In-Silico Simulations of Ultrasound Imaging in the Far-Field For Histotripsy Therapy Monitoring

Avery Antes[1] | Erik Saucedo[1] | Eric Galindo[1] | Kenneth Bader, PhD[1]

[1]Department of Radiology, University of Chicago, Chicago, IL

2026 JULY 19–22 VANCOUVER, BC JOINT AAPM | COMP MEETING

THE UNIVERSITY OF CHICAGO Committee on Medical Physics

ABSTRACT

Purpose: Ultrasound imaging is used for therapy guidance in focused ultrasound procedures. A discrepancy between focused ultrasound source design and diagnostic imaging probes means targets can lie in the far field of the imaging system, reducing image quality and complicating real-time monitoring. This study developed and validated in-silico methods for three-dimensional ultrasound imaging to support real-time monitoring of cavitation clouds during histotripsy therapy [1,2].

Methods: A fully populated 32 × 32 matrix array was modeled to characterize three-dimensional point spread functions (PSFs) [8] over focal depths from 1.0 to 10.0 cm. Axial and lateral PSF profiles were evaluated, and spatial resolution was quantified using the −6 dB full-width at half maximum (FWHM). Linear regression assessed depth dependence and lateral symmetry.

Results: Axial PSF exhibited a narrow main lobe with sidelobes decaying below −50 dB within millimeters of the focus, remaining approximately constant across all depths. Lateral PSF widths increased linearly with depth, showing strong x–y symmetry with identical regression fits (R^2=0.9996). These results reveal depth-invariant axial resolution governed by pulse bandwidth and aperture-limited lateral resolution dominated by diffraction.

Conclusions: The proposed in-silico framework demonstrates predictable, stable 3D imaging performance across clinically relevant depths, supporting reliable real-time volumetric guidance of histotripsy therapy.

Key Words: Histotripsy · Cavitation · Point Spread Function · Volumetric Imaging · Ultrafast Ultrasound

INTRODUCTION

Histotripsy is a focused ultrasound therapy that uses controlled cavitation to mechanically destroy pathological tissue (e.g., tumors, clots) without incisions or ionizing radiation [1]. The non-invasive nature of histotripsy makes real-time image guidance critical for safe and effective treatment.

Current Limitation: Existing histotripsy systems rely on two-dimensional ultrasound imaging for treatment monitoring. However, histotripsy generates a volumetric *"cavitation cloud"* [2] demanding three-dimensional, real-time monitoring that 2D imaging cannot provide.

Challenge: Structural differences between focused ultrasound therapy transducers and diagnostic imaging probes place treatment targets in the far field of the imaging system, degrading image quality and complicating cavitation cloud visualization [3].

Objective: Develop and validate in-silico computational methods that model how ultrasound waves interact with cavitation clouds in three dimensions, enabling ultrafast volumetric monitoring of histotripsy therapy.

METHODS & MATERIALS

Parameter	Value
Array configuration	32 × 32 (1,024 elements)
Center frequency	3 MHz
Fractional bandwidth	70%
Element size	250 µm × 250 µm
Inter-element pitch	300 µm
Sound speed	1,540 m/s
Focal depth range	1.0 – 10.0 cm (0.5 cm steps)
Beamforming	Delay-and-Sum (DAS)
Simulation toolbox	MUST (MATLAB) [4,5]

Simulation Workflow:

- Transmit delays computed for focal depths 1.0 – 10.0 cm at (0, 0, z)
- Pressure-field simulation for transmit-field consistency [8]
- RF channel simulation using a unit-amplitude point scatterer at focus [6]
- RF data demodulated to complex baseband I/Q signals [4]
- DAS beamforming on a 3D grid: ±5 mm axial, ±5 mm lateral [5]
- Lateral sampling: 1λ | Axial sampling: λ/10
- 1D point spread function (PSF) profiles extracted along x-, y-, z-axes through peak voxel [7]
- FWHM at −6 dB computed for each depth and axis
- Linear least-squares regression with R^2 and RMSE goodness-of-fit

Figure 1. 3.5 MHz fully populated matrix array ultrasound probe for research and preclinical imaging. Its high-density piezocomposite matrix array enables real-time 3D imaging with ultrafast frame rates, high contrast, and volumetric super-resolution across near and far imaging depths.

RESULTS

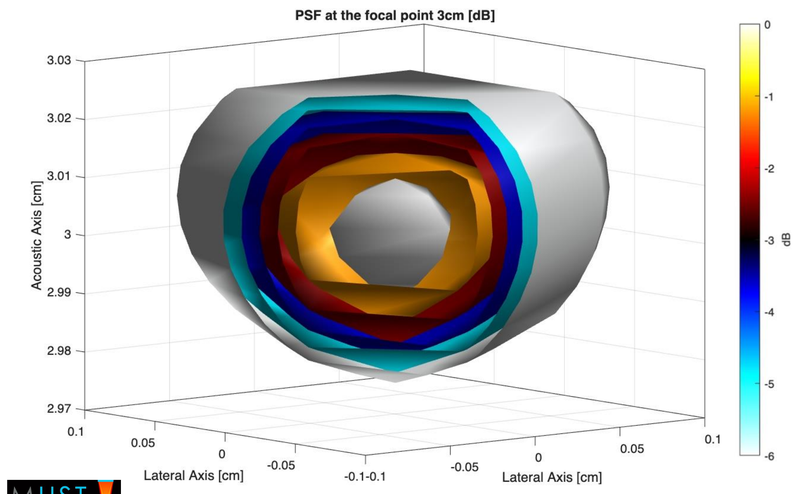
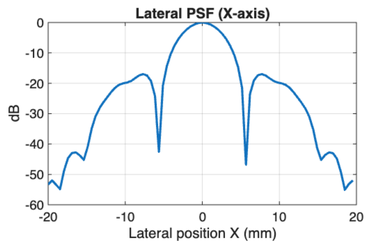
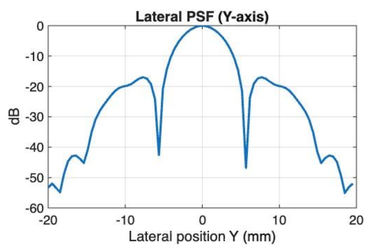


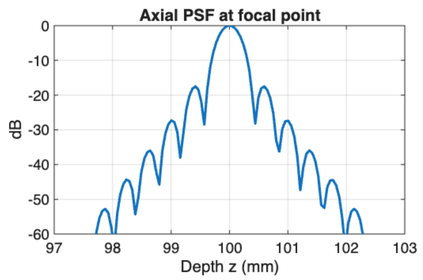
Figure 2. Three-dimensional PSF iso-surface rendering at focal depth 3 cm (dB scale). Nested shells represent −1 to −6 dB contours. The near-spherical inner core demonstrates excellent 3D beam symmetry. Color Bar is in units of dB relative to the pressure maximum.

Lateral FWHM fit (x and y identical) **R^2 = 0.9996**

Axial sidelobe level within ±5 mm of focus **< −50 dB**







Figures 3–5. PSF profiles at 10 cm focal depth. Top Left: Lateral X-axis: broader lobe, aperture-diffraction limited. Bottom Left: Lateral Y-axis: identical to X, confirming azimuthal symmetry. Right: Axial (z-axis): narrow main lobe, sidelobes below −50 dB, depth-invariant.

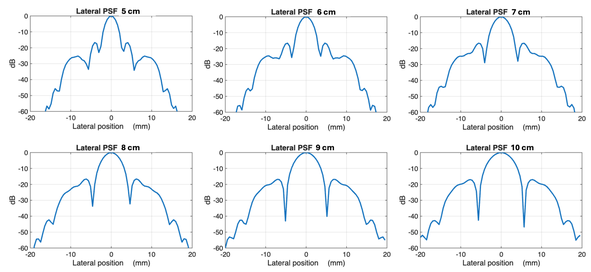


Figure 6. Lateral PSF profiles at source-to-detector distances of 5–10 cm, showing broadening and increasing side-lobe prominence with distance.

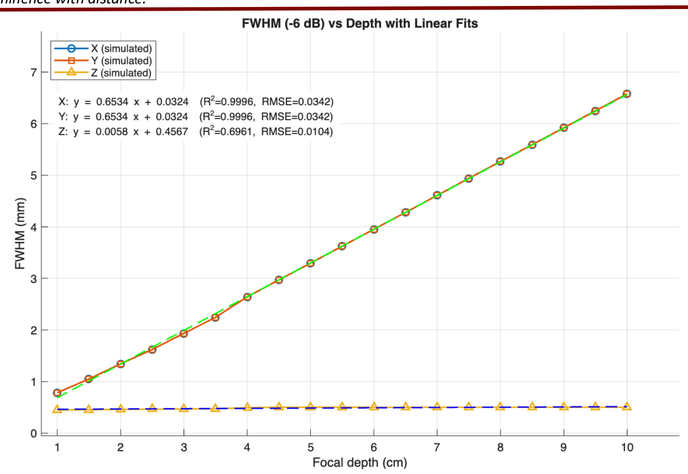


Figure 7. FWHM (−6 dB) vs. focal depth for X, Y (lateral) and Z (axial) axes with linear fits. Lateral: y = 0.6534x + 0.0324, R^2=0.9996. Axial: y = 0.0058x + 0.4567, R^2=0.696.

Acknowledgments: The authors thank the Committee on Medical Physics for resources and support. This work is funded in part by the National Institutes of Health (grant # R01 HL133334). Travel was funded by the University of Chicago Medicine Comprehensive Cancer Center Trainee Associate Member Travel Award

DISCUSSION

Axial Resolution (Depth-Invariant):

The axial PSF width remained approximately constant across all focal depths (1.0–10.0 cm), with a near-zero regression slope (y = 0.0058x + 0.4567) and low RMSE. This confirms that axial resolution was governed primarily by the center frequency of the transmitted pulse, not by focusing geometry. This observation is consistent with prior theoretical and experimental ultrasound studies.

Lateral Resolution (Aperture-Limited):

Lateral PSF widths increased linearly and symmetrically with depth (R^2=0.9996 for both x and y axes, RMSE=0.034 mm). Identical regression fits for X and Y confirm the azimuthal symmetry expected from a square matrix array. Over the clinically relevant depth range for focused ultrasound sources (4–6 cm), the lateral FWHM increased by approximately 1.86–2.65 mm relative to the shallow baseline at ~1 cm, an important consideration for target localization in therapy guidance.

Clinical Relevance:

The predictable, depth-dependent behavior of lateral resolution enables quantitative correction strategies. The stable axial resolution ensures reliable time-of-flight ranging regardless of target depth. Together, these characteristics support accurate 3D localization of histotripsy cavitation clouds throughout the therapeutic range.

Limitations:

- PSF simulated in homogeneous, lossless medium. Tissue-induced aberration and attenuation were not modeled.
- Resolution was characterized by −6 dB FWHM only. The sidelobe structure and contrast performance were not fully captured.
- Lower axial R^2 (0.696) despite near-zero slope may reflect measurement noise in the flat regime.

Future Directions:

- Tissue-mimicking and in vivo environment evaluation
- Aberration-corrected beamforming strategies
- Contrast-based imaging metrics for cavitation characterization
- Analysis of ultrafast image sequences to quantify bubble cloud dissolution rate, a promising metric correlated with histotripsy treatment outcomes

CONCLUSIONS

1. Developed and validated an in-silico 3D ultrasound simulation framework for real-time histotripsy monitoring using a 32 × 32 matrix array transducer.
2. Axial resolution was depth-invariant (governed by pulse bandwidth), remaining stable across 1–10 cm, essential for reliable acoustic time-of-flight imaging.
3. Lateral resolution increased linearly and symmetrically with depth (R^2=0.9996) due to aperture diffraction, predictable and correctable in future work.
4. Lateral FWHM increase of 1.86–2.65 mm over the 4–6 cm therapeutic range quantifies the resolution cost of far-field imaging relevant to focused ultrasound guidance.
5. The framework provides a foundation for 3D volumetric passive and ultrafast cavitation imaging during histotripsy, addressing a core limitation of current 2D monitoring.

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CONTACT

Avery Antes
Medical Physics Graduate Program
University of Chicago, Department of Radiology
aantes@uchicago.edu

Kenneth Bader, PhD (PI)
Biomedical Acoustics Development and Engineering Research (BADER) Lab
University of Chicago, Department of Radiology
baderk@uchicago.edu