Innovation to Breast Cancer Detection: A Study of Adjunct SoftVue™ Automated Whole Breast Ultrasound Tomography (SV) to Digital Mammography on Enhancing Lesion Localization and Characterization

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Disclosures

- Delphinus Med. Tech. (DMT), sponsor
- Univ. of Chicago, reader study (grant, consulting fee, travel)
- M Yamashita, reader training (consulting fee)
- Avania, statistical analysis

- Y Jiang, consultant, QT

Background: Breast Cancer Screening in Dense Tissue

- Dense breasts can mask cancer on mammography
- Increasing breast density is associated with an increased risk of breast cancer
  - 4.64-fold (3.64-5.91) for extremely dense compared with fatty

Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E, Jong RA, Hislop G, Chiarelli A, Minkin S, Yaffe MJ. Mammographic density and the risk and detection of breast cancer. N Engl J Med. 2007 Jan 18;356(3):227-36. doi: 10.1056/NEJMoa062790. PMID: 17229950

Background: Breast Cancer Screening in Dense Tissue

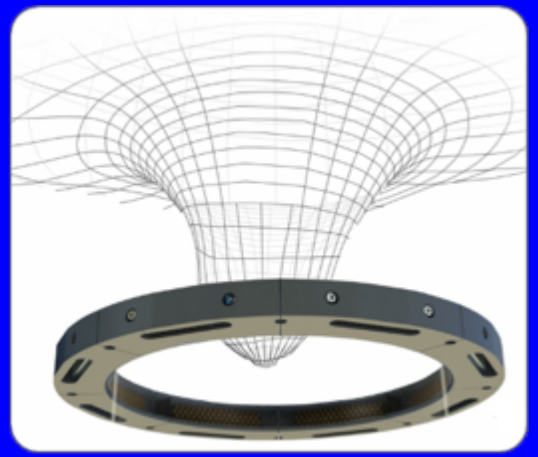
- Adding ultrasound to mammography increases cancer detection:

- Limitations of handheld ultrasound
  - Shortage of trained technologists
  - Small field of view
  - Operator dependence
  - Increase in false positives; Reduced specificity
  - Increased recall rates; High rate of unnecessary biopsies

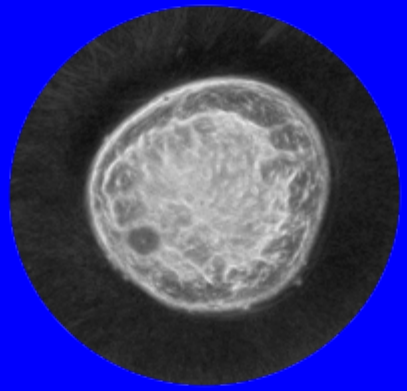
- Limitations of automated ultrasound
  - Several thousand images to review
  - Long interpretation time
  - False positives
  - Learning curve

Vourtsis A, Berg WA. Breast density implications and supplemental screening. Eur Radiol. 2019 Apr;29(4):1762-1777. doi: 10.1007/s00330-018-5668-8. Epub 2018 Sep 25. PMID: 30255244; PMCID: PMC6420861.

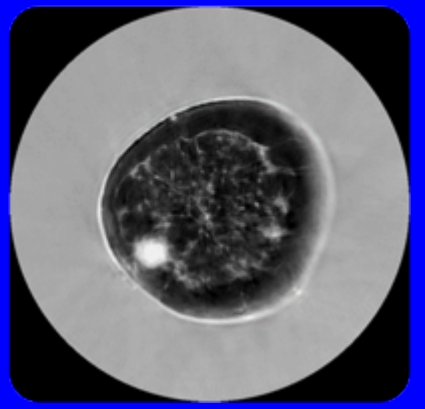
SoftVue by Delphinus



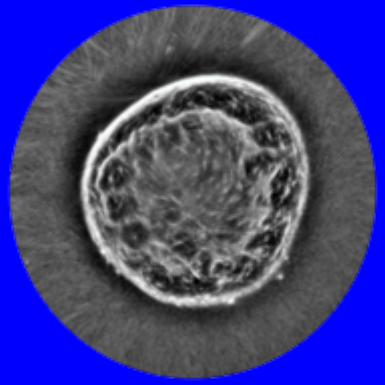
Wafer
(fat suppressed reflection)



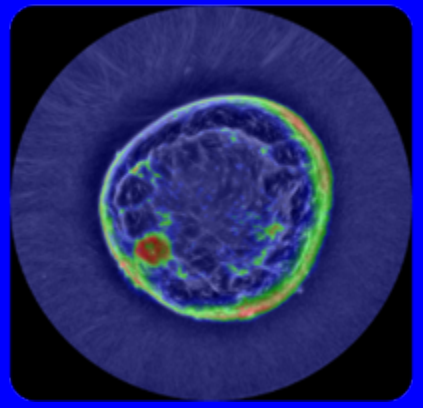
Sound Speed

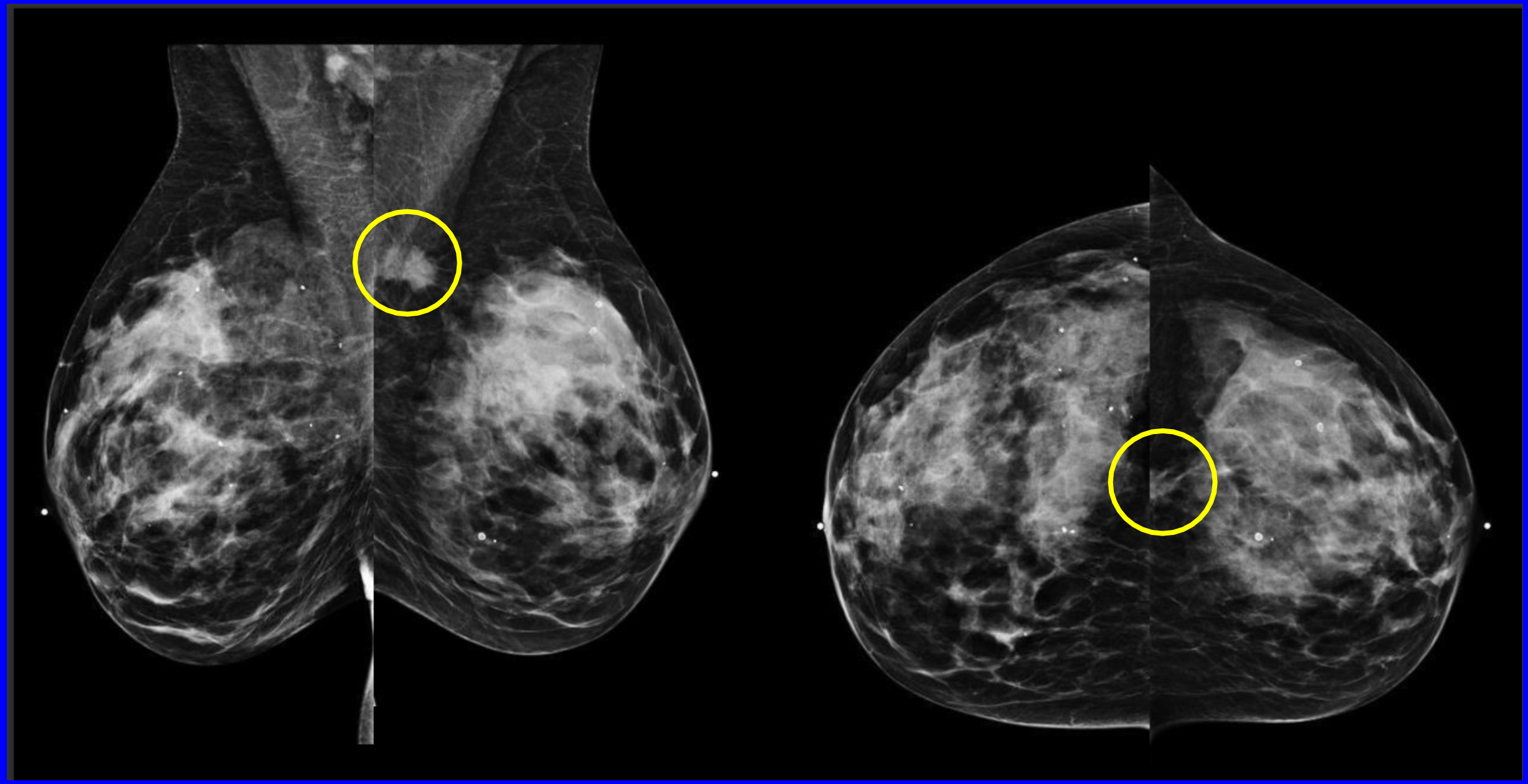


Reflection
(B-mode)



Stiffness Fusion





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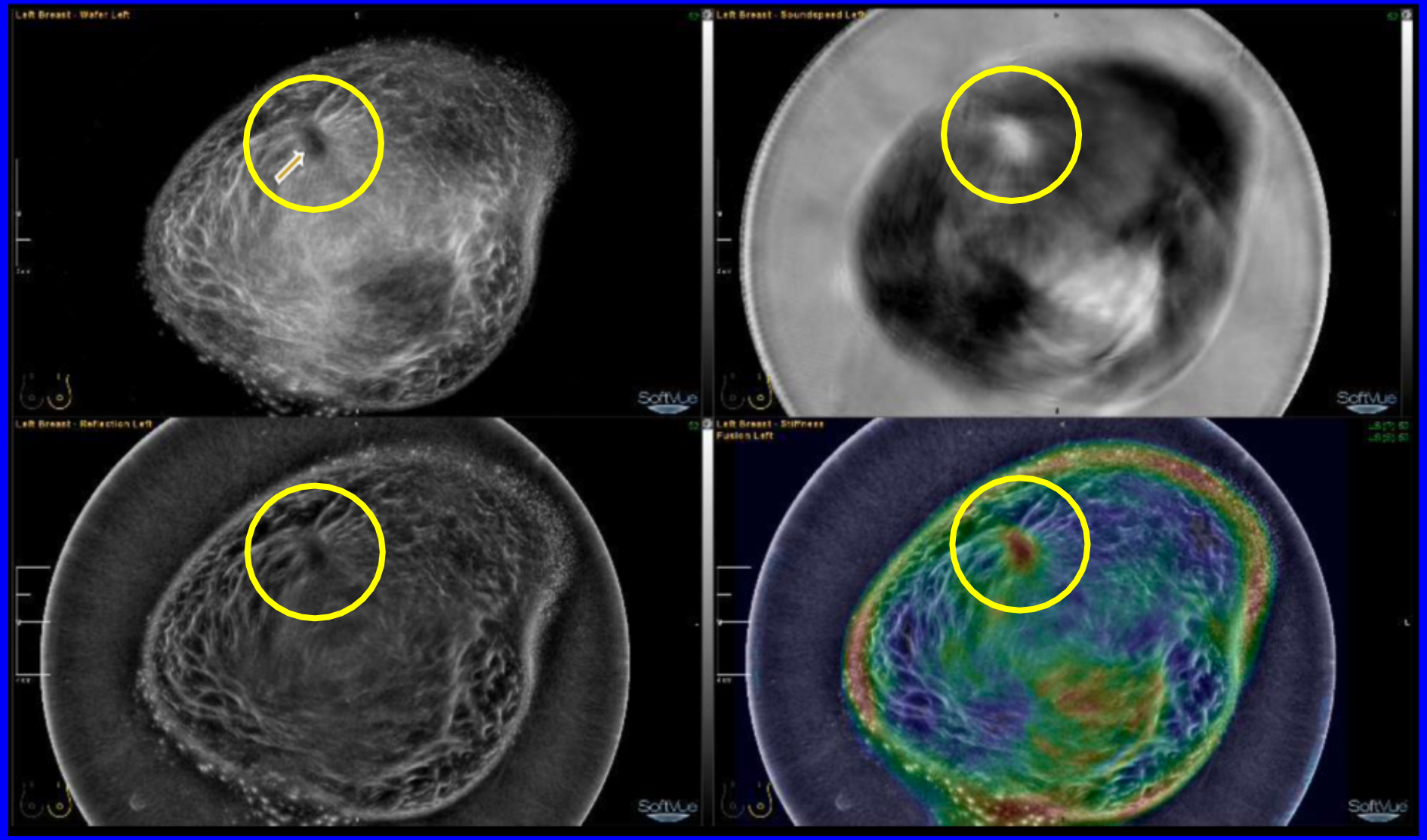


Reflection (B-mode)

Stiffness Fusion

Purpose and Study Endpoint

- Test hypothesis for breast cancer screening
  - FFDM + SoftVue better than FFDM alone

- Multi-reader multi-case (MRMC) reader study
  - Primary endpoint
    - Area under the ROC curve (AUC)
  - Secondary endpoints
    - Sensitivity (superiority test)
    - Specificity (non-inferiority test)

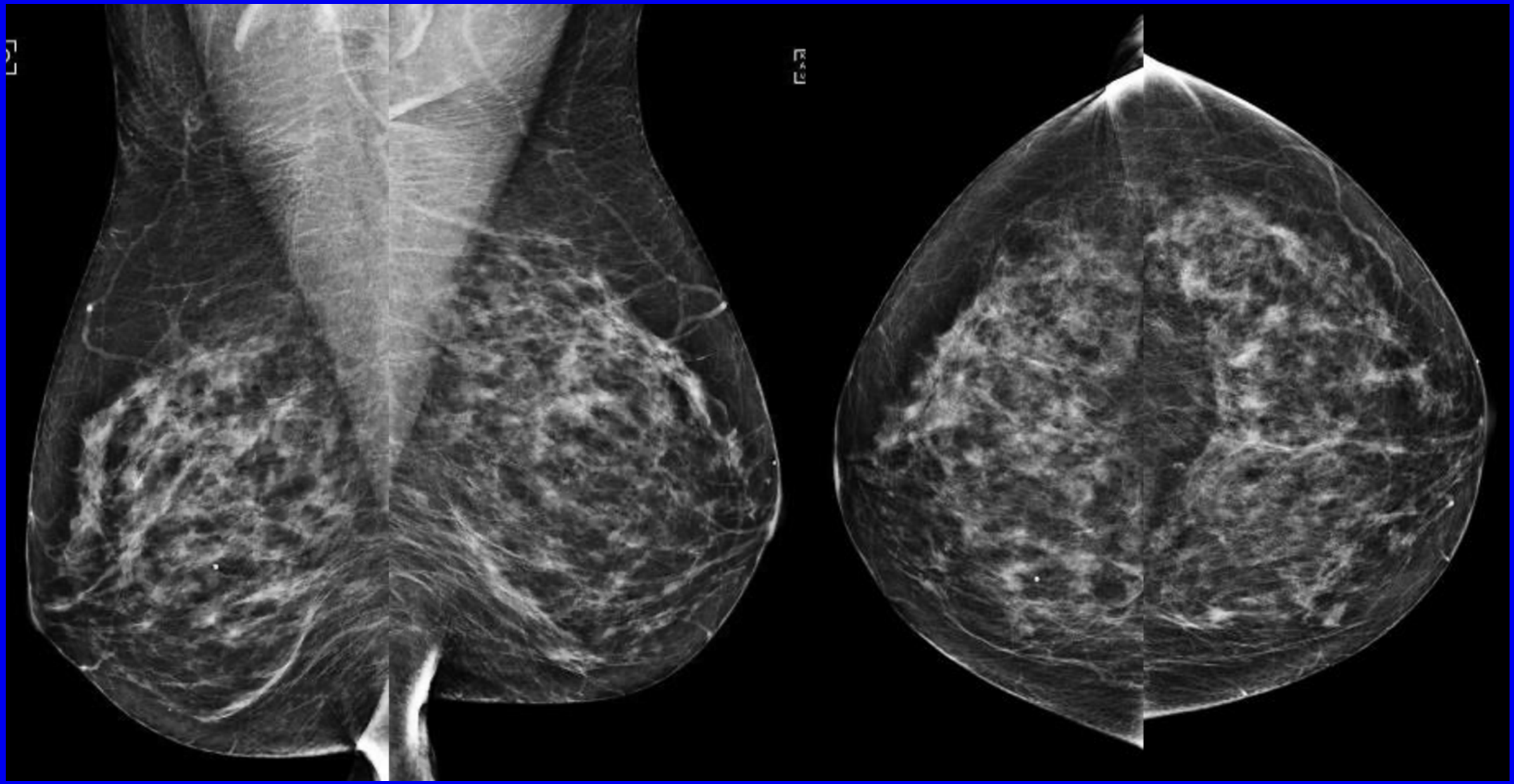
Cases and Readers

- 140 cases (36 cancers, 104 random-sample non-cancers)
  - 4-view screening FFDM
  - All BI-RADS density c or d
  - All patients had SoftVue scans
- 32 MQSA-qualified radiologists from the United States
  - Academic, private, community
  - Breast imaging experience 2–37 years
  - Mammograms/Year median 5900 (range 500–25k)
  - Geographically diverse

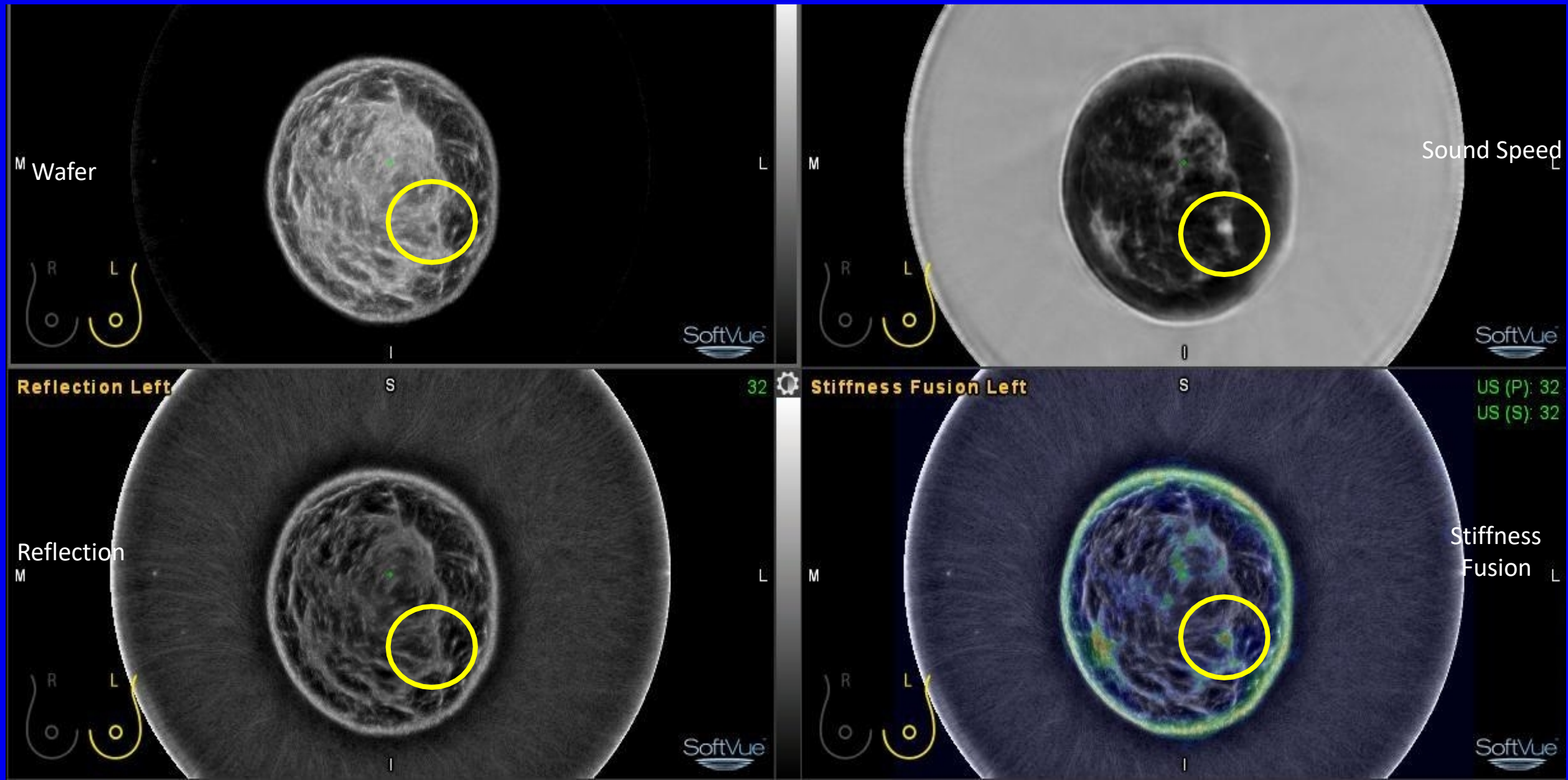
Study Design

- Read cases individually in randomized order
- No more than 3 findings per case
- Malignancy score (0–100) — ROC analysis
- BI-RADS assessment (1–5) — sensitivity, specificity

Reader Workflow: 4 views of FFDM

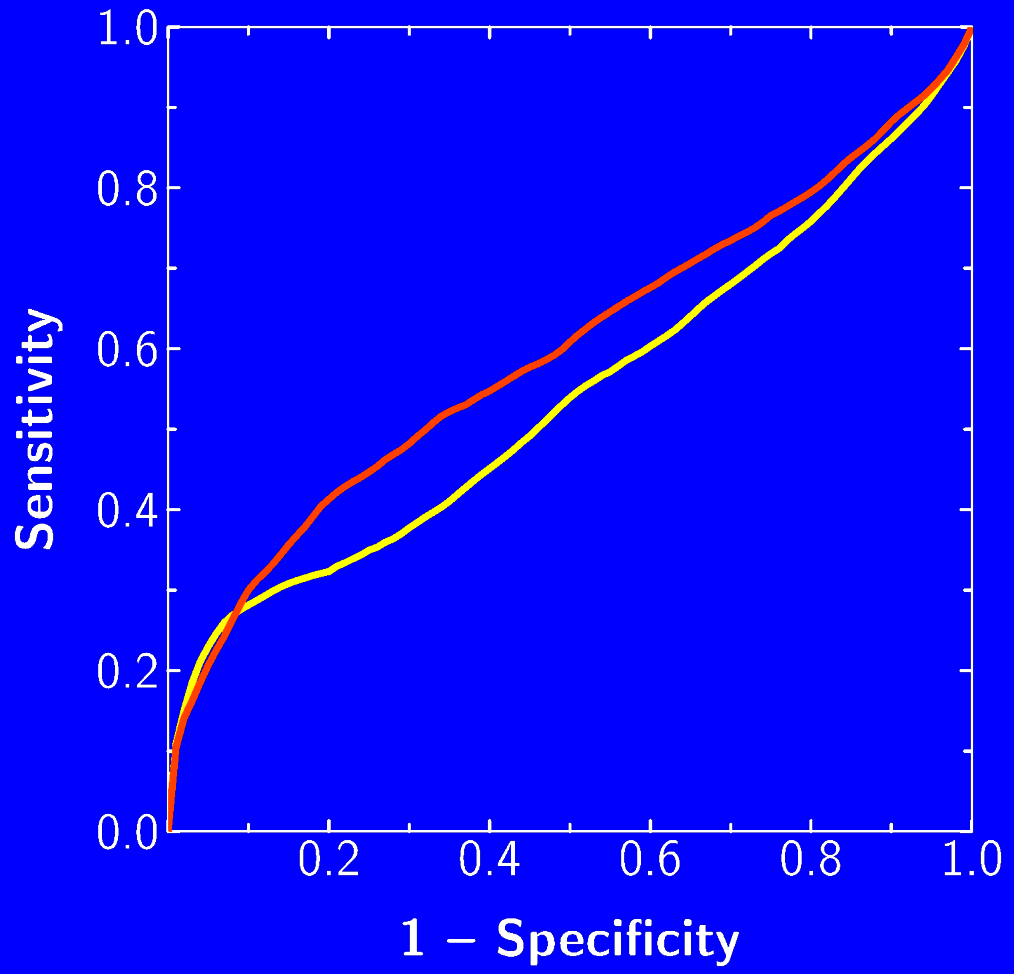


Reader Workflow: 4 Sequences of SoftVue



ROC Results

32 Readers, 140 Cases, Lesion Localization (15-mm)



	AUC
FFDM	0.54 ± 0.05
FFDM + SoftVue	0.60 ± 0.05
95% CI of Δ	(0.006, 0.103)
p-value	0.03
Stat. Sig.	*
Null Hypothesis	$\Delta = 0$

MRMC statistical analysis allows for generalization of readers and cases

Sensitivity, Specificity: Biopsy

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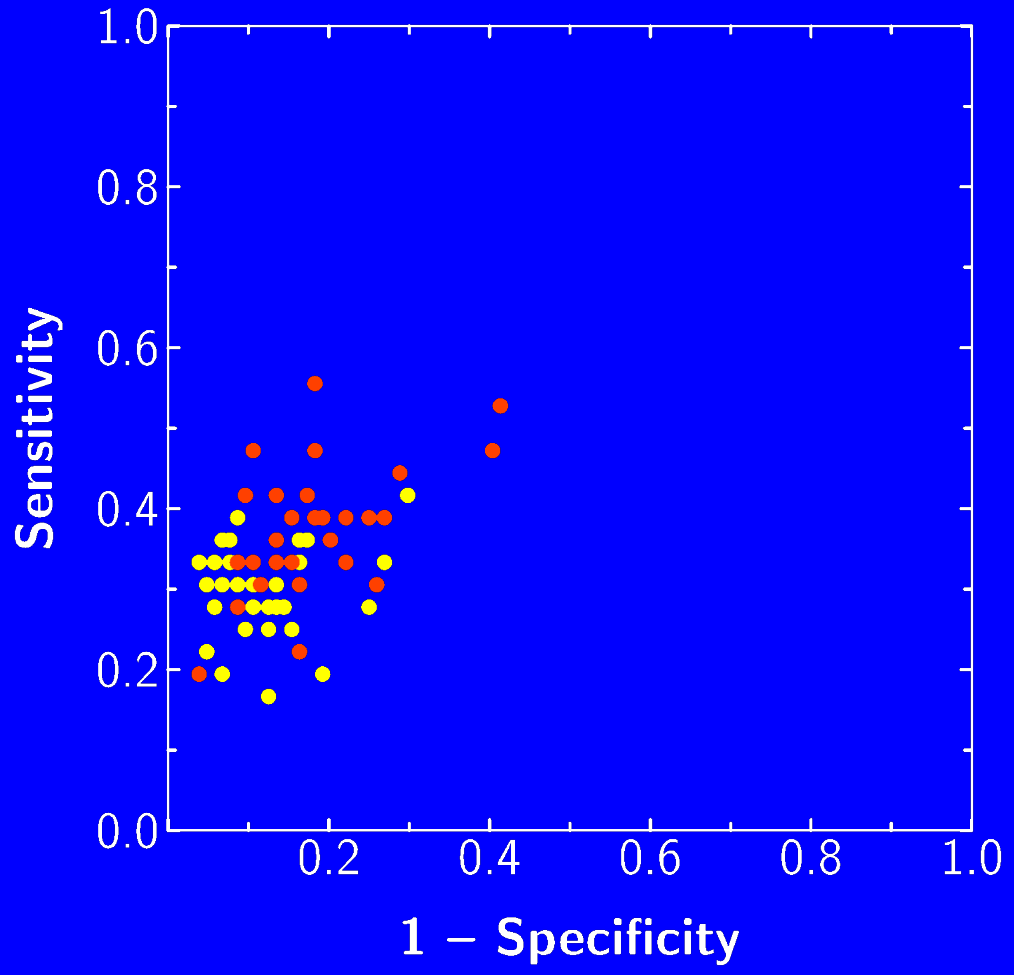

	Sensitivity	1–Specificity
FFDM	30 ± 6%	12 ± 2%
FFDM+SoftVue	37 ± 6%	18 ± 3%
95% CI of Δ	(0.7%, 14%)	(2%, 9%)
p-value	0.03	0.004
Stat. Sig.	*	*
Null Hypothesis	Δ = 0%	Δ > 10%

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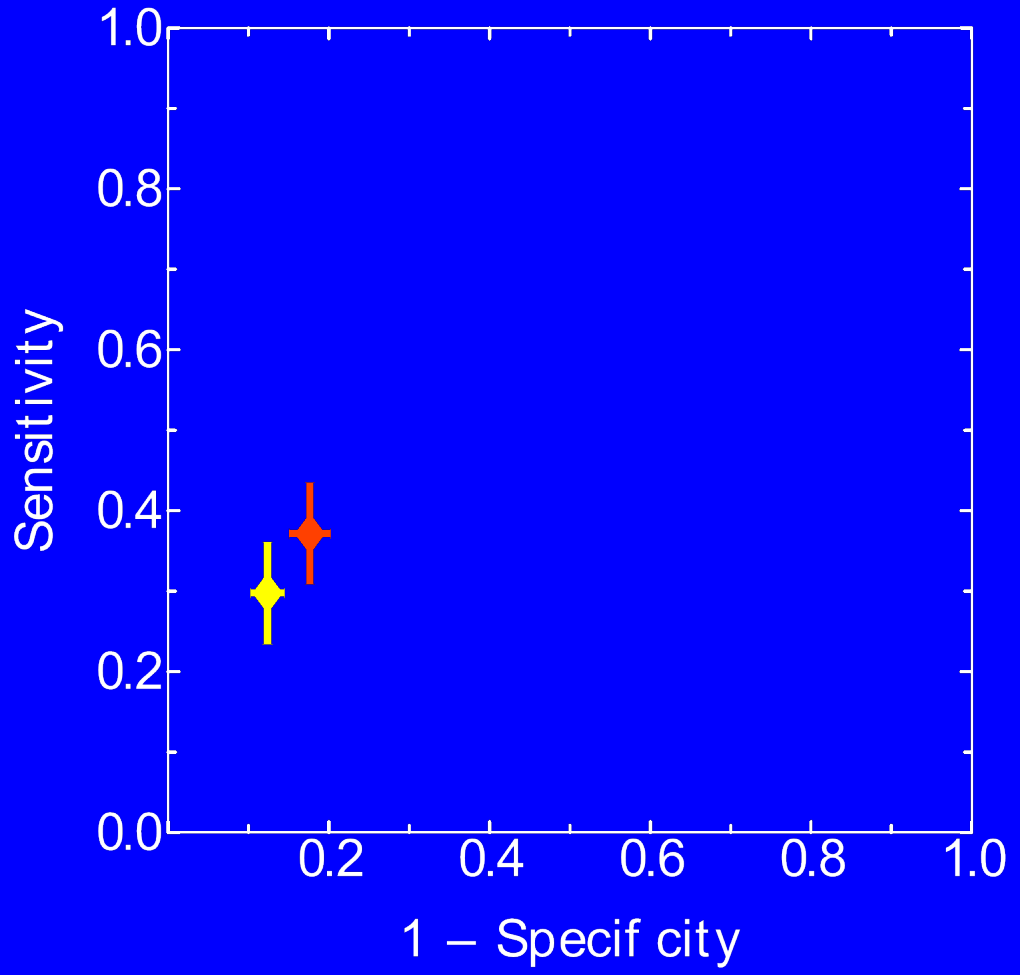

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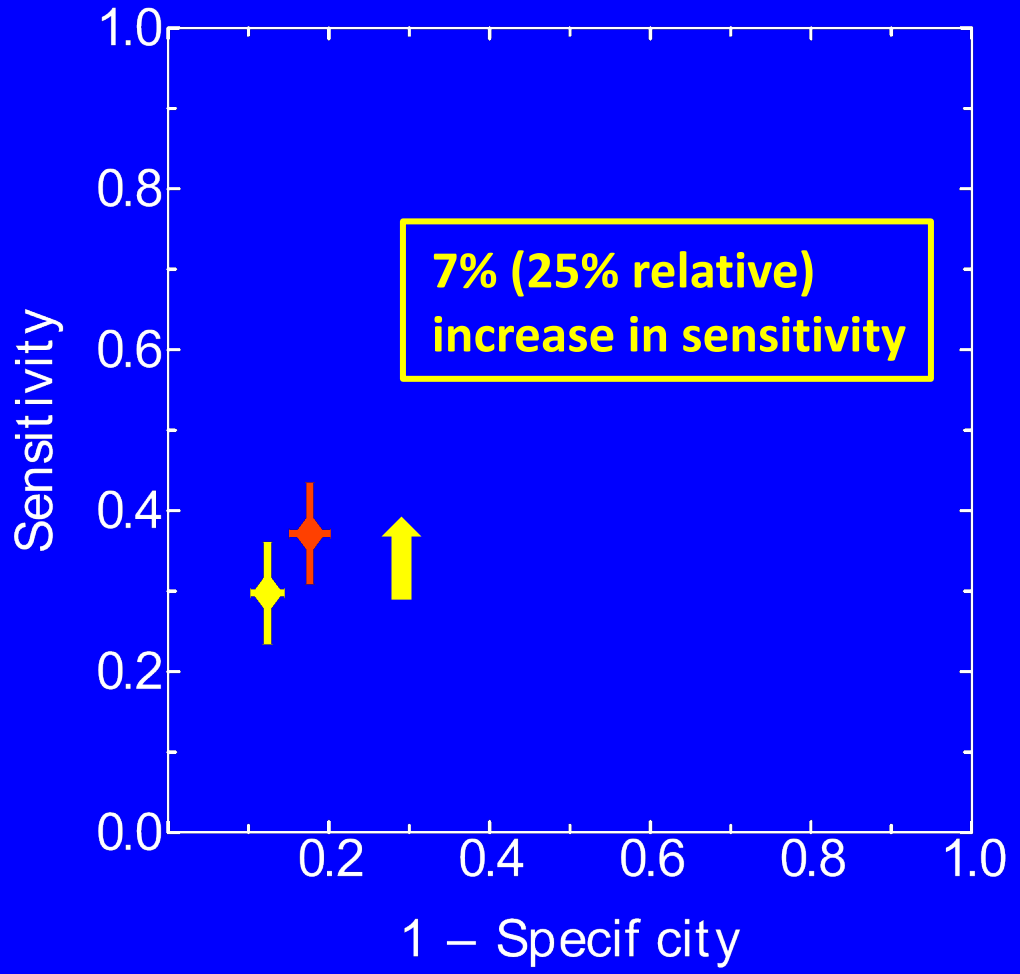

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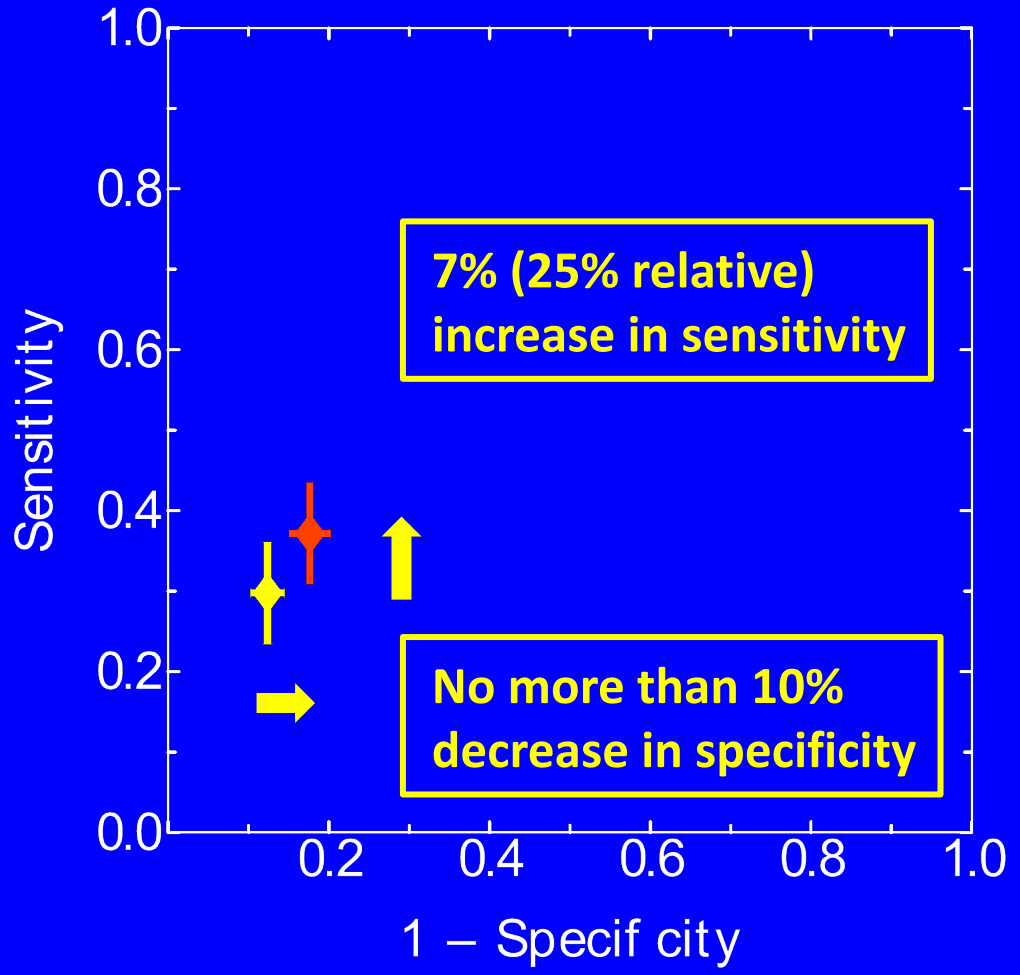

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Sensitivity, Specificity: Short-term Follow-up or Biopsy

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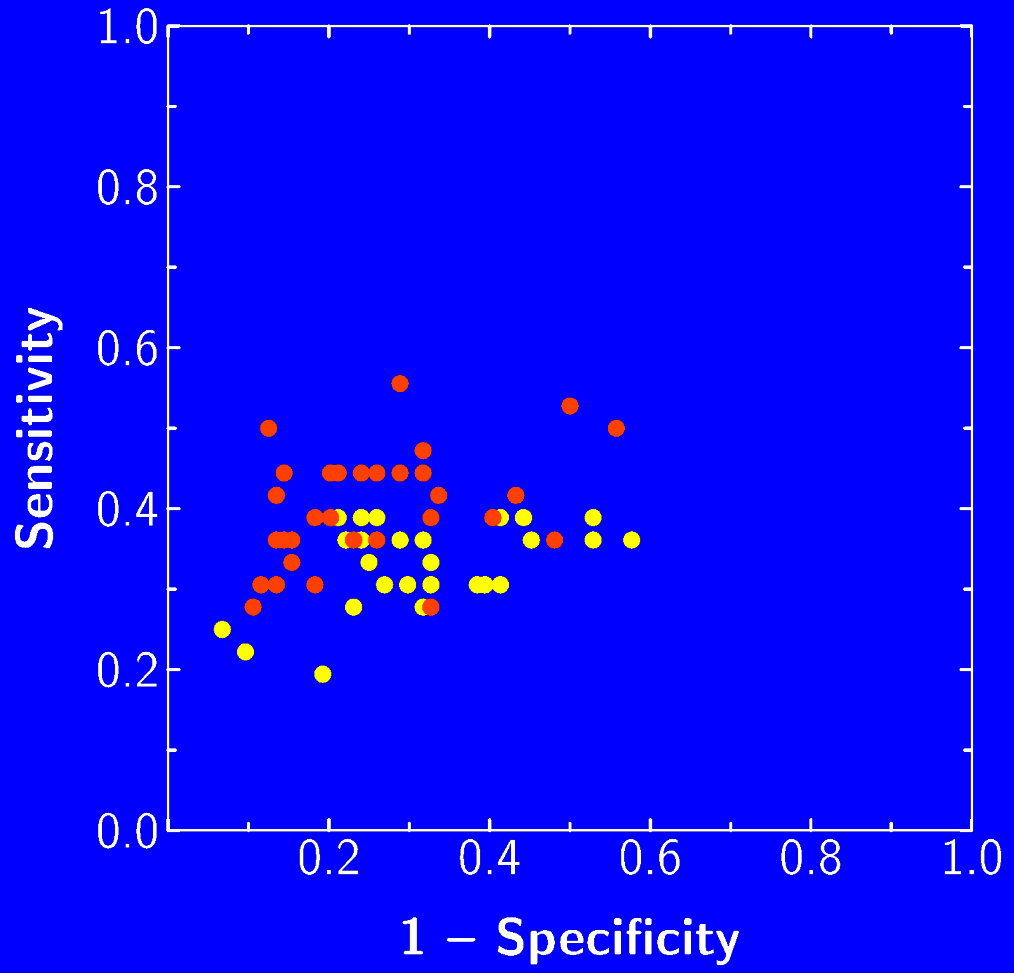

	Sensitivity	1–Specificity
FFDM	33 ± 7%	31 ± 3%
FFDM+SoftVue	40 ± 6%	25 ± 3%
95% CI of Δ	(-1%, 14%)	(-11%, -0.3%)

Sensitivity, Specificity: Short-term Follow-up or Biopsy

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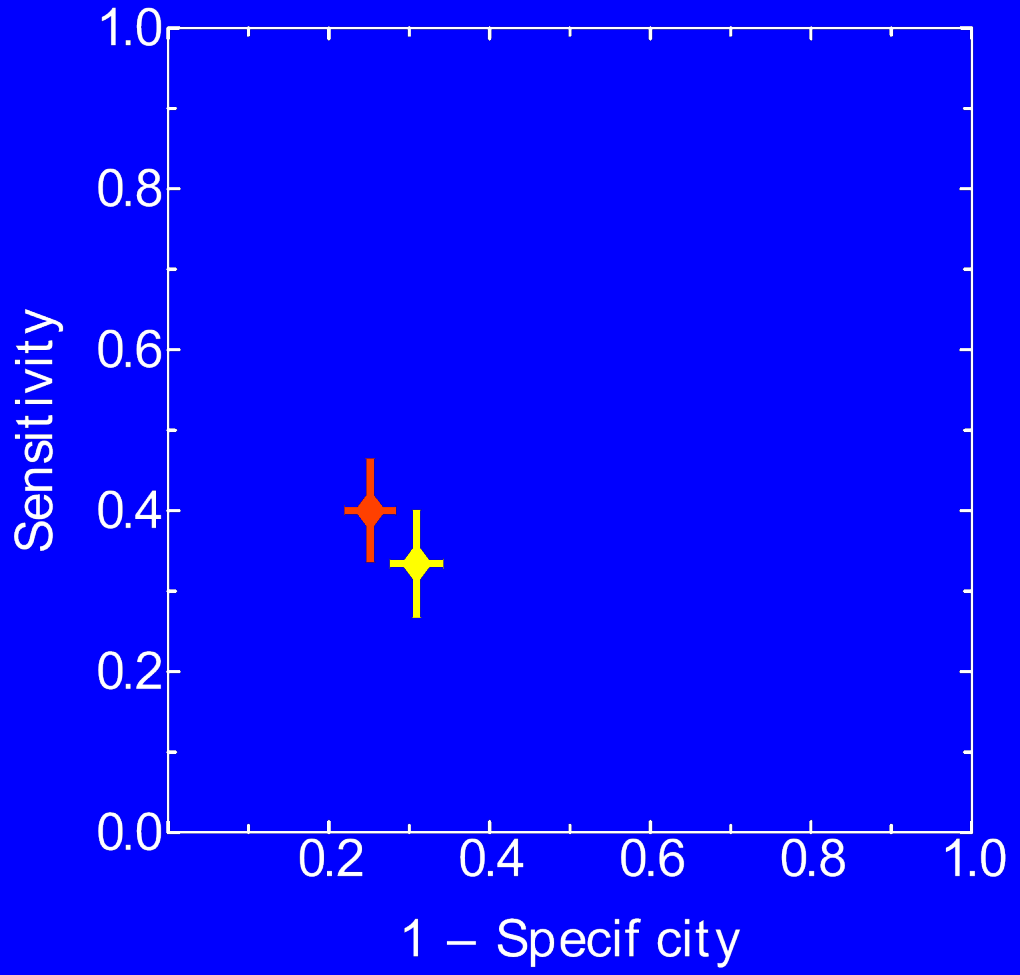

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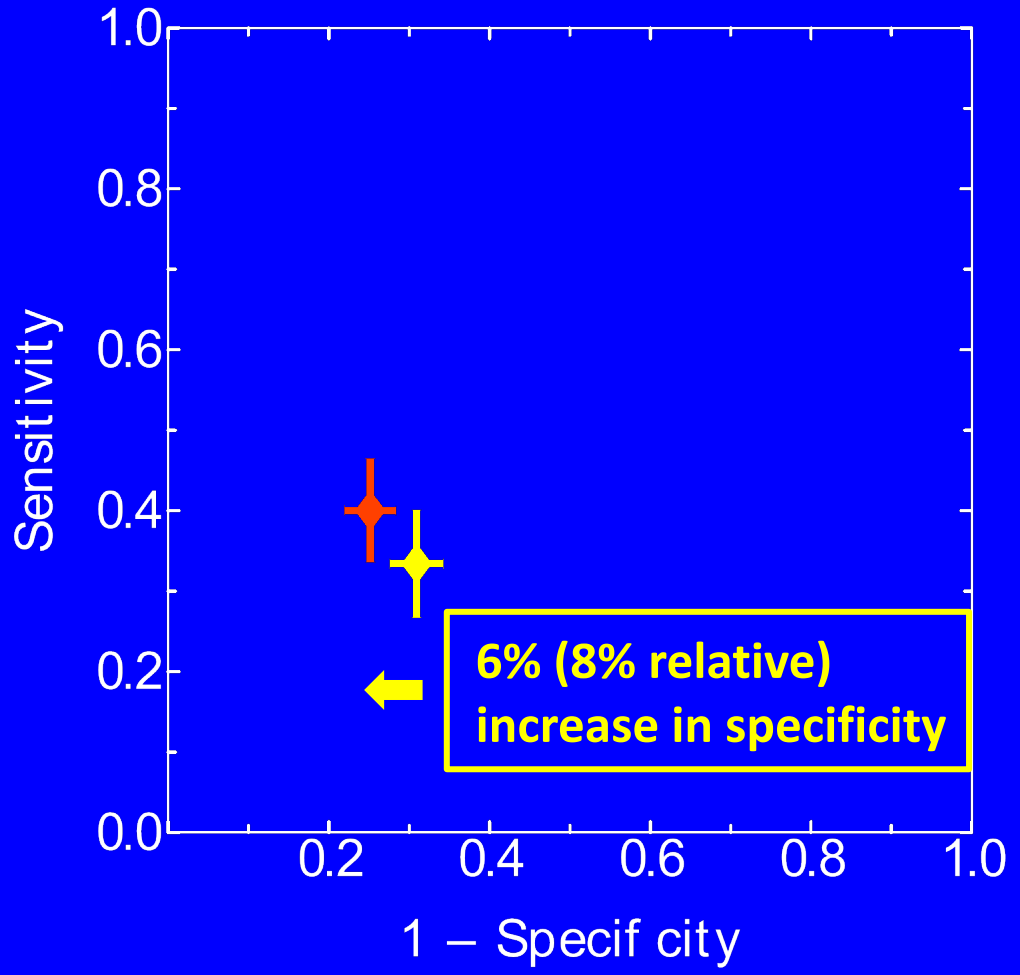

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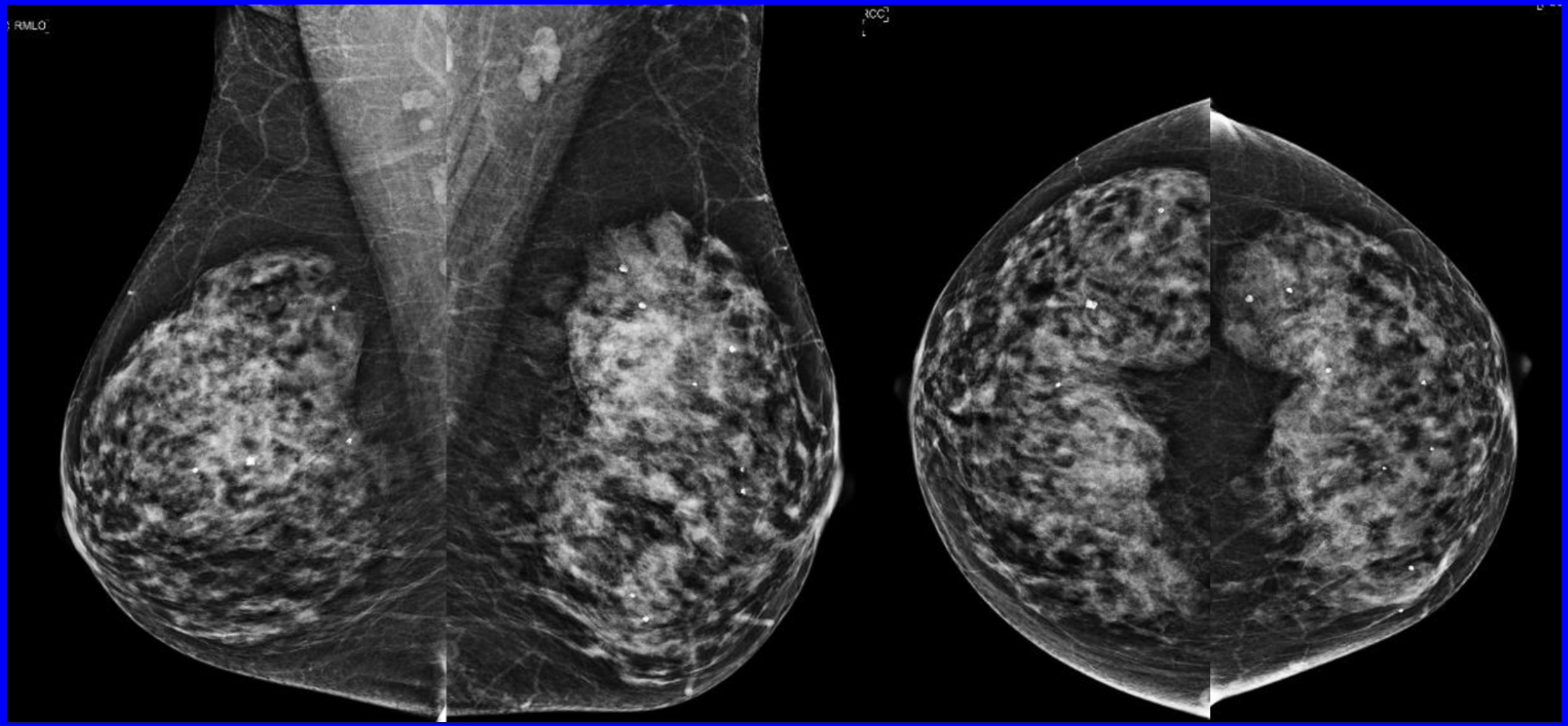
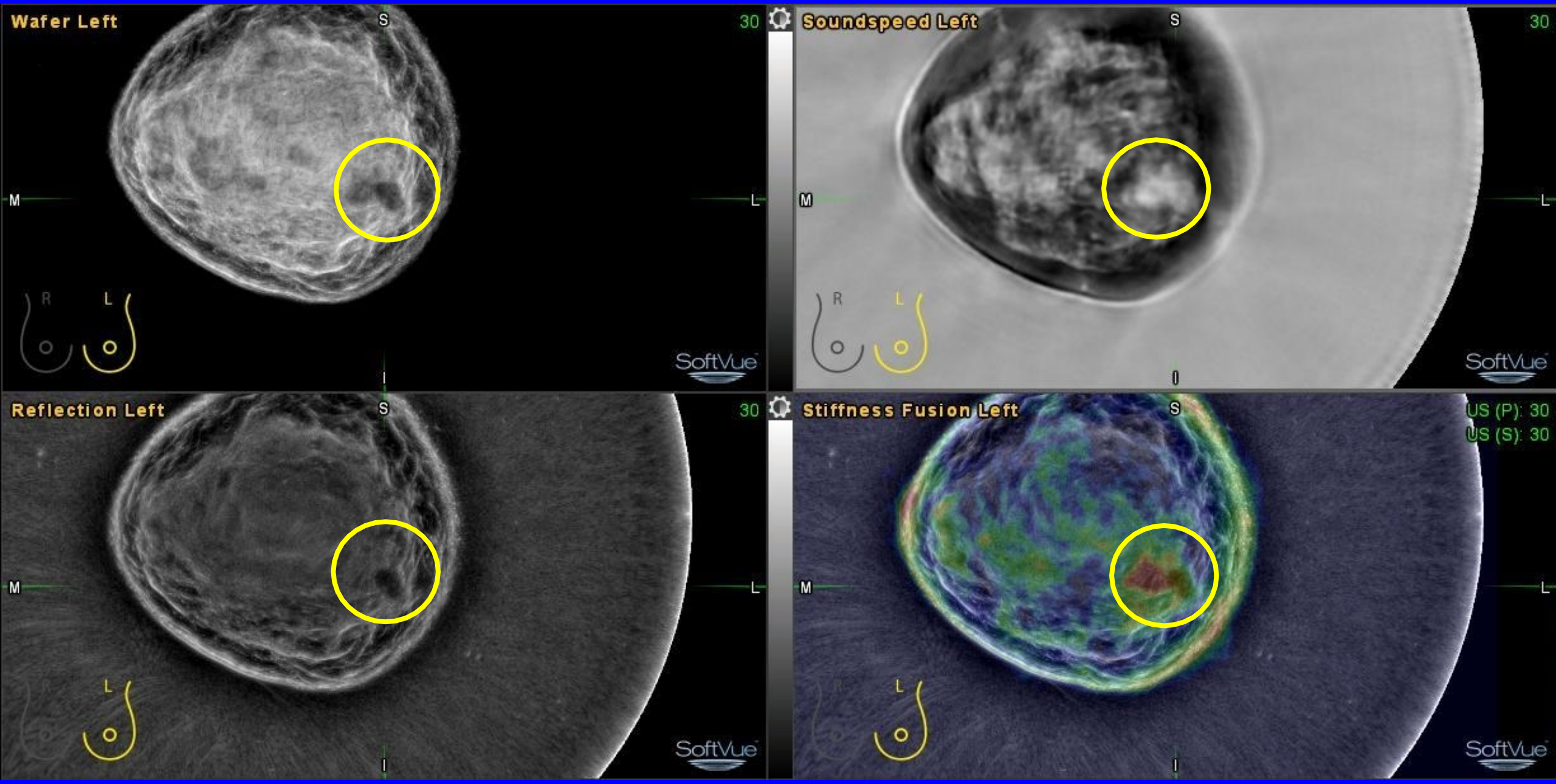
BI-RADS Density C, Negative FFDM




Wafer Left
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30
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R
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SoftVue
Soundspeed Left
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30
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SoftVue
Reflection Left
S
30
M
L
I
L
SoftVue
Stiffness Fusion Left
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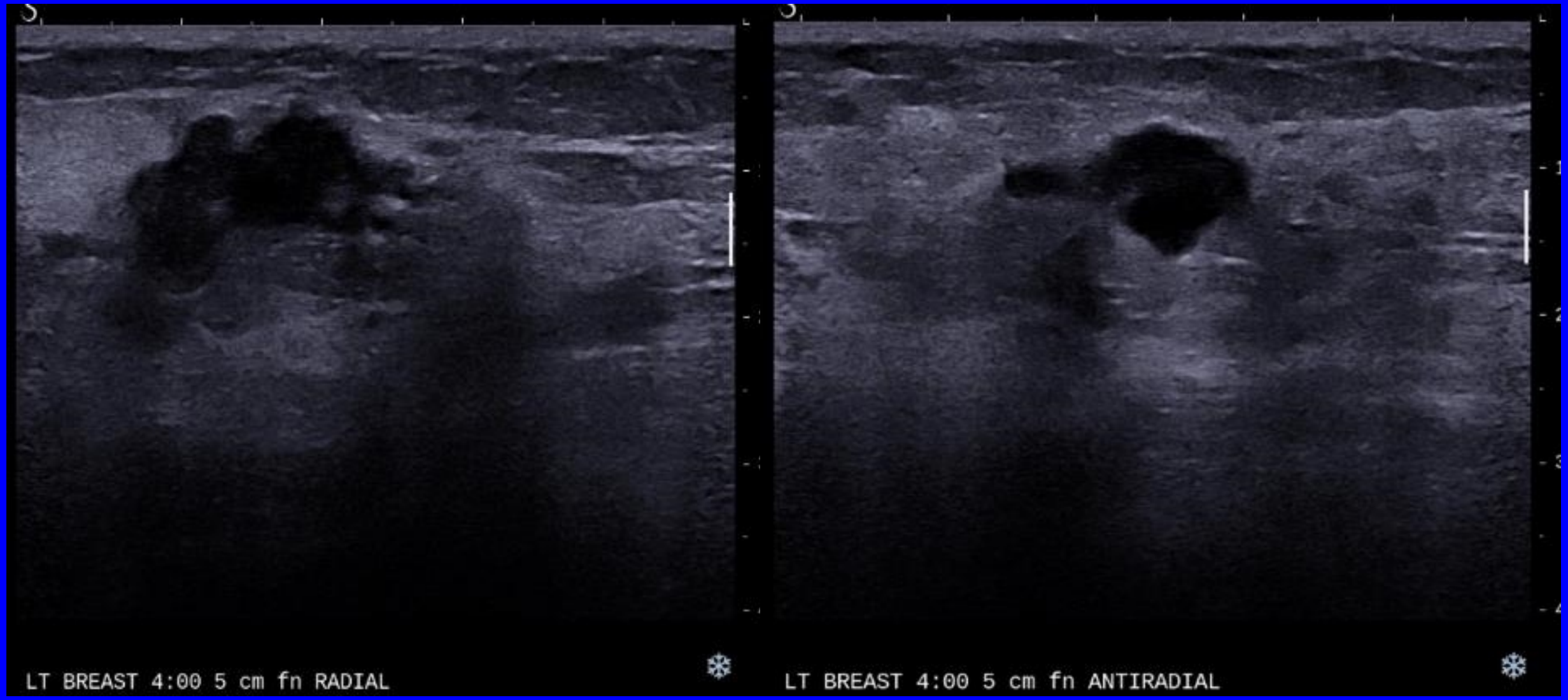
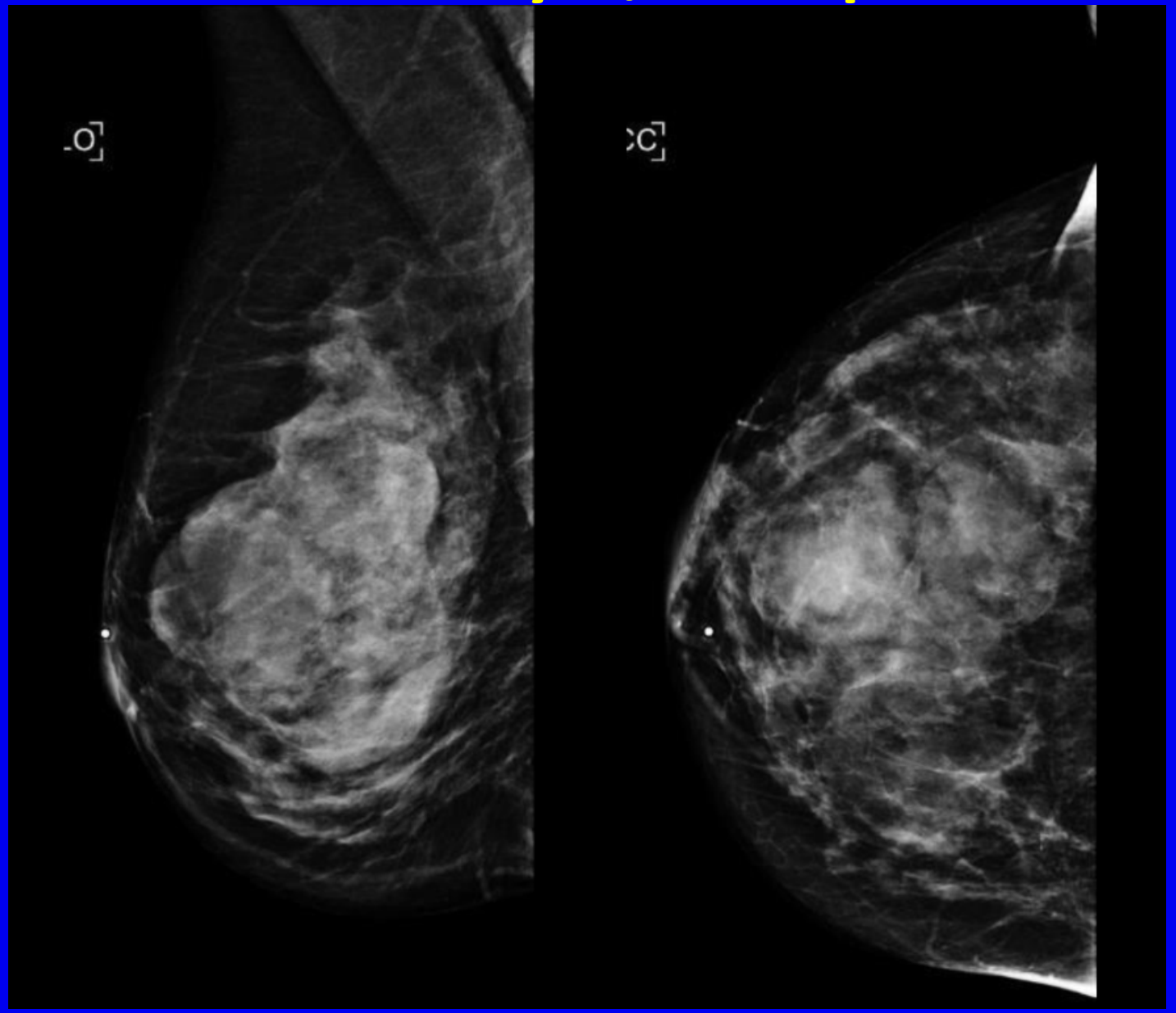
US (P): 30
US (S): 30
M
L
I
L
SoftVue

Invasive Ductal Carcinoma

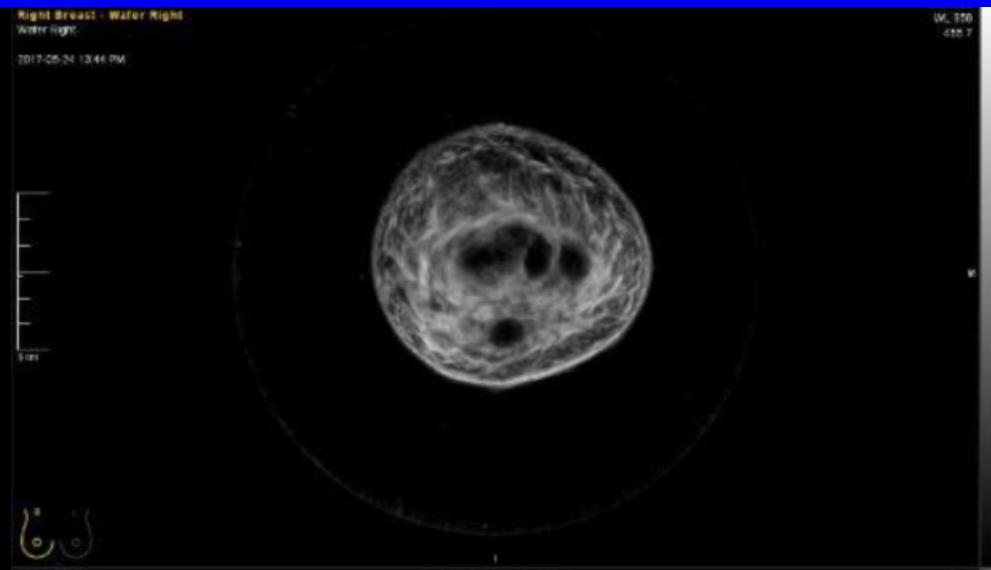


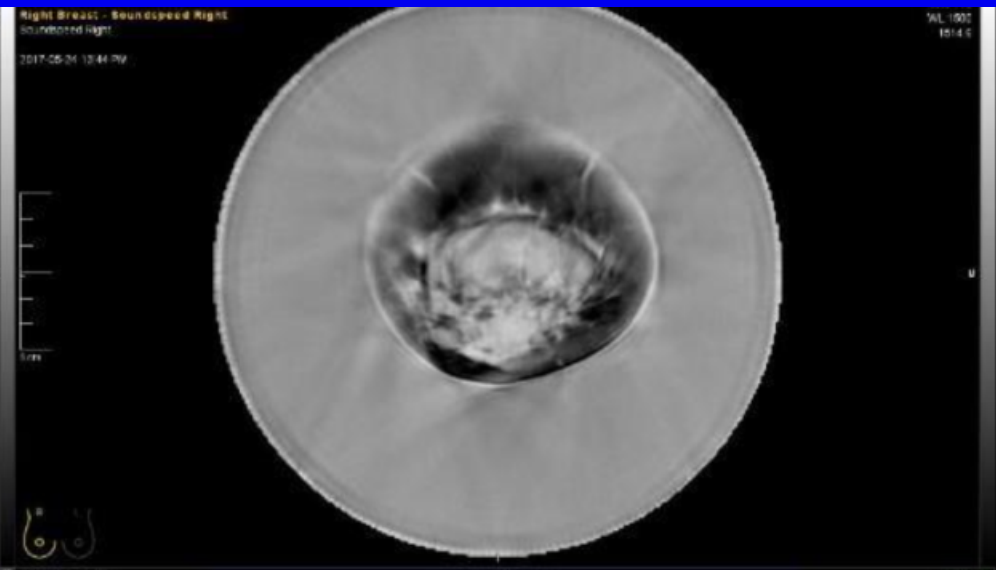
BI-RADS Density D, Multiple Masses



RT
Slice #16

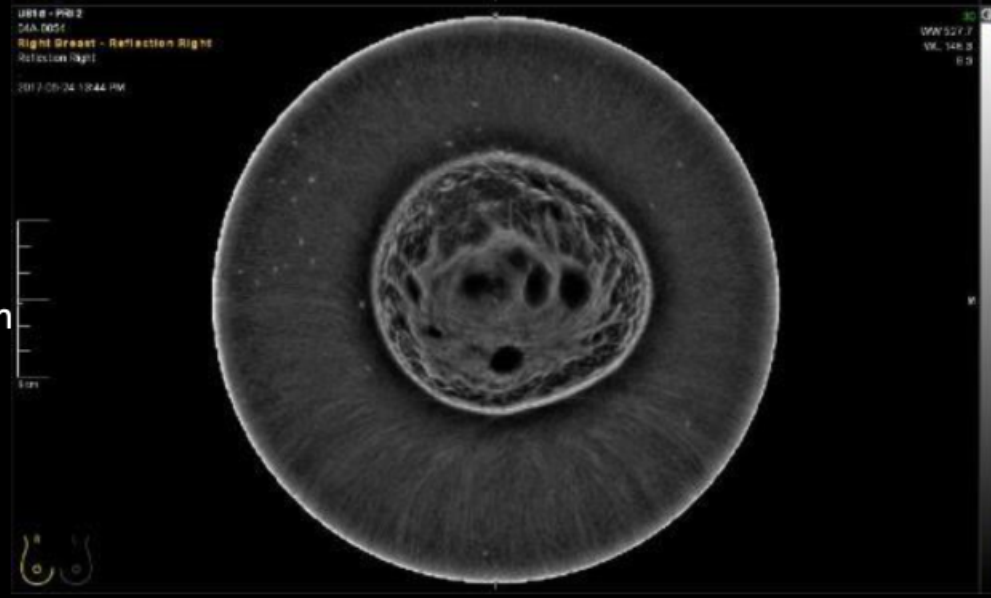
Wafer

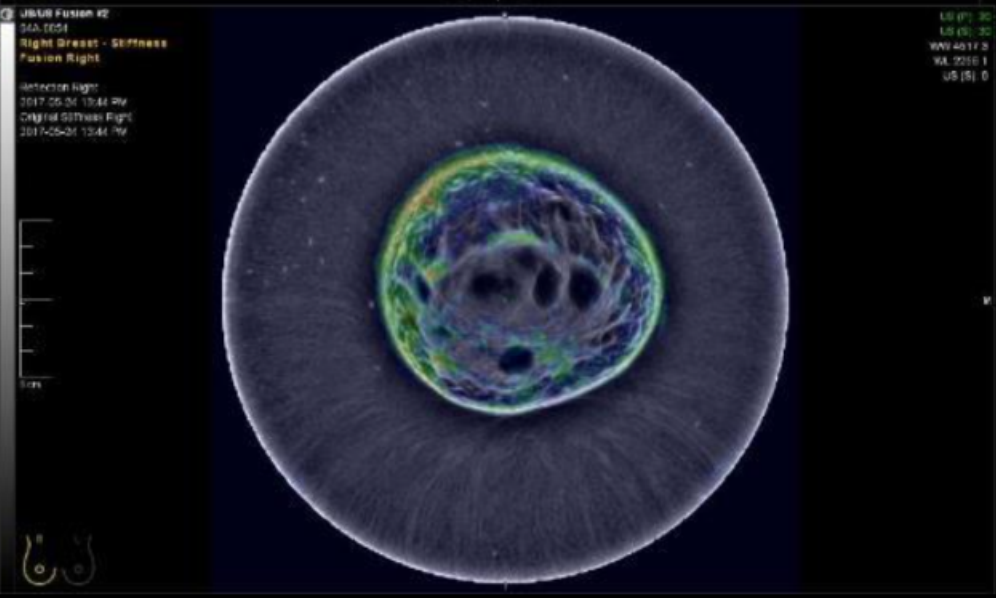




Sound Speed

Reflection





Stiffness
Fusion

Multiple Cysts on HHUS

Conclusion

Adding SoftVue to screening FFDM for dense breast can improve cancer detection without decreasing specificity.