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Diagnosis of Breast Masses Using Opto-Acoustics

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Disclosures

1. Erin I. Neuschler, MD: Northwestern University Feinberg School of Medicine, Assistant Professor of Radiology, research grant from Seno Medical Instruments, Inc.

2. A. Thomas Stavros, MD: Seno Medical Instruments, Inc., Medical Director, Seno stock

3. Philip T. Lavin, PhD: Boston Biostatistics Research Foundation, Consultant to Seno Medical Instruments, Inc., analytical services provider

4. Michael J. Ulissey, MD: Breast Diagnostic Center, Seno Stock

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Imagio® is an investigational device that embodies the opto-acoustic technology. The information presented in this presentation is preliminary and not based on an FDA-approved device using this opto-acoustic technology.

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Purpose

- Gray-scale ultrasound is limited in its specificity for characterization of breast masses
- Limited ultrasound 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?

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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

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Opto-Acoustic Imaging

- Optical energy from a laser is absorbed[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 laser light at two wavelengths are applied sequentially to breast tissue
    - Near-infared light (757nm) is absorbed predominantly by hypoxic (de-oxygenated) blood
    - Laser light (1064 nm) is absorbed predominantly by normally oxygenated blood

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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 are used to 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 than laser alone in diffuse optical tomography

Fusion of anatomy and function

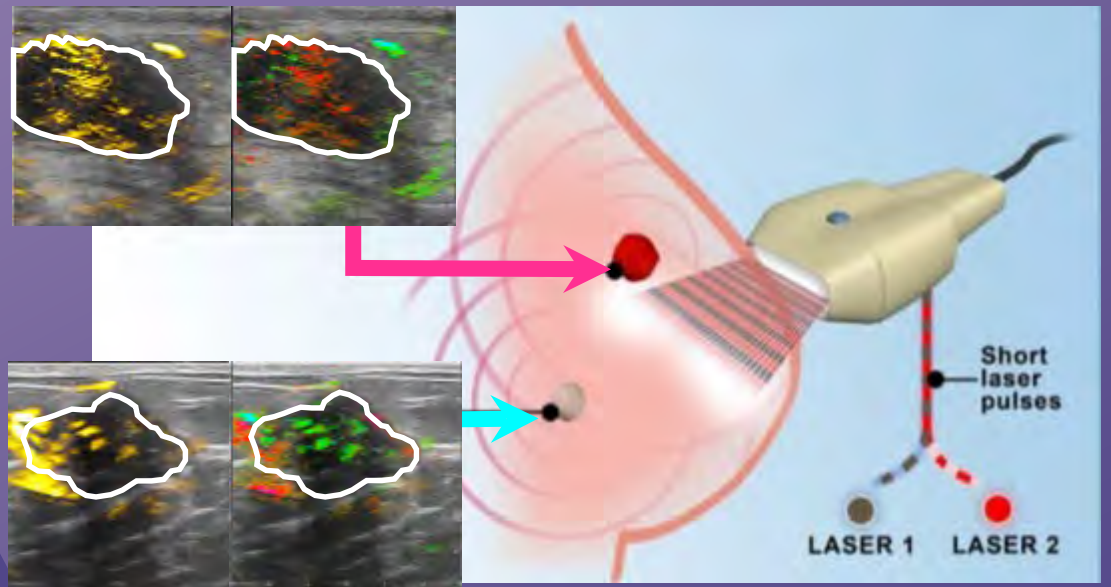
- Anatomy – gray-scale ultrasound anatomy as well as OA demonstration of tumor angiogenesis
- Function – OA demonstration of relative degrees of oxygenation/deoxygenation

Opto-Acoustic (OA) and Ultrasound Images

Real Time Hemoglobin Map

Malignant more deoxygenated hemoglobin

Benign more oxygenated or absent hemoglobin



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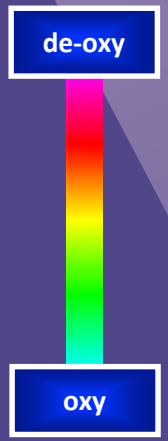
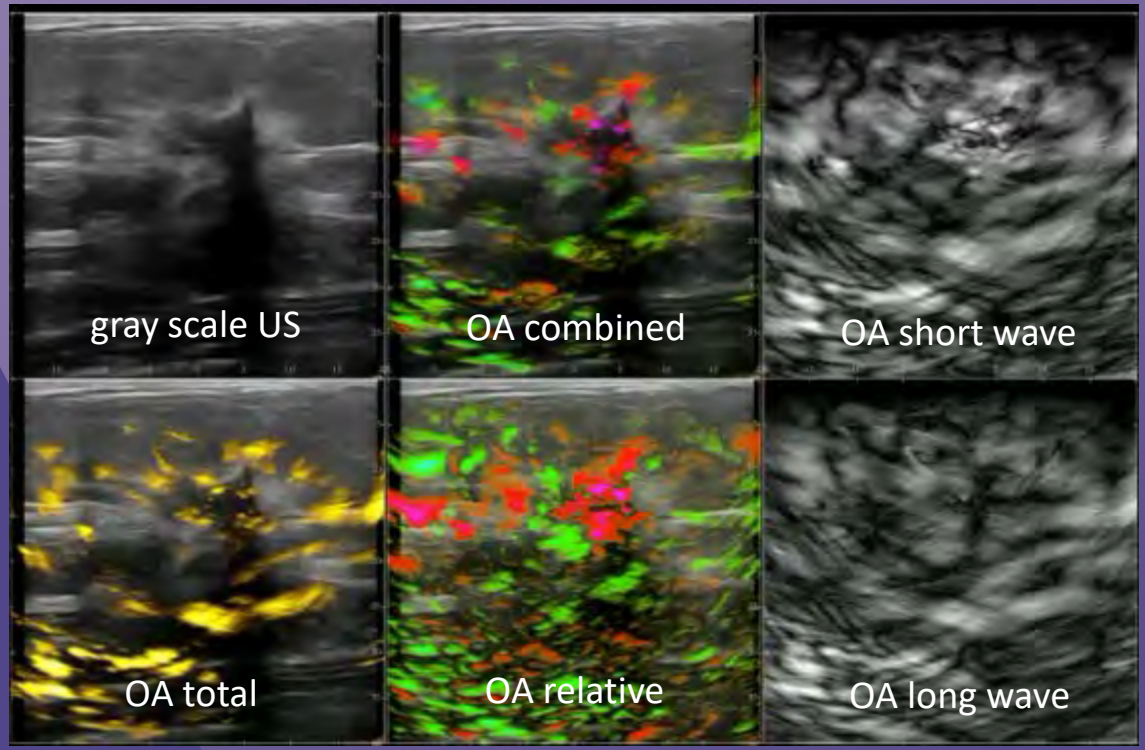
Opto-Acoustics (OA) 6-on-1 Real Time Display

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

Invasive ductal carcinoma, grade II





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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 OA upgrade the BI-RADS (BR) categories of malignant masses?

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PIONEER Pivotal Study

2,097 subjects	7 blinded readers	16 sites in the USA

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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, Imagio Ultrasound (IUS), immediately before acquiring the OA images

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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 were 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

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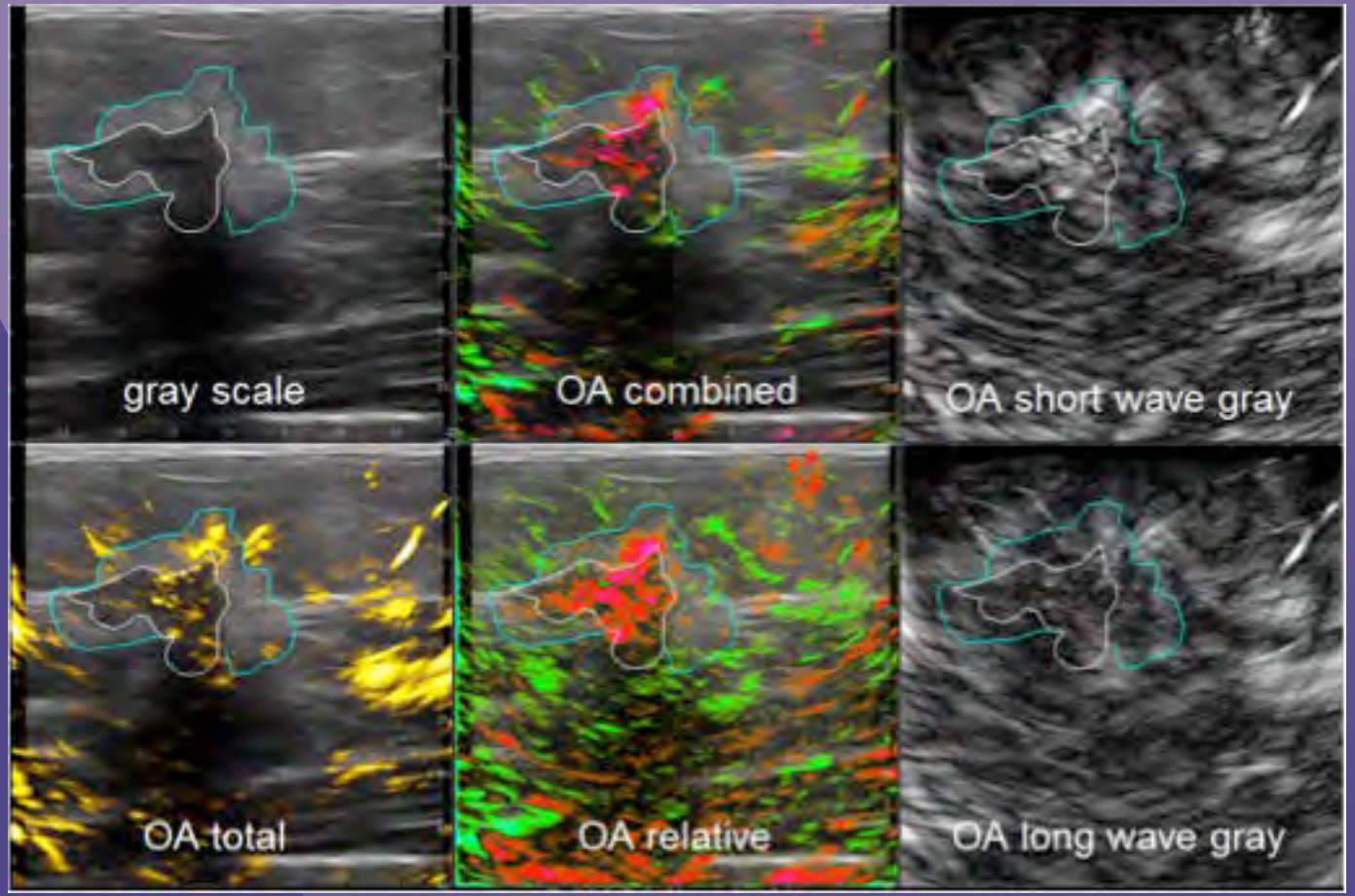
OA Findings

Internal OA Findings

- Internal vessels
- Internal blush
- Internal hemoglobin

External OA Findings

- Capsular or boundary vessels
- Peri-tumoral vessels



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Materials and Methods

- 103 masses from the 100 pilot study cases
- 101 were evaluable
- 6 masses were not biopsied and did not have 12 month follow-up
- 95 masses were either biopsied or had 12 month follow-up
  - 84 biopsied masses (39 malignant and 45 benign)
  - 11 masses were coded BR 3 and had 12 month follow-up

Results

- IRs had 97.0% sensitivity for IUS and OA
- IRs had a 44.3% specificity with OA, which was a 7.6 % improvement over IUS
- There were higher OA scores for malignant vs. benign masses for each feature score

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Results – Benign Masses: OA vs. CDU

- Using OA, 52% of benign masses classified as BR 4a by CDU were **downgraded** to BR 3 or 2
- Using OA, 35% of benign masses classified as BR 4b by CDU were **downgraded** to BR 3 or 2
- Using OA, 24% of benign masses classified as BR 3 by CDU were **downgraded** to BR 2

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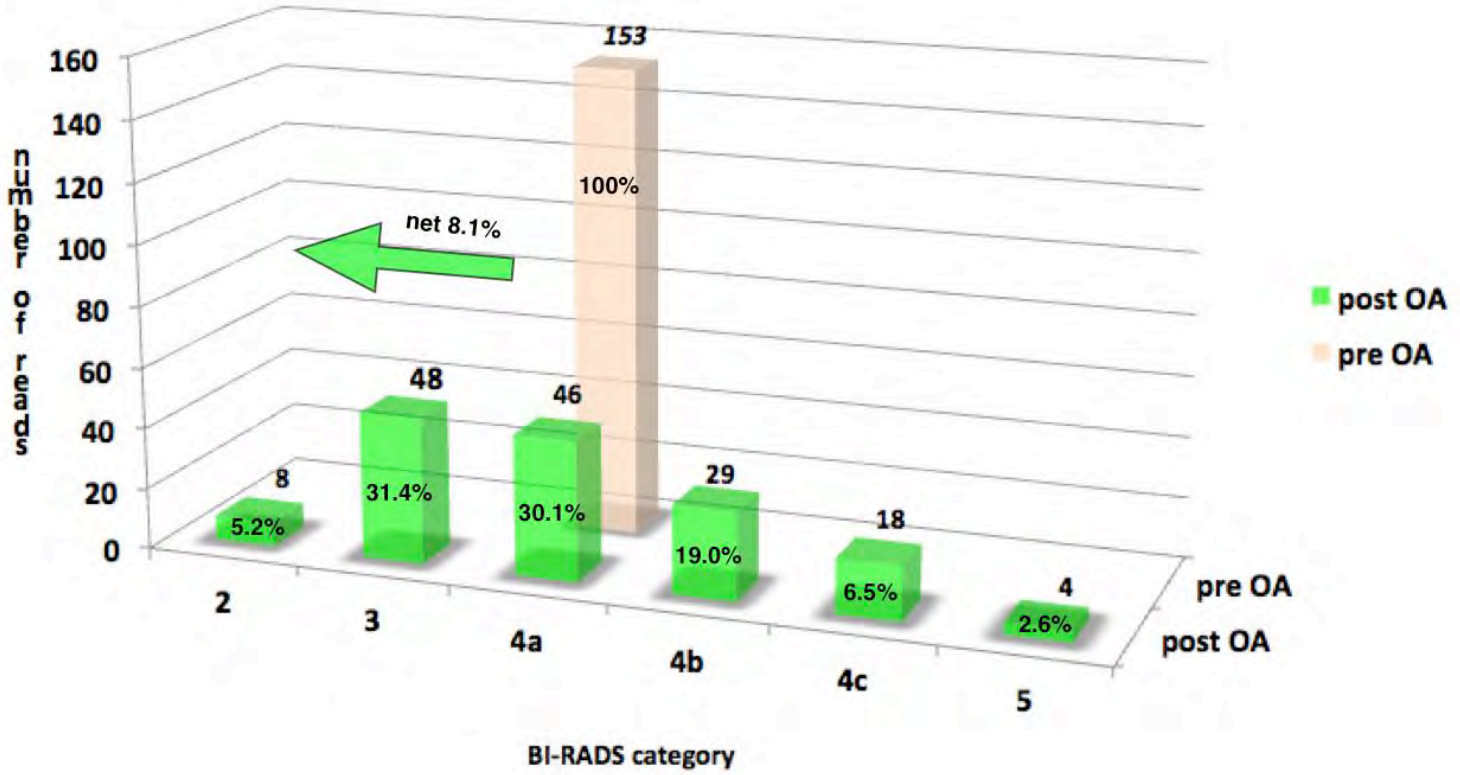
Results – Benign Masses: OA vs. IUS

- Using OA, 37% of benign masses classified as BR 4a by IUS were **downgraded** to a BR 3 or 2

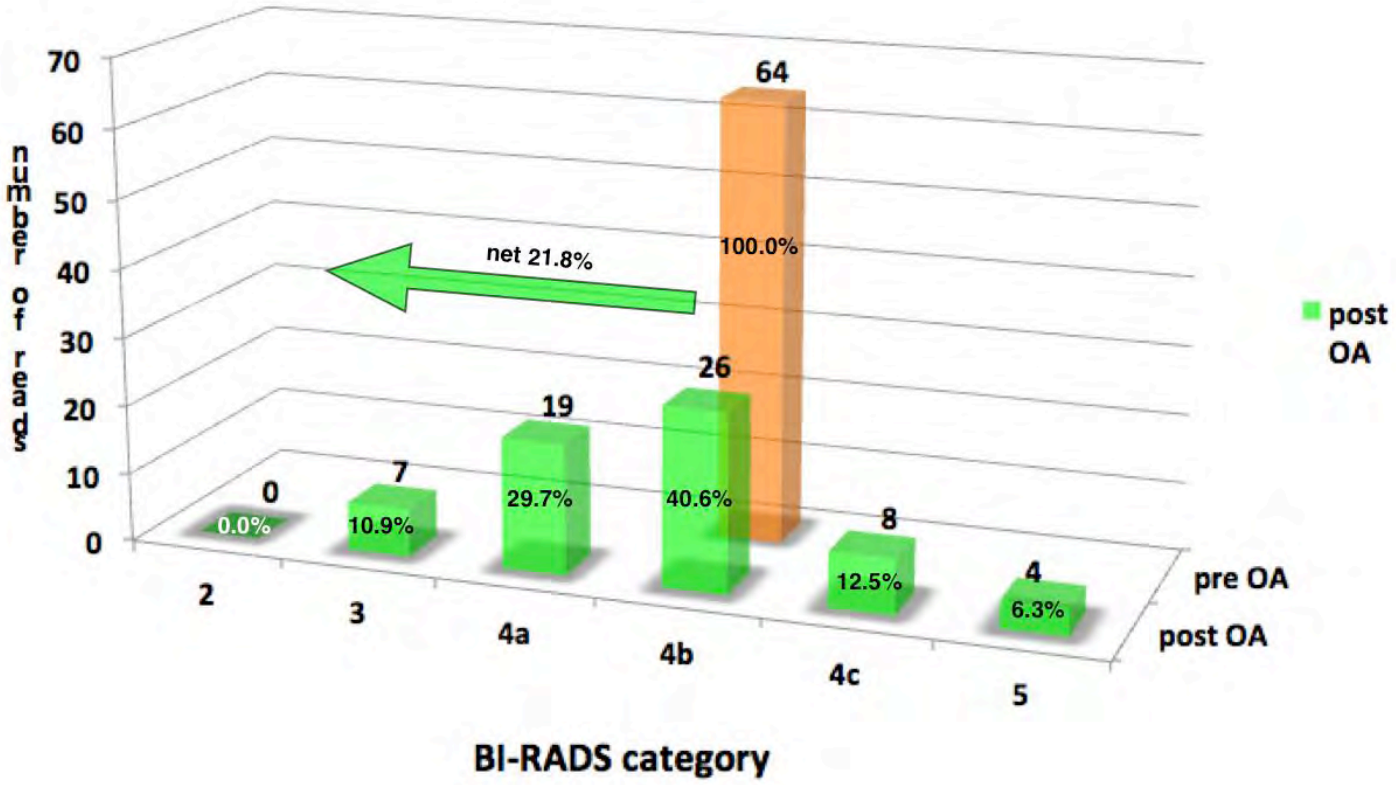
- Using OA, 11% of benign masses classified as BR 4b by IUS were **downgraded** to a BR 3 or 2

- Using OA, 37% of benign masses classified as BR 3 by IUS were **downgraded** to BR 2

benign BR 4a masses - shift in BI-RADS category after OA versus IUS



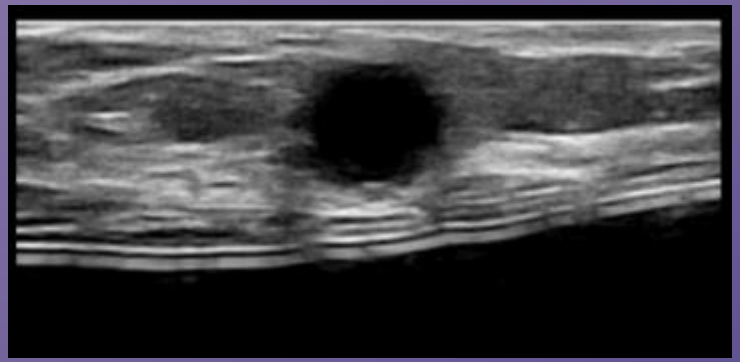
benign BR 4b masses - shift in BI-RADS category after OA versus IUS



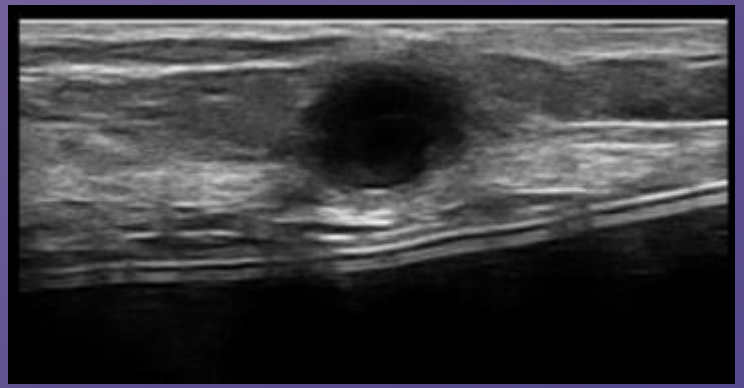
Case #1

0.9 cm mass in left breast at 3:00, 7 cm from the nipple

- CDU: BI-RADS 4B
- IUS: BI-RADS 4B



ARAD



RAD

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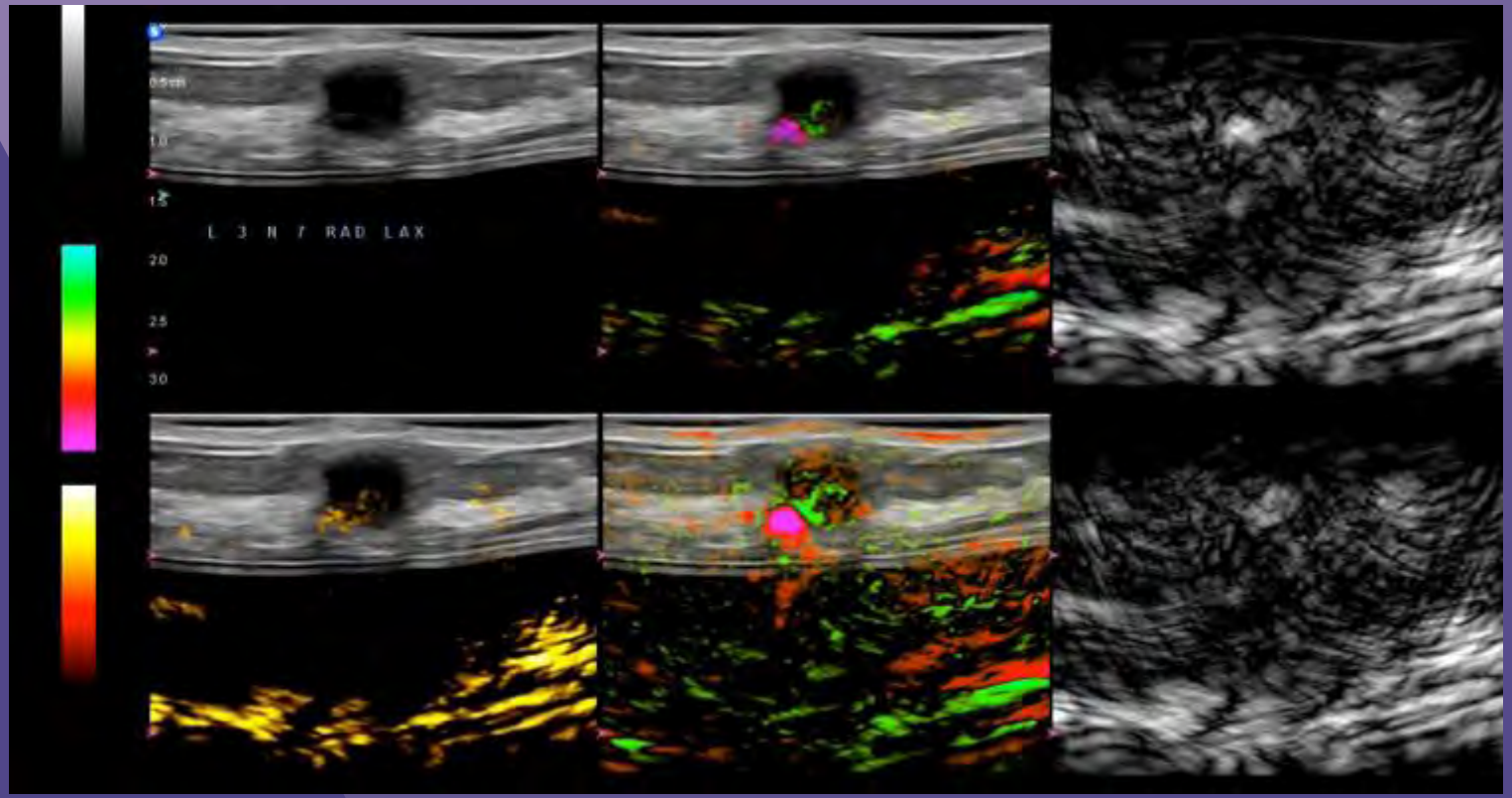
OA



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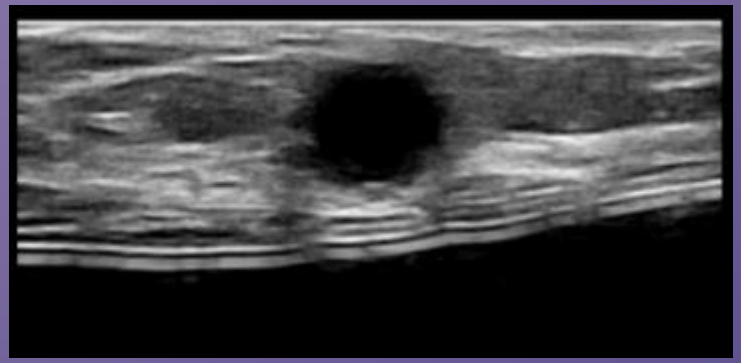
FIBROADENOMA

0.9 cm mass in left breast at 3:00, 7 cm from the nipple

- CDU: BI-RADS 4B
- IUS: BI-RADS 4B
- OA: BI-RADS 3



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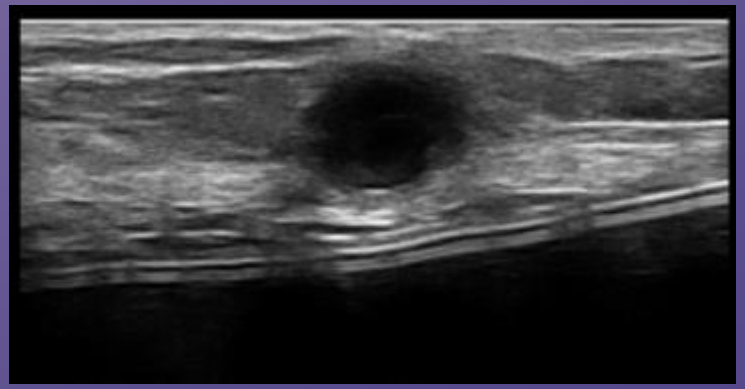

RAD

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Results – Malignant Masses: OA vs. CDU

- Using OA, the IRs **upgraded** 33% of the malignant masses classified as BR 4b by the CDU to 4c or 5

- No masses were given a BR 4a by the site-CDU

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Results – Malignant Masses: OA vs. IUS

- Using OA, the IRs **upgraded** 42% of the malignant masses classified as 4a by the IUS to 4c or 5

- Using OA, the IRs **upgraded** 57% of the malignant masses classified as 4b by the IUS to 4c or 5

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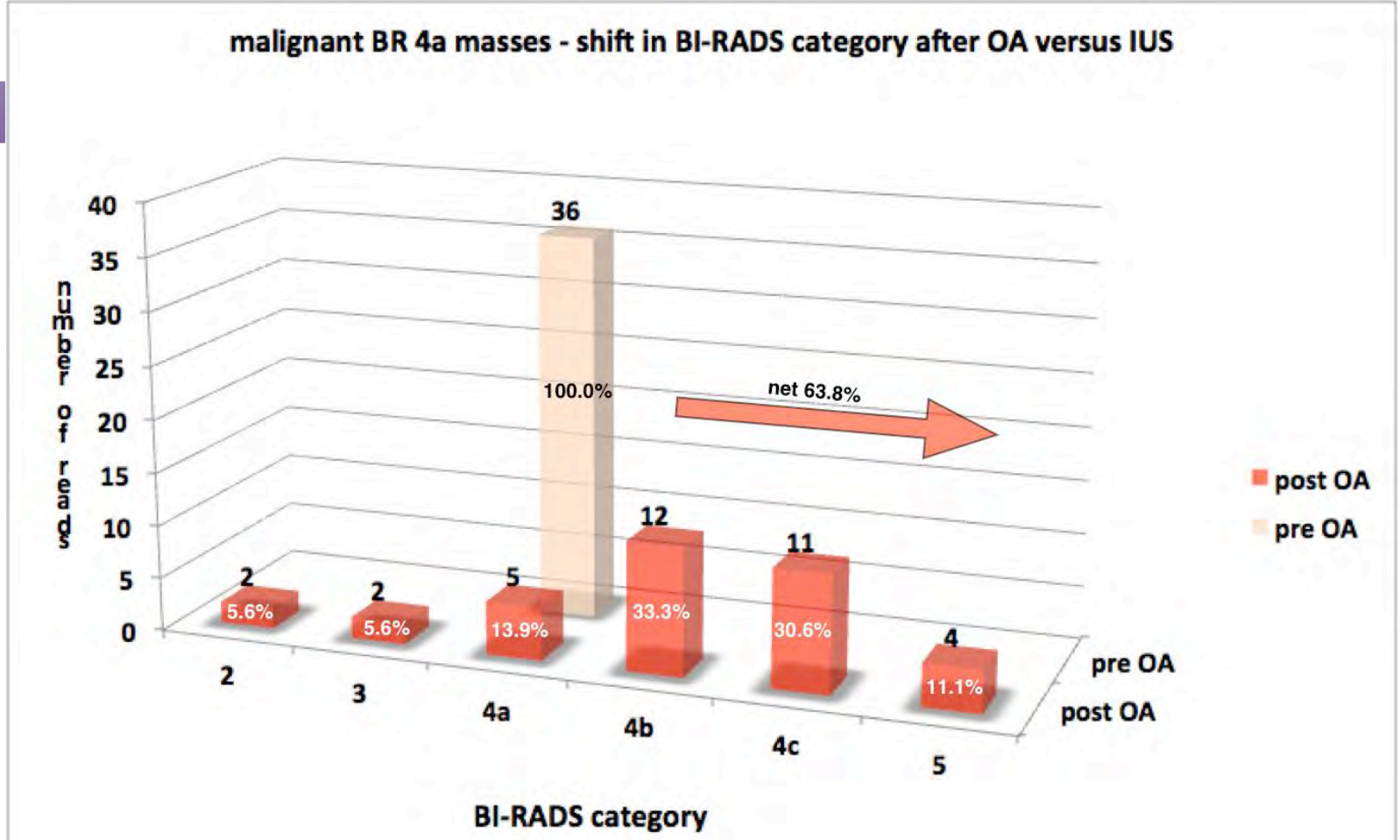
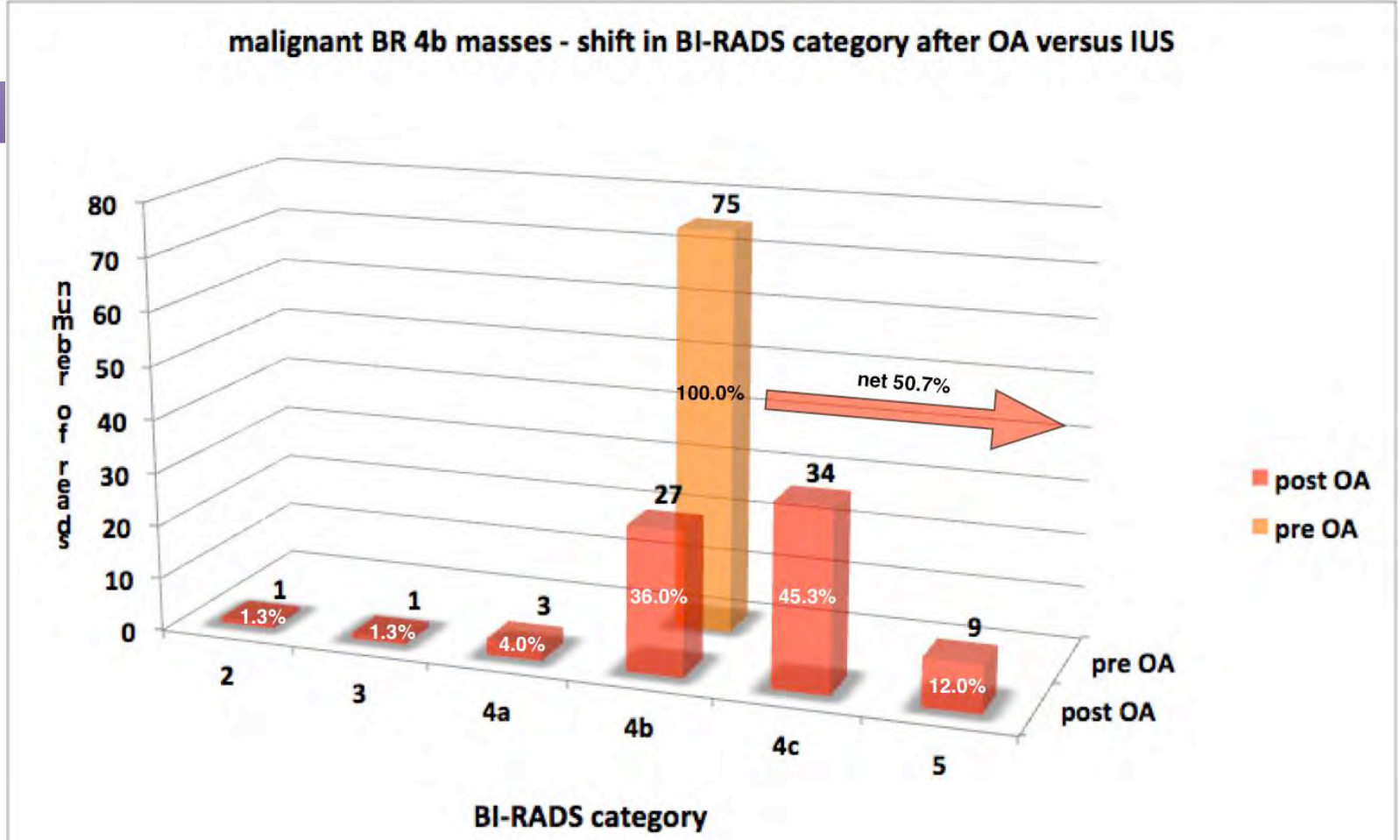
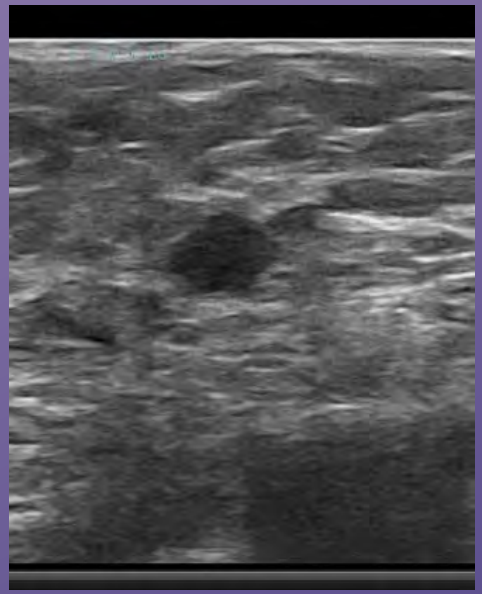


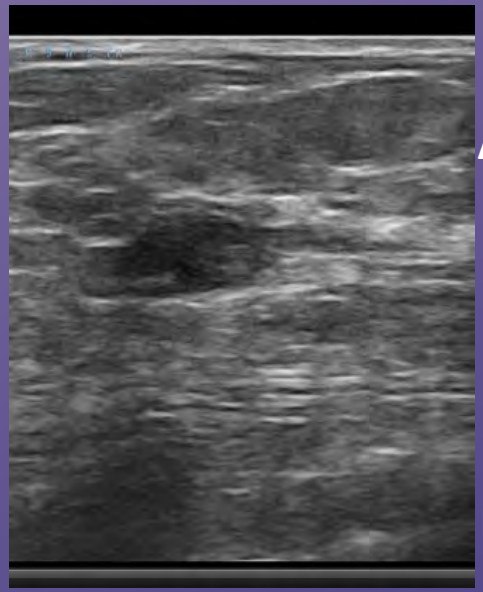


Case #2

1.1 cm mass in right breast at 9:00, 5 cm from the nipple

- IUS: BI-RADS 4A





ARAD

RAD

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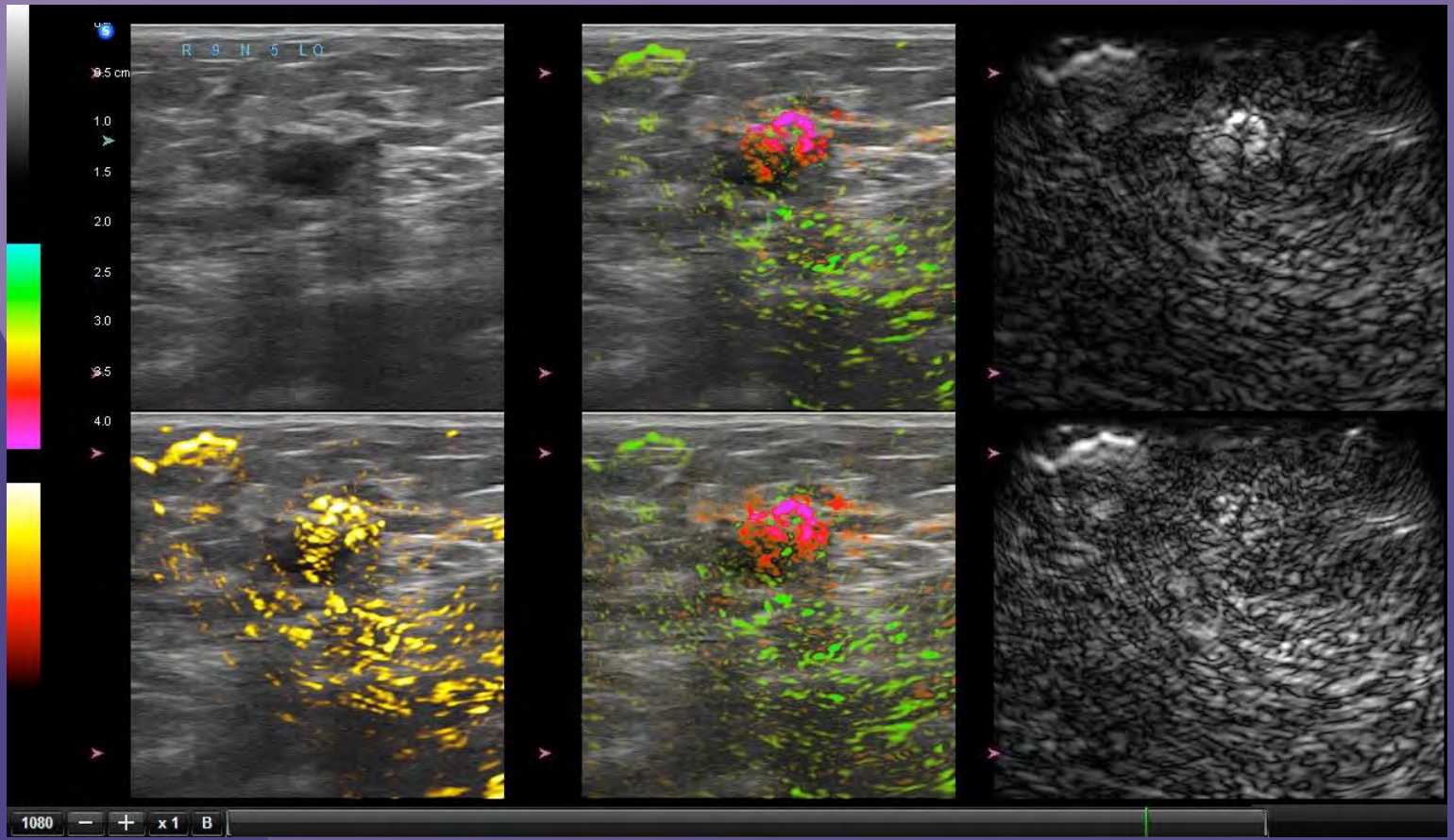
OA



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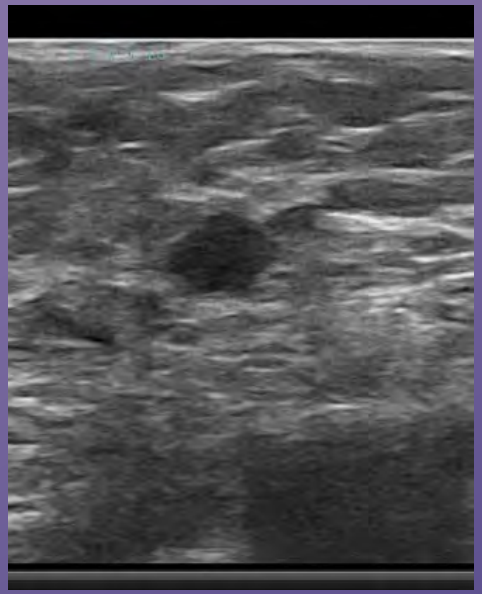
DCIS Grade 2 (Solid Type)

1.1 cm mass in right breast at 9:00, 5 cm from the nipple

- IUS: BI-RADS 4A
- OA: BI-RADS 4C



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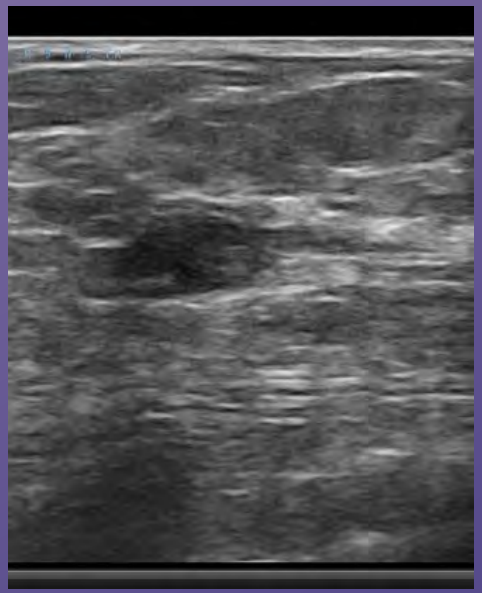

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Results

- Using OA, more BR 2 and 3 categories were assigned for biopsy-proven benign lesions.
- Using OA, for biopsy-proven malignant lesions there were more BR 4c and 5 categories assigned.

Conclusions

- Benign masses classified as BR 3, 4a, and 4b by IUS and CDU could be downgraded 1-3 categories while malignant masses may be upgraded one to two categories with OA.
- If the findings are confirmed by the Pivotal study, OA findings may help identify masses that do not require biopsy, and in some cases, even avoid short interval follow-up.
- Conversely, OA findings may increase suspicion and add certainty to the need for biopsies in malignant masses.

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Thank You

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