ORIGINAL RESEARCH

High-Frame-Rate Doppler Ultrasound with Contrast Agents Enables Deep Vein Thrombosis Delineation

Jiaming Sun '27, Jacob Elliot Ph.D., Julianna Simon Ph.D.
Washington University in St. Louis

Deep vein thrombosis (DVT) affects approximately 1 to 2 per 1,000 individuals each year and remains a leading cause of pulmonary embolism-related deaths. Conventional ultrasound imaging is widely used for DVT detection but often fails to precisely delineate thrombus boundaries, limiting diagnostic confidence. High-frame-rate (HFR) Doppler ultrasound, built on plane-wave transmissions rather than sequential focused beams, enables ultrafast acquisition and improved sensitivity to subtle and transient blood flow signals, providing sharper definition of clot–lumen interfaces than standard color Doppler.

In this study, a DVT flow phantom was constructed from a silicone vessel embedded in a 2% agar block with an attached 3D-printed clot. A dual-channel peristaltic pump generated continuous physiologic circulation, while sodium dodecyl sulfate-stabilized perfluoropentane (SDS-PFP) nanoemulsions were introduced as ultrasound contrast agents. These droplets vaporize under acoustic excitation to form microbubbles that act as strong backscatterers, enhancing Doppler signal intensity and flow visualization. Imaging was conducted on a Verasonics NXT® research platform using an L7-4 linear probe (center frequency approximately 5 MHz). Plane-wave flash Doppler sequences with in-phase/quadrature (IQ) acquisition were implemented through MATLAB-controlled scripts on the system's PC interface, capturing 1,134 frames over 120 seconds at an effective frame rate of approximately 9.5 fps. The acquired IQ data were reconstructed into Doppler power maps to visualize flow disruption and clot boundaries.

Compared with conventional B-mode and color Doppler imaging, HFR Doppler produced crisper transitions between perfused and occluded regions and revealed localized flow disturbances around the thrombus. This work establishes a proof of concept that plane-wave HFR Doppler ultrasound combined with SDS-PFP contrast agents enhances delineation of thrombus boundaries in a DVT phantom model. Future studies will quantify contrast-to-noise and boundary-sharpness metrics and explore in vivo validation toward clinical translation.

Deep vein thrombosis (DVT) is a vascular disorder in which thrombi form in deep veins, most commonly in the lower extremities. DVT and pulmonary embolism (PE) together constitute venous thromboembolism, with an incidence of about 1 to 2 per 1,000 person-years in Western countries and substantial morbidity and mortality worldwide [1, 2]. PE occurs when a thrombus or thrombus fragment travels to and obstructs branches of the pulmonary artery, which can be rapidly fatal without timely diagnosis and treatment [2].

High-frame-rate (HFR) Doppler based on plane-wave transmissions acquires unfocused insonifications of the whole field of view and reconstructs images from all receive channels. This ultrafast strategy improves temporal sampling and the quality of the slow-time ensemble for Doppler estimation, increasing sensitivity to low or transient velocities near thrombus margins compared with conventional color Doppler [3]. Acoustic backscatter refers to echo energy returned to the transducer by tissues or particles; higher backscatter and a better signal-to-noise ratio improve the detectability of weak blood-flow signals along boundary layers.

Recent super-resolution methods, such as ultrasound localization microscopy (ULM) further demonstrate the value of ultrafast acquisitions by mapping microvasculature beyond the diffraction limit using tracked microbubbles [4, 5]. These advances motivate evaluating HFR Doppler for sharper delineation of the clot–lumen transition in DVT models.

As shown in Figure 1, a conventional color Doppler example depicts macroscopic flow disruption near a thrombus but provides limited definition at the clot boundary. In contrast, Figure 2 illus

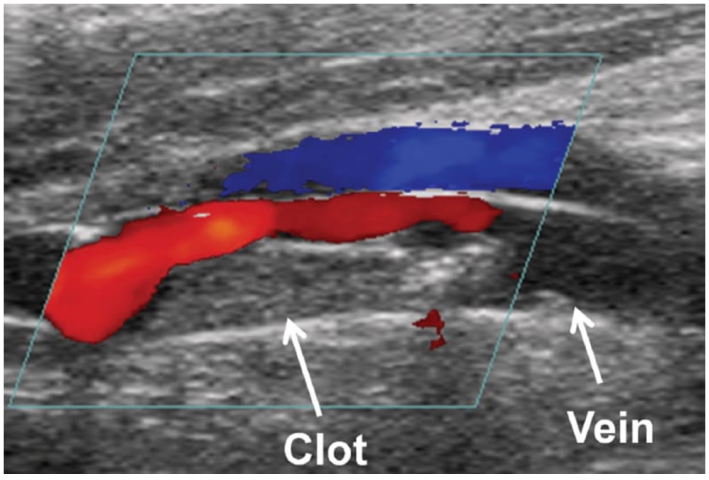

Fig. 1

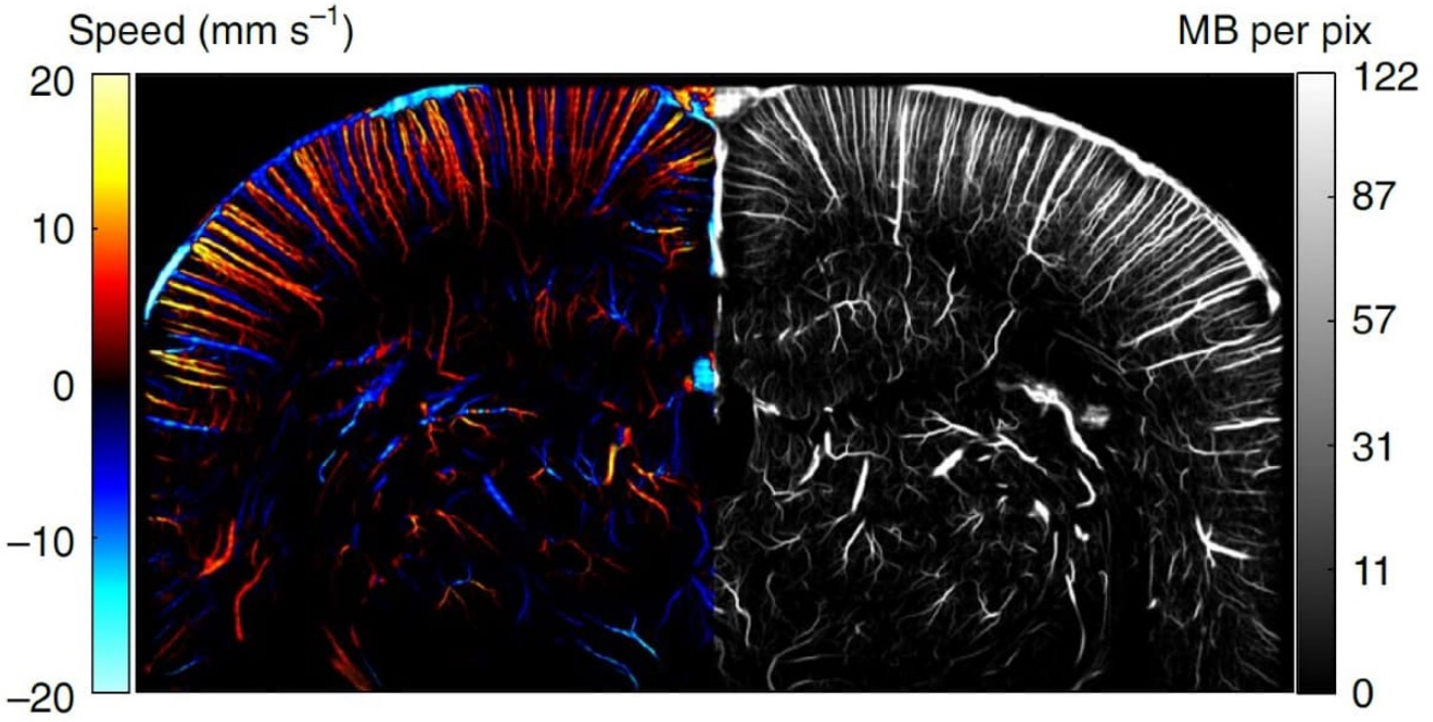

Fig. 2

trates an ultrafast ULM result (6.5 µm resolution in rat brain), highlighting how ultrafast acquisitions enable fine vascular detail. Building on these ideas, we investigated whether HFR Doppler combined with sodium dodecyl sulfate–stabilized perfluoropentane (SDS-PFP) nanoemulsions—nanodroplets that vaporize into highly scattering microbubbles under acoustic excitation—can enhance thrombus boundary delineation in a controlled DVT flow phantom.

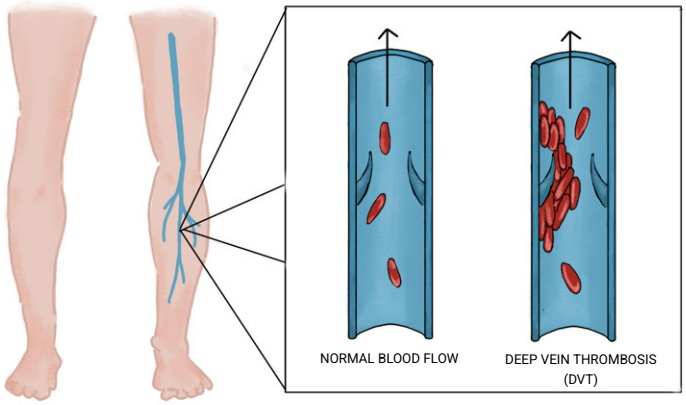

Illustration by | Lucy Wei '29

Materials and Methods

Phantom Fabrication

A deep vein thrombosis (DVT) flow phantom was constructed to emulate a partially occluded vessel. An 8 mm inner-diameter silicone tube was embedded horizontally in a 2% agar hydrogel block. A 4 mm diameter 3D-printed clot, fabricated from the same silicone material compatible with the Formlabs 3B Plus printer, was affixed to the inner wall to mimic a wall-adherent thrombus. Using the same material for both components minimized acoustic impedance mismatch and ensured consistent elastic properties throughout the model. The 4 mm size was selected to represent a moderate obstruction that preserved some flow for Doppler visualization while maintaining stability during repeated scans. A thin neoprene acoustic absorber was placed beneath the phantom to suppress reflections from the container base and prevent imaging artifacts.

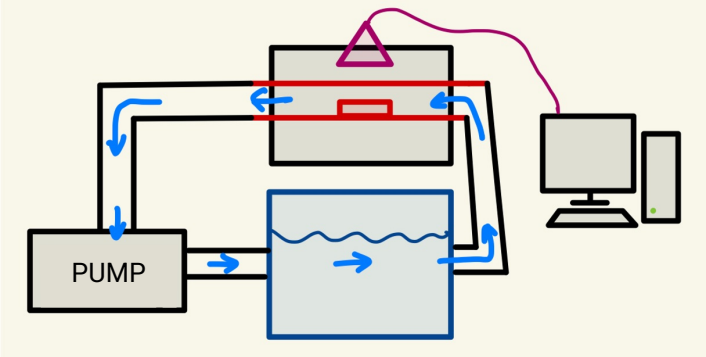

Fig. 3

Flow System

The phantom was connected in series with a dual-channel peristaltic pump and a fluid reservoir to establish a closed-loop circulation (Figure 1). A peristaltic pump transports liquid by sequential compression of flexible tubing, thereby generating smooth, controllable flow without exposing the working fluid to moving mechanical parts. This mechanism replicates low-pulsatility physiologic venous flow while maintaining sterility and consistency across runs. The system operated at the pump's minimum calibrated setting, producing steady laminar circulation through the phantom. The circulating fluid consisted of deionized water containing 2.1% sodium dodecyl sulfate–perfluoropentane (SDS-PFP) nanoemulsions, which served as ultrasound contrast agents. Under acoustic excitation, these droplets underwent acoustic droplet vaporization, forming transient microbubbles that acted as

strong backscatterers and markedly enhanced Doppler signal intensity. Figure 3 illustrates the closed-loop circuit, including the reservoir, pump tubing, and contrast flow path.

Imaging Setup and Acquisition

Ultrasound imaging was performed using a Verasonics® Vantage NXT research platform controlled via MATLAB R2022b and equipped with an L7-4 linear array probe (center frequency ≈ 5 MHz). The probe was positioned perpendicular to the phantom surface, with the imaging plane orthogonal to the vessel axis. Flash plane-wave Doppler sequences with in-phase/quadrature (I/Q) acquisition were executed through MATLAB scripts on the system's PC interface. The acquisition captured 1,134 frames over 120 seconds, which were later beamformed and reconstructed into Doppler power maps for quantitative flow analysis. The B-mode image was grayscale inverted and resized to align with the Doppler -power map, producing a composite overlay that emphasized vessel boundaries and thrombus margins. All post-processing, including quadratic filtering, ensemble summation, thresholding, and morphological smoothing, was conducted in MATLAB to derive the final clot mask. Figure 4 shows the complete experimental setup, including the probe, vessel phantom, contrast reservoir, and peristaltic pump.

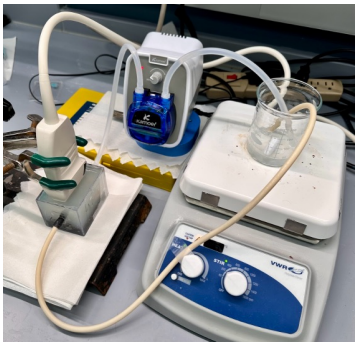

Fig. 4

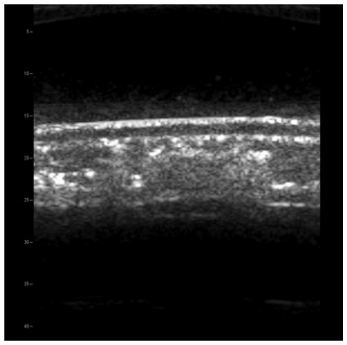

Fig. 5

Results

Conventional B-mode (brightness mode) imaging, which displays echo amplitude from stationary tissue, provided limited structural detail in this phantom. Only faint reflections were visible near the clot, and the thrombus–lumen interface was indistinct. Figure 5 shows the B-mode appearance of the vessel phantom.

Applying standard color Doppler revealed macroscopic flow disruption at the thrombus site. Regions occupied by the 3D-printed clot exhibited reduced or absent Doppler signal, while surrounding lumen showed persistent flow. The introduction of SDS-PFP nanoemulsions increased acoustic backscatter by vaporizing into microbubbles under ultrasound excitation, which acted as strong moving scatterers and thereby improve flow detectability. With contrast present, Doppler imaging captured motion more sensitively, delineating flow over and around the clot, while the clot itself remained a signal void. Figure 6 shows the same imaging plane with standard color Doppler rendering that outlines the intraluminal clot.

To more robustly separate moving from stationary regions, we reconstructed Doppler power maps from the acquired I/Q ensembles. Doppler power integrates the magnitude of slow-time fluctuations independent of flow direction, which is advantageous in this geometry where recirculation and complex angles can cause direc

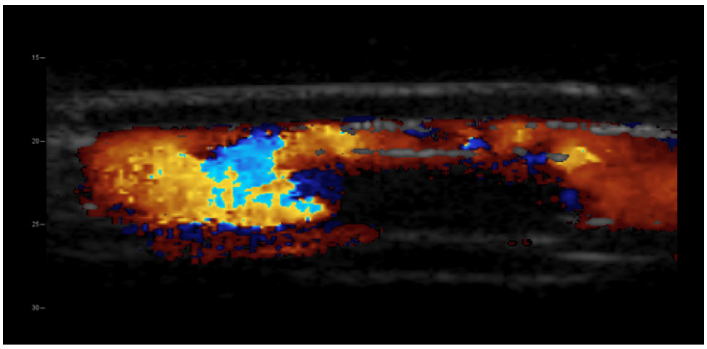

Fig. 6

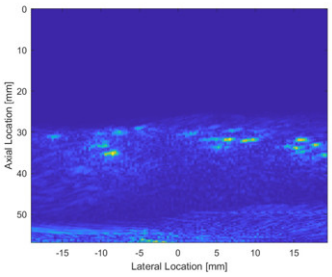

Fig. 7

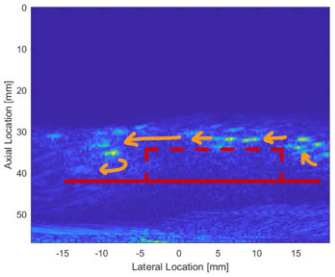

Fig. 8

tional velocity estimates to cancel or alias. Figure 7 presents the HFR Doppler-power reconstruction, in which brighter clusters correspond to stronger motion of contrast agents and lumenal blood.

Compared with the corresponding conventional Doppler frames, the high frame rate (HFR) Doppler reconstructions provided crisper transitions between perfused and occluded regions. Stationary and moving areas were separated more cleanly, allowing clearer identification of the clot boundary within the phantom. Figure 8 annotates the HFR Doppler pattern that completes an outline of the thrombus. Overlaying the Doppler-power maps on grayscale inverted B-mode images further confirmed that flow signals terminated at the clot interface, producing a composite that localized the thrombus and emphasized its margins. Figure 9 shows the I/Q-based B-mode and HFR Doppler overlay.

Discussion

These experiments demonstrate that high frame rate (HFR) Doppler ultrasound with vaporized SDS-PFP nanoemulsions enhances thrombus boundary delineation in a DVT phantom. Conventional bright mode imaging failed to resolve clot margins, and standard Doppler showed only coarse flow disruption. In contrast, HFR Doppler produced clearer spatial separation between occluded and perfused regions. The IQ-based overlays measured clot lengths of 13.6–14.2 mm versus 11.6 mm from standard Doppler, representing an approximately 17–20% improvement in boundary accuracy.

HFR Doppler outperformed conventional imaging because its rapid plane wave acquisitions increased temporal sampling and ensemble size, improving sensitivity to low-velocity flows and reducing aliasing.

When combined with the strong acoustic backscatter of vaporized SDS-PFP droplets, this produced superior contrast-to-noise ratios and sharper clot outlines.

Limitations include the idealized phantom environment, absence of tissue heterogeneity or motion, and the instability of SDS-

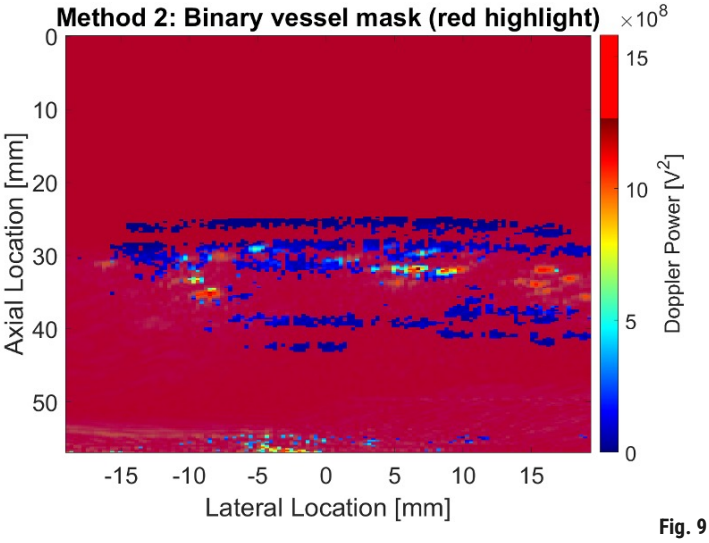

Fig. 9

PFP nanoemulsions, which may coalesce or recondense over time. Translating this technique in vivo will require optimizing droplet formulation, dosing, and acoustic parameters to balance stability and activation efficiency.

Overall, this study provides a proof of concept that contrast enhanced HFR Doppler imaging improves thrombus visualization beyond conventional Doppler. Future work should quantify edge sharpness and contrast-to-noise ratios under pulsatile and in vivo conditions to refine its diagnostic potential.

Conclusion

This study demonstrates that high-frame-rate Doppler ultrasound, augmented with SDS-PFP nanoemulsions, improves delineation of thrombus boundaries in a DVT phantom relative to conventional Doppler. The approach yielded sharper separation of perfused and occluded regions and more accurate boundary measurements under controlled conditions. These findings suggest potential clinical value for refining thrombus assessment, risk stratification, and treatment planning, contingent on validation in pulsatile and in vivo settings. Looking ahead, integrating this acquisition and processing pipeline with ultrasound localization microscopy (ULM) could enable super-resolution mapping of clot morphology by localizing and tracking contrast microbubbles beyond the diffraction limit, thereby providing quantitative metrics such as edge sharpness, contrast-to-noise ratio, and microvascular flow patterns that are not accessible with standard methods. Future work will evaluate these metrics in more physiologic models and establish parameter choices that balance contrast stability, activation efficiency, and acquisition time for practical clinical use.

References

[1] Lutsey, P. L., & Zakai, N. A. (2022). Epidemiology and prevention of venous thromboembolism. *Nature Reviews Cardiology*, 20(4), 248–262. https://doi.org/10.1038/s41569-022-00787-6

[2] Farmakis, I. T., Valerio, L., Bikdeli, B., Connors, J. M., Giannakoulas, G., Goldhaber, S. Z., Hobbom, L., Hunt, B. J., Keller, K., Spyropoulos, A. C., & Barco, S. (2022). Annual mortality related to pulmonary embolism in the U.S. before and during the COVID-19 pandemic. *Journal of the American College of Cardiology*, 80(16), 1579–1581. https://doi.org/10.1016/j.jacc.2022.08.721

[3] Dong, Z., Li, S., Duan, X., Lowerison, M. R., Huang, C., You, Q., Chen, S., Zou, J., & Song, P. (2023). High volume rate 3-D ultrasound imaging using fast-tilting and redirecting reflectors. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, Advance online publication. https://doi.org/10.1109/TUFFC.2023.3282949

[4] Renaudin, N., Demené, C., Dizeux, A., Ialy-Radio, N., Pezet, S., & Tanter, M. (2022). Functional ultrasound localization microscopy reveals brain-wide neurovascular activity on a microscopic scale. *Nature Methods*, 19, 1004–1012. https://doi.org/10.1038/s41592-022-01549-5

[5] Opacic, T., Dencks, S., Theek, B., Piepenbrock, M., Ackermann, D., Rix, A., Lammers, T., Stickeler, E., Delorme, S., Schmitz, G., & Kiessling, F. (2018). Motion model ultrasound localization microscopy for preclinical and clinical multiparametric tumor characterization. *Nature Communications*, 9, 1527. https://doi.org/10.1038/s41467-018-03973-8