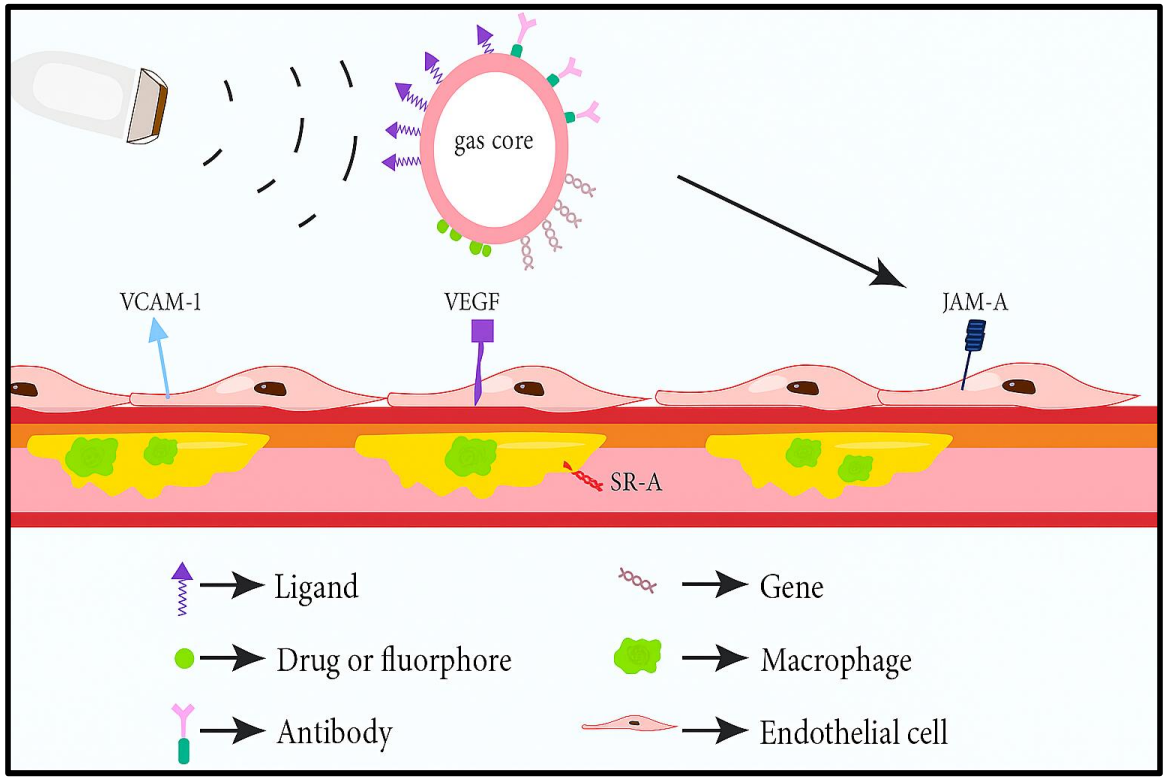
Real-time Convolutional Neural Network for Nondestructive Detection of Targeted Microbubbles in Ultrasound Molecular Imaging

Stanford SCIT Program
Presenter: Hoda Hashemi, PhD
Mentors: Dr. Jeremy Dahl, Dr. Ramasamy Paulmurugan, Dr. Steven Poplack

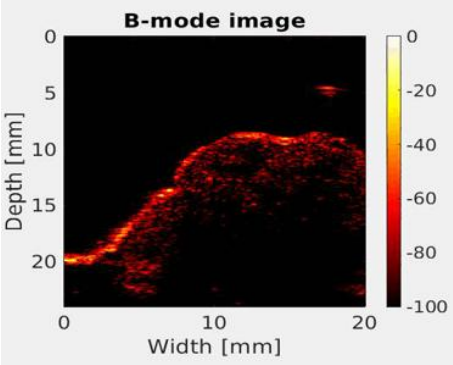
Department of Radiology, Stanford University
February 2026

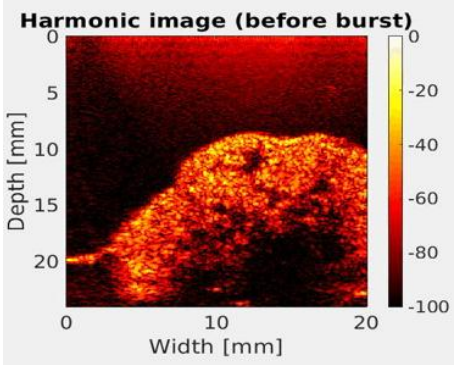
Motivation: Ultrasound Molecular Imaging for Early Cancer Detection



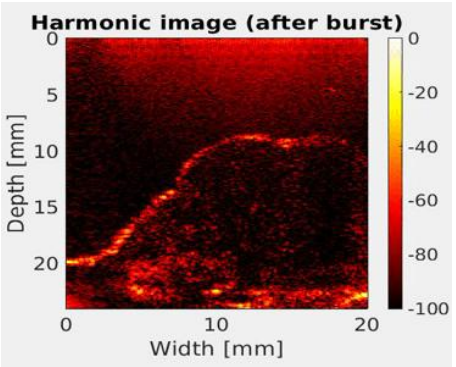
Yao, et al., Frontiers in Cardiovascular Medicine, 2023.

Conventional Method for Capturing the Molecular Signal



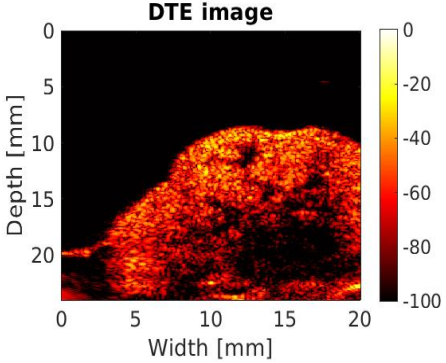


Busting the microbubbles



- Differential targeted enhancement (DTE) method
- Preclinical approach for detecting bound microbubbles

Before – after burst



Disadvantage:

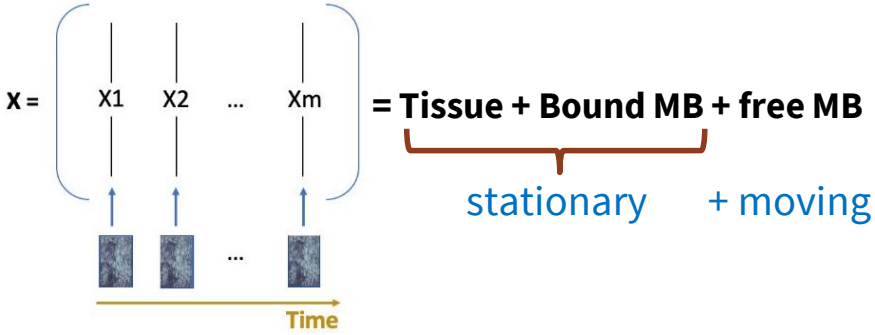
- Destroys the contrast agents;
- Cannot be performed in real-time;
- Needs precise tumor localization;
- Does not exclude free microbubbles.

RPCA-Based Filtering: Separating Bound and Free MBs

- **Non-destructive** optimization approach
- Based on Robust Principal Component Analysis (RPCA)
- Filtering out the free floating MBs

- The motion of tissue & bound MBs:
  - High spatiotemporal coherence
  - Low-rank matrix L
- The flow of free MBs:
  - low coherence
  - Sparse matrix S

- $\|L\|_*$: nuclear norm (sum of singular values)
- $\|S\|_1$: L1 norm
- Can be solved by the ADMM method.



= Tissue + Bound MB + free MB

stationary + moving

X = L + S → stationary + moving

$$\text{minimize } \|L\|_* + \lambda\|S\|_1$$
$$\text{subject to } L + S = X$$

[1] Hashemi, et al., IEEE Trans. on Ultrasonics, 2025.

[2] Hashemi, et al., IEEE IUS, 2024.

Real-Time MB Separation With Minimal Tissue Leakage

Our main goals:

- Non-destructively separating bound and free MBs → RPCA-based filtering
- Minimizing tissue signal leakage → DTE, but destructive

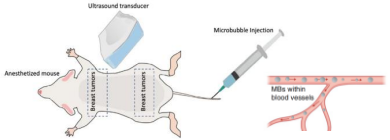
Our new idea:

- Combining **RPCA & DTE** to leverage the strengths of both methods.
- Using the images as **labels** to train a neural network (non-destructive)
- Capable of working in **real-time**
- To be **integrated** to the ultrasound scanner

Summary of Our Proposed Imaging Approach & Analysis

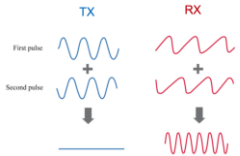
Data Collection

- 36 Transgenic mice with breast cancer
- Targeted MBs: B7-H3, PD-L1
- Non-Targeted MBs



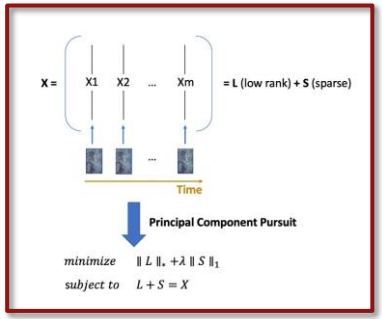
Verasonics scanner

Contrast Enhanced Ultrasound

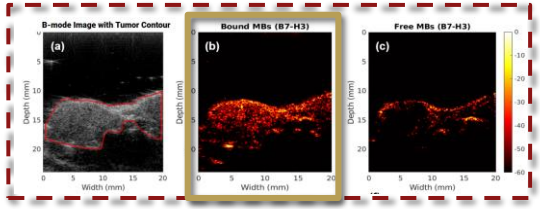


RPCA-based Labels + DTE

RPCA-Based Separation Method



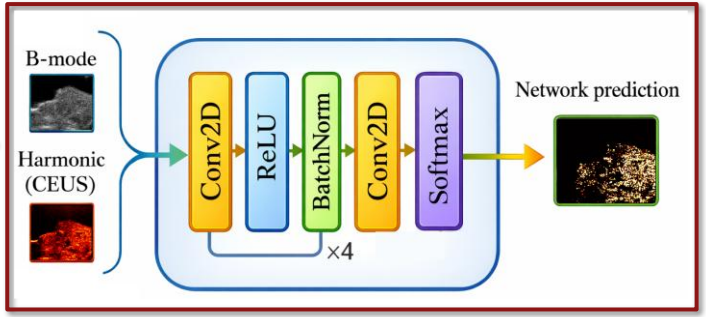
Bound vs free MBs sequences



DTE (before–after burst)

Eliminating tissue signal leakage

Convolutional Neural Network (CNN)



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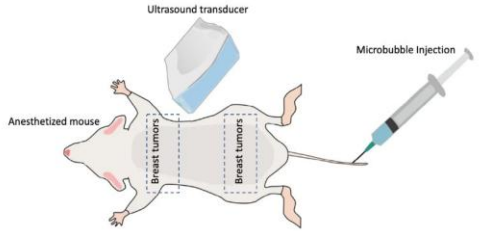
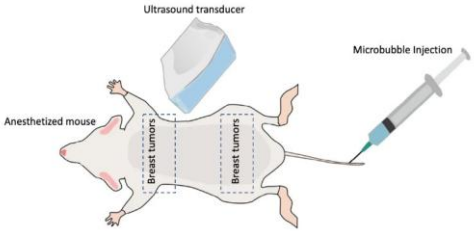
Data Collection

Mouse 1



Mouse 2



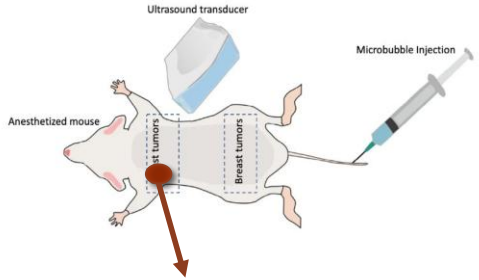
…

Mouse 36

…

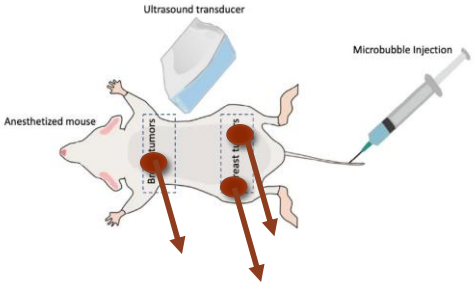
Data Collection

Mouse 1



Tumor

Mouse 2



3 Tumors

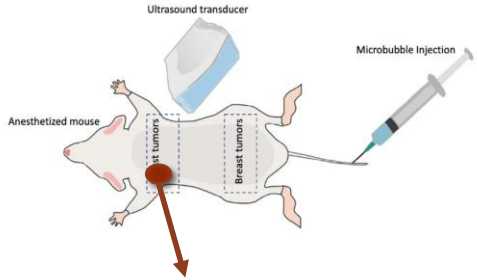
…

Mouse 36

…

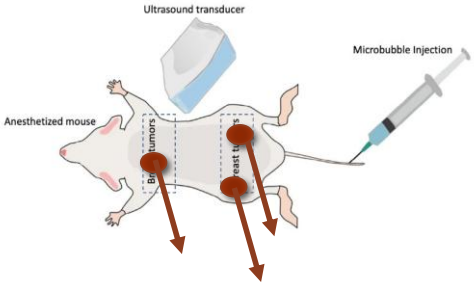
Data Collection

Mouse 1



Tumor

Mouse 2



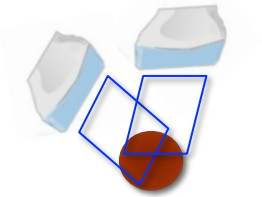
3 Tumors

…

Mouse 36

…

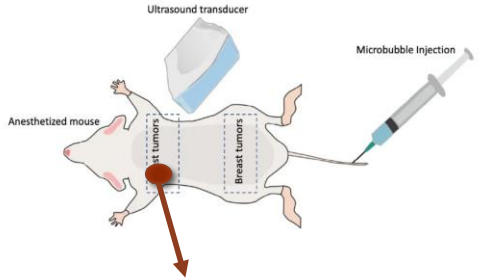
Each Tumor:



Results in a total of 114 scans

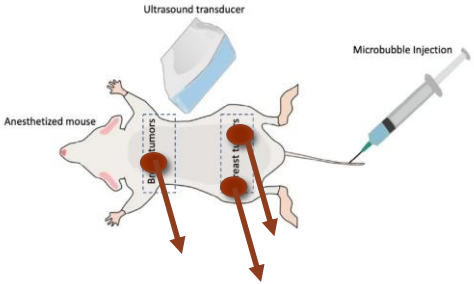
Data Collection

Mouse 1



Tumor

Mouse 2



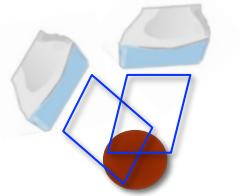
3 Tumors

…

Mouse 36

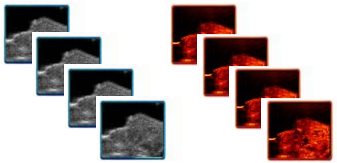
…

Each Tumor:



Results in a total of 114 scans

Each Scan:

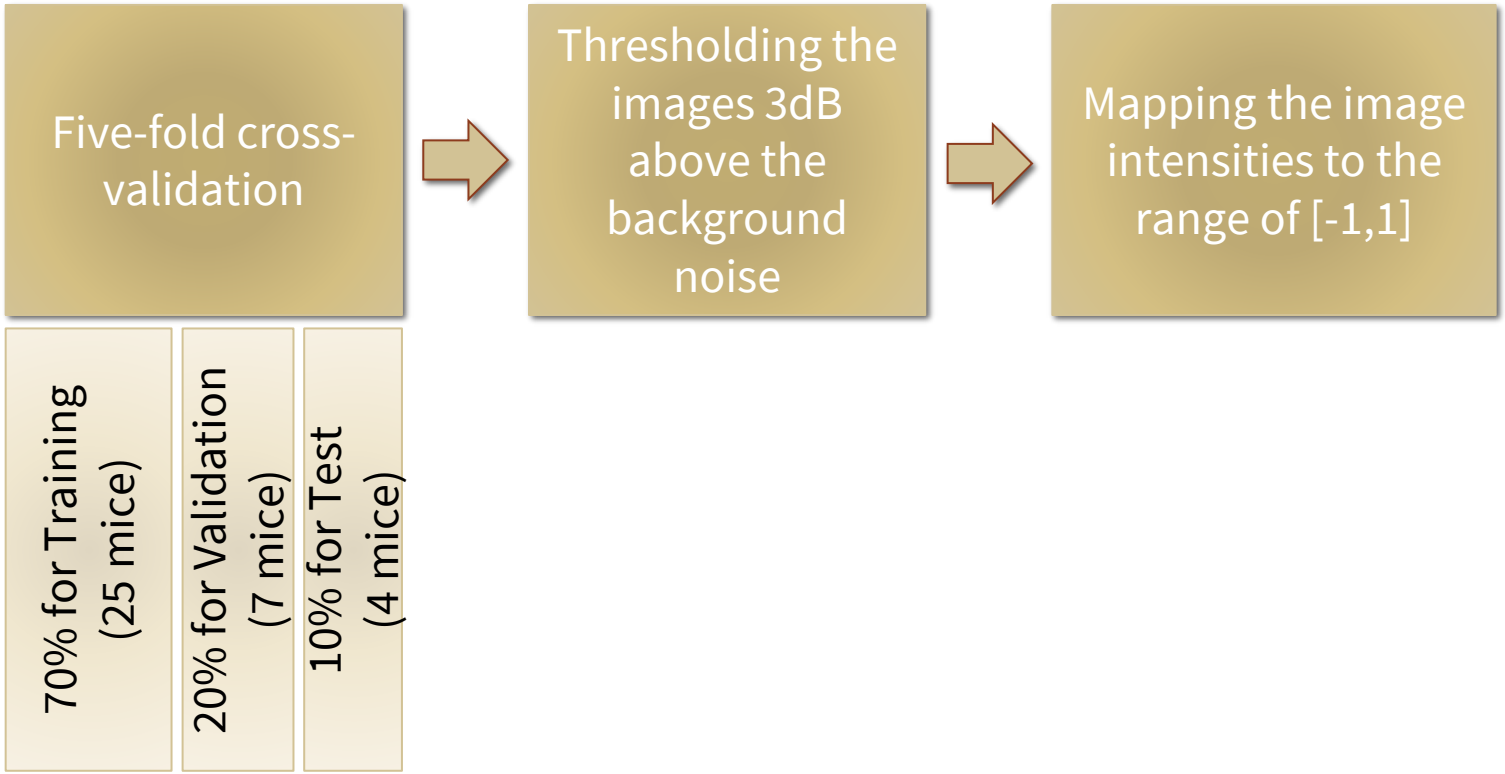


B-mode & CEUS sequences:

153 frames before burst → for training the network

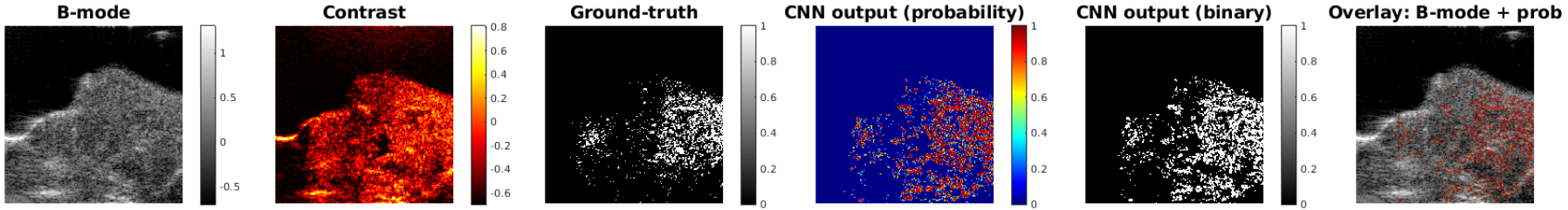
153 frames after burst → for making labels using DTE

Data Preparation

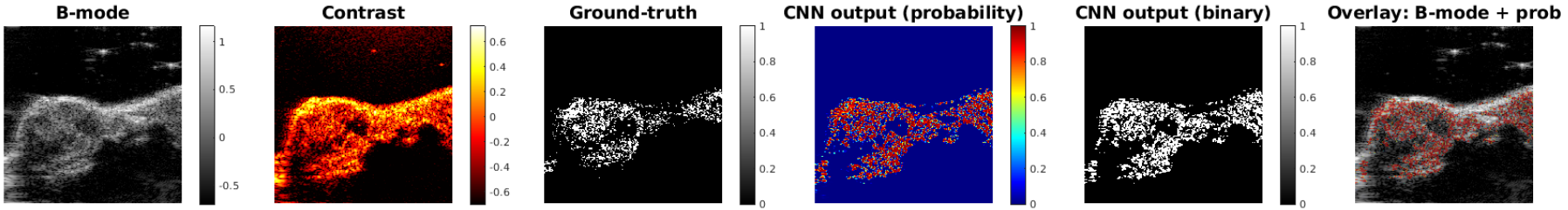


Results: Targeted Microbubbles

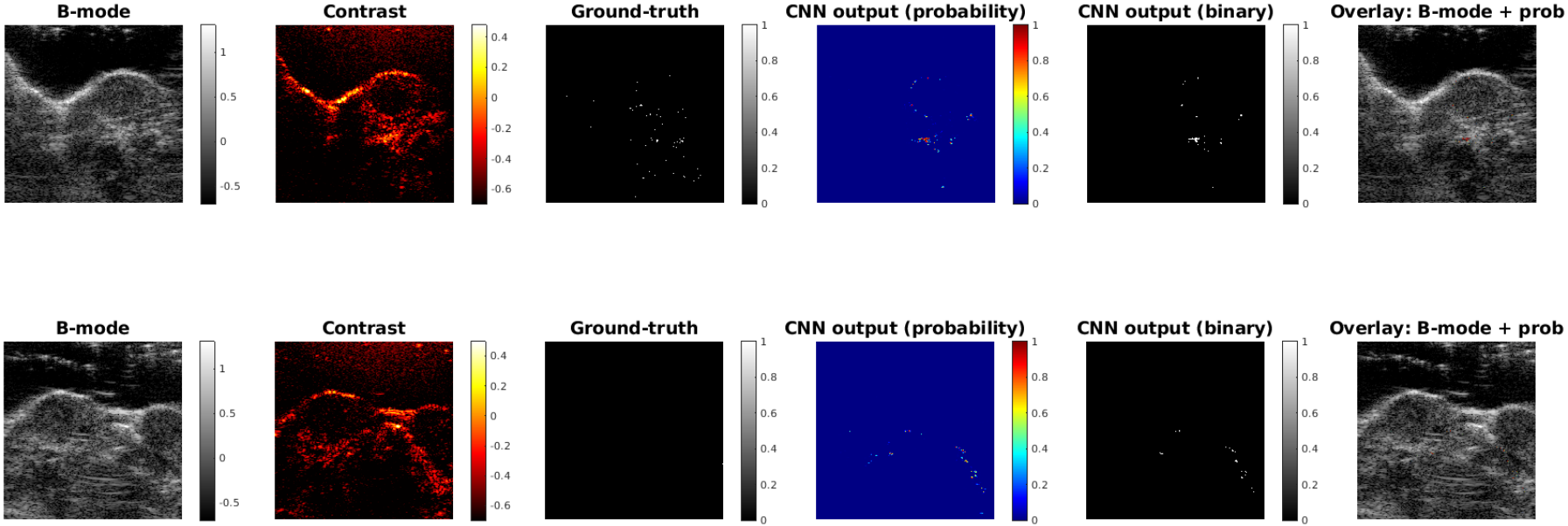
B7-H3 Targeted MBs:



PD-L1 Targeted MBs:

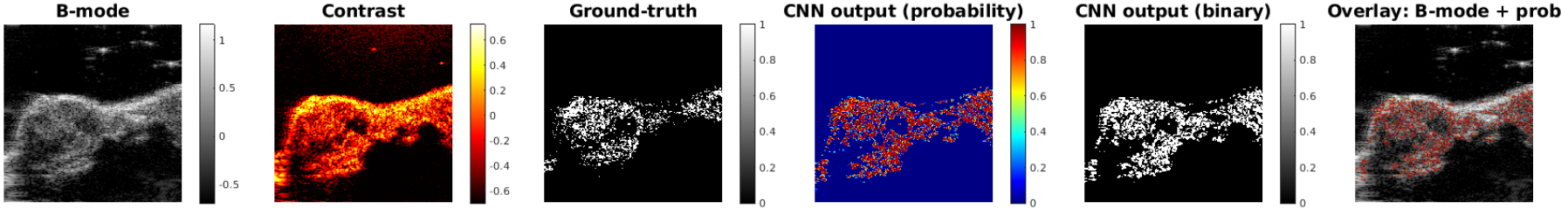


Results: Non-Targeted Microbubbles



Results:

- The average Dice coefficient = 0.65
- Calculated over all examples in the test set.
- Encouraging result given the highly sparse nature of microbubble signals and the class imbalance between background and positive pixels.
- Small boundary differences can noticeably reduce the Dice value.
- Qualitative inspection shows the CNN consistently captures the main regions of UMI signal with good spatial agreement to the ground-truth.



Real-Time Implementation on Verasonics Scanner

TX/RX sequence for B-mode and contrast imaging

Raw channel data for B-mode

Raw channel data for CEUS

Beamforming and image reconstruction

B-mode

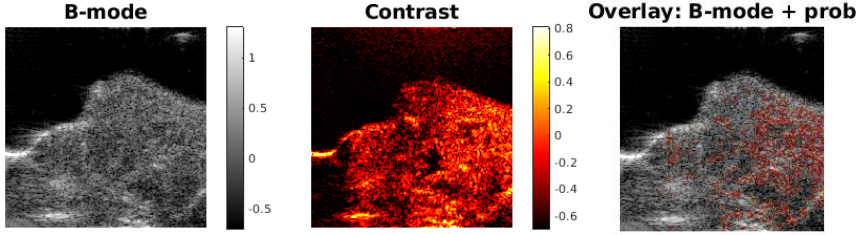
CEUS

Resizing + normalizing

Catching these two for NN

Call NN (external function)

update images on the screen



Overall System Frame-Rate

With this pipeline, we have multiple flexible parameters to set.

Imaging Depth	No. of Angles	Lateral Resolution	Update Rate (Hz)	Frame Rate (Hz)
4 cm	25	0.5λ	1	7
4 cm	11	λ	1	11
3 cm	11	λ	1	13
3 cm	11	0.5λ	5	13
3 cm	11	λ	5	30

Conclusion

- UMI enables early detection of **breast cancer**.
- **Detecting bound microbubbles** is vital for UMI, but **challenging** due to the presence of free microbubbles.
- We proposed a **non-destructive real-time CNN** to visualize bound microbubbles.
- We applied an **RPCA-based filtering** method as well as DTE to make the labels for the neural network.
- The results show that the CNN consistently captures the main regions of UMI signal with good spatial agreement to the ground-truth.
- The real-time implementation of the method on the Verasonics scanner is able to run at 30 frames/s.

Acknowledgment

- Ultrasound Imaging & Instrumentation Lab
- Stanford Cancer Imaging Training (SCIT) Program
- Diagnostic Sciences Laboratory (DSL)
- NIH/NCI T32 Training Grant
- NIH NIBIB Funding Grant
- Canary Center at Stanford

Pr. Jeremy Dahl, Principal Investigator
Pr. Ramasamy Paulmurugan, PhD, Principal Investigator
Arutselvan Natarajan, PhD, Senior Scientist
Farbod Tabesh, PhD, Postdoctoral Scholar
Jihye Baek, PhD, Postdoctoral Scholar
Nathan Nguyen, Undergrad. Intern
Hoda S. Hashemi, PhD, Postdoctoral Scholar
Louise Zhuang, PhD Candidate
Benjamin N. Frey, PhD Candidate
Caelia Thomas, PhD Candidate
Brian Boitnott, PhD Candidate
Andrew Andrzejek, Lab Manager
Samuel Beuret, PhD, Postdoctoral Scholar
Thurston Brevett, PhD, Recent Graduate

Sofia Gonzales
Program Manager

Jeremy Dahl
Program Director

Bruce Daniel
Program Director