

## Super Resolution Vascular Ultrasound Imaging for Clinical Diagnostics

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## Overview

Alterations in the microvasculature characterize various pathologies, including cancers and inflammatory diseases (i.e., Crohn's disease). Therefore, precise in vivo microvascular imaging at the capillary level could be a valuable tool for early diagnosis and clinical management. Ultrasound (US) is a highly useful imaging tool since it does not involve exposure to ionizing radiation, and it is accessible and cost-effective. However, conventional US cannot be applied for microvasculature imaging due to insufficient resolution. Super-resolution Ultrasound localization microscopy (ULM) is a promising method; however, it is not routinely used in clinical practice due to several technical challenges in the analysis, which is time-consuming and requires prior knowledge. Prof. Eldar and her team developed an advanced deep learning method for US analysis that effectively addresses these technical challenges and quickly resolves the microvasculature structure. Their method was successfully applied on breast cancer US scans, suggesting that this method could potentially assist clinicians in breast cancer early diagnosis.

## The Need

Numerous pathologies involve alterations in the microvasculature, including malignant tumors, inflammatory diseases (i.e., Crohn's disease), myocardial and brain pathologies. Therefore, precise and fast in-vivo microvascular imaging at the capillary level may be of great importance for early detection and clinical management. Among the currently available methods for vasculature imaging, CT involves high exposure to ionizing radiation, and MRI is expensive and highly inaccessible, making Ultrasound (US) an attractive alternative. Although the conventional Doppler US only applies for larger vessels, the recently developed super-resolution Ultrasound (US) localization microscopy (ULM) enables imaging of the microvasculature at the capillary level. It is based on administrating encapsulated gas microbubbles, with a size similar to red blood cells, as a US contrast agent. After scanning with a US scanner, the images are analyzed for the localization of each microbubble, the accumulation of frame-by-frame localizations is calculated, resulting in a super-resolved map of the microvasculature. Various works based on the above idea were illustrated in vitro and in vivo on animal models. However, this technique is not routinely used in clinical practice due to technical challenges, such as long reconstruction time, dependency on prior knowledge of the system Point Spread Function (PSF), and separability of the Ultrasound Contrast Agents (UCAs).

## The Solution

Prof. Yonina Eldar and her team developed advanced deep learning methods for US analysis that effectively and quickly resolved microvasculature structure without prior knowledge of the PSF or the UCA.

## Technology Essence

Prof. Eldar and her team developed an analysis method for ULM that effectively recovers the microvasculature

structure. The network architecture is devised by unrolling the Iterative Soft Threshold Algorithm (ISTA) into a deep neural network where the algorithm's parameters are replaced with learnable convolutional parameters filters. Since each layer of the network assimilates an action from the algorithm, the unrolled network naturally inherits prior structures and domain knowledge rather than learn them from intensive training data, prompting its generalization ability. Importantly, the team has employed this method in a clinical study on breast cancer, which was conducted in collaboration with radiologists from Beilinson hospital. In the study, 21 female subjects with benign or malignant breast lesions were scanned after a UCA administration. The super-resolved recoveries, presenting a  $31.25 \text{ \AA}\mu\text{m}$  spatial resolution, exhibit different vascular patterns of the lesions that correspond with their known histological structure, assisting differentiation between the different types of lesions (Figure 1).

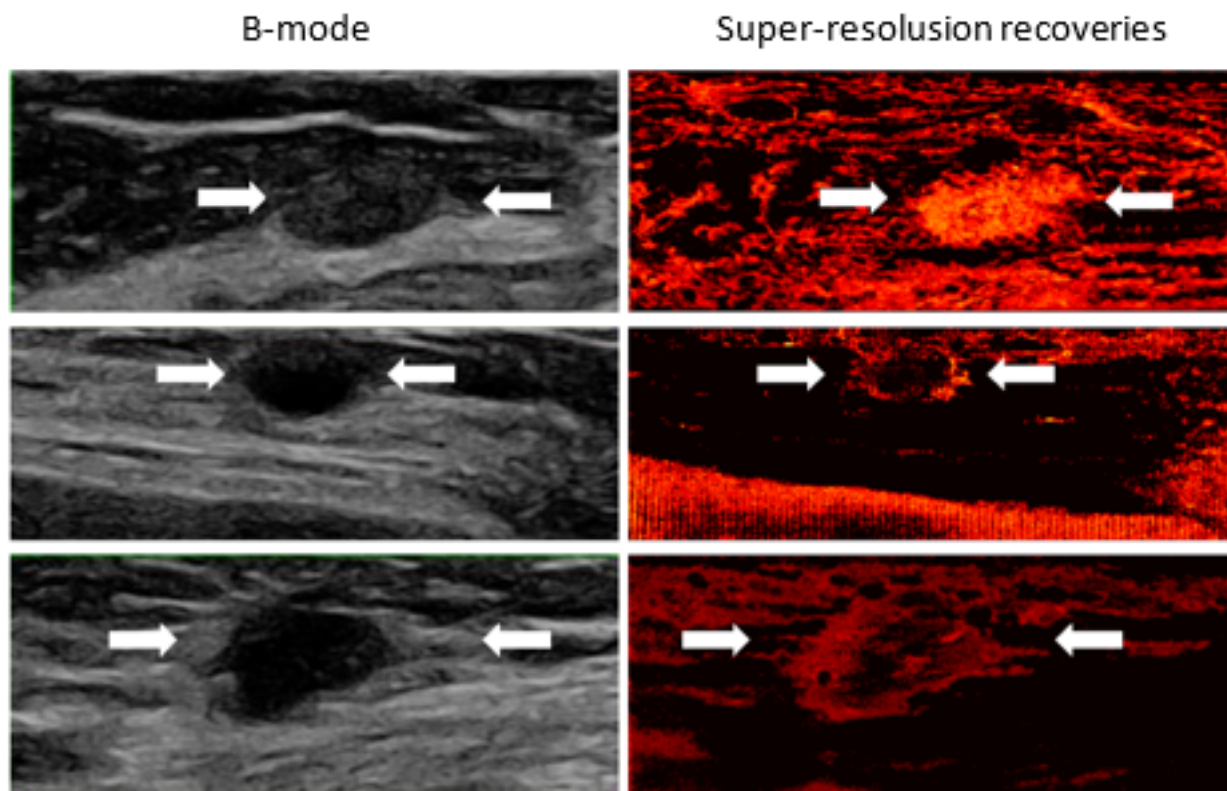


Figure 1- Super-resolution recoveries of three human US breast scans. The white arrows point at the lesions; Top: fibroadenoma (benign). The super-resolution recovery shows an oval, well-circumscribed mass with homogeneous high vascularization. Middle: cyst (benign). The super-resolution recovery shows a round structure with a high concentration of blood vessels at the periphery of the lesion. Bottom: invasive ductal carcinoma (malignant). The super-resolution recovery shows an irregular mass with ill-defined margins, a high concentration of blood vessels at the periphery of the mass, and a low concentration of blood vessels at the center of the mass.

## Applications and Advantages

### Applications

- Microvascular imaging using super-resolution US for clinical use
- Supporting tool in distinction between different types of breast tumors.
- Supporting tool in the diagnosis and monitoring of various diseases characterized by microvasculature alterations

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### Advantages

- Quick, radiation-free, cost-effective, and accessible
- Fast analysis
- Does not require prior knowledge of the PSF or the UCA

## Development Status

The team developed the analysis method described above and tested it in a clinical study on breast cancer patients. Additional clinical applications, such as other malignancies and inflammatory diseases, will be validated in future clinical studies.

## References

Bar-Shira O. et al. (2021) Learned Super Resolution Ultrasound for Improved Breast Lesion Characterization. In: de Bruijne M. et al. (eds) Medical Image Computing and Computer Assisted Intervention – MICCAI 2021. MICCAI 2021. Lecture Notes in Computer Science, vol 12907. Springer, Cham.  
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## Patent Status

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