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Imaging Young Women With Breast Cancer: Challenges and Opportunities

Samantha L. Heller

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Disclosures

None

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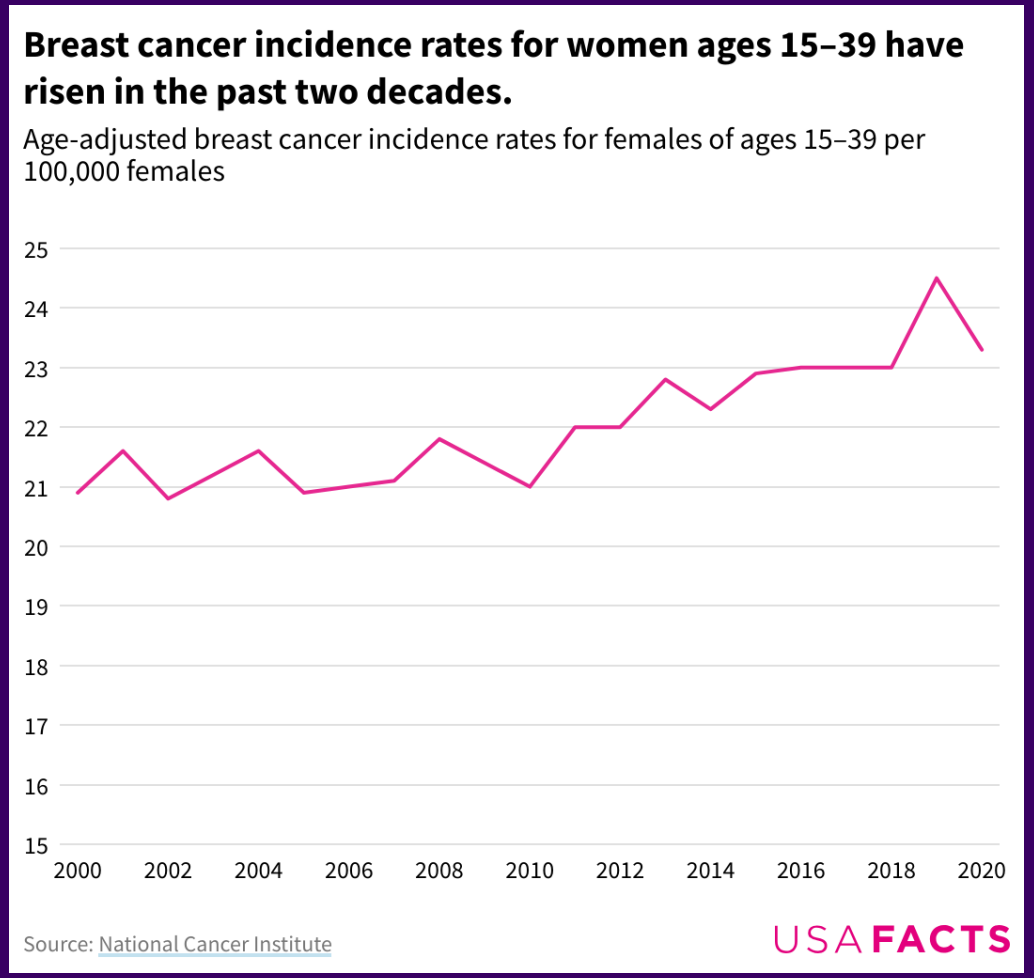
Background

- BC is the leading cause of cancer death in YW
- Increasing incidence of advanced breast cancer in women<40
- Young age at dx=risk factor for poor prognosis



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Background

- YW with surgically treatable BC have >recurrence/death at any clinical stage
- Higher BC-specific mortality rate results from:
  - Typically more-aggressive tumors (HER2-enriched, TN tumors)
  - More advanced disease stage at dx, even with “more favorable” luminal cancers

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Lian W, Fu F, Lin Y, et al. Sci Rep 2017

Purpose

1. Review imaging based tools for breast cancer detection
2. Discuss imaging-based detection and advances in young women with known >average risk of BC
3. Discuss imaging-based detection in young women with unknown risk
4. Imaging focus

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Part 1: Young Women/Known Risk

Imagine the perfect (breast cancer) screening test

Inexpensive

Easy to Administer

Specific

Detects Disease Early

Sensitive

Improves Outcomes/ Decreases mortality

Tolerable/ Safe

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Mammography

- [x] Improves outcomes
- [x] Inexpensive
- [x] Minimal discomfort
- [x] Easy to administer
- [x] High specificity
- [ ] High sensitivity (?)
- [ ] Detects disease early (?)

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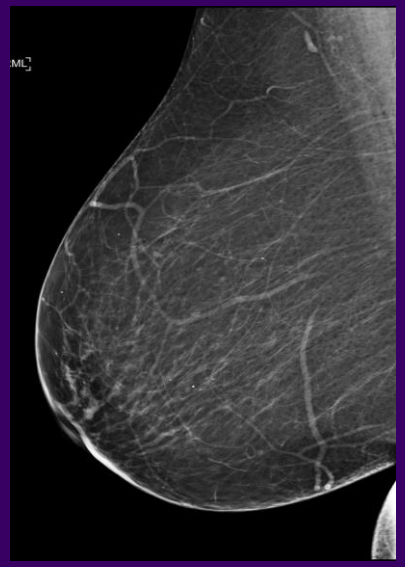
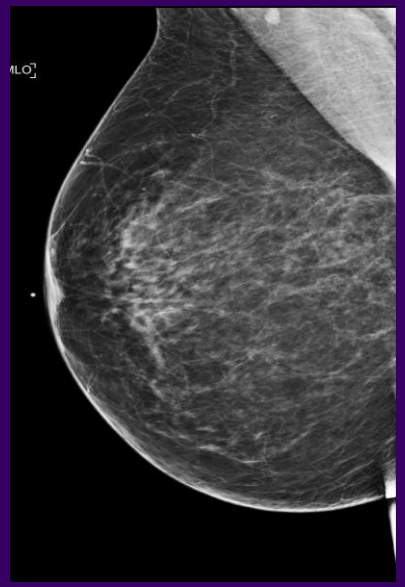
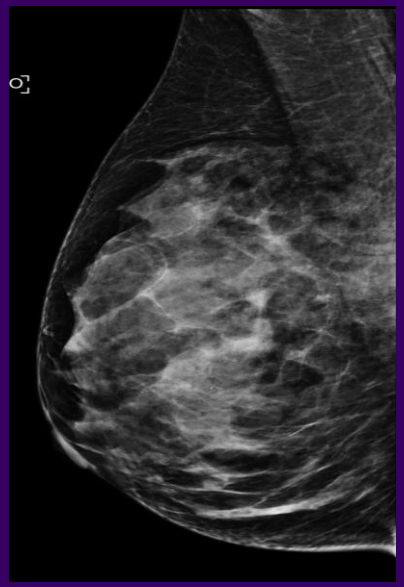
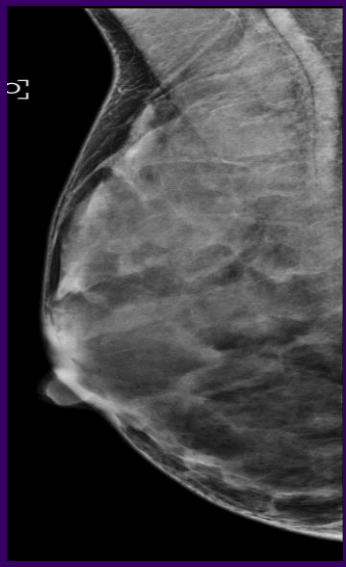
Sensitivity and Density (proportion of FG tissue to Fat)
YW are more likely to be dense

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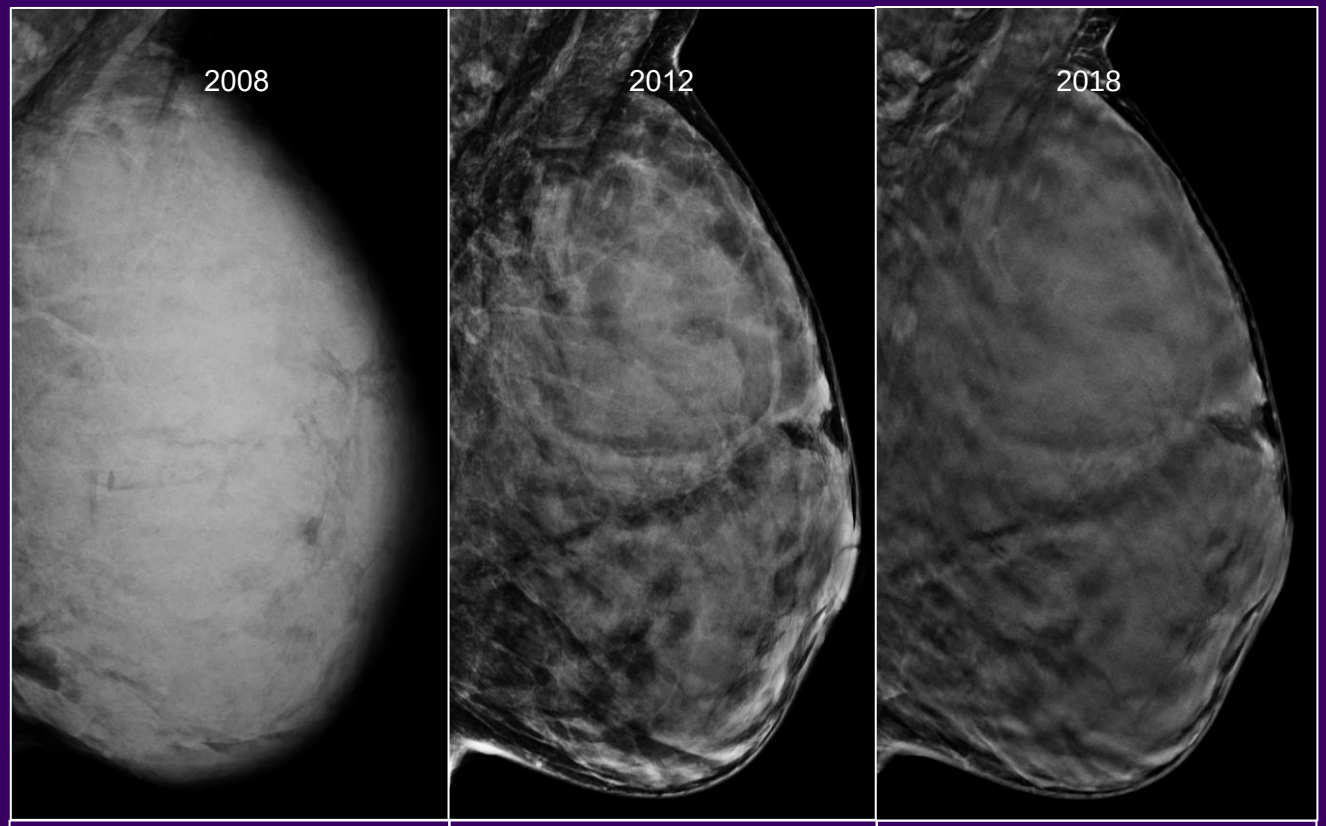
Density

Challenge: Intrinsic Limitations



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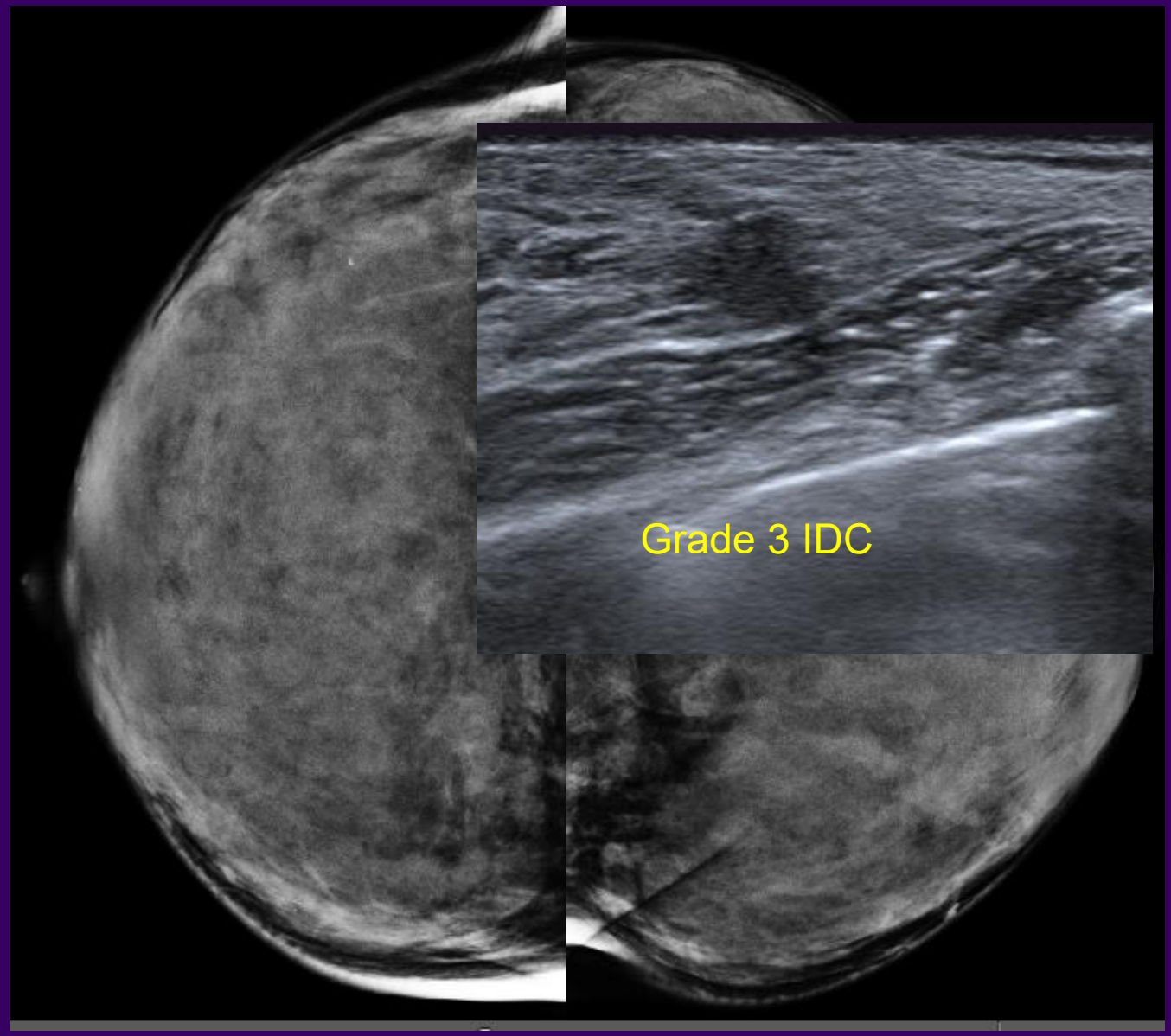

36-year-old woman for high risk screening (family history)

Ultrasound

- Commonly used for screening
- Relatively inexpensive and available
- Mammo CDR 4-5/1000
- US incremental CDR 2-4/1000*
- Usually invasive, small, node negative

*varies by study, population, risk level

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Gao Y et al. RG 2021; Ohuchi N et al. Lancet 2016; Corsetti V et al. Eur J Cancer 2008; Berg WA et al. JAMA 2012

Ultrasound

- Operator dependent
- Increased FPs vs. mammo
- Increased biopsy rate vs mammo (>5x mammo/1000)
- Lack of evidence re: mortality reduction or disease free survival benefit
- No benefit if MRI performed

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Scheel JR et al Am J Obstet Gynecol. 2015 Jan; 212(1): 9–17.Gao Y et al. RG 2021; Ohuchi N et al. Lancet 2016; Corsetti V et al. Eur J Cancer 2008; Berg WA et al. JAMA 2012; Lee JM et al . JAMA 2019

MRI

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36-year-old for HR screening

Mammo negative

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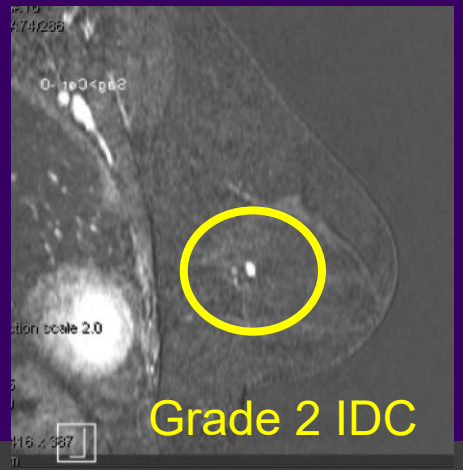
Screening MRI



MORE CANCERS DETECTED ON MRI

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Kuhl CK et al. Rofo 2005; Berg WA et al. JAMA 2012

CDR MRI vs. Mammo

EVA Trial: CDR MRI 16/1000 vs. 7.7/1000 mammo/sono

ACRIN 6666: Incremental CDR MRI 14.7/1000 vs. mammo/sono

Table 4.4 Magnetic Resonance Imaging Cancer Detection and Cancer Yield

Study	Year	Cancers		Interval Cancers	Cancers Found		Cancer Yield for MRI Alone (%)
		Total	*Invasive Breast*		*With MRI*	*With Mammography*	
Sardanelli et al.[24]	2011	52	44	3	48	25*	16/501 (3.2)
Hagen et al.[46]	2007	25	21	5	18	10	8/491 (1.6)
Lehman et al.[8]	2007	6	6	NA (No FUP)	6	2	4/171 (2.3)
Kuhl et al.[36]	2005	43	34	1	39	14†	19/529 (3.6)
Leach et al.[18]	2005	35	29	2	19	6	19/649 (2.9)
Kriege et al.[44]	2004	51‡	44	4	32	18	22/1909 (1.2)
Warner et al.[45]	2004	22	16	1	17	8	7/236 (3.0)

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Heller SL et al. Breast MRI 2014

MRI impact

- Detects small cancers & node negative disease
- Decreases advanced-stage BC incidence in HR women
- Offers longer survival in populations with HR family history and/or HR genetic mutations

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Warner et al., J Clin Oncol. 2011; Evans DG et al., Hered Cancer Clin Pract. 2016; Saadatmand S et al. Lancet Oncol 2019

American Cancer Society MRI Screening Guidelines (2007)

TABLE 1 Recommendations for Breast MRI Screening as an Adjunct to Mammography

Recommend Annual MRI Screening (Based on Evidence*)
BRCA mutation
First-degree relative of *BRCA* carrier, but untested
Lifetime risk ~20–25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history
Recommend Annual MRI Screening (Based on Expert Consensus Opinion†)
Radiation to chest between age 10 and 30 years
Li-Fraumeni syndrome and first-degree relatives
Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives
Insufficient Evidence to Recommend for or Against MRI Screening‡
Lifetime risk 15–20%, as defined by BRCAPRO or other models that are largely dependent on family history
Lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH)
Atypical ductal hyperplasia (ADH)
Heterogeneously or extremely dense breast on mammography
Women with a personal history of breast cancer, including ductal carcinoma in situ (DCIS)
Recommend Against MRI Screening (Based on Expert Consensus Opinion)
Women at < 15% lifetime risk

*Evidence from nonrandomized screening trials and observational studies.
†Based on evidence of lifetime risk for breast cancer.
‡Payment should not be a barrier. Screening decisions should be made on a case-by-case basis, as there may be particular factors to support MRI. More data on these groups is expected to be published soon.

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Saslow D et al. CA Cancer J Clin 2007

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Why not screen everyone with MRI?

More FPs
More Recalls
More Biopsies

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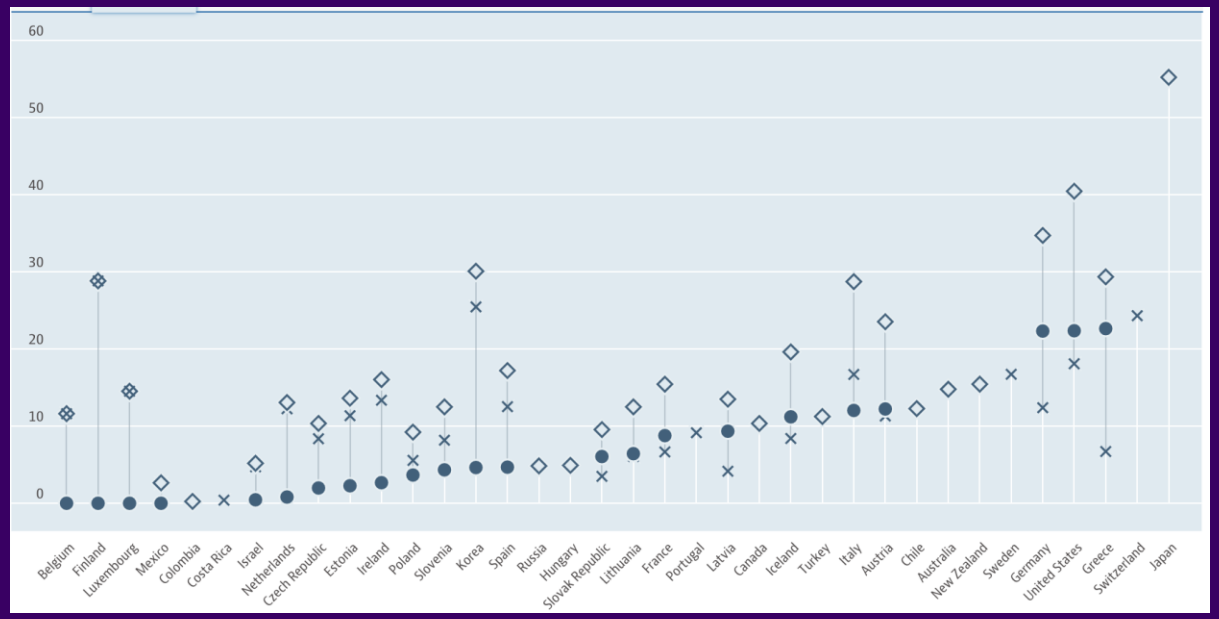
Global: MRI Units in Selected Countries

Per 1,000,000 inhabitants



Many studies show low uptake of MRI screening among eligible high risk women, even at sites with onsite MR availability (6.6% in one study)

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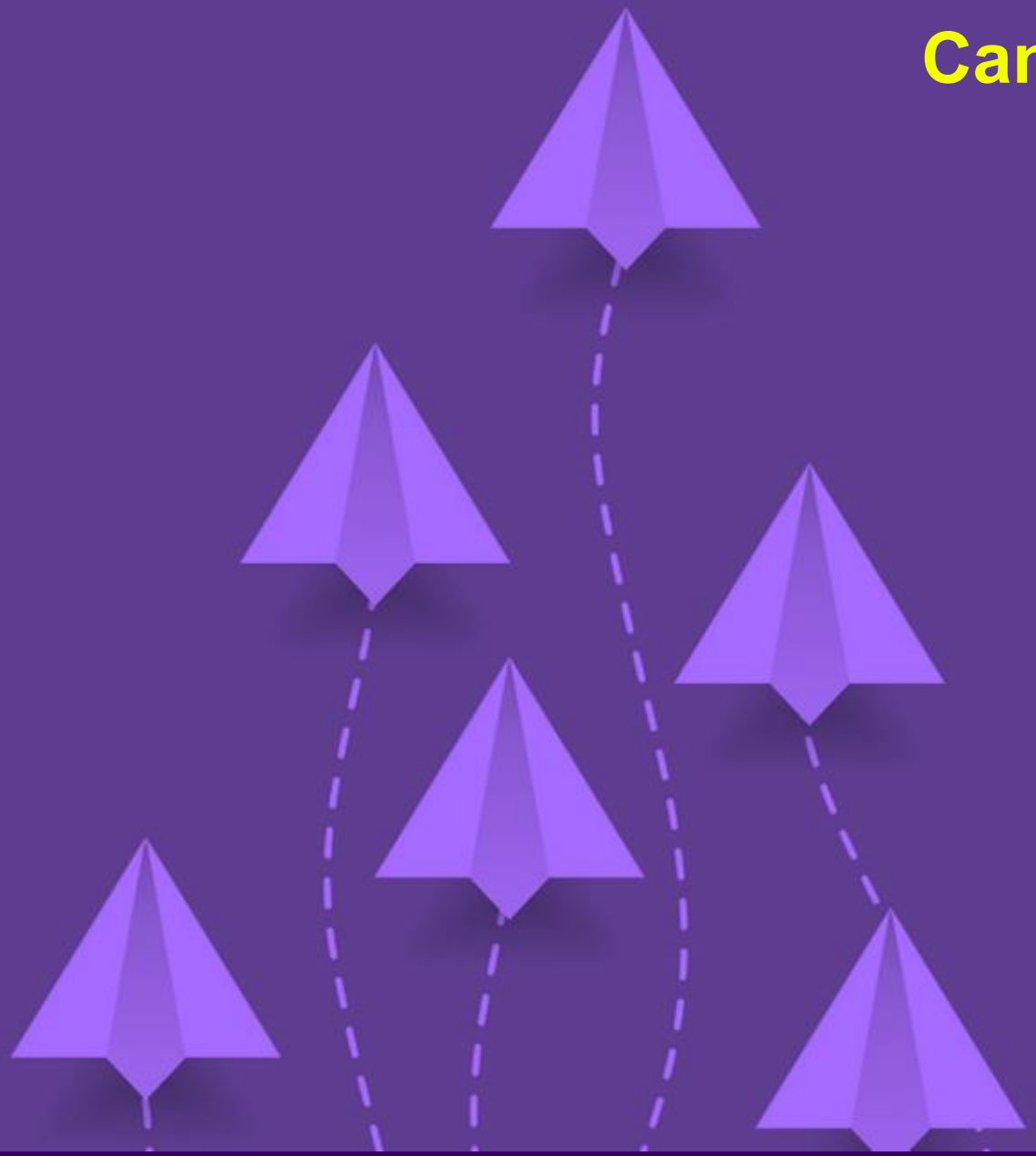
https://data.oecd.org/healthcqt/magnetic-resonance-imaging-mri-units.htm; Miles R et al J Women's Health 2018

Newer Approaches:
Can we change the MR exam?



https://createvalue.org/blog/shifting-paradigms-work-virtual-world/

Abbreviated Exams

faster, shorter, cheaper, more tolerable?

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Classic aka full protocol MRI exam

Multiple images after injection of contrast over several minutes

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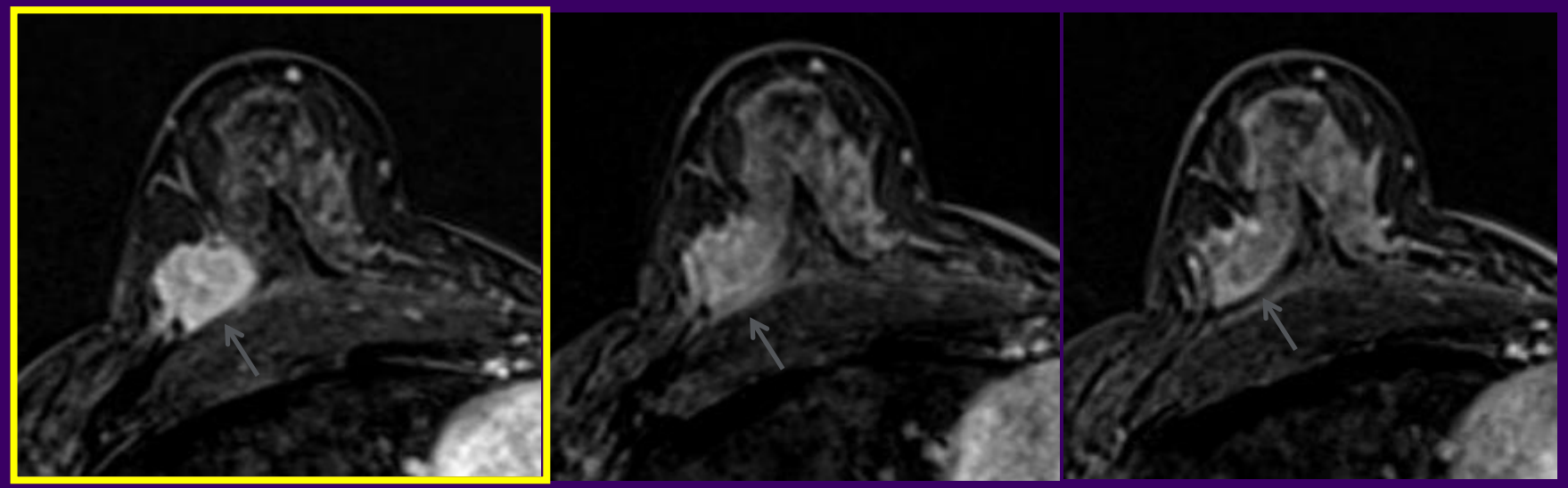
Tumor enhancement peaks early (1-2 min)
Tumor washes out as tissue washes in



T1W C+ Phase 1
~ 100 seconds

T1W C+ Phase 2
~ 200 seconds

T1W C+ Phase 3
~ 300 seconds

TP: AB-MR maximizes tumor conspicuity by imaging at the greatest tumor/BPE divergence

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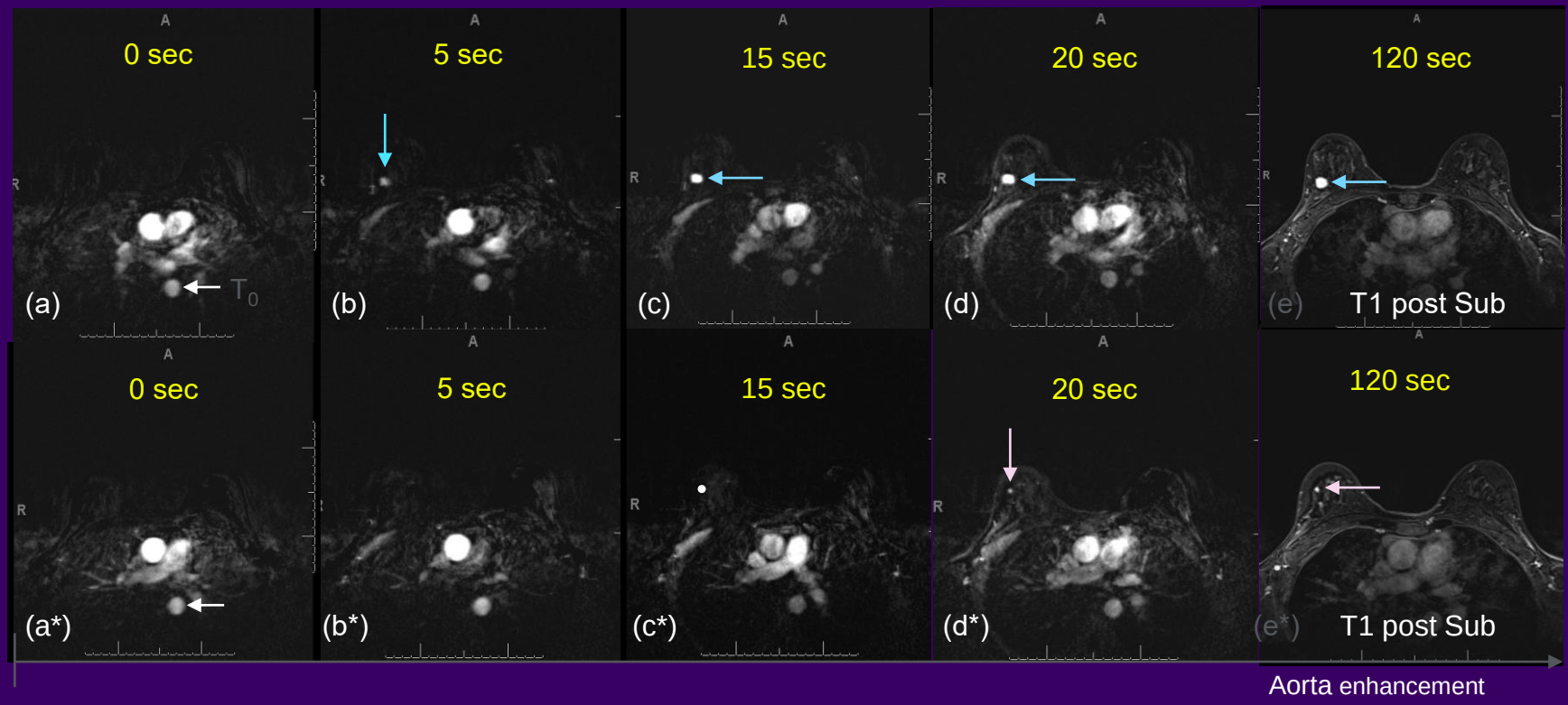
Gao Y, Heller SL, RG 2020

Benefit: Ultrafast MRI allows further ↑ discrimination between malignant vs. benign

High temporal resolution MRI further increases the ability to distinguish between benign and malignant lesions. Malignant lesions typically enhance early and briskly. Benign lesions typically enhance later and gradually.



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Abe 2016 AJR

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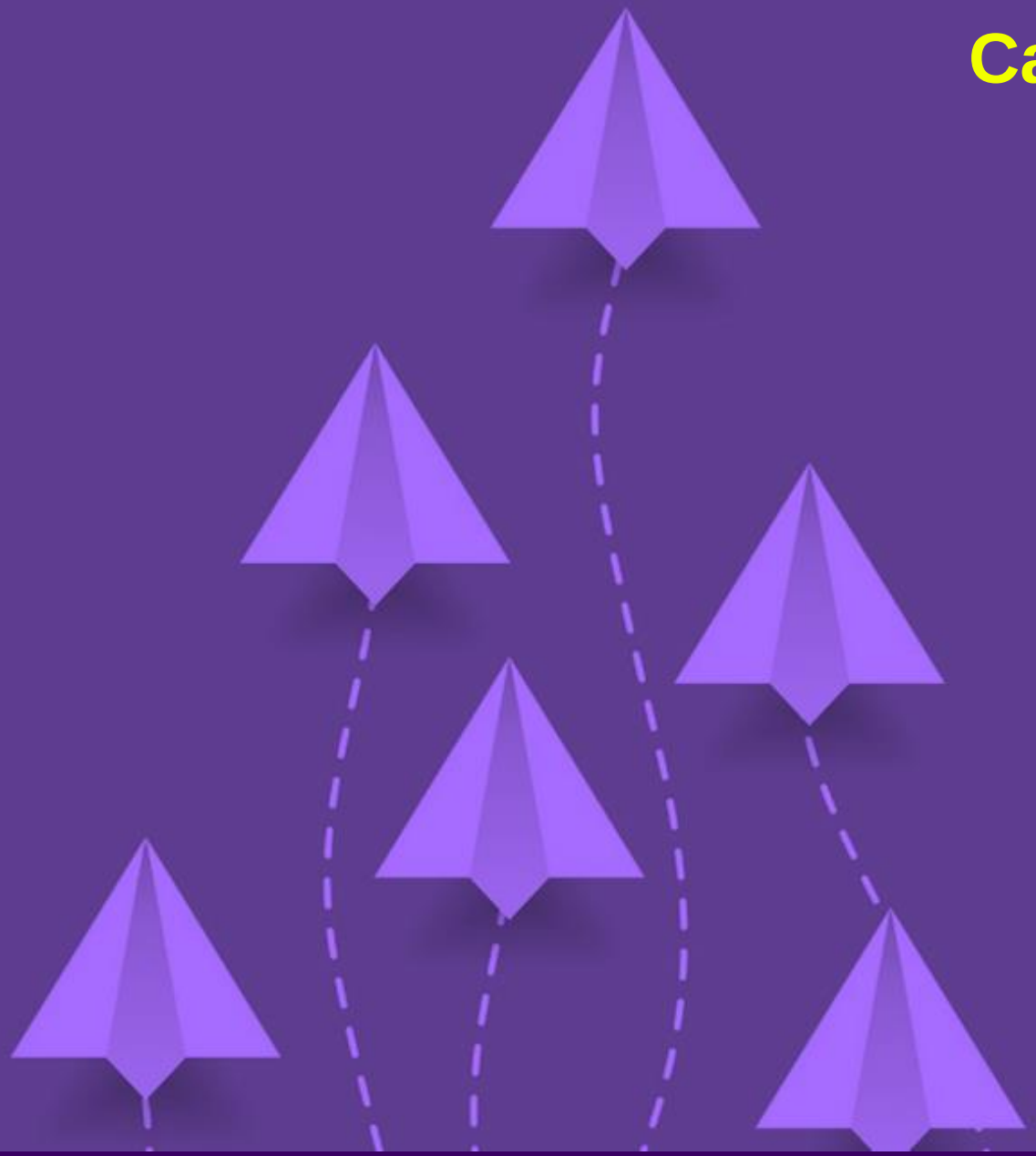
Expansion of Screening
(high risk vs greater than average risk)

ACR/SBI 2023

Indication	Recommendation
Genetic mutation carriers/untested 1st degree relatives	Annual DM+/-DBT at age 40 if annual MRI; at age 30 if not Annual MRI ages 25-30
Calculated Lifetime Risk of >=20%	Annual DM+/-DBT Annual MRI (age 30)
History of chest/abdominal XRT at a young age	Annual DM+/-DBT Annual MRI Consider abdominal RT that overlaps breast in risk (age 25 or 8 years after tx, whichever is later)
PH of BC before age 40	Annual DM+/-DBT Consider annual MRI if dense or If dx before age 50; others with PHx consider from age at dx
History of atypia/LCIS diagnosed before age 40	Annual DM+/-DBT Consider annual MRI if other risk factors (from age at diagnosis)
Dense breast tissue	Annual DM+/-DBT Annual MRI Consider CEM or US as alternatives to MRI (age 40 or earlier if other risk factors)

Newer Approaches:
Can we improve detection?



https://createvalue.org/blog/shifting-paradigms-work-virtual-world/

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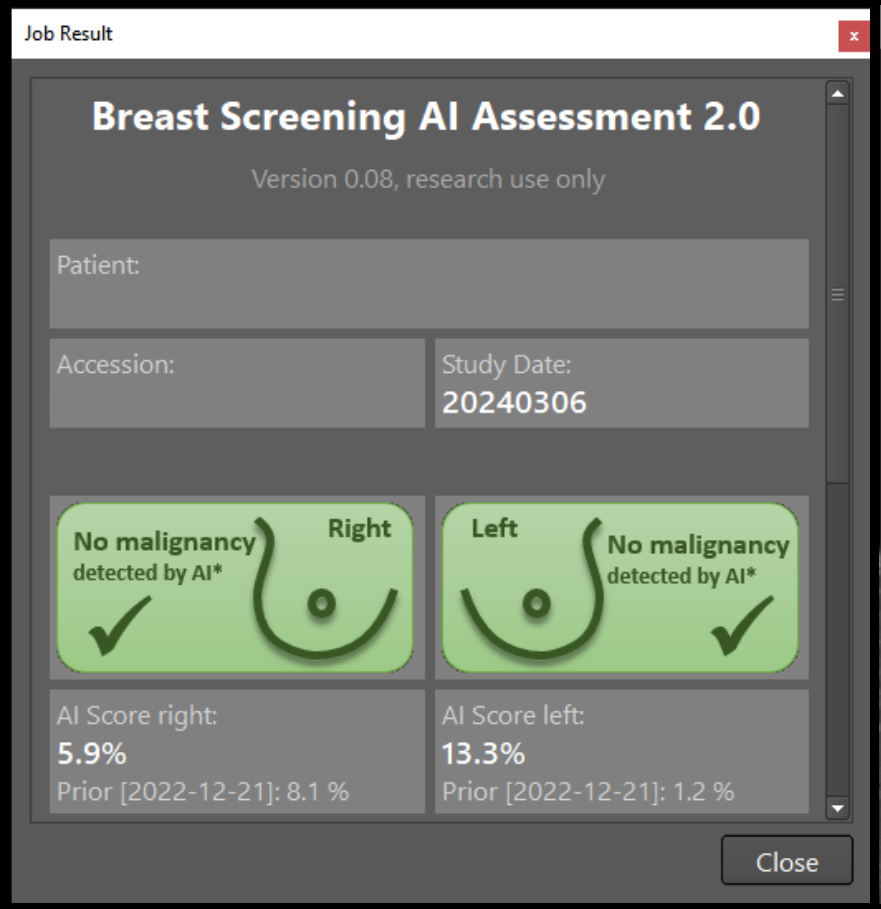
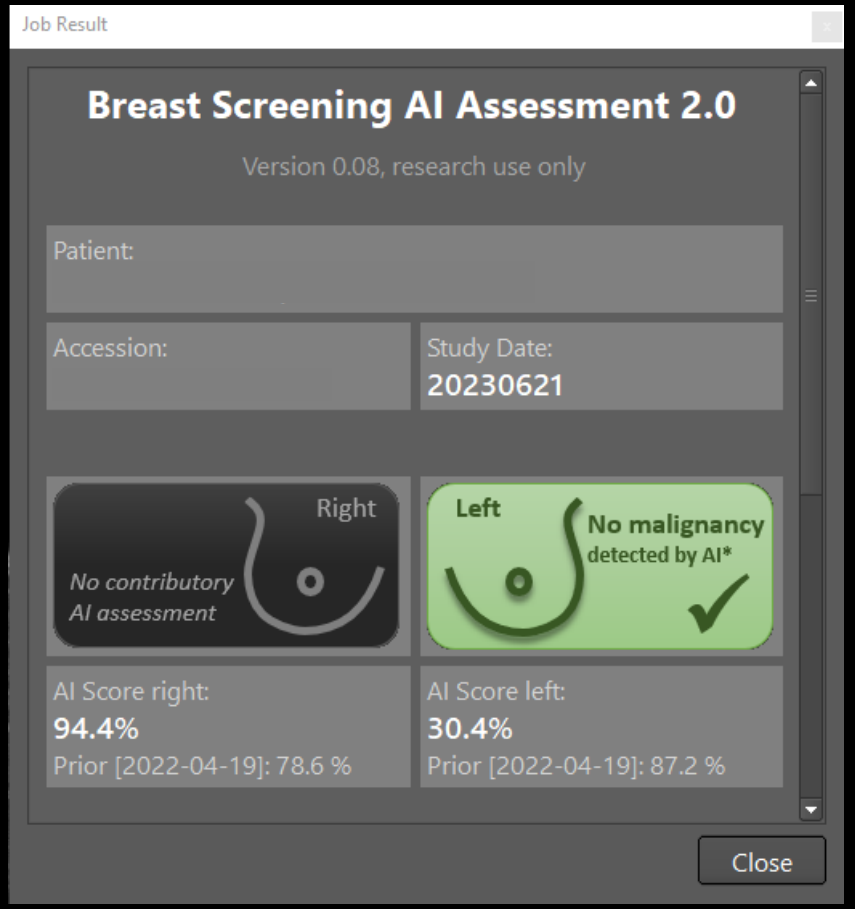
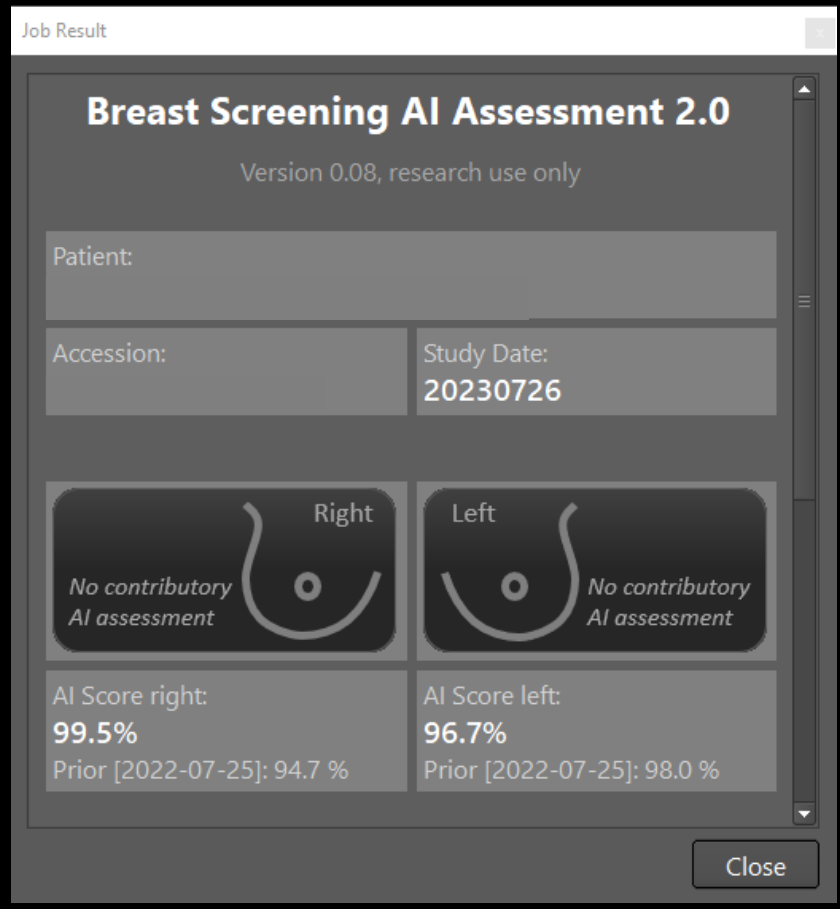
AI: Improved Cancer Detection

Materials and Methods

- AI-DBT model produces a high specificity threshold score for each breast

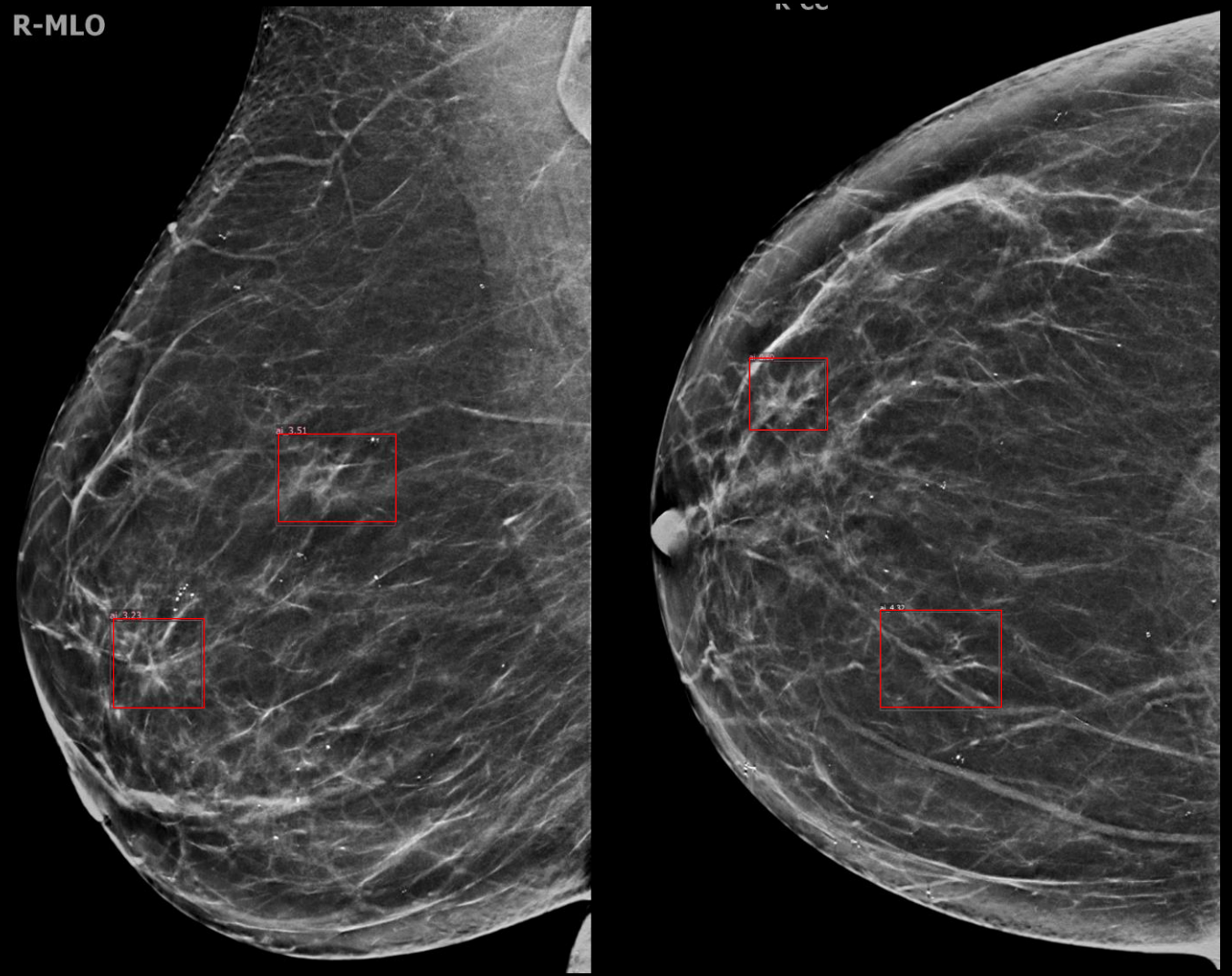


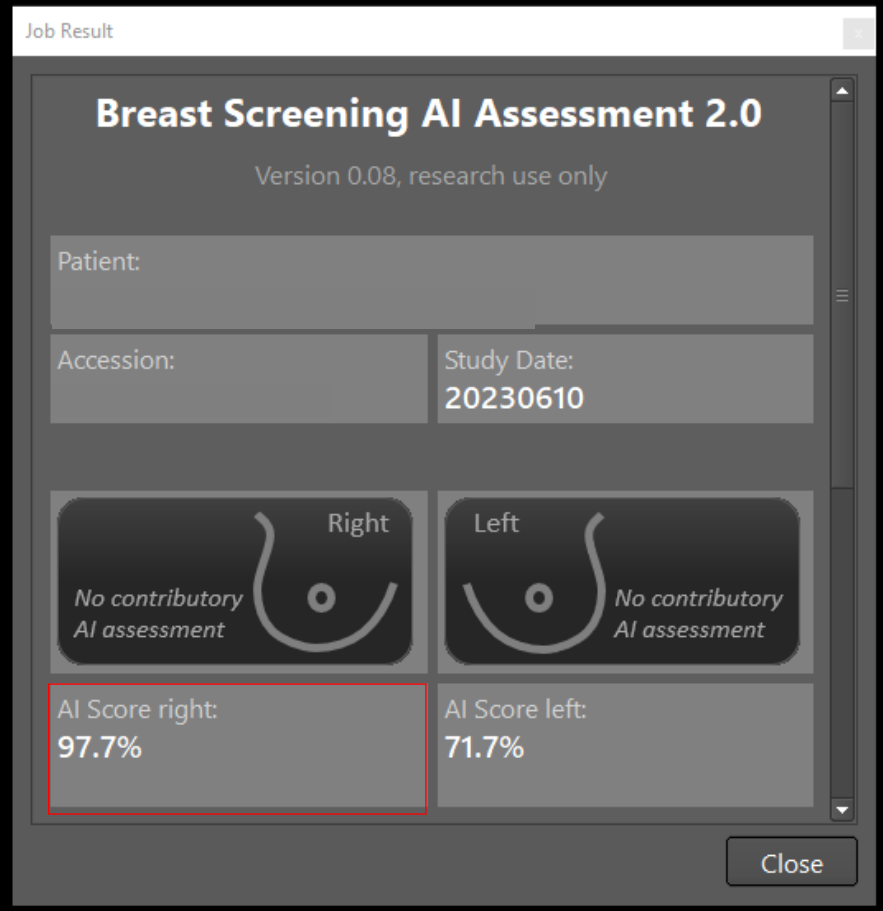




Materials and Methods

- AI-DBT model produces a high specificity threshold score for each breast and bounding boxes denoting the suspicious areas





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Part 2: Young Women/Unknown Risk

Case

22-year-old woman with a palpable left breast lump
No known genetic or family history

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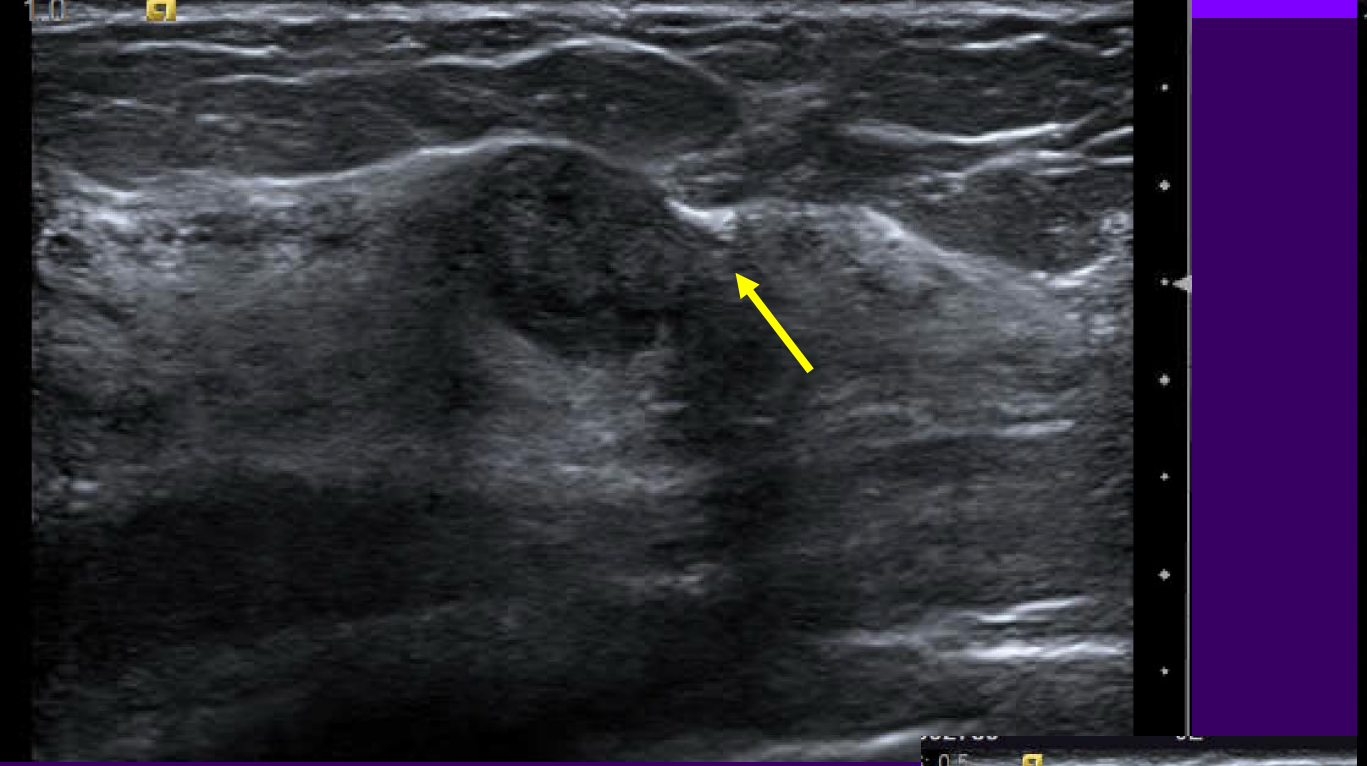

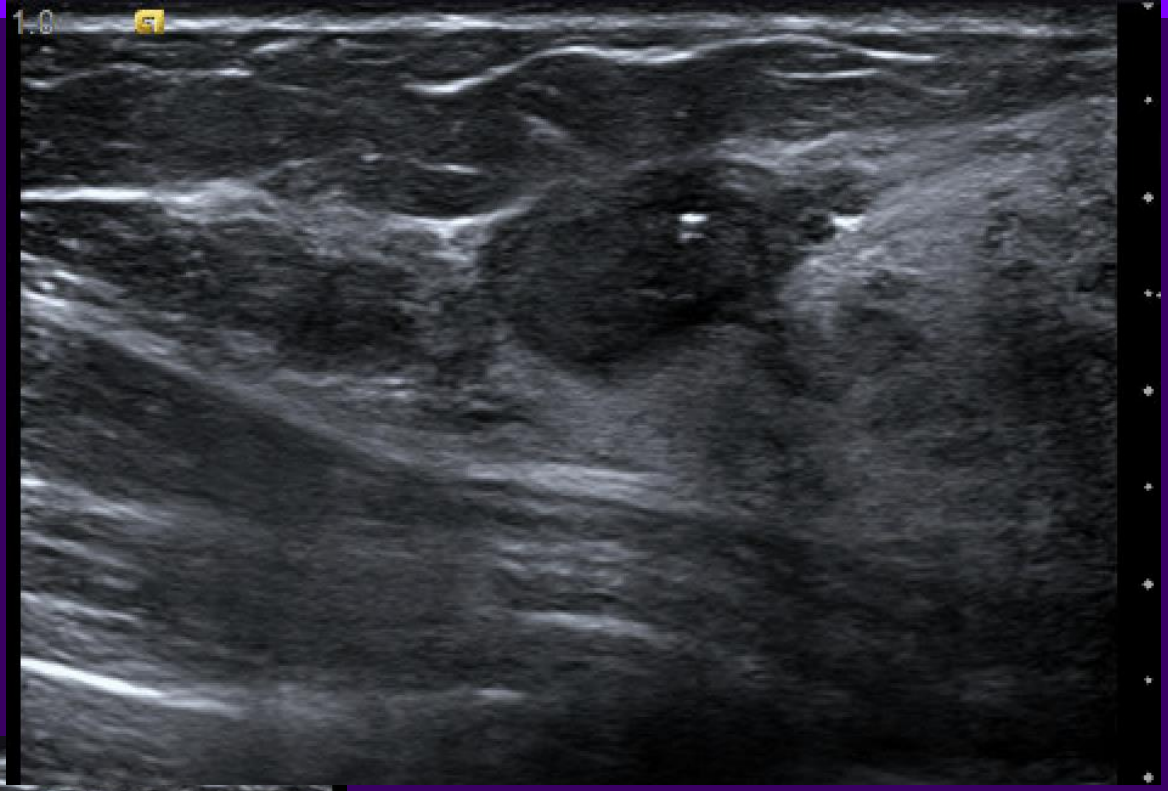

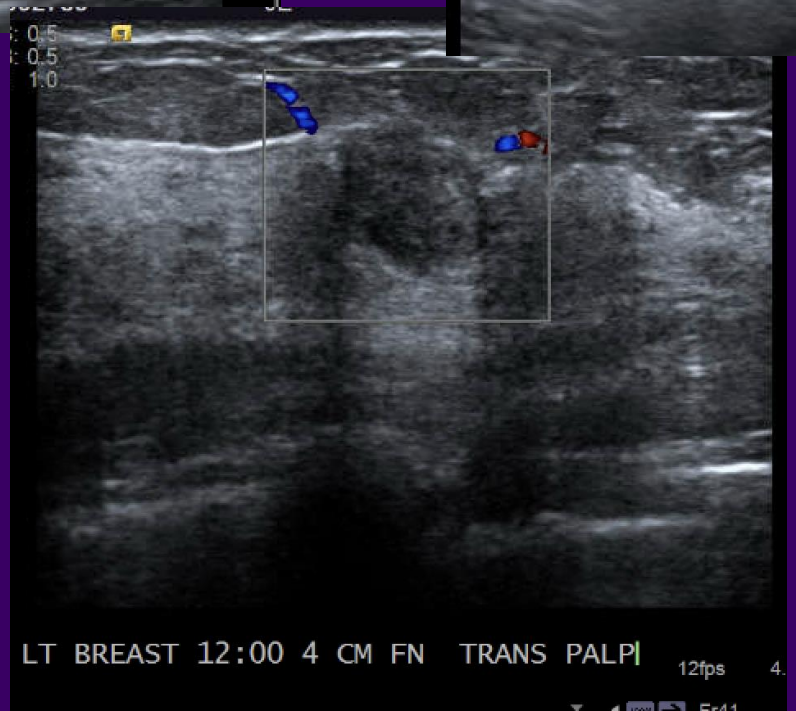

TN BC

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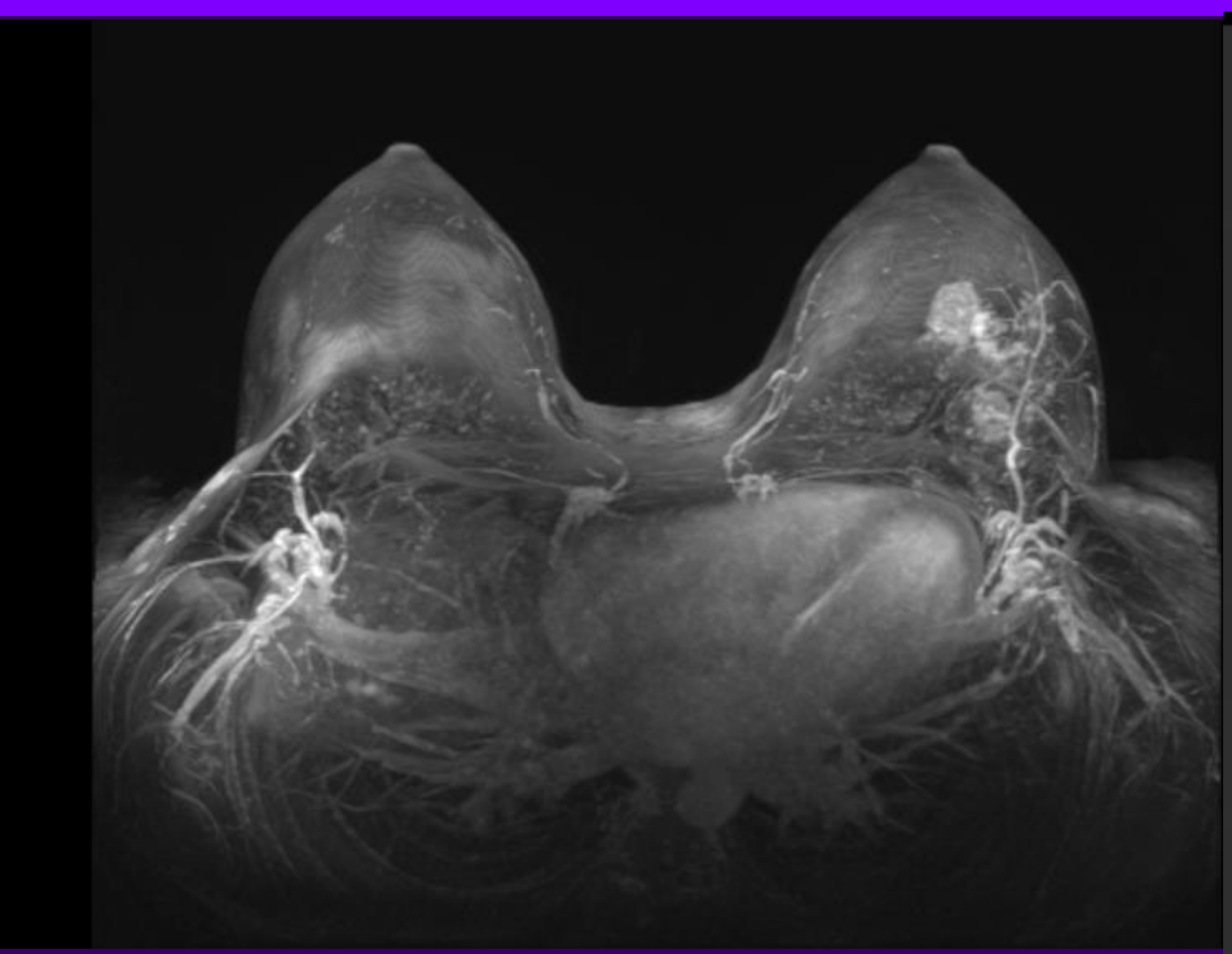

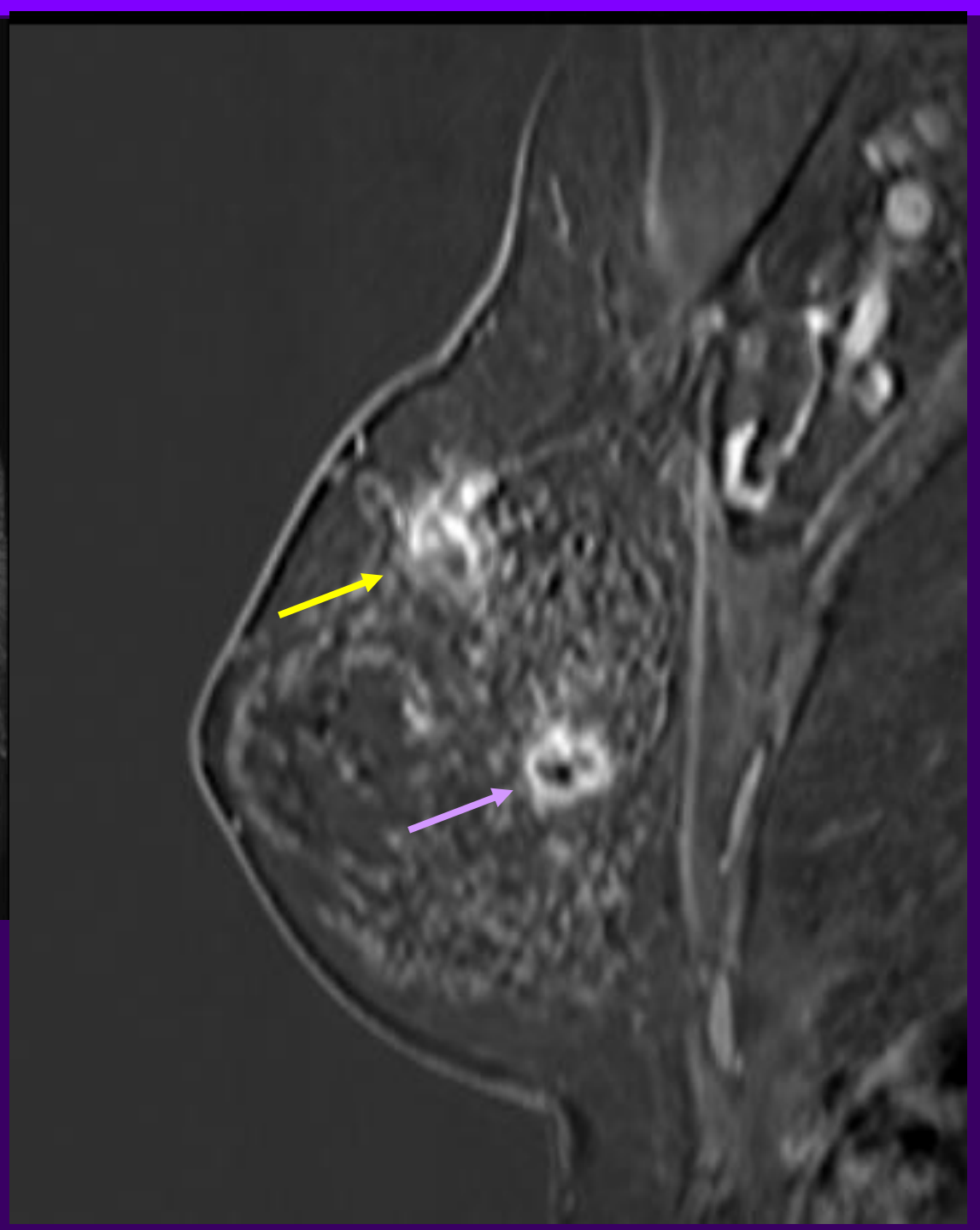

Key Point: Diagnostic presentation

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Corollary Case

32-year-old woman—breast-feeding—lump for 5 months

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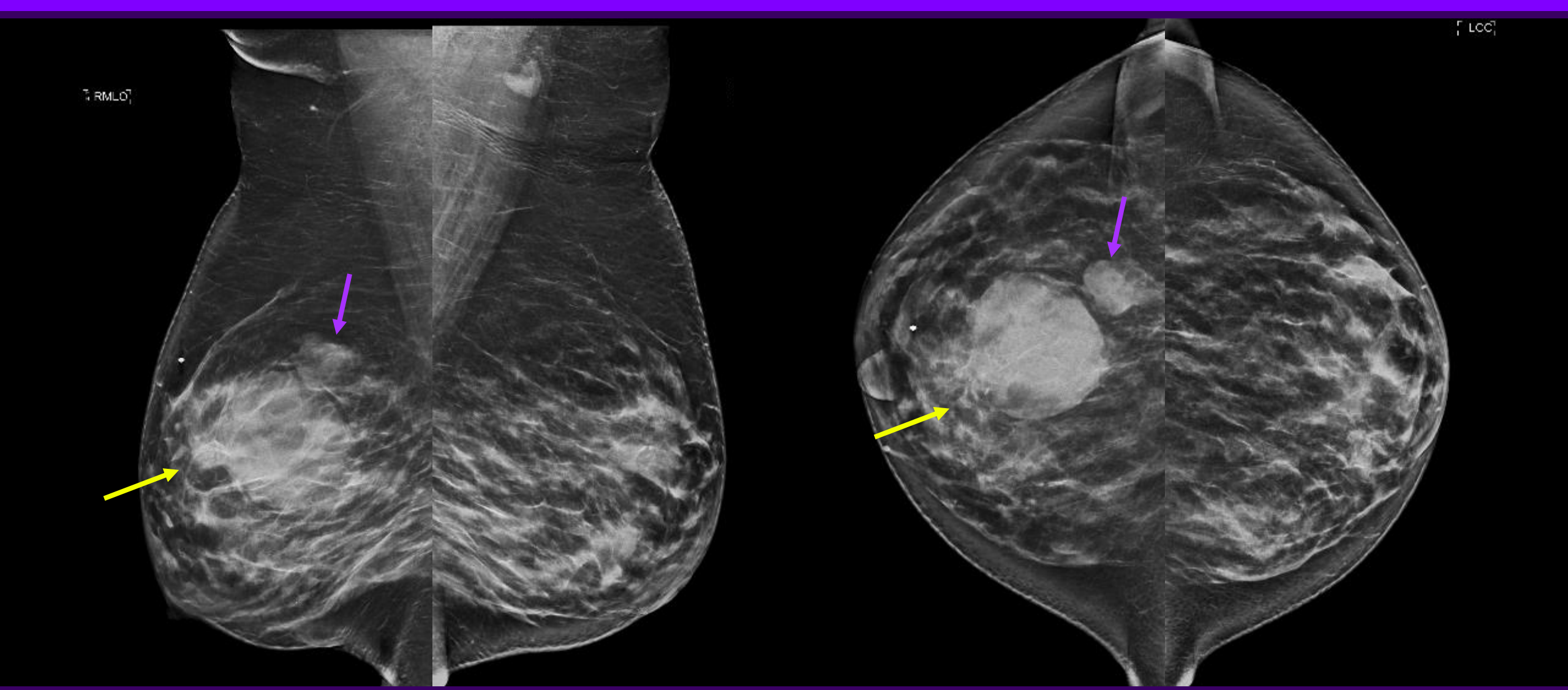

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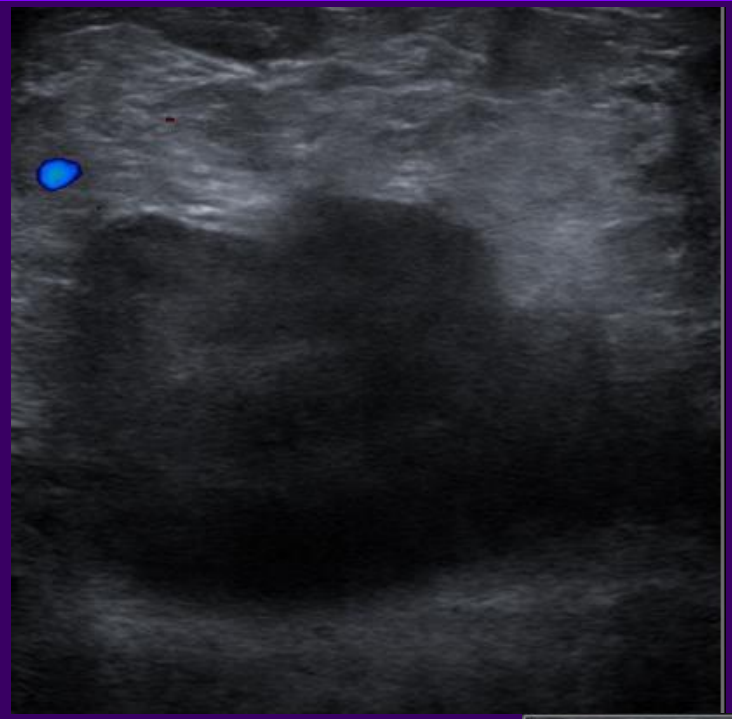

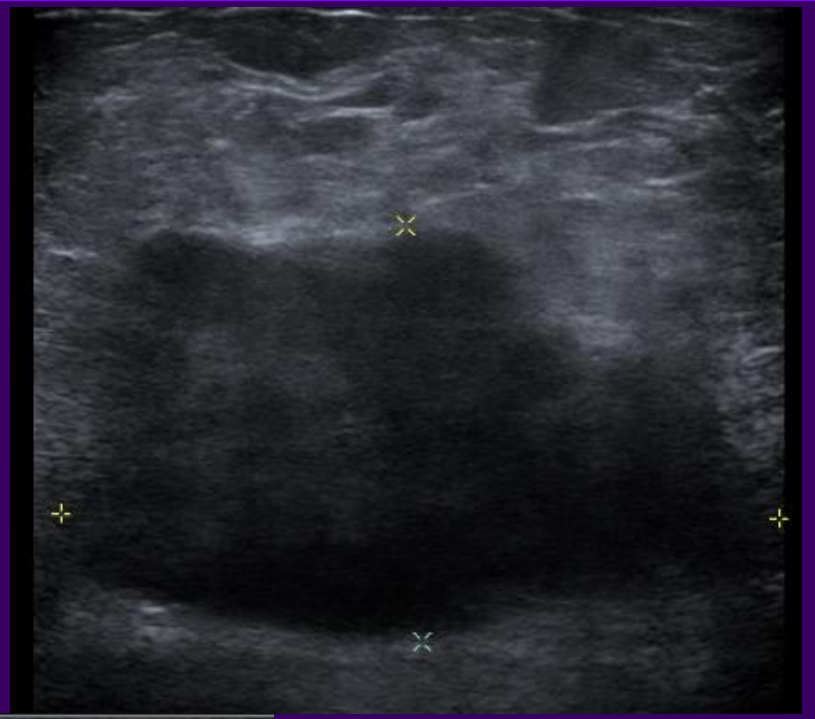

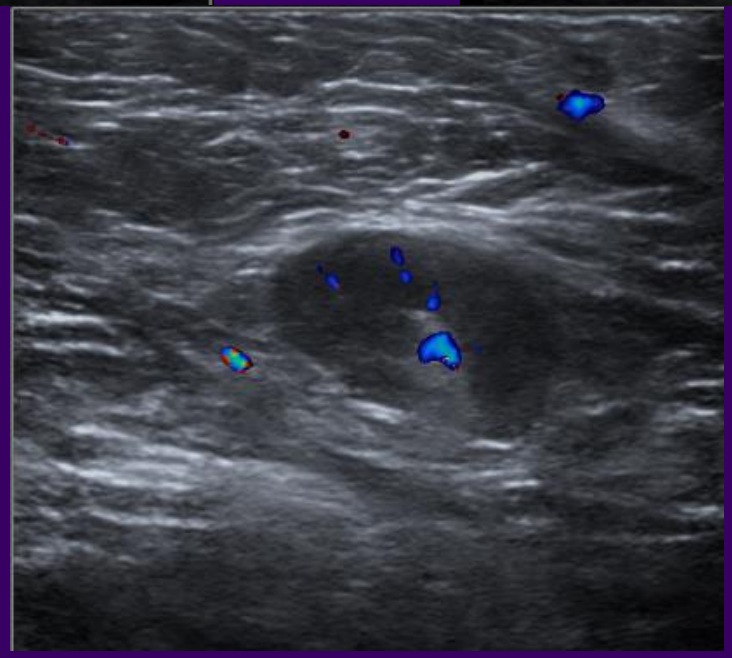

TN G3 IDC

Metastatic R axillary LN

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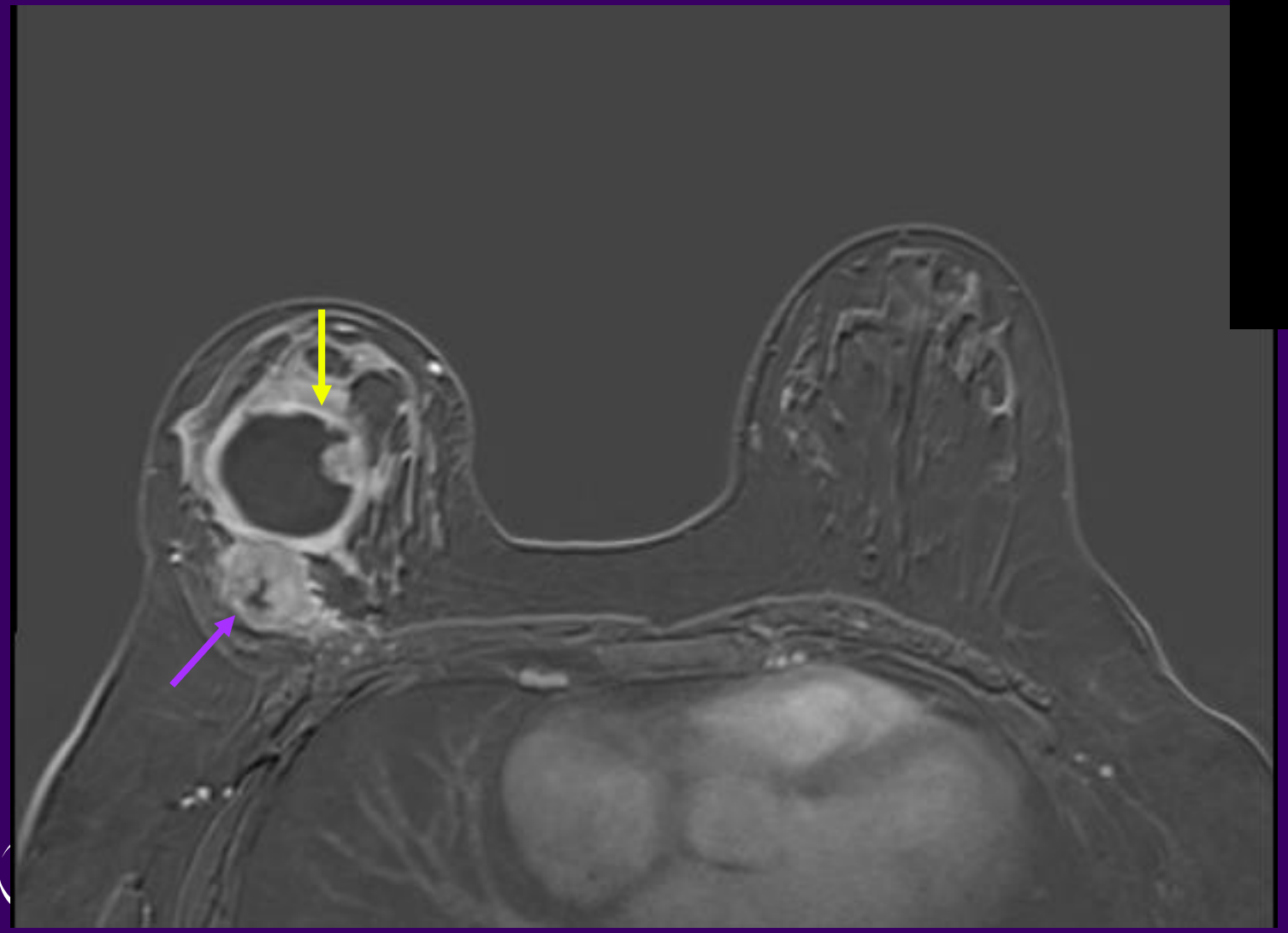

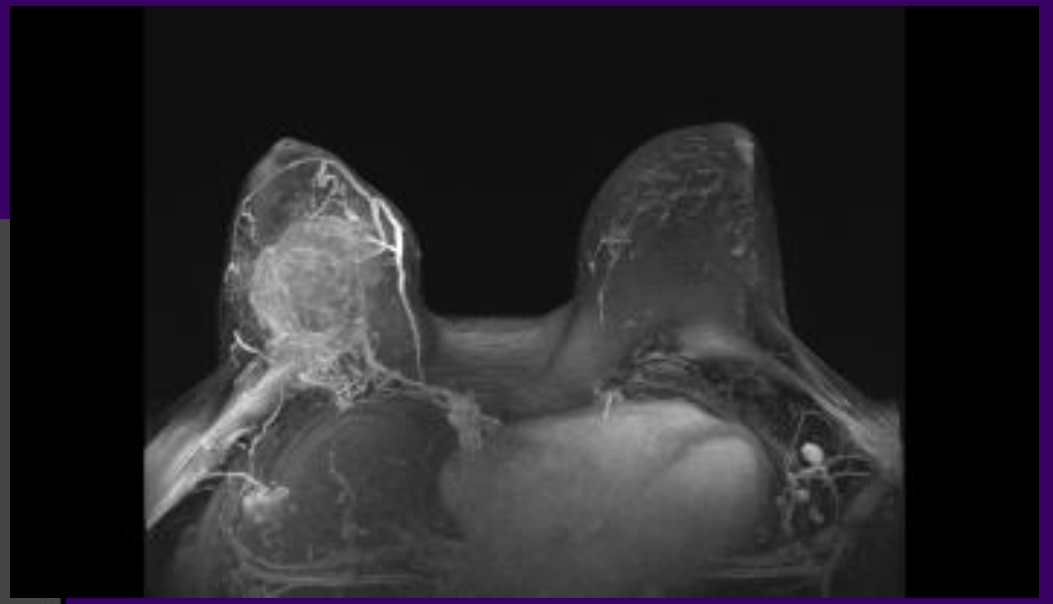

Referral to risk assessment clinic→ BRCA1 mutation carrier

Pregnancy-Associated Breast Cancer

- BC during pregnancy or within 1 year peripartum
- Commonly age <40
- Increasing incidence (older age at pregnancy)
  - Swedish registry study >four million deliveries over 5 decades
    - 1963 16/100000 deliveries
    - 2002 37.5/100000 deliveries

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Andersson TM et al. **Obstet Gynecol** 2009

True or False

- Mammo is not helpful during lactation because the breasts are too dense
- Radiation from mammography during lactation has a toxic effect on breast milk
- Mammo is contraindicated during pregnancy

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Imaging in Pregnancy and Lactation

- No contraindication to mammo during breast-feeding
- No contraindication to mammo in pregnant patients at any point in pregnancy
- Radiation exposure to the fetus from a mammogram is expected to be inconsequential
- Only contrast-enhanced MRI is contraindicated in pregnancy

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Unknown Risk

- Individuals <40 years without identifiable risk factors do not undergo screening
- Most women with BC do not have a known 1st degree family history of breast cancer (89%) or germline genetic mutation (90%–95%)
- Most sporadic early-onset breast cancers are discovered clinically

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Goodwin PJ et al. J Clin Oncol 2012;30(1):19–26; Copson ER et al, Lancet Oncol 2018; Claus, EB et al. Cancer 1996

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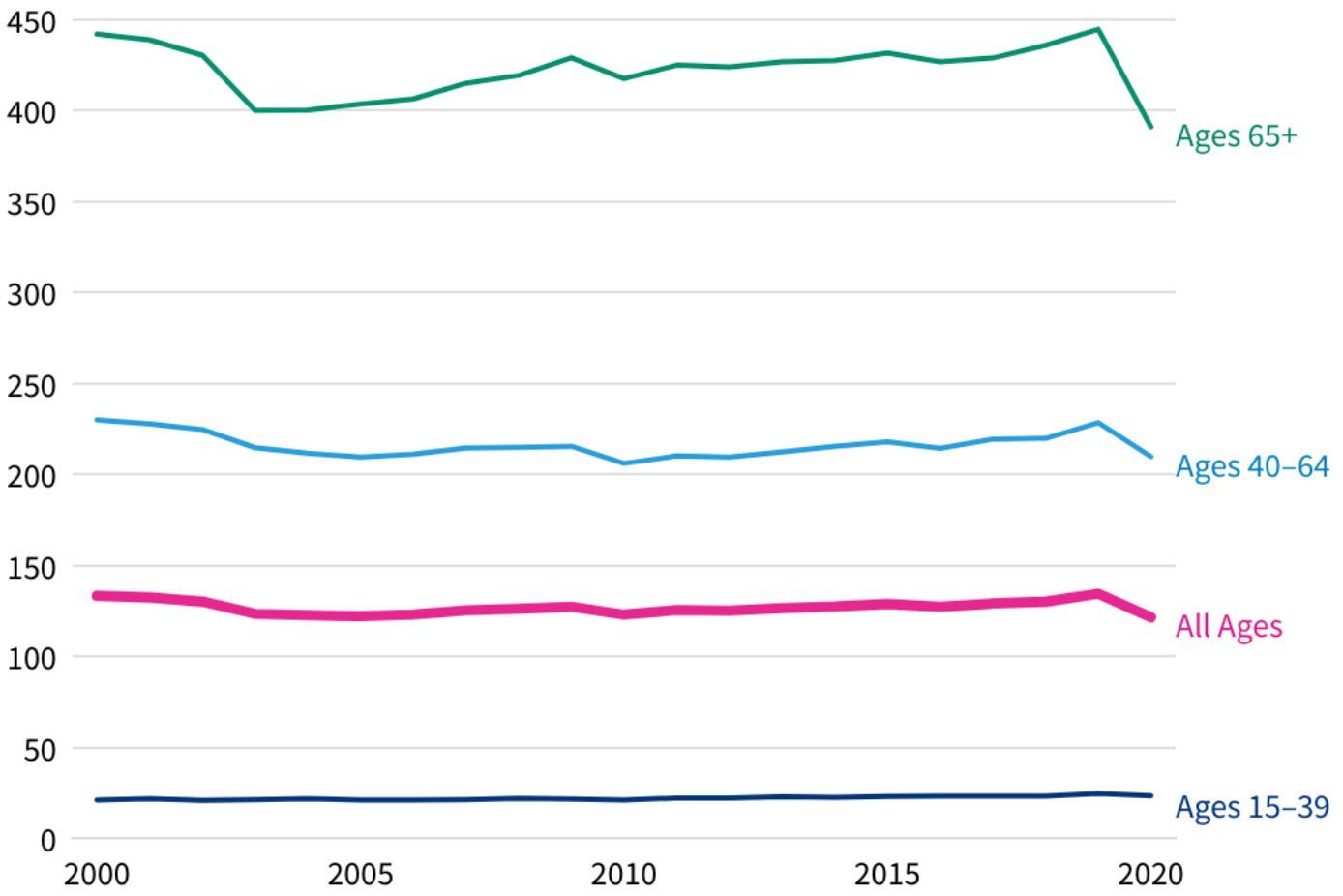
Age-Based Screening and Imaging: Should we start younger?

The incidence of breast cancer increased for all ages in 2019.

Age-adjusted breast cancer incidence rates for females per 100,000 females, by age group



Source: National Cancer Institute

USAFACTS

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Limitations of modalities at the population level

density, false positives, cost, access

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ACR/SBI recommends

- Risk assessment by age 25
- Discussion with provider whether earlier screening with mammo
- and/or MRI is needed
- Attention to higher risk populations

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Attention must be paid (USA)

- Early-onset BC disproportionately affects patients of certain racial and ethnic groups
- Black, Native American, and Hispanic individuals have > likelihood of stage III or IV disease, higher-grade tumors→worse prognosis
- Black women <45 years have the highest BC mortality rate

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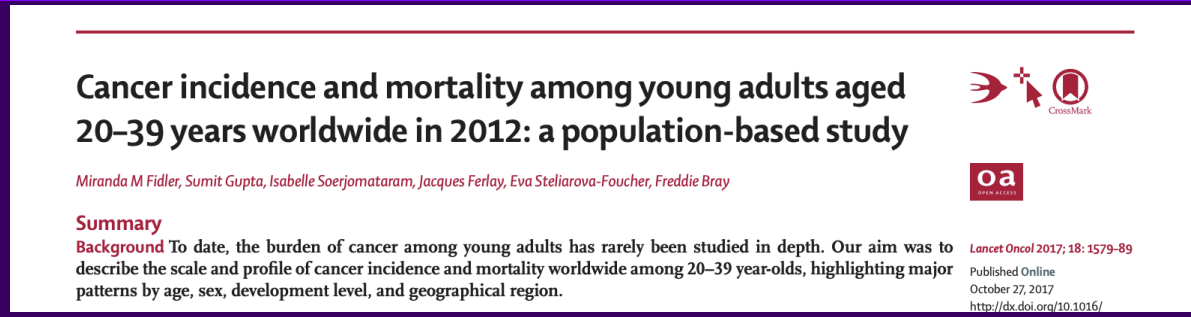
Shoemaker ML et al. Breast Cancer Res Treat 2018

Attention must be paid (Global)



Cancer incidence and mortality among young adults aged 20–39 years worldwide in 2012: a population-based study

Miranda M Fidler, Sumit Gupta, Isabelle Soerjomataram, Jacques Ferlay, Eva Steliarova-Foucher, Freddie Bray

Summary

Background To date, the burden of cancer among young adults has rarely been studied in depth. Our aim was to describe the scale and profile of cancer incidence and mortality worldwide among 20–39 year-olds, highlighting major patterns by age, sex, development level, and geographical region.

Lancet Oncol 2017; 18: 1579–89
Published Online
October 27, 2017
http://dx.doi.org/10.1016/

	Cancer Incidence per 100,000	Cancer Mortality Rate per 100,000
H-HDI	64.5	9.2
L-HDI	46.2	25.4

HDI=Human Development Index countries
Age-standardized Rates

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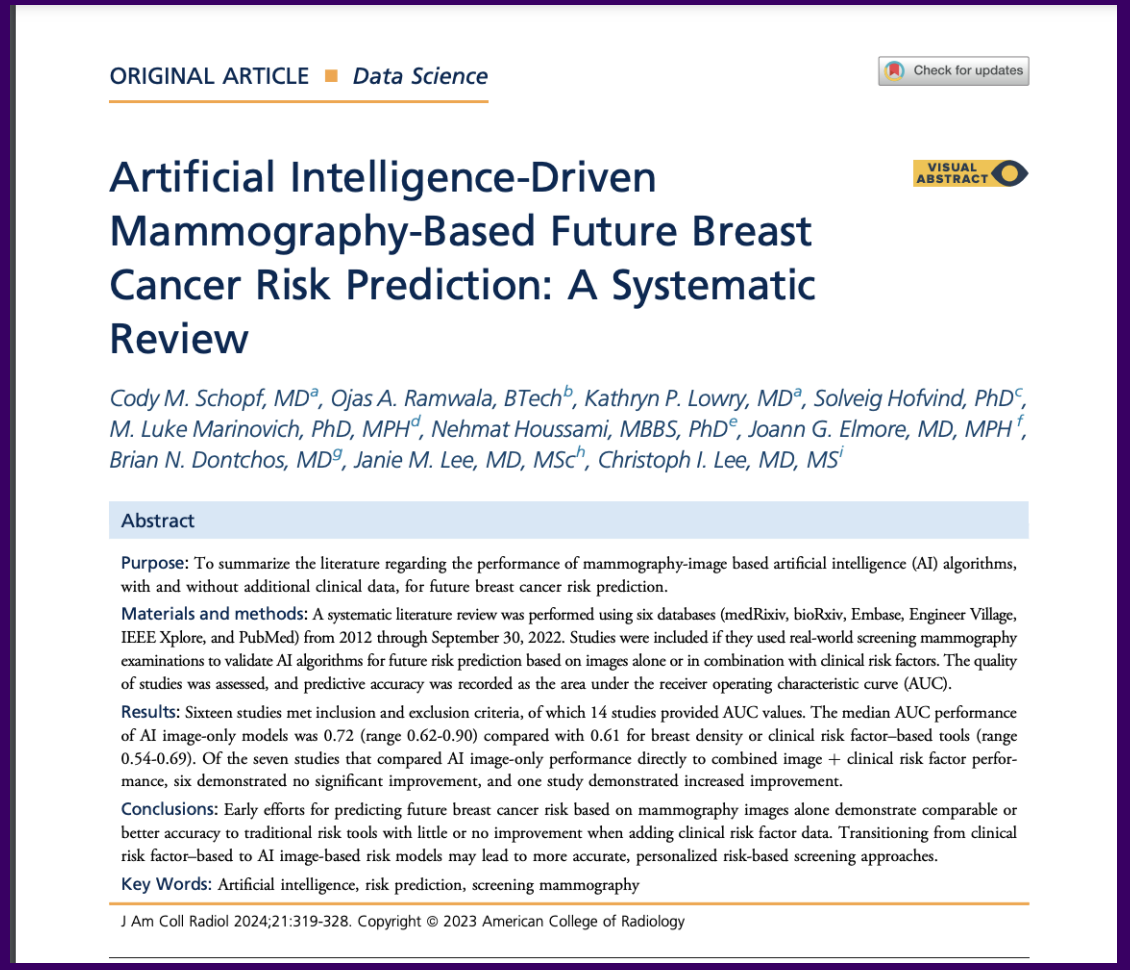
Opportunities: AI and Risk Prediction

- Multiple traditional risk models (TC, Gail, etc.,)
- Self-reported factors, variable predictive accuracy
- Review of 16 studies of AI assessment (mammo based)→
  - Comparable or improved risk assessment vs traditional tools
  - Little or no improvement with addition of clinical risk factors
- Future directions???



ORIGINAL ARTICLE ■ *Data Science*

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VISUAL ABSTRACT

Artificial Intelligence-Driven Mammography-Based Future Breast Cancer Risk Prediction: A Systematic Review

Cody M. Schopf, MD[a], Ojas A. Ramwala, BTech[b], Kathryn P. Lowry, MD[a], Solveig Hofvind, PhD[c], M. Luke Marinovich, PhD, MPH[d], Nehmat Houssami, MBBS, PhD[e], Joann G. Elmore, MD, MPH[f], Brian N. Dontchos, MD[g], Janie M. Lee, MD, MSc[h], Christoph I. Lee, MD, MS[i]

Abstract

Purpose: To summarize the literature regarding the performance of mammography-image based artificial intelligence (AI) algorithms, with and without additional clinical data, for future breast cancer risk prediction.

Materials and methods: A systematic literature review was performed using six databases (medRixiv, bioRxiv, Embase, Engineer Village, IEEE Xplore, and PubMed) from 2012 through September 30, 2022. Studies were included if they used real-world screening mammography examinations to validate AI algorithms for future risk prediction based on images alone or in combination with clinical risk factors. The quality of studies was assessed, and predictive accuracy was recorded as the area under the receiver operating characteristic curve (AUC).

Results: Sixteen studies met inclusion and exclusion criteria, of which 14 studies provided AUC values. The median AUC performance of AI image-only models was 0.72 (range 0.62-0.90) compared with 0.61 for breast density or clinical risk factor–based tools (range 0.54-0.69). Of the seven studies that compared AI image-only performance directly to combined image + clinical risk factor performance, six demonstrated no significant improvement, and one study demonstrated increased improvement.

Conclusions: Early efforts for predicting future breast cancer risk based on mammography images alone demonstrate comparable or better accuracy to traditional risk tools with little or no improvement when adding clinical risk factor data. Transitioning from clinical risk factor–based to AI image-based risk models may lead to more accurate, personalized risk-based screening approaches.

Key Words: Artificial intelligence, risk prediction, screening mammography

J Am Coll Radiol 2024;21:319-328.

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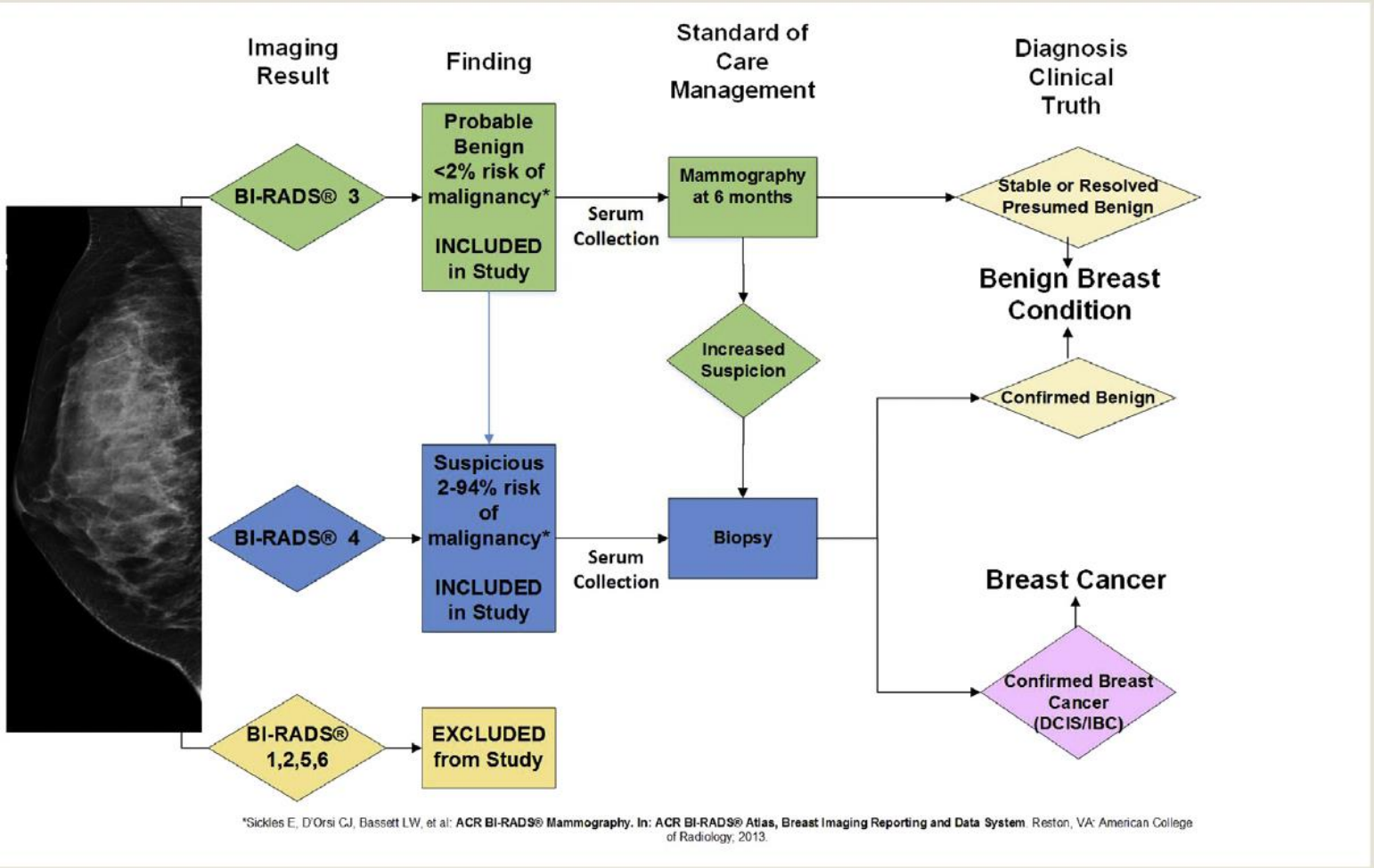
Opportunities: Combined approaches

Equivocal or suspicious imaging findings→serum for proteins/tumor antibodies



Lourenco AP et al. Clinical Breast Cancer 2017

Opportunities

Screening

- Assessing risk at a young age
- Developing potential for tailored screening (AI, synergy with non-imaging based screening options)
- Increasing access to screening
- Continuing development of detection

Diagnostic

- Increasing awareness of potential for BC in YW presenting with symptoms (including in pregnancy and peripartum period)
- Referral pathway to risk clinics for YW who present with diagnostic concerns

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Thank you

Samantha.Heller@nyulangone.org