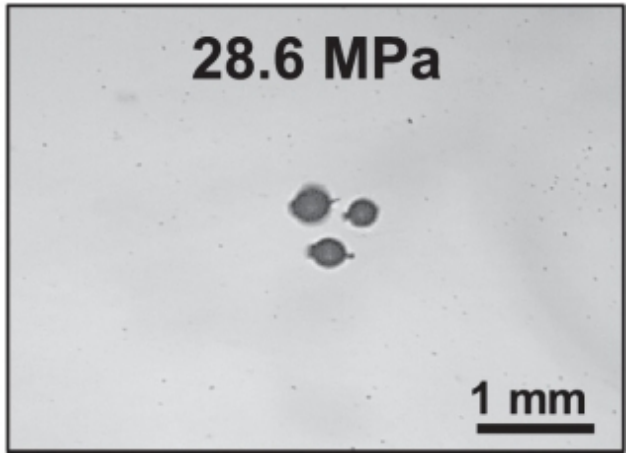
Maxwell et al. *J. Acoust. Soc. Am.* 2011

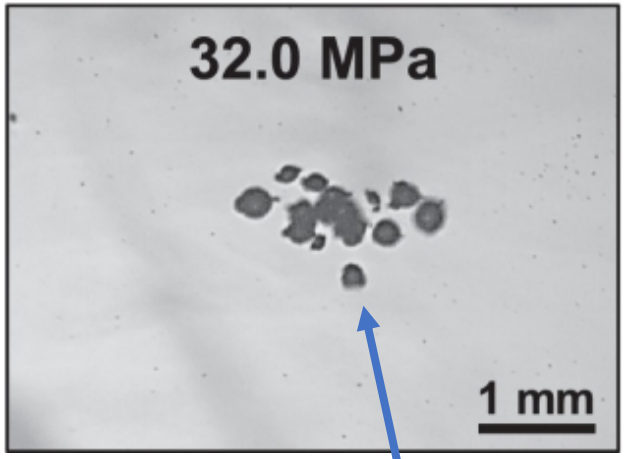
- 3-20 cycle excitations
- Incident shock wave scattered by intrinsic nuclei
- Requires highly asymmetric waveforms
- Potential off-target cavitation[3]



[3]Maxwell et al. *J. Vasc. Interv. Radiol.* 2011

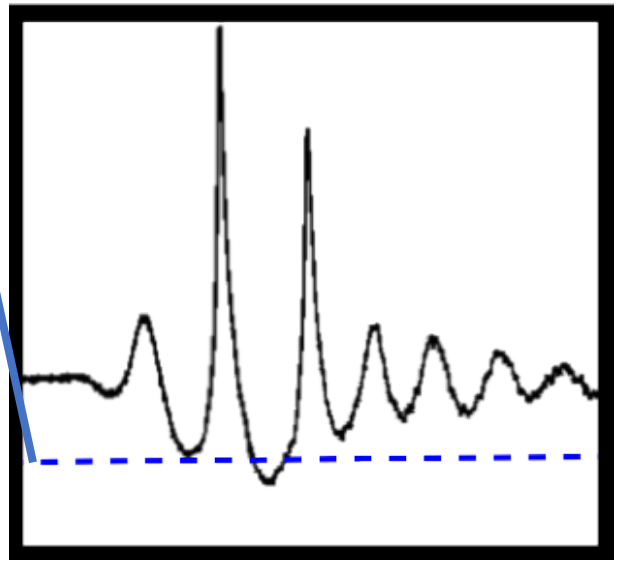
Histotripsy: Intrinsic Threshold Cavitation





Bader et al. *Ultrasound Med Biol* 2019

- Single cycle excitations
- Only peak negative pressure matters
- Large tensile phase needed for inertial cavitation
- Contained in vessel[4]



[4]Zhang *Ultrasound Med Biol* 2017

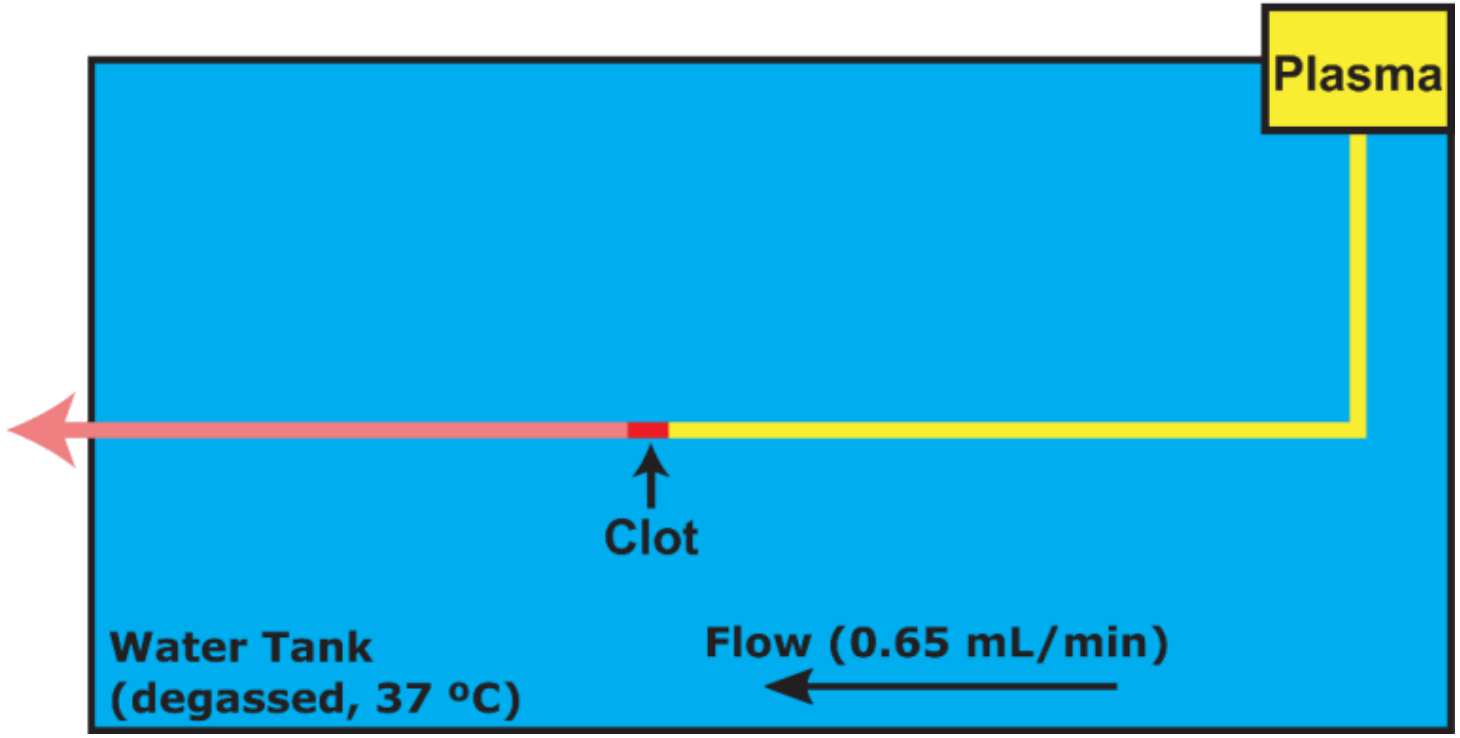
Research Questions

- How does pulse duration affect thrombolytic efficacy?

- Can thrombolytic efficacy be assessed by passive cavitation imaging?

Methods: Experimental Setup

- Human plasma alone or mixed with $2.68\ \mu g/mL$ of rt-PA

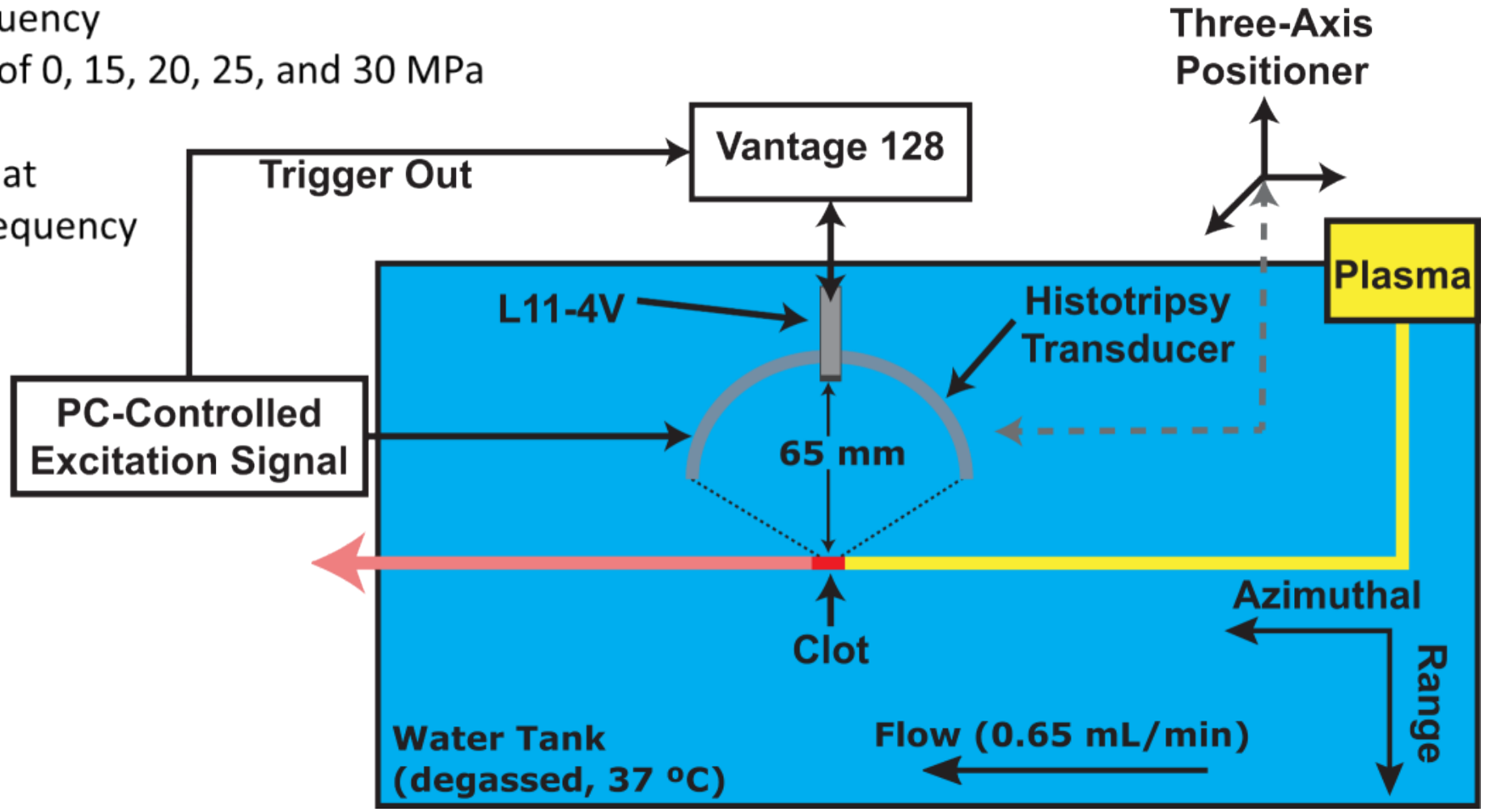


Methods: Experimental Setup

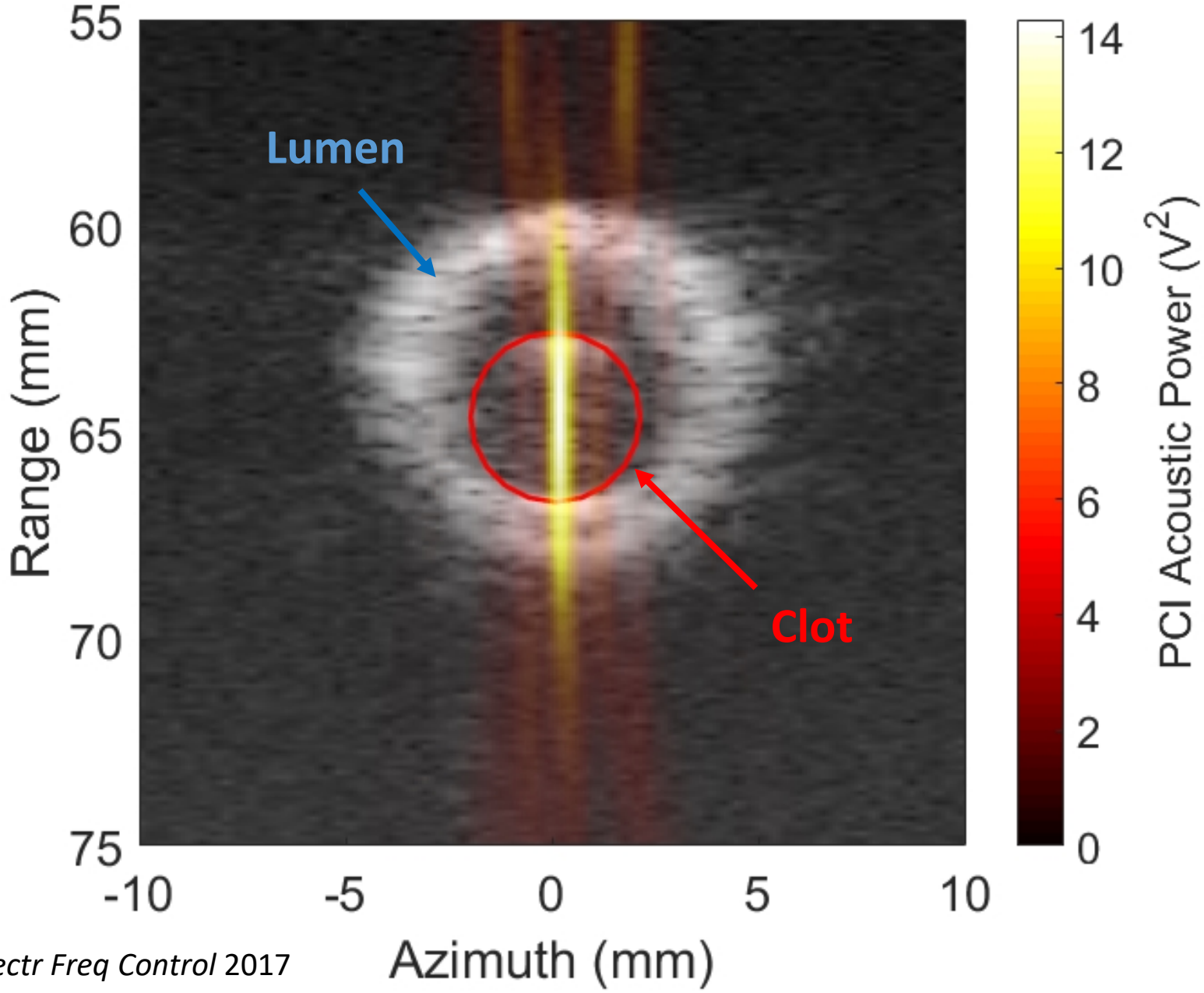
- Human plasma alone or mixed with $2.68\ \mu g/mL$ of rt-PA

- 1 (intrinsic threshold) and 5 (shock scattering) cycle pulses
- 1 MHz fundamental frequency
- Peak negative pressures of 0, 15, 20, 25, and 30 MPa

- 2000 pulses per location at
  40 Hz pulse repetition frequency

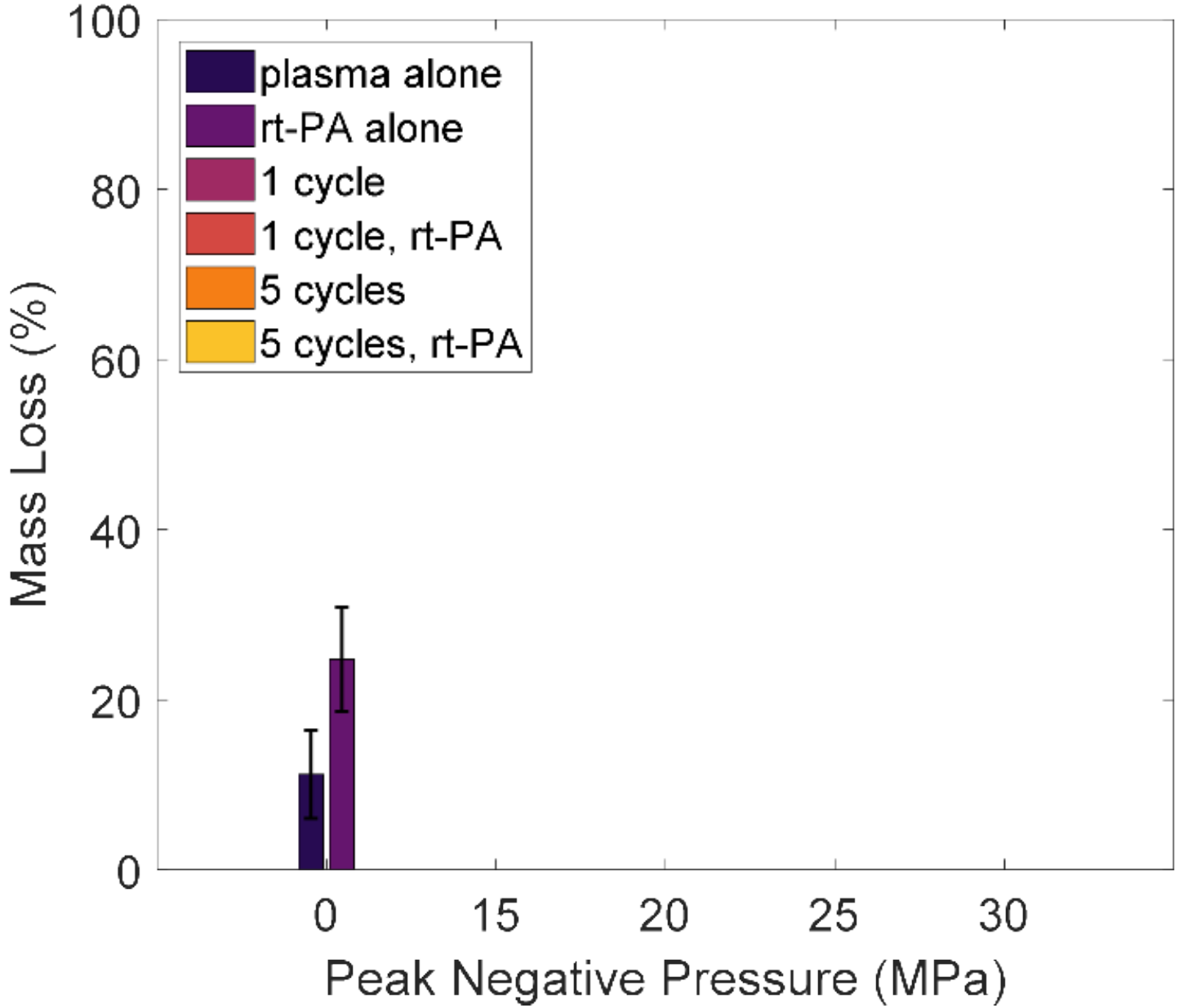


Methods: Acoustic Power Dose from Passive Cavitation Imaging



Haworth et al.
IEEE Trans Ultrason Ferroelectr Freq Control 2017

Results: Thrombolytic Efficacy



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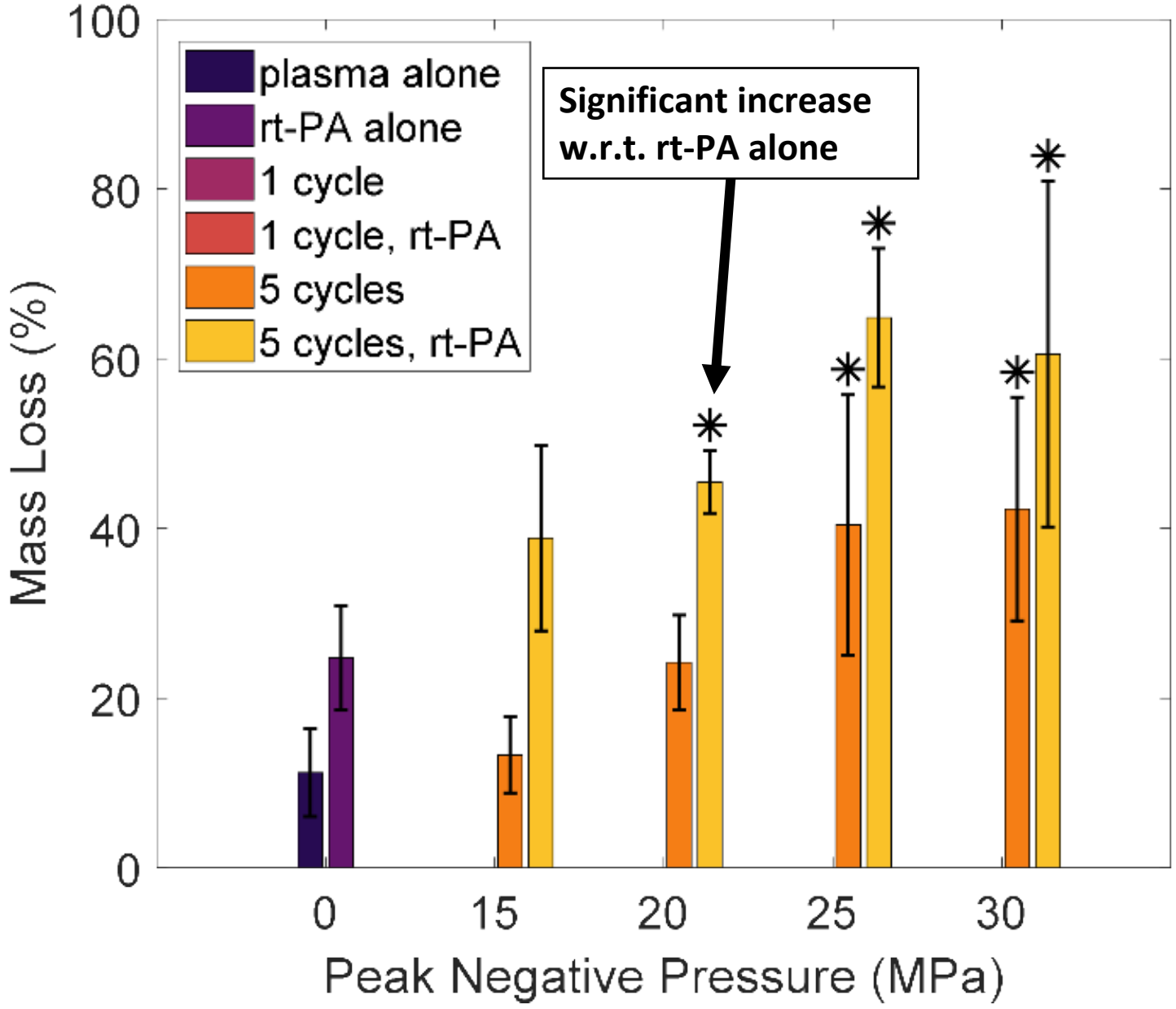

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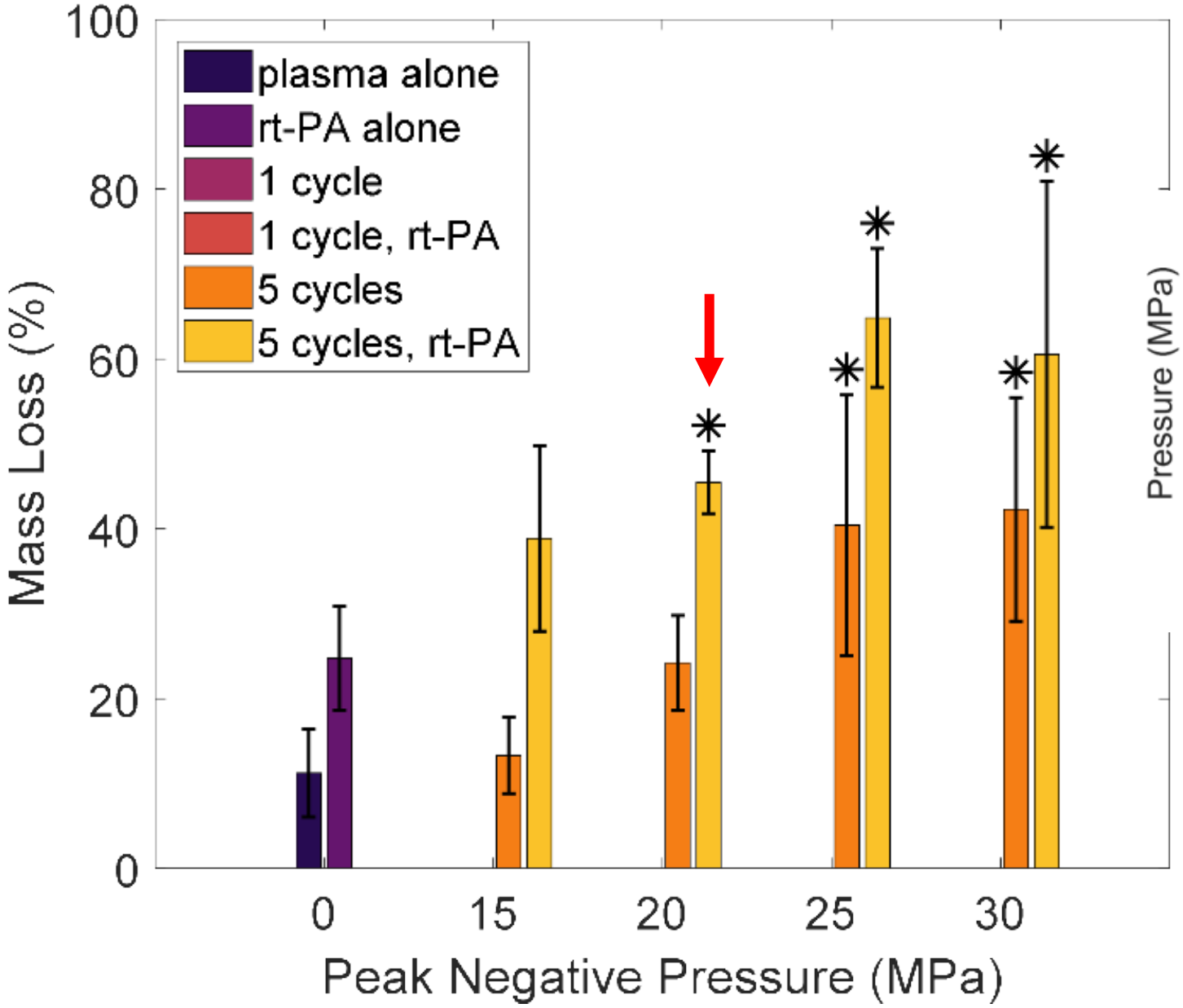
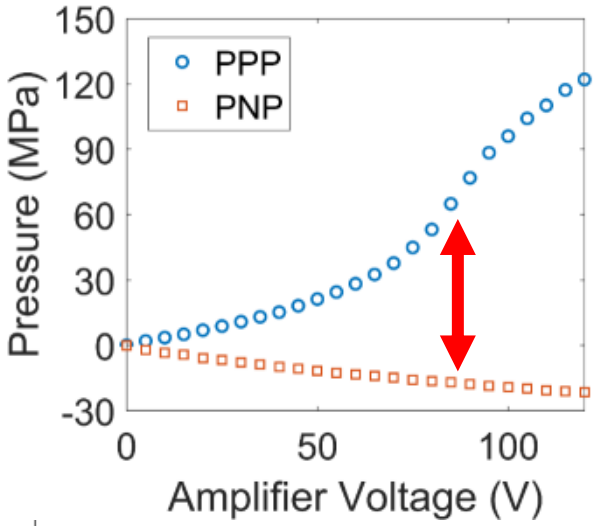
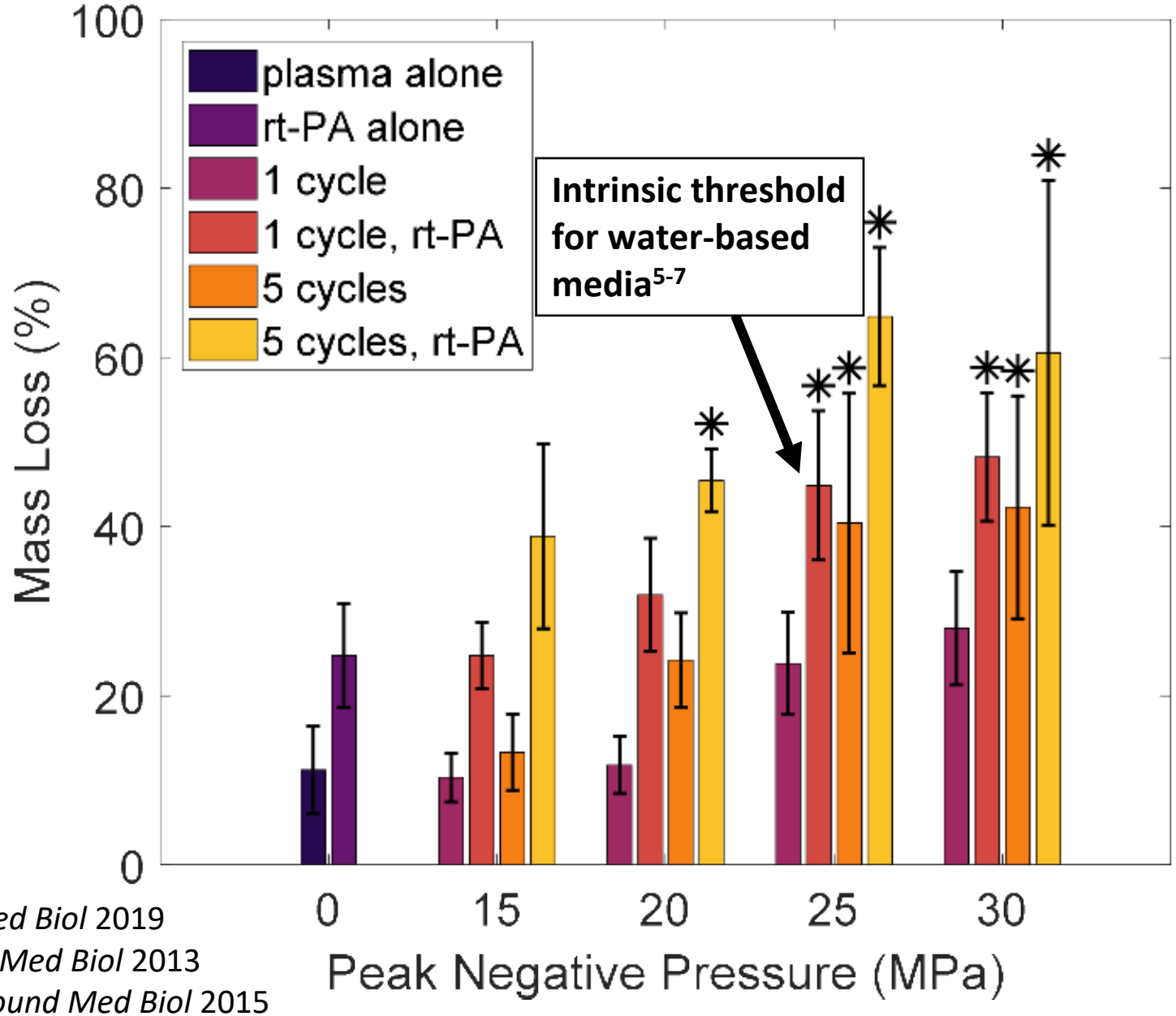


Five Cycle

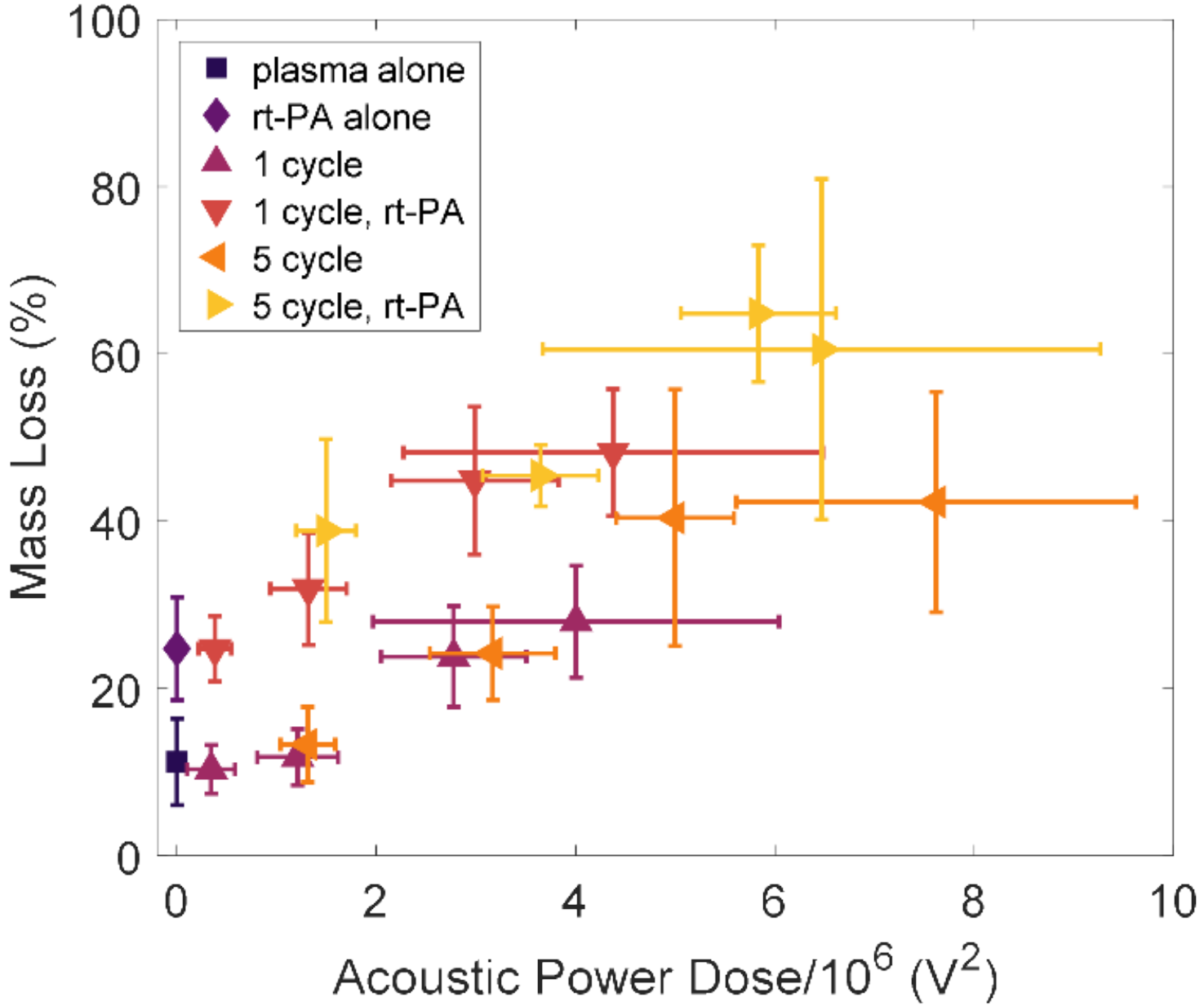


Results: Thrombolytic Efficacy



[5]Bader et al. *Ultrasound Med Biol* 2019
[6]Maxwell et al. *Ultrasound Med Biol* 2013
[7]Vlaisavljevich et al. *Ultrasound Med Biol* 2015

Results: Thrombolytic Efficacy to Acoustic Power Dose



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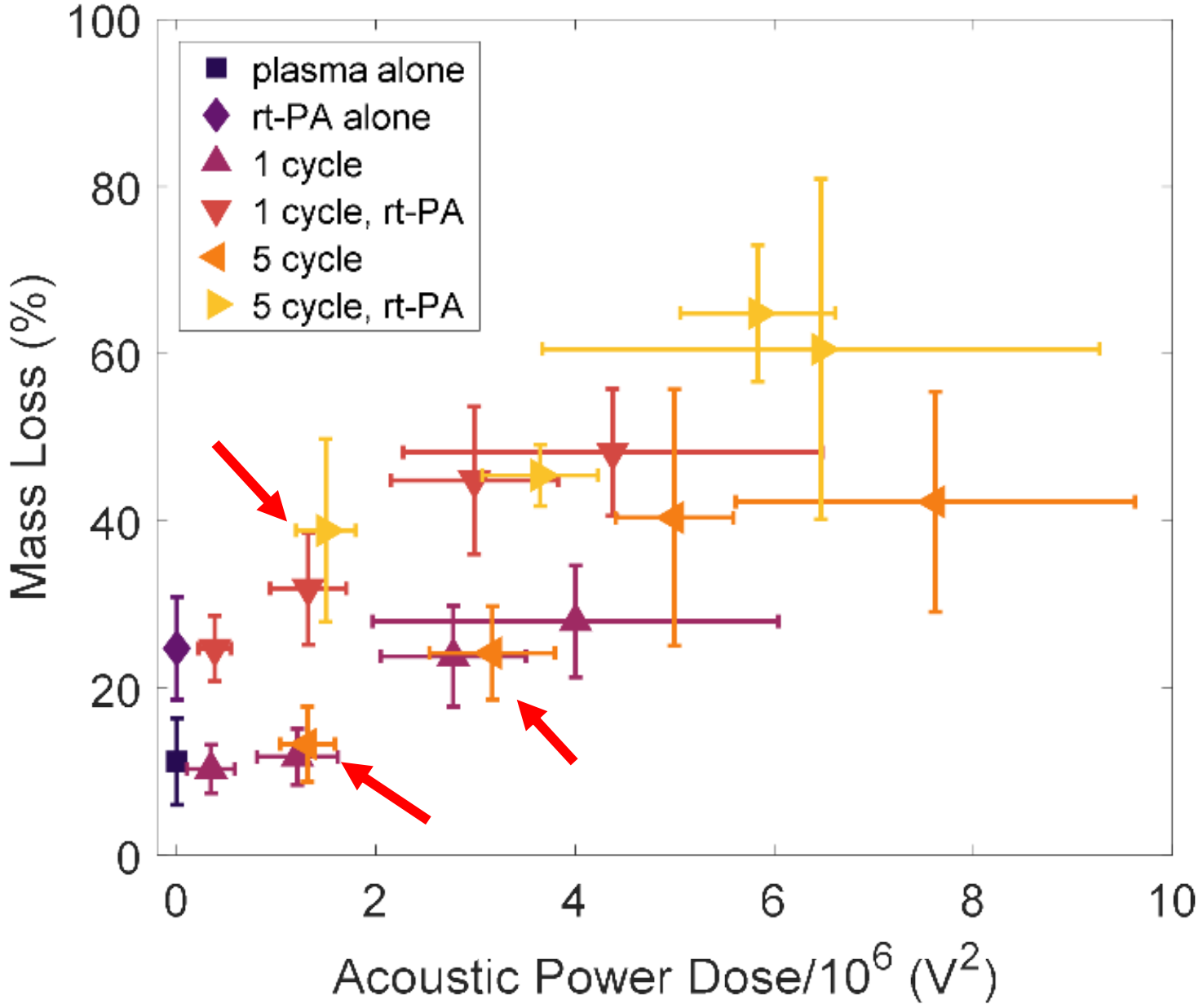

Conclusion

- Enhancement in thrombolytic efficacy in combination with histotripsy depends on mechanism based threshold
- Thrombolytic efficacy correlates with acoustic power dose, independent of pulse duration

Contact Information

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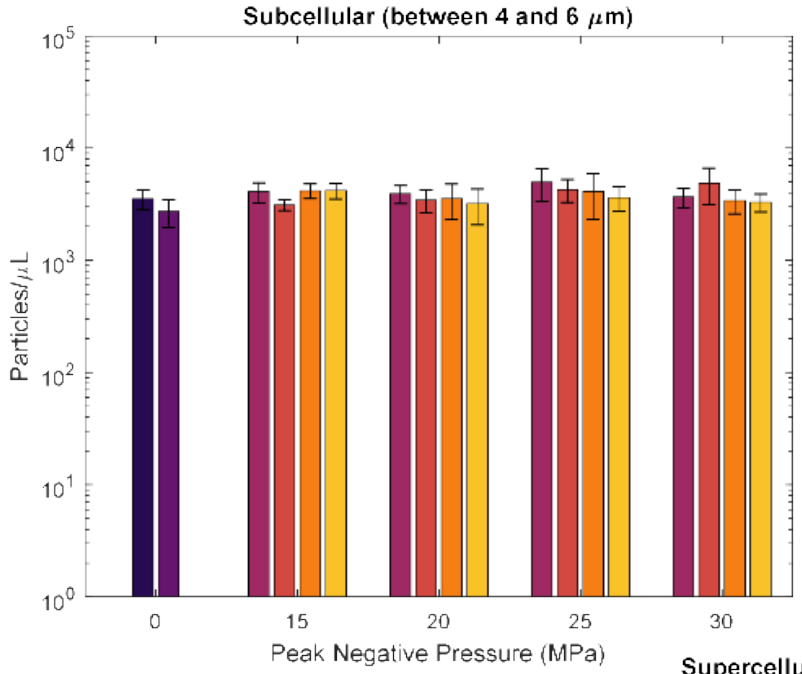
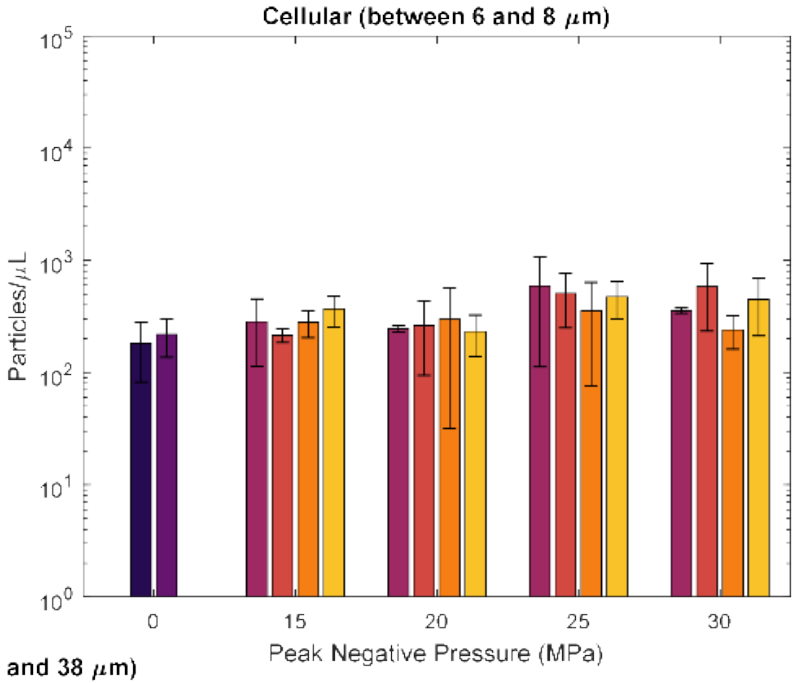
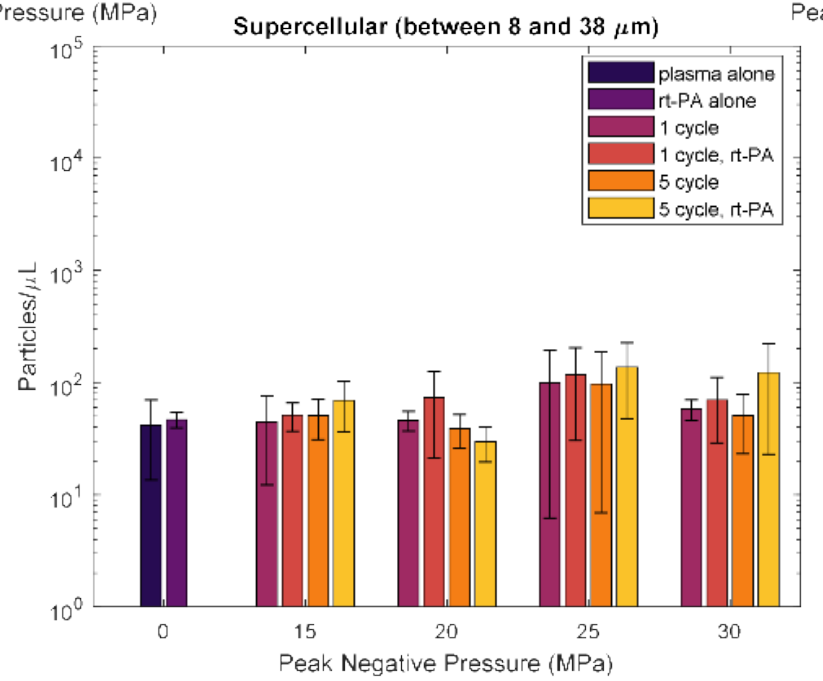
Results: Particle Debris







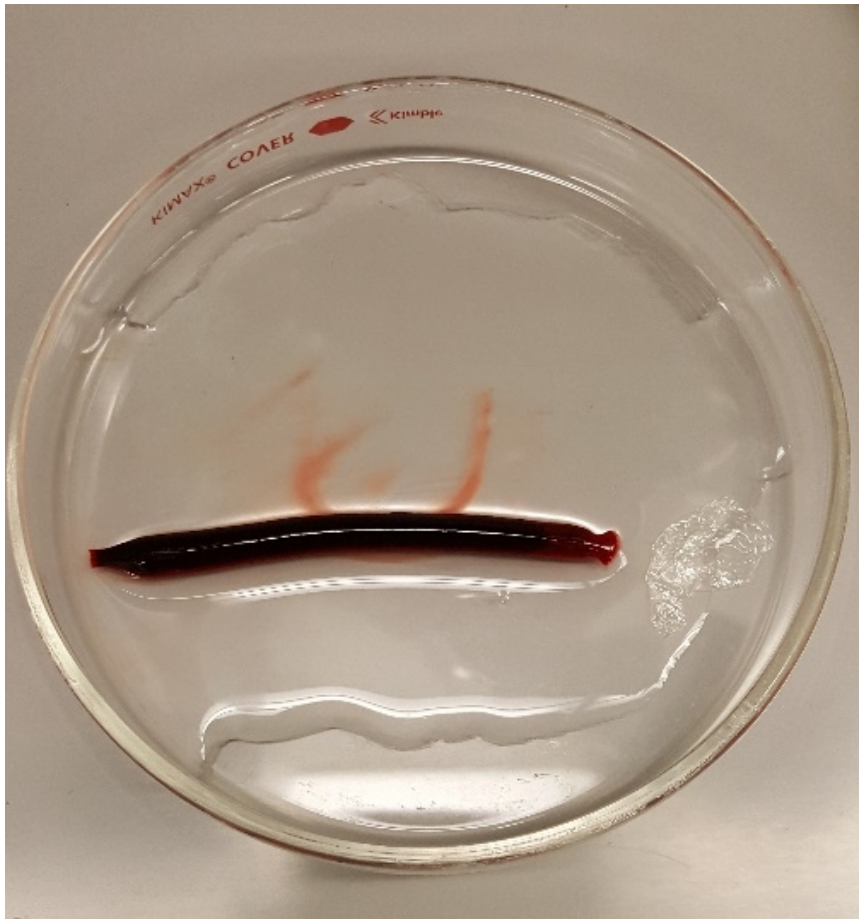
Methods: Whole Blood Clot Model

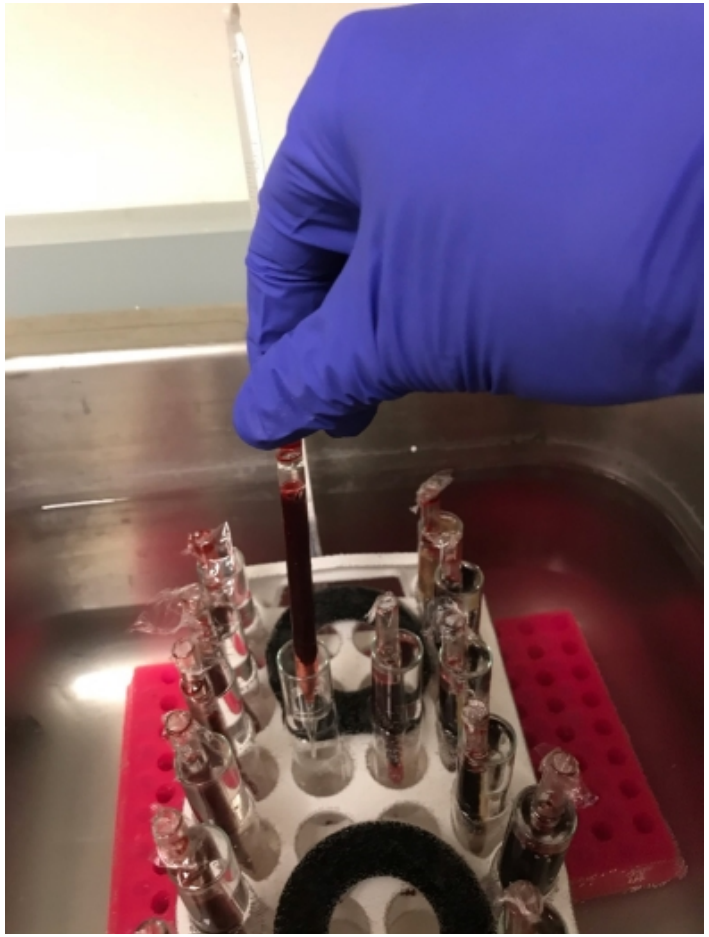
Protocol

- Venous blood drawn from volunteer patients at the catheter lab
- Aliquots of 2 mL were transferred into Pasteur pipettes
- Incubated at 37 °C for 3 hours
- Stored at 4 °C for 3 days to allow for full retraction

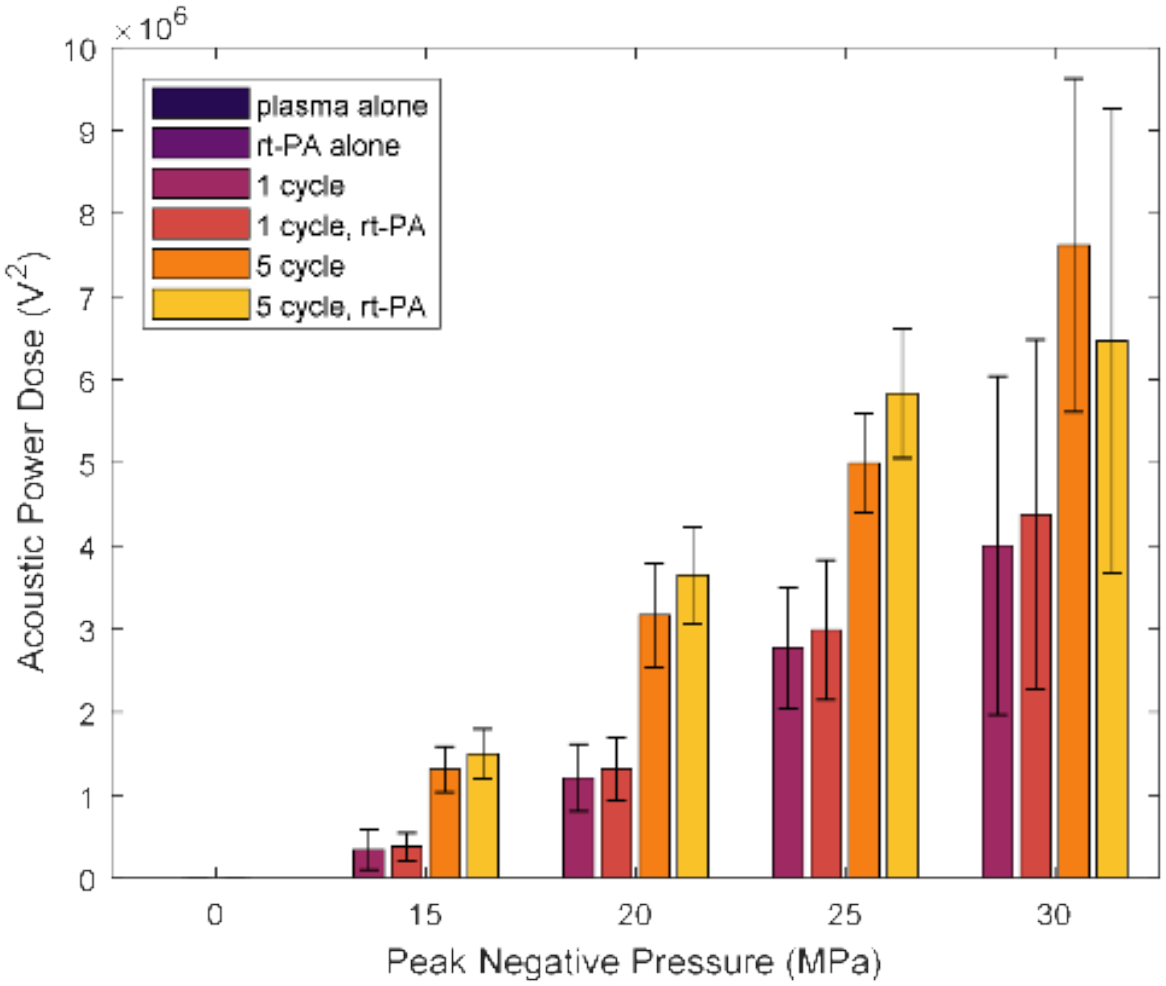
Subject Demographics

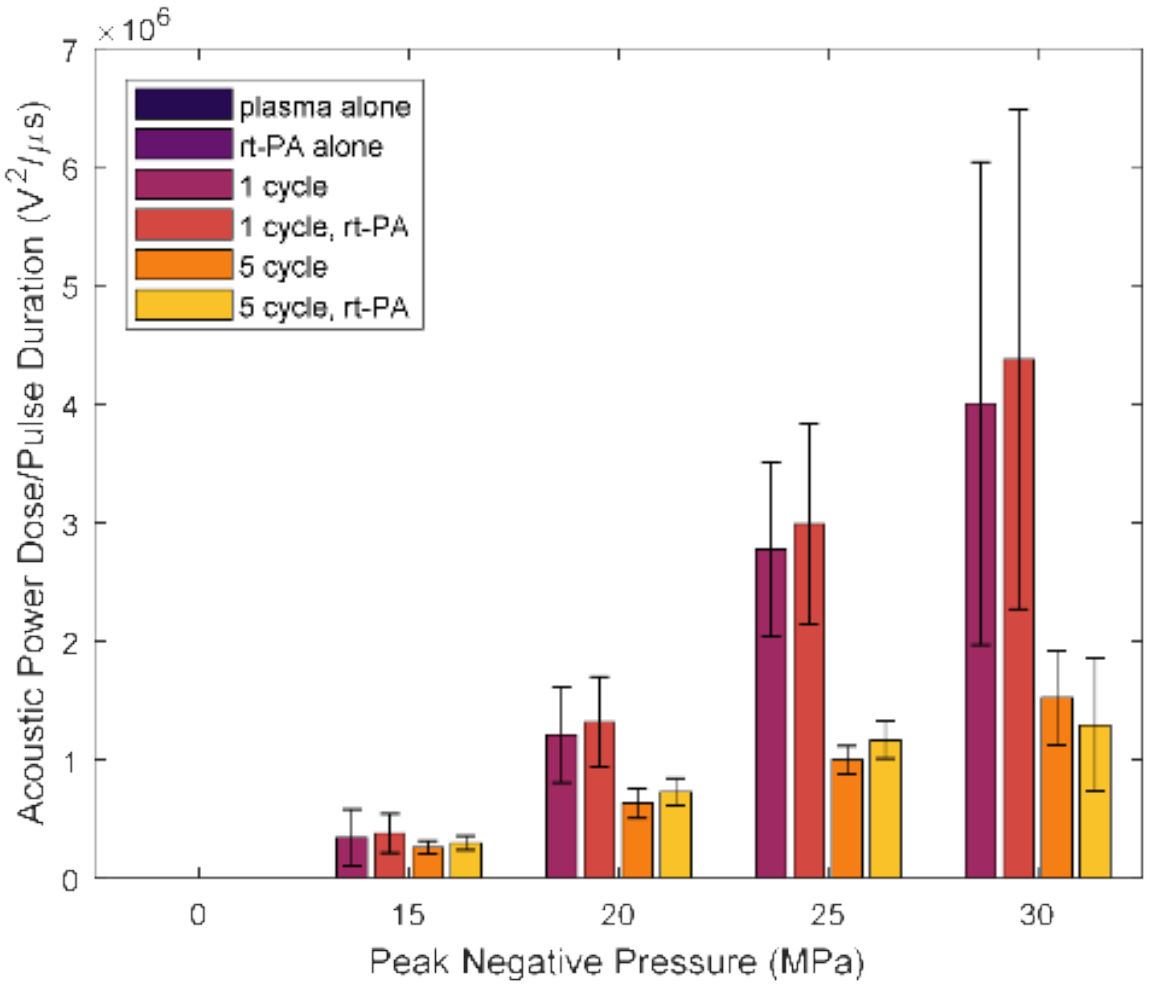
- 15 volunteer patients
- 55 ± 12 years of age
- 8 African American, 7 white
- 9 female, 6 male



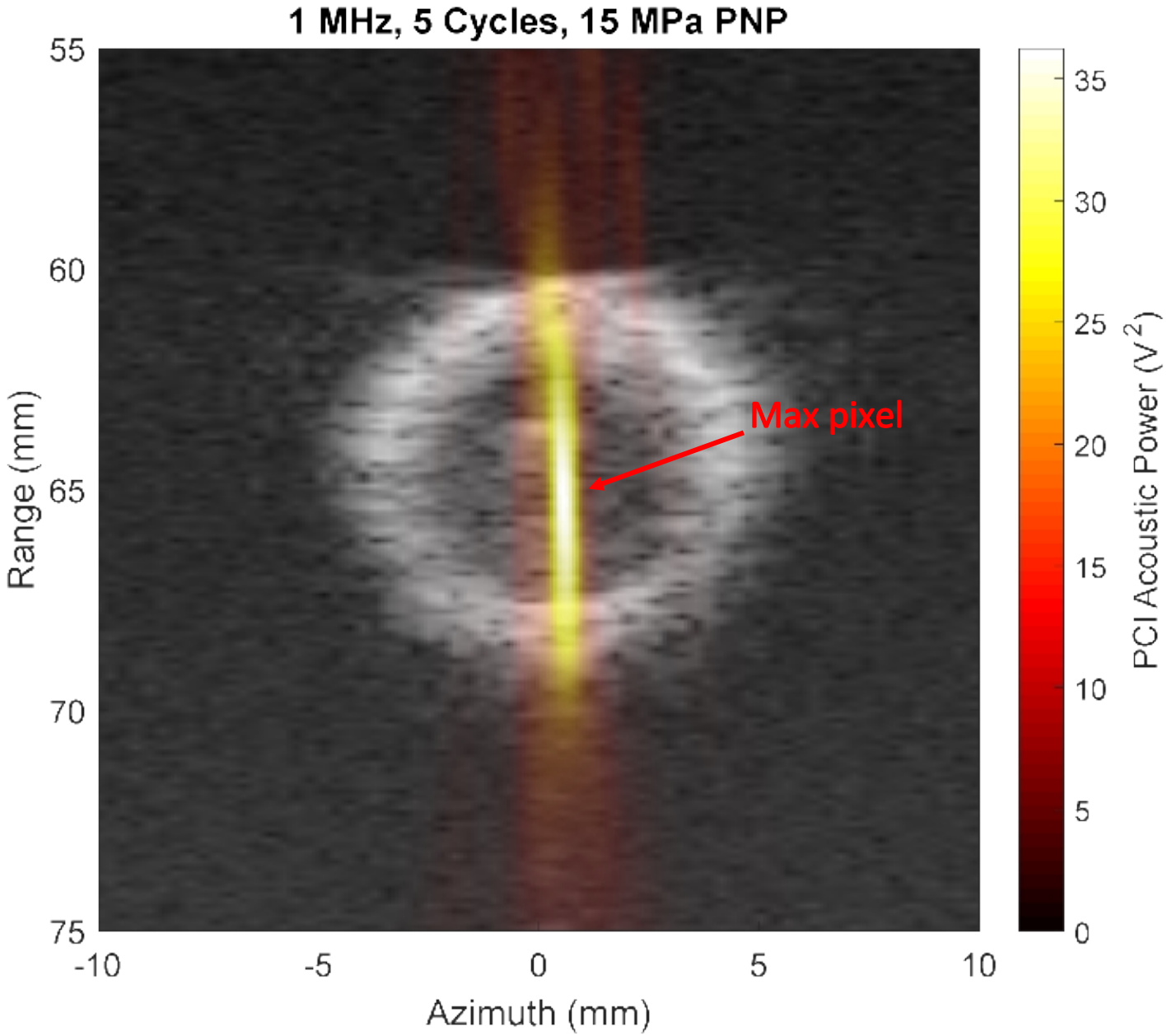


Results: Acoustic Power Dose Inside Clot





Methods: Spectrum from Maximum Pixel Location



Results: Normalized Spectra of Bubble Cloud Emissions