Downclassification of Suspicious Breast Masses Using Opto-Acoustic Imaging

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Purpose

- Gray-scale ultrasound is limited in its specificity for characterization of breast masses
- Limited specificity results in false positives and negative biopsies
- Can opto-acoustic (OA) imaging increase the specificity of gray-scale ultrasound for characterization of breast masses?

Basis for Opto-Acoustic Imaging

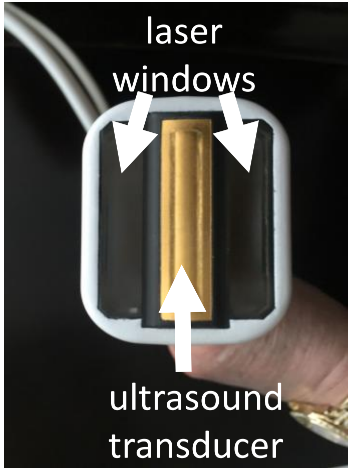
- Cancers do not grow beyond 2-mm without developing neovascularity[1]
- With angiogenesis there is increased blood flow to cancerous tissue
- Cancers are generally more metabolically active and deoxygenate hemoglobin more than benign entities or normal tissue

Opto-Acoustic Imaging

- Optical energy from a laser is absorbed and emitted acoustically[2,3,4]
- Light excitation causes thermalelastic expansion within a mass which then emits a pressure (acoustic) wave that is detected by an array of acoustic sensors within a hand-held breast probe[5]
- Pulses of near-infared light at two wavelengths are applied sequentially to breast tissue
    - Red light (757nm) is absorbed predominantly by hypoxic (de-oxygenated) blood
    - Near-infared light (1064 nm) is absorbed predominantly by normally oxygenated blood

Investigational Device - Imagio®

- Hand-held linear probe which can perform both gray-scale ultrasound as well emits optical pulses via a class 3b laser
- Dual wavelength optical pulses generate the OA images
- Ultrasound images are acquired and temporally interleaved and co-registered with the OA images in real-time



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Opto-Acoustic Imaging: Fusion Imaging

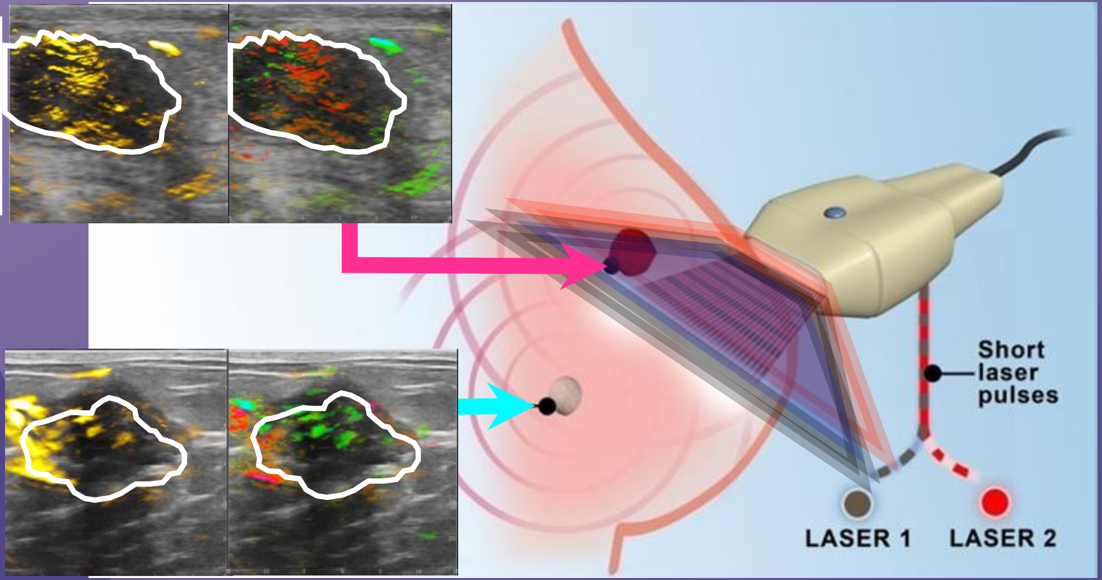
- Fusion of laser optic imaging and gray-scale imaging in real-time[6-12]
    - Optics – high contrast resolution (about 20/1)
    - Ultrasound – high spatial resolution and better penetration
- Fusion of anatomy and function
    - Anatomy – gray-scale ultrasound anatomy as well as OA demonstration of tumor angiogenesis
    - Function – OA demonstration of relative degrees of oxygenation/deoxygenation

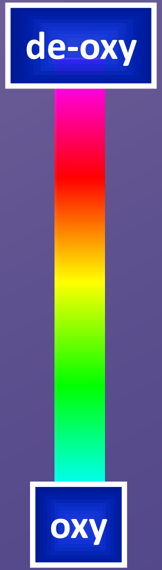
Opto-Acoustic (OA) and Ultrasound Images

Real Time Hemoglobin Map

Malignant
more
deoxygenated
hemoglobin

Benign
more oxygenated
or absent
hemoglobin





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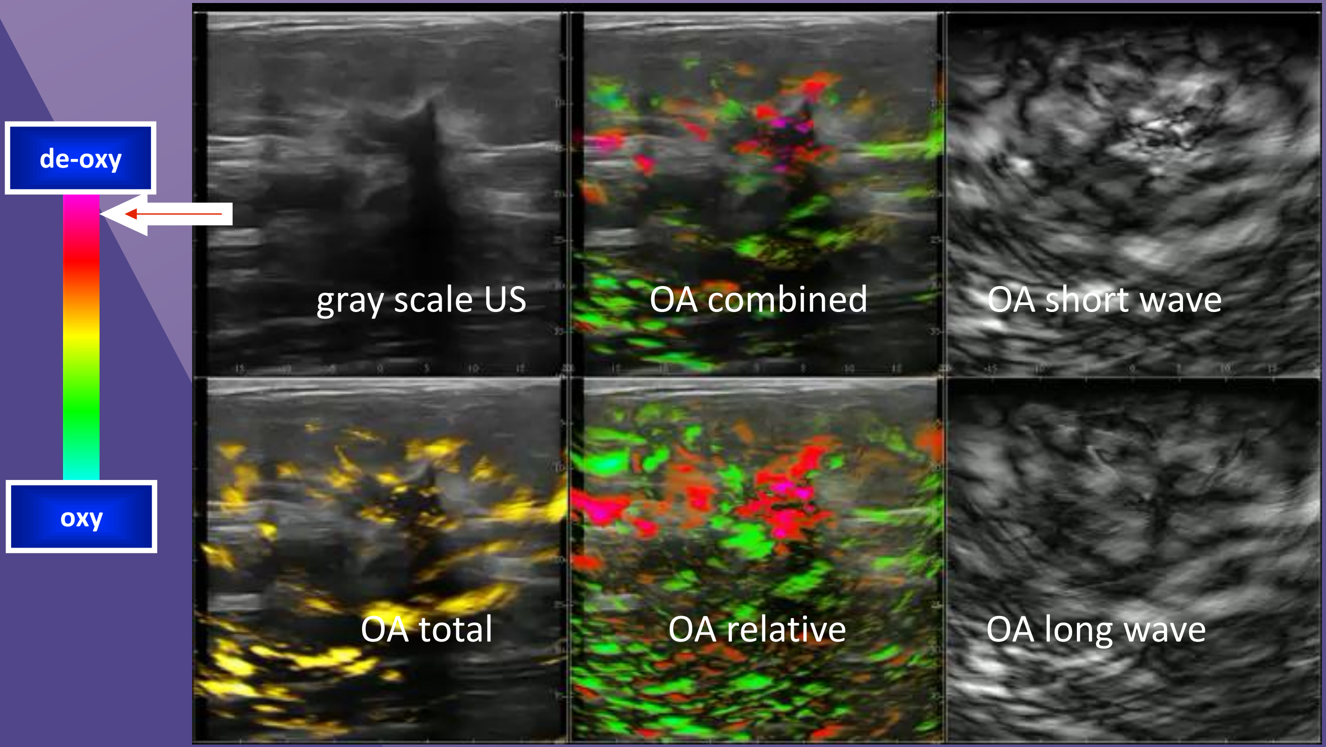
Opto-Acoustics (OA) 6-on-1 Real Time Display

1 gray scale map and 5 OA maps are complementary to each other

Invasive ductal carcinoma, grade II



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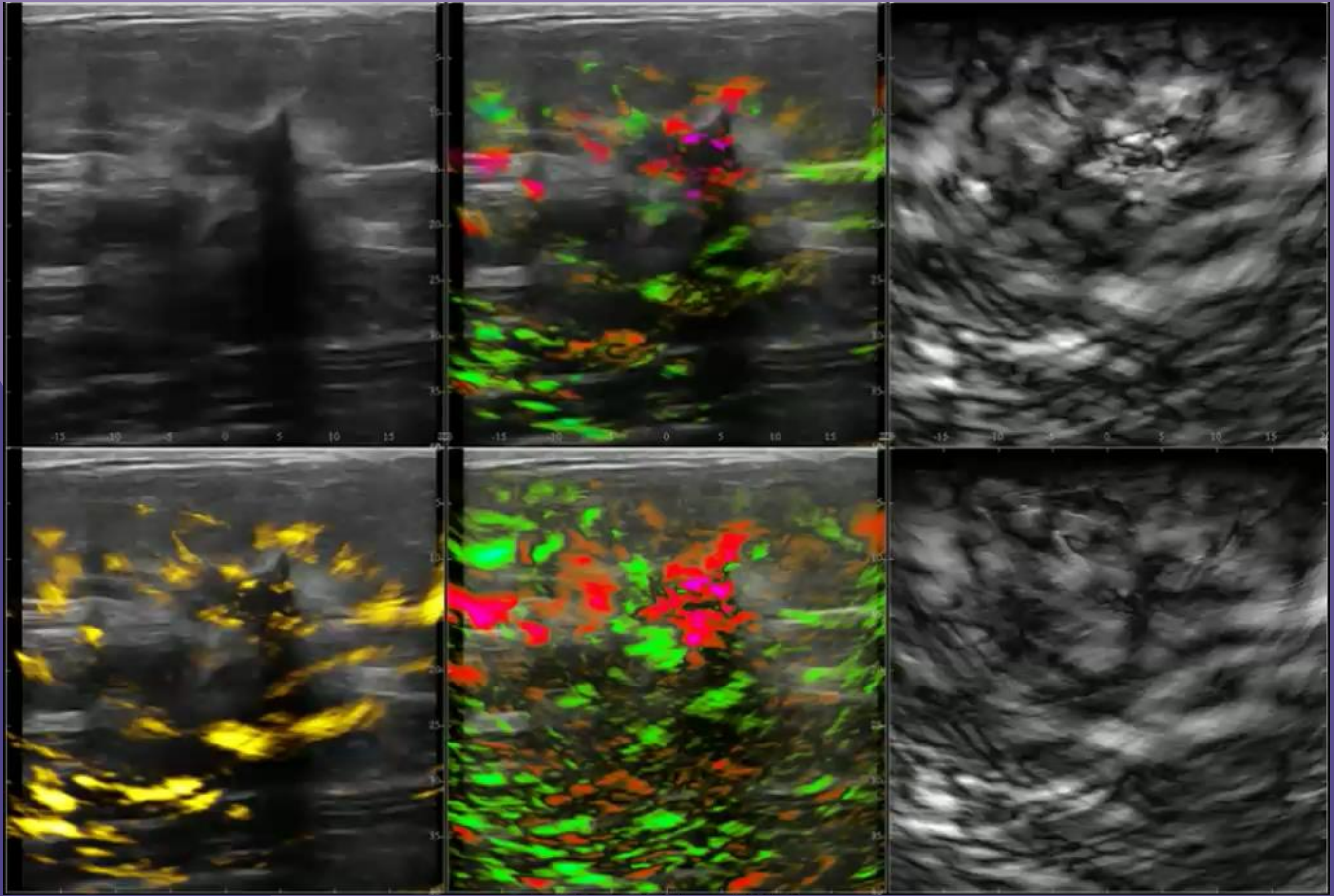

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PIONEER-01 Pilot Study

- A **P**ivotal Study of **I**maging with **O**ptoacoustics to diagnose breast masses detected by mammography and/or clinical findings: A **NE**w Evaluation Tool for **R**adiologists
- Pilot study of 100 patients was evaluated for the potential ability of OA to downgrade BI-RADS scores in benign masses
- Can BI-RADS (BR) 4a or 4b masses be downgraded to either BI-RADS 3 or 2 with OA?
- Can masses coded BI-RADS 3 be downgraded to BI-RADS 2 with OA?

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PIONEER-1 Investigator Sites

- Northwestern Medicine
- Yale University School of Medicine
- New York Presbyterian Hospital
- Georgetown University Hospital
- Cleveland Clinic
- The University of Texas MD Anderson Cancer Center
- The University of Texas Health Science Center at San Antonio
- Elizabeth Wende Breast Care
- Invision Sally Jobe
- Weinstein Imaging Associates
- Boca Raton Regional Hospital
- Radnet, Inc.
- Austin Radiological Association
- Solis Women's Health (Texas and North Carolina)
- Breast Care Specialists

Materials and Methods

- 6 of the 16 sites contributed to the pilot cases
- Women referred for diagnostic breast ultrasound due to a palpable mass or a suspicious mammographic finding
- Patients with BI-RADS 3, 4a, 4b, 4c and 5 lesions at conventional diagnostic ultrasound (CDU) were eligible for the study
- Investigators obtained gray-scale images with the Imagio® device, the internal ultrasound control (IUC), immediately before acquiring the OA images

Materials and Methods

- Independent readers (IRs) blinded to clinical data, site imaging and pathology
- 7 IRs were trained by expert reader to identify and score three OA internal features and two OA external features for each mass
- IRs offered the results of two nomograms (that were calculated from their OA feature scores) to help predict the Probability of Malignancy (POM)
- 2% or less POM → downgrade to BI-RADS 3
- 0% POM → downgrade mass to BI-RADS 2

Materials and Methods

- 102 masses from the 100 pilot study cases
- 75 biopsied masses (39 benign, 36 malignant)
- BI-RADS classification by site radiologists of conventional diagnostic ultrasound:

  4 BI-RADS 3
  18 BI-RADS 4a
  18 BI-RADS 4b
  12 BI-RADS 4c
  23 BI-RADS 5

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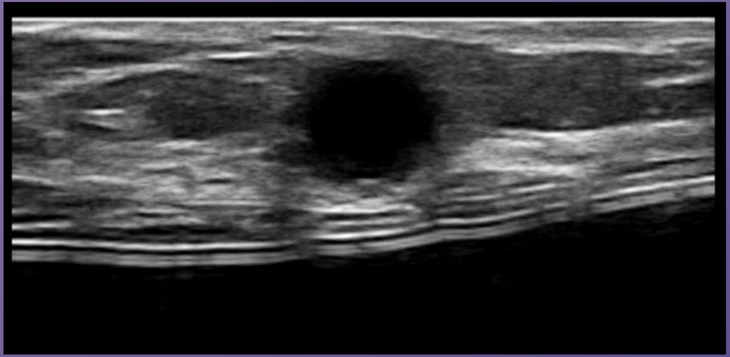
Case #1

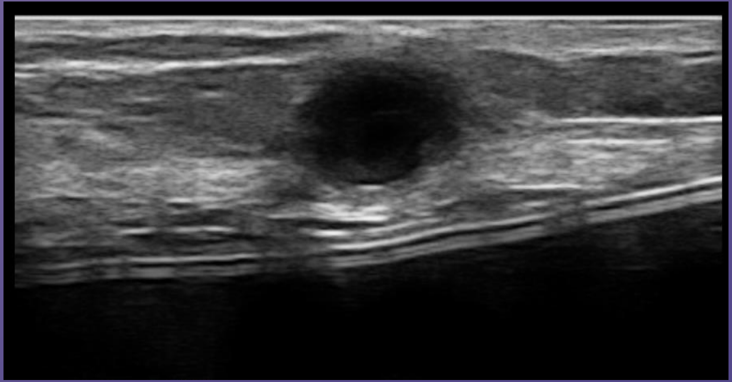
9-mm mass in left breast at 3:00 7 cm from the nipple

- CDU: BI-RADS 4B

- IUC: BI-RADS 4B

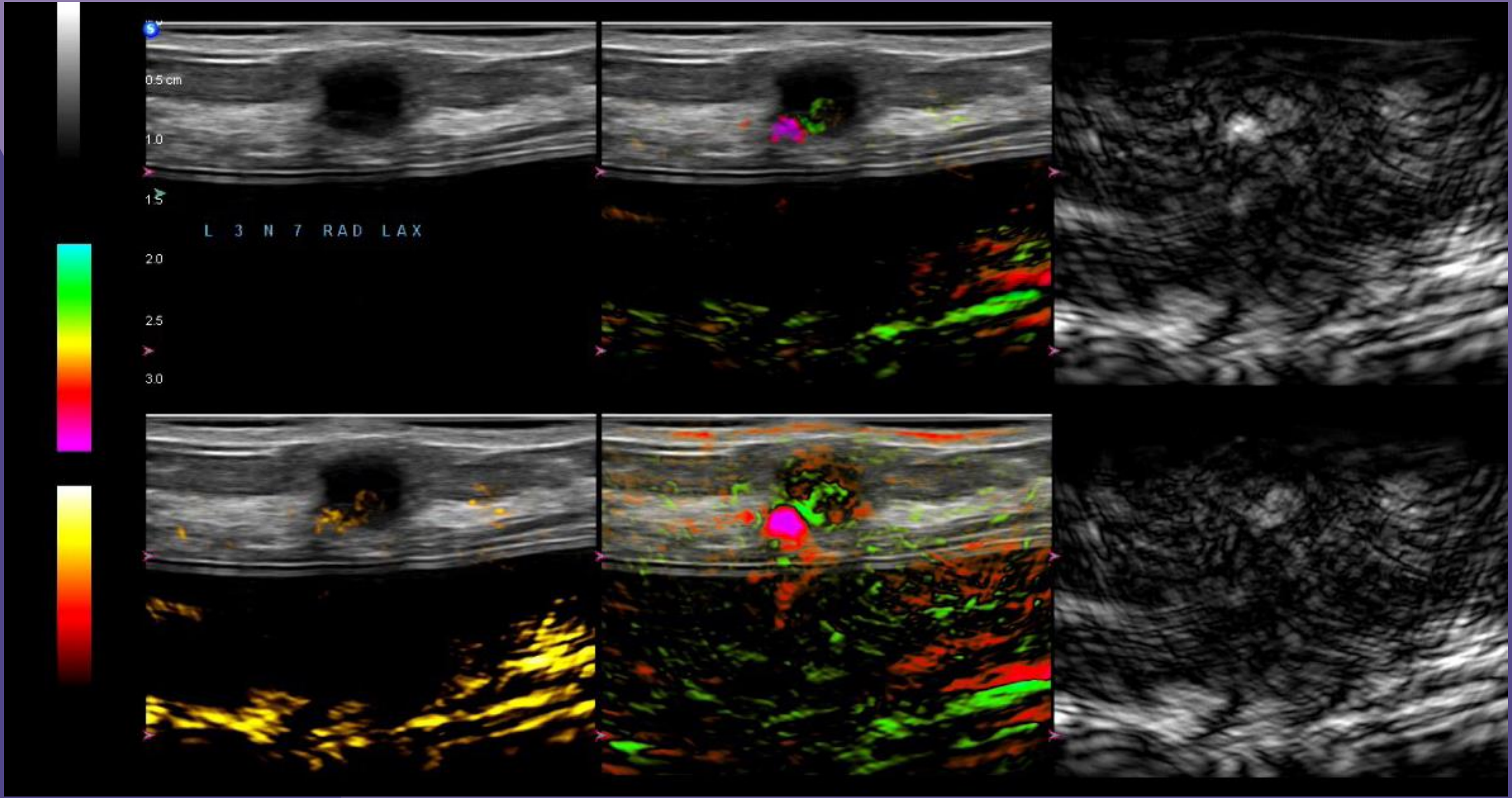


ARAD



RAD

OA



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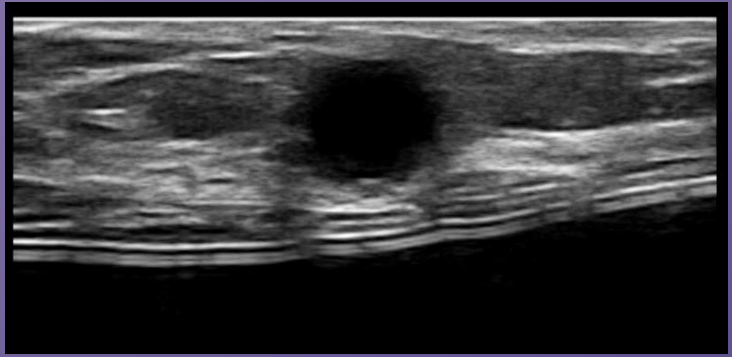
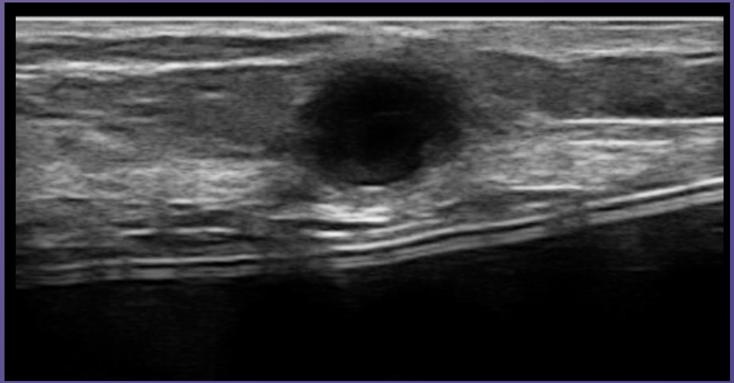
FIBROADENOMA

9-mm mass in left breast at 3:00 7 cm from the nipple

- CDU: BI-RADS 4B
- IUC: BI-RADS 4B
- **OA: BI-RADS 3**



ARAD

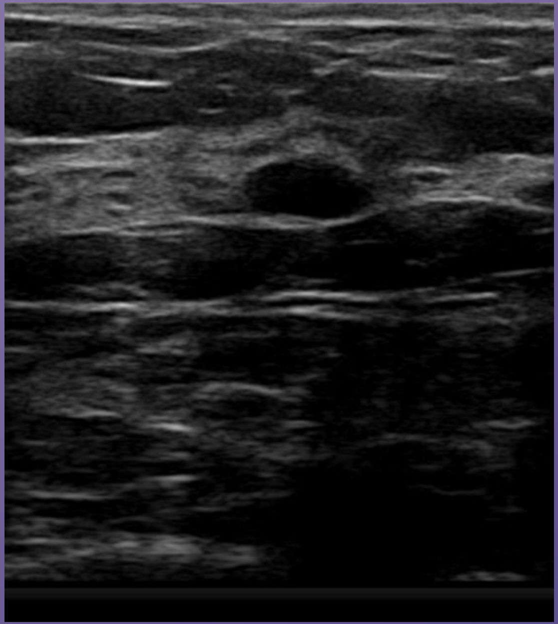


RAD

Case #2

7-mm mass in the right breast at 10:30 8 cm from the nipple

- CDU BI-RADS: 3
- IUC BI-RADS: 3



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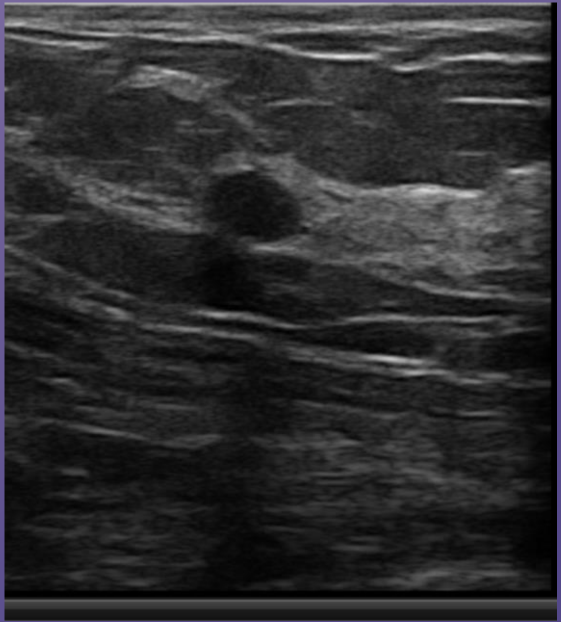

RAD

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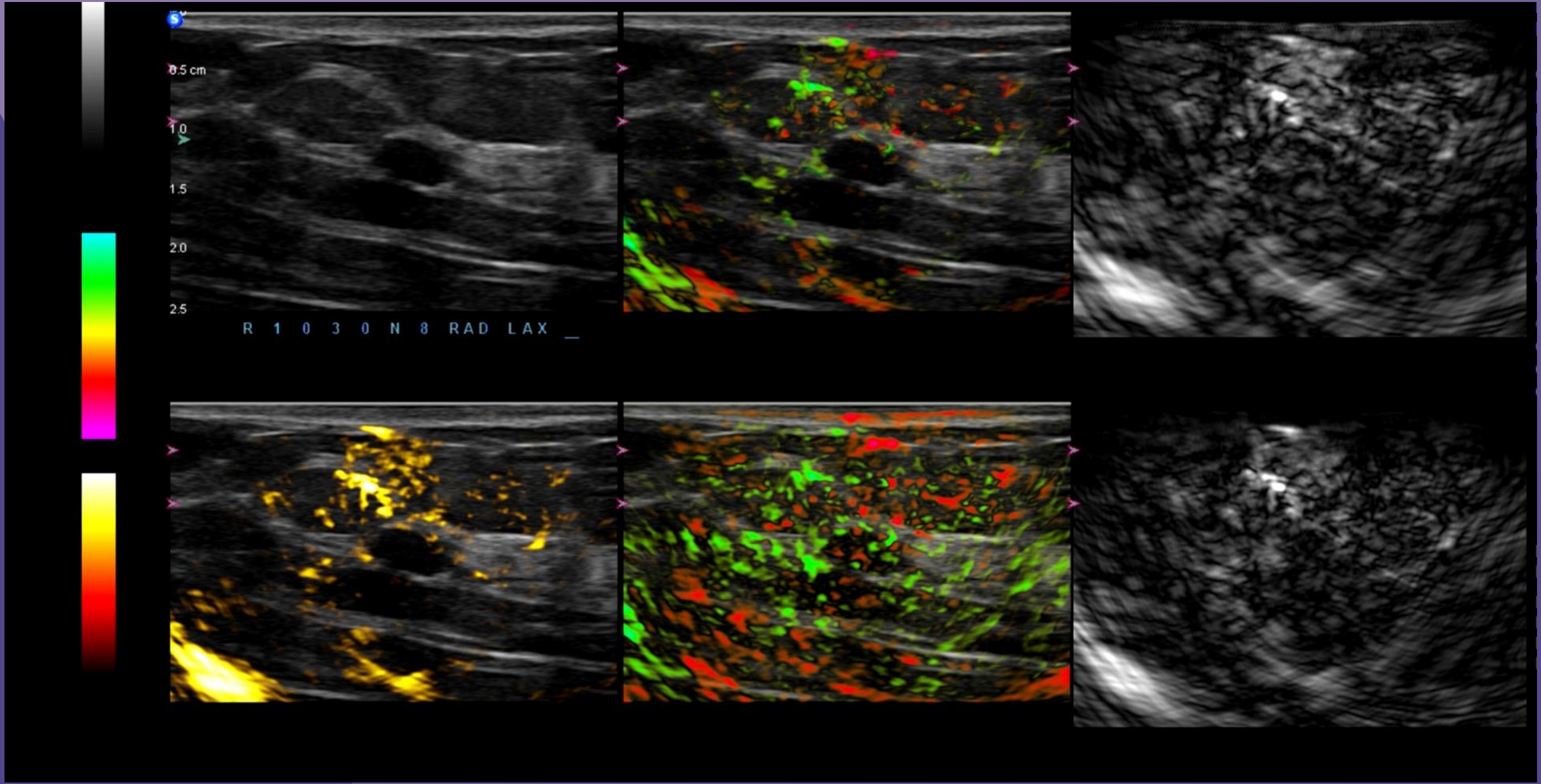
OA



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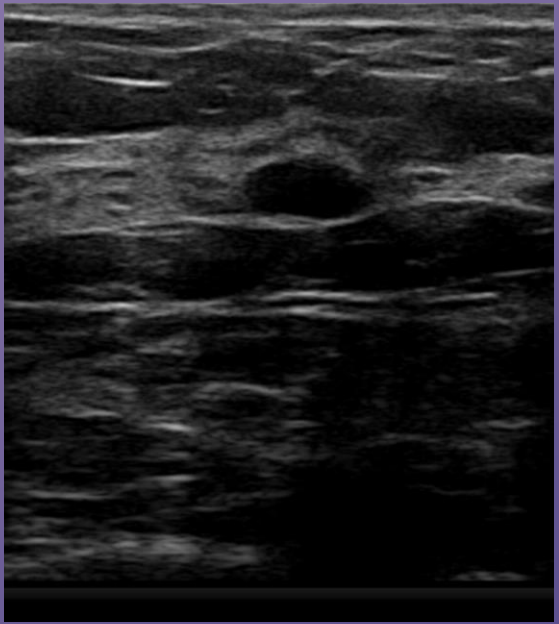
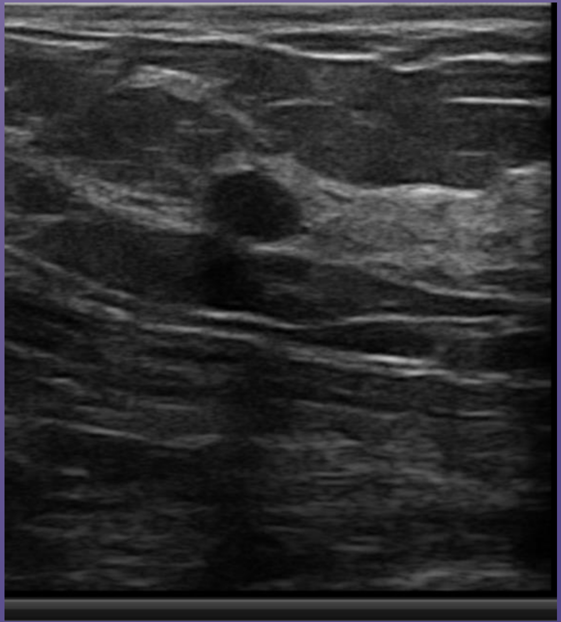
FIBROADENOMA

7-mm mass in the right breast at 10:30 8 cm from the nipple

- CDU BI-RADS 3
- IUC BI-RADS 3
- **OA: BI-RADS 2**



ARAD



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Results

- Using OA the IRs had 97.6% sensitivity and 44.4% specificity
- Net absolute gain in specificity of 13%

Results

- Using OA, the IRs were able to downgrade site-CDU masses as follows:
  - BR 4a masses to BR 3 or 2 in 53% of cases
  - BR 4b masses to BR 3 or 2 in 33% of cases
  - BR 3 masses to BR 2 in 33% of cases
- Using OA, the IRs downgraded IUC-classified masses as follows:
  - BR 4a to either BR 3 or 2 in 43% of cases
  - BR 4b masses to either BR 3 or 2 in 13% of cases
  - BR 3 masses to BR 2 in 43% of cases

Conclusions

- Benign masses classified as BR 3, 4a and 4b could be downgraded to BR 3 or 2 by using OA with the aid of nomograms
- The use of OA could potentially decrease false positives and decrease negative biopsies
- The larger 1997 subject 16 center pivotal study will allow for confirmation

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