# NEXT-GENERATION ULTRASOUND IMAGING FOR ASSESSING THE MICROVASCULAR FINGERPRINT OF CANCER

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## 1. INTRODUCTION

Angiogenesis, the physiologic development of new blood vessels, has been understood as one of the hallmarks of cancer for more than four decades. Microvascular evolution associated with malignancy has been observed with microscopy, histology, and other imaging tools at multiple scales, and thus presents as an encouraging biomarker for both cancer diagnostics and assessment of response to therapy. The ability to differentiate lesions based on microvascular fingerprint, rather than tumor anatomy, would be a paradigm shift in ultrasound diagnostics. We hypothesize that microvascular imaging techniques could improve the specificity of ultrasound to malignancy, an advance clinically needed in breast, prostate, thyroid, and other oncological applications

## 2. METHODS

Acoustic angiography is an approach to high-resolution contrast enhanced ultrasound imaging enabled by ultra-broadband transducer designs. The high frequency imaging technique is based on superharmonic imaging, and provides signal separation from tissue which does not produce significant harmonics in the same frequency range, as well as high resolution. This approach enables imaging of microvasculature in-vivo with high resolution and signal to noise, producing images that resemble x-ray angiography. Data shows that acoustic angiography can provide important information about the presence of disease based on vascular patterns, and may enable a new paradigm in medical imaging.[1,2]

Super-resolution imaging, also called ultrasound localization microscopy, is a technology originally developed in the optical field. The acoustic version of approach involves detection of thousands signals from individual micron-sized microbubble scatterers, and reconstructing images based on localizing their position. The result is images of blood flow, and thus the microvasculature, based on motion paths of micron-scatterers, thereby enabling resolution of blood vessels as small as 10 microns, well below the diffraction limit of ultrasound at clinical frequencies.[3]

## 3. RESULTS, DISCUSSION, & CONCLUSION

We have utilized both acoustic angiography and super-resolution ultrasound to visualize microvascular angiogenesis associated with tumor growth. Both techniques illustrate significant changes in microvascular density and tortuosity involved with growing tumors, as opposed to healthy tissue, and present a non-traditional way of identifying malignancy based on microvascular features as opposed to tumor size, shape, density, or elasticity. Analysis indicates that readers can identify the presence of spontaneous tumors arising in rodents with a diameter of 5 mm with a sensitivity and specificity of approximately 90% based on microvascular images. Although both super resolution and superharmonic imaging techniques such as acoustic angiography have challenges which need to be overcome prior to clinical translation, data suggests that microvascular imaging provides an alternative approach to lesion diagnosis which can provide high sensitivity and specificity. With the development of new hardware and software which will make these imaging techniques commercially available, we hypothesize that microvascular imaging will undoubtedly play an increasing role in both pre-clinical and clinical ultrasound diagnostics.

## 11. REFERENCES

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