

# **A CLOSER LOOK AT CONTRAST ENHANCED MAMMOGRAPHY**

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# Why Contrast Mammography

- Mammography is the only tool demonstrated to reduce breast cancer mortality- but it is an imperfect tool
- Supplemental imaging can improve breast cancer detection
- Screening ultrasound finds 3-4 additional cancers/1000 women but with a large number of false positive findings
- Contrast Enhanced Breast MRI is the most sensitive imaging tool using enhancement of neovascularity to find cancer sometimes before a mass is seen, but is expensive & not readily available for large numbers of women
- Contrast Enhanced mammography uses the enhancement of neovascularity in a fashion like MRI to improve the sensitivity of mammography at a lower cost with the potential to reach a larger number of women
- Called CEDM, CESM and now CEM
- What are the indications?

# What is Contrast Mammography

- **Digital mammo unit w/ the ability to do dual energy**
- **Iodinated contrast 1.5 ml/kg w/ maximum of 150 ml.**
- **Power injector: 3ml/sec. through 20-gauge needle**
- **First imaging ~ 2 minutes post-injection**
- **Provides low energy images = 2D mammo**
- **Provides contrast images enhancing abnormalities not seen on mammo alone**

# Risks

- **Contrast reactions: pooled rate: 0.82%\* (can have Gadolinium allergy too)**
- **Reaction rate MSKCC: 0.5%\*\***
- **Renal failure- rare if avoid pts w/ renal impairment**
- **Additional radiation ~20-50% > routine 2D (0.9 mGy) or DBT alone (0.5 mGy)**
- **1.5 mGy less than DM + DBT**
- **Falls w/i MQSA guidelines**

**\*Zandaro et al Insights into Imaging 2019**

**\*\*Coffey et al personal communication**

# Mitigating risks

## Contrast allergy:

- Take a good history
- If a patient has had **ANY** reaction in the past, do not premedicate & do the exam unless there are no other options. Premedication is **not** a guarantee. There is always MRI

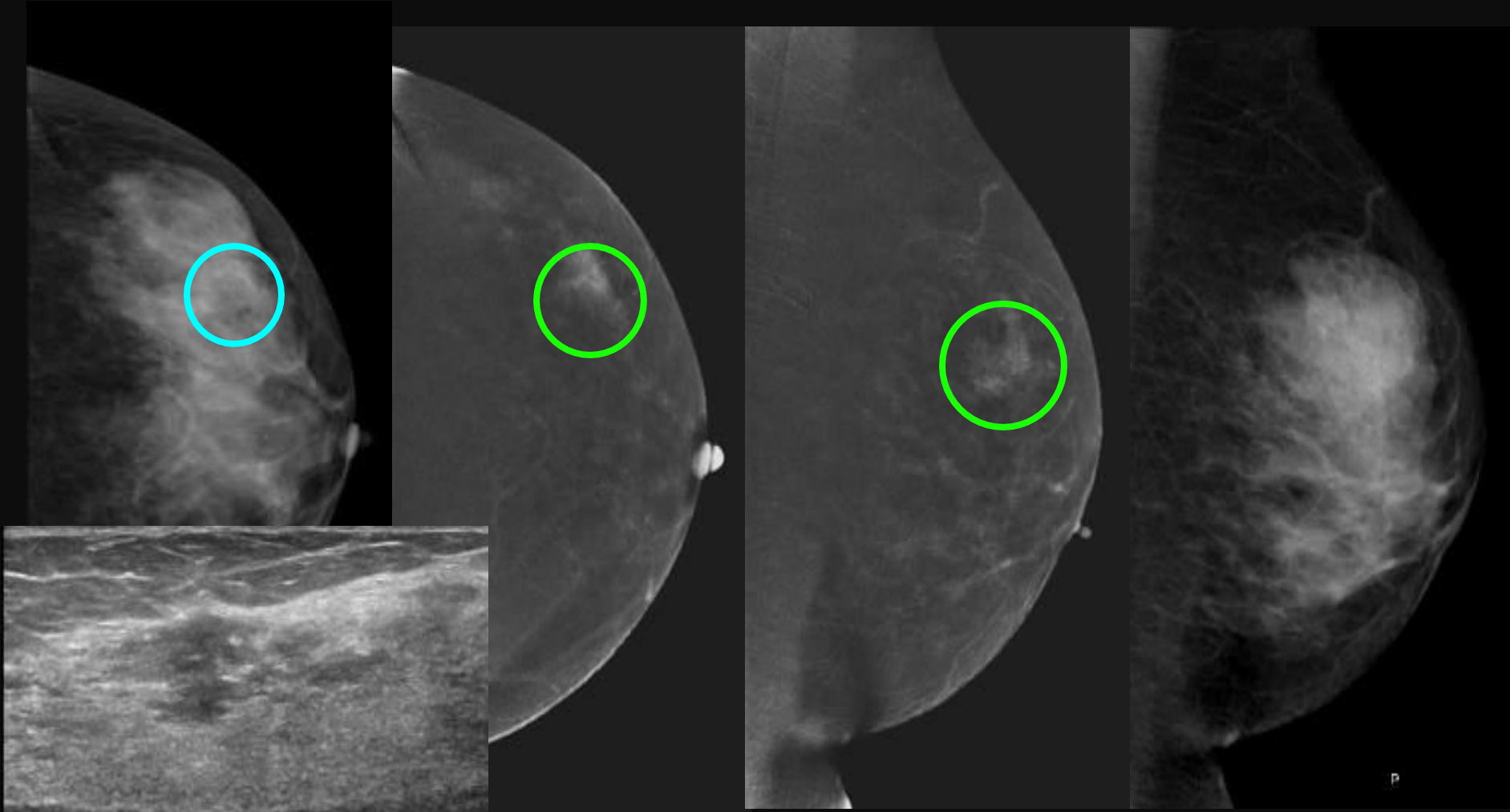
## Renal toxicity:

- Rare in patients w/ normal renal function
- Check renal function in patients > 70, diabetics, or patients with risk for renal failure

# Let's go!!!

- **Patient seated for IV & contrast injection followed by saline flush**
- **At 2-2.5 minutes, contrast is in**
- **Tech should wear gloves when dealing w/ contrast but remove when positioning the pt.**
- **Pt. stands to have what to her perception is a regular 2D mammo ~ a minute an image**
- **Techs can do the mammo in any order they are used to**
- **Contrast sticks around for up to 10 minutes so additional views can be obtained**
- **Some radiologists monitor in real time/ others don't**

# Distortion



Images courtesy of Dr Mizutani  
Mikawa Breast Cancer Clinic –Miakawa-anio. JAPAN

# What are the indications?

1. Call- back from screening/ problem solving
2. Staging known cancer
3. Palpable or clinical abnormalities
4. Staging & follow up after neoadjuvant chemotherapy
5. Follow up after lumpectomy
6. Screening women at increased risk & even dense breasts
7. When beginning either pick one or 2 or get an idea of what your referring faculty may be interested in

Each site may lean one way or the other



# Call back from screening/ problem solving

- N=120
- **UNILATERAL** CESM + mammo c/w mammo or mammo + US:
- Sensitivity: CESM **93%** vs mammo 78%
- CESM + mammo > mammo alone (p=0.045) & mammo + US (trend)
- **CESM + mammo significantly more accurate than mammo + US due to better specificity**

# Call back from screening/ problem solving

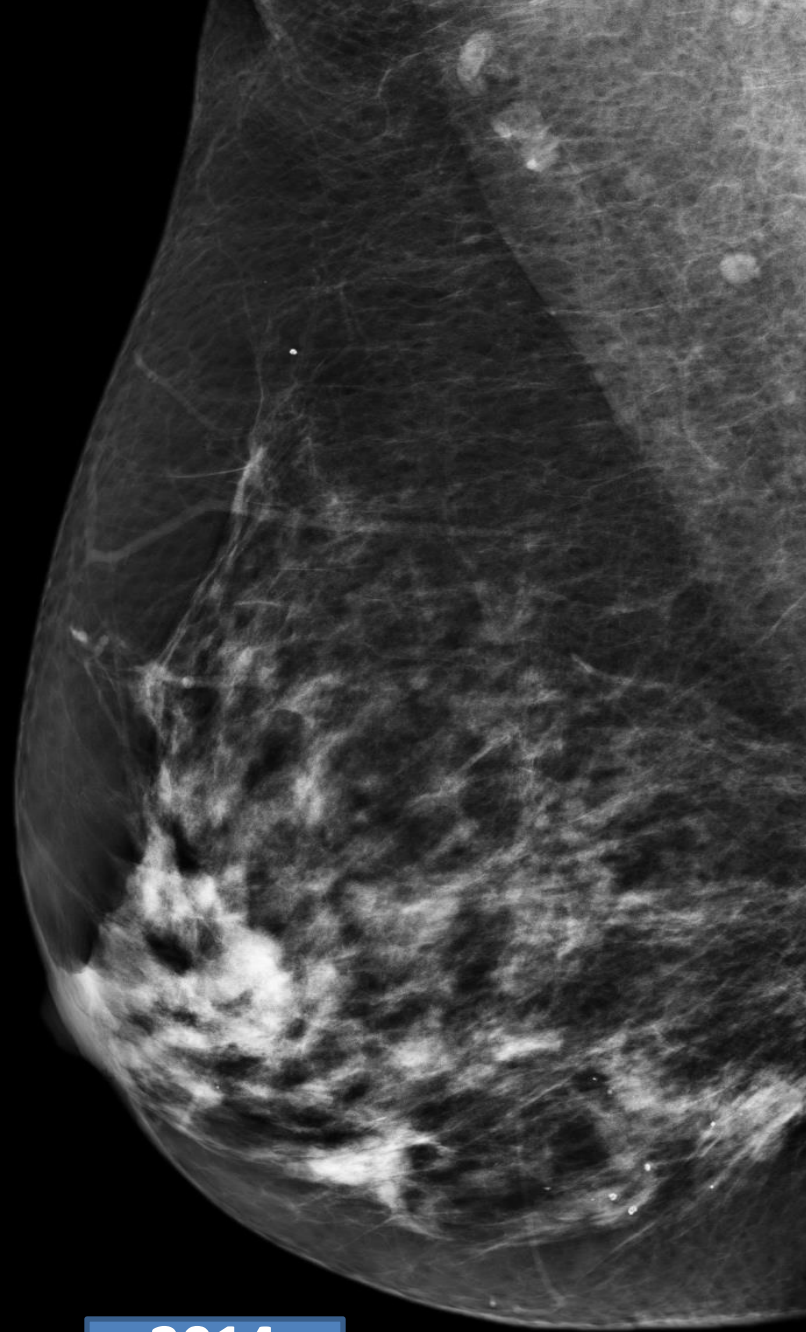
## N=113

### MAMMO

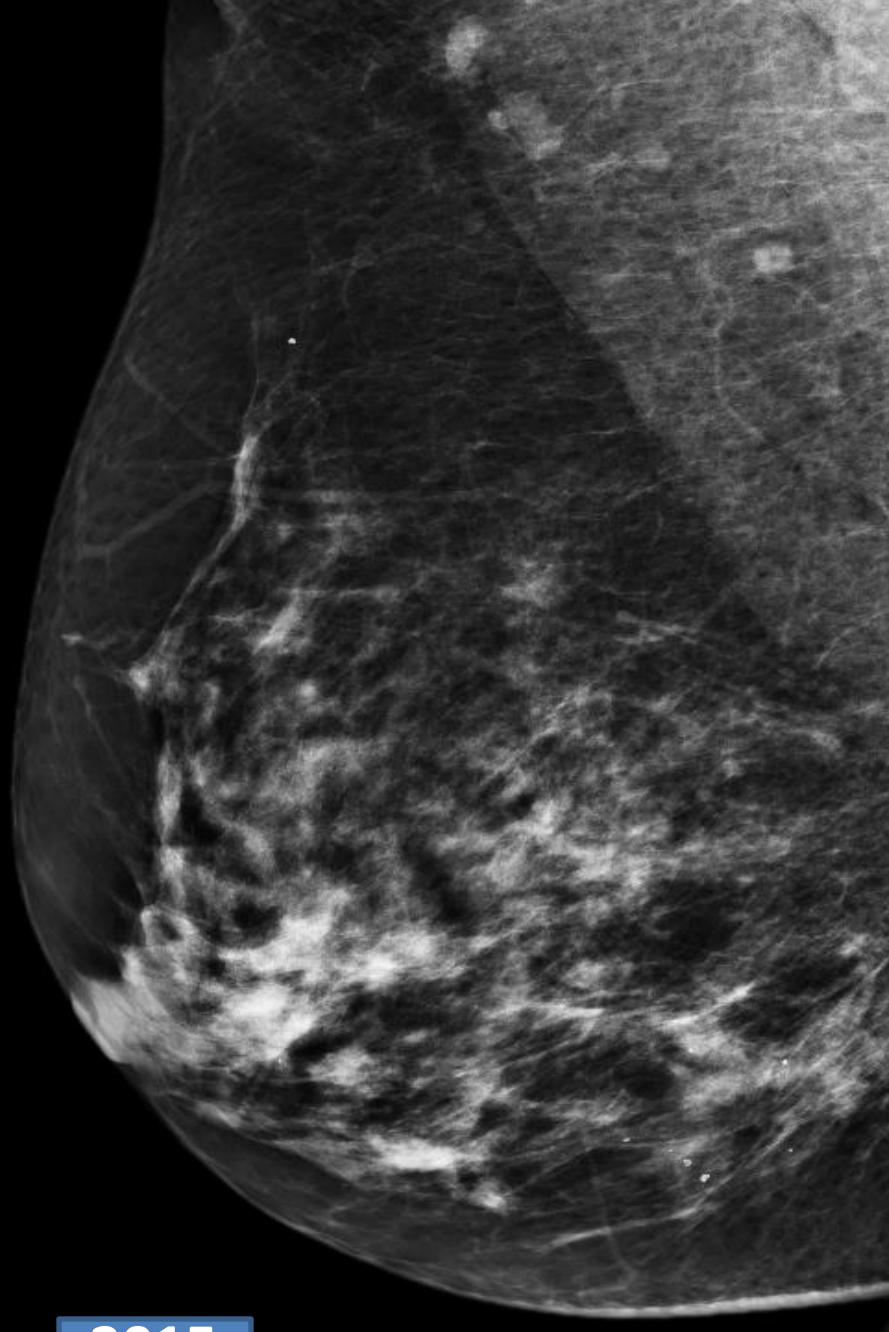
- Sensitivity: 96.9%
- Specificity: 42.0%
- PPV: 39.7%
- NPV: 97.1%

### CEM

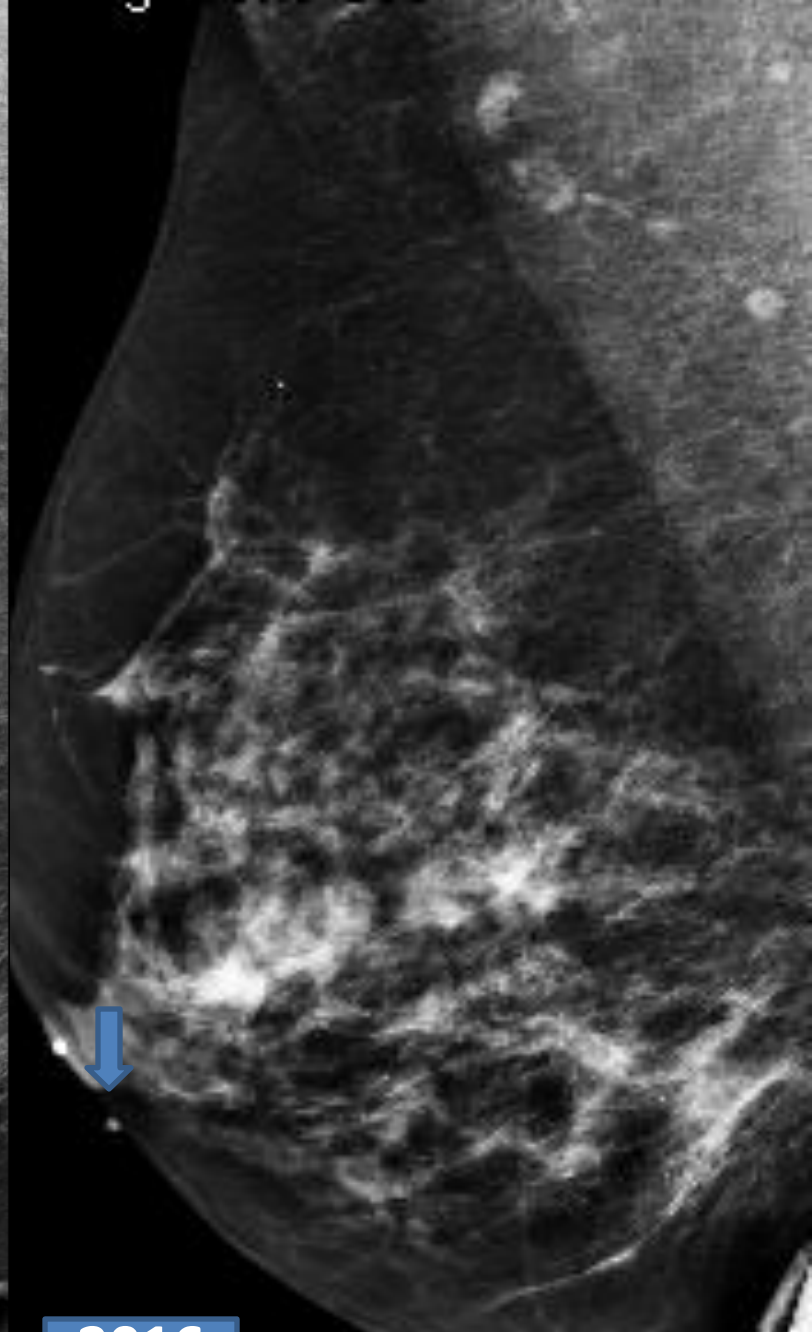
- Sensitivity: 100%
- Specificity: 87.7%
- PPV: 76.2%
- NPV: 100%



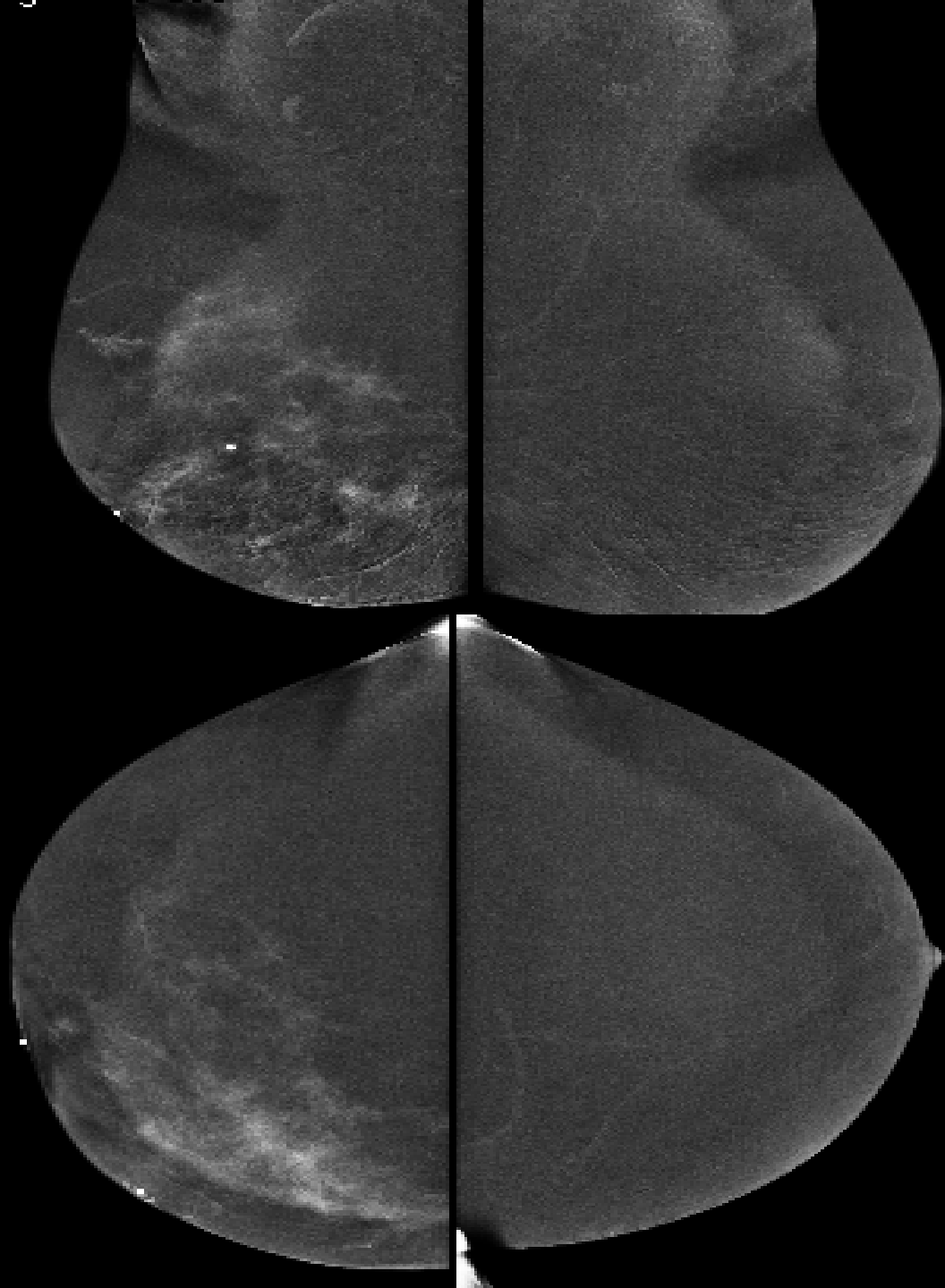
2014



2015



2016



# Palpable abnormalities

- **N=237 women/ 262 palpable abnormalities**
- **116/262 (44%) no imaging correlates**
- **242/262 (92%) benign**
- **Contrast images had better specificity & were more accurate c/w low energy plus ultrasound**
- **CEM plus US was not significantly different in performance than LE plus ultrasound**

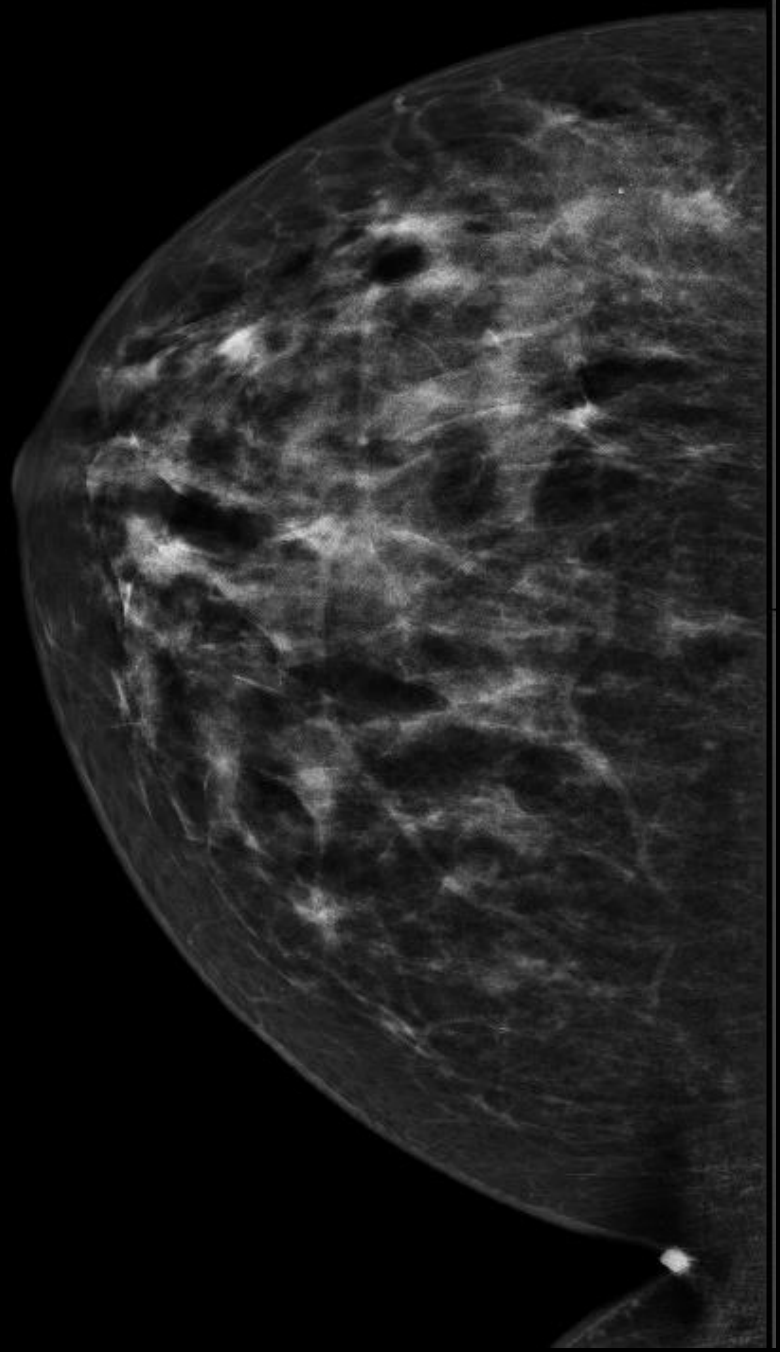
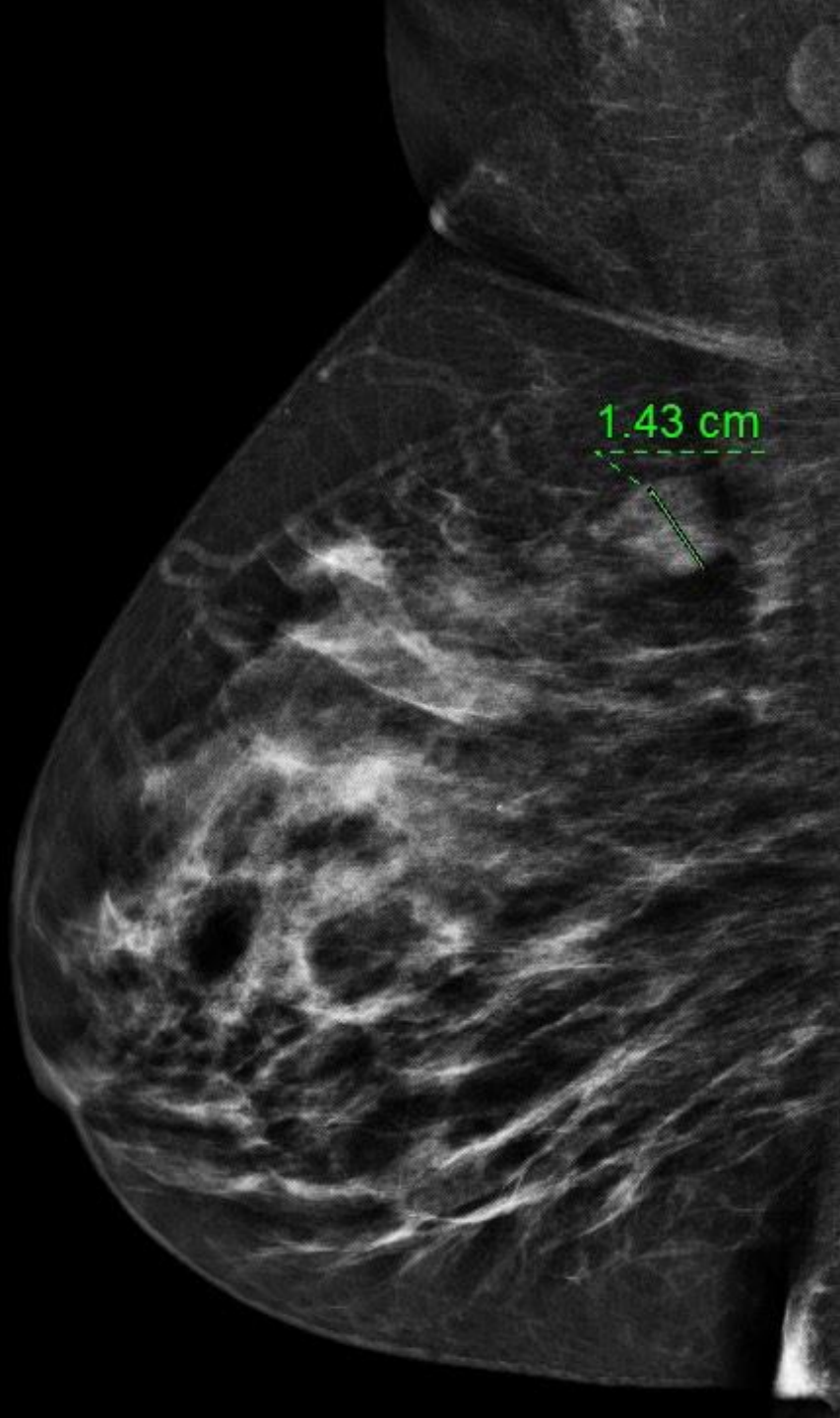
Amir et al CEM for women w/ palpable breast abnormalities, Academic Radiology 2023

# Known cancer

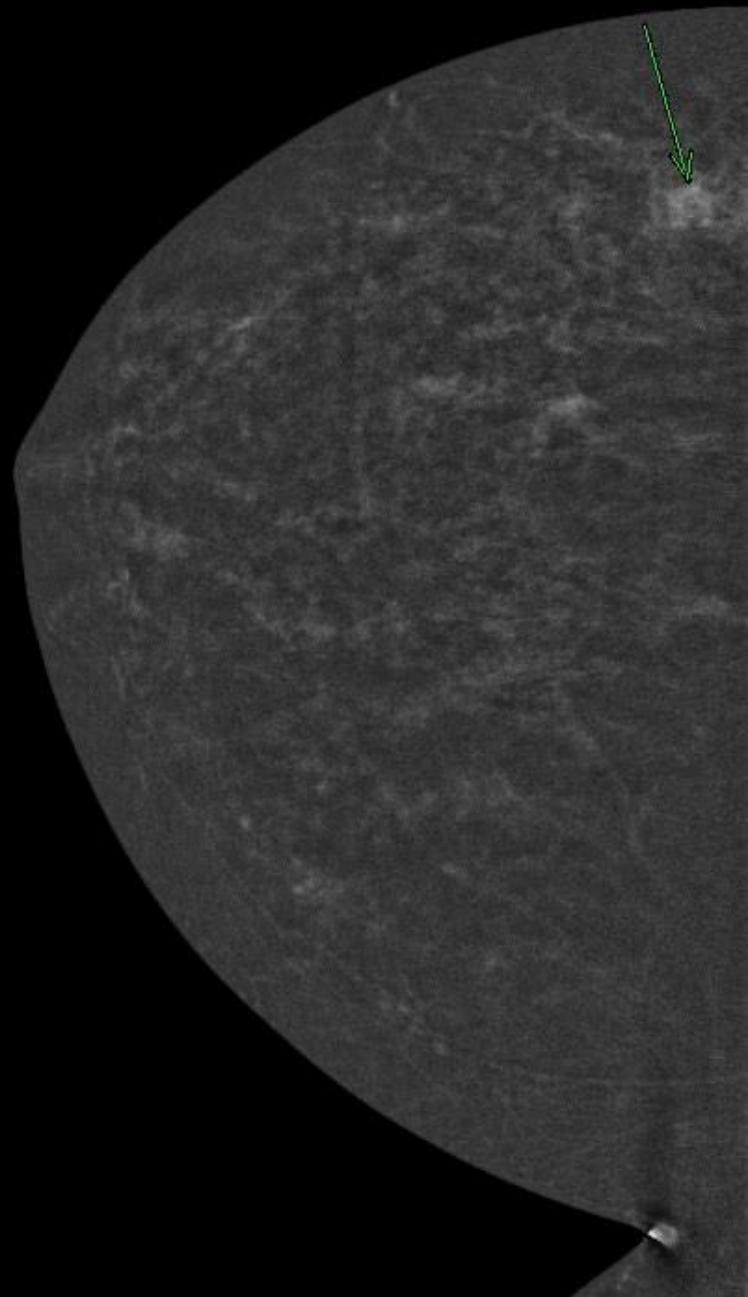
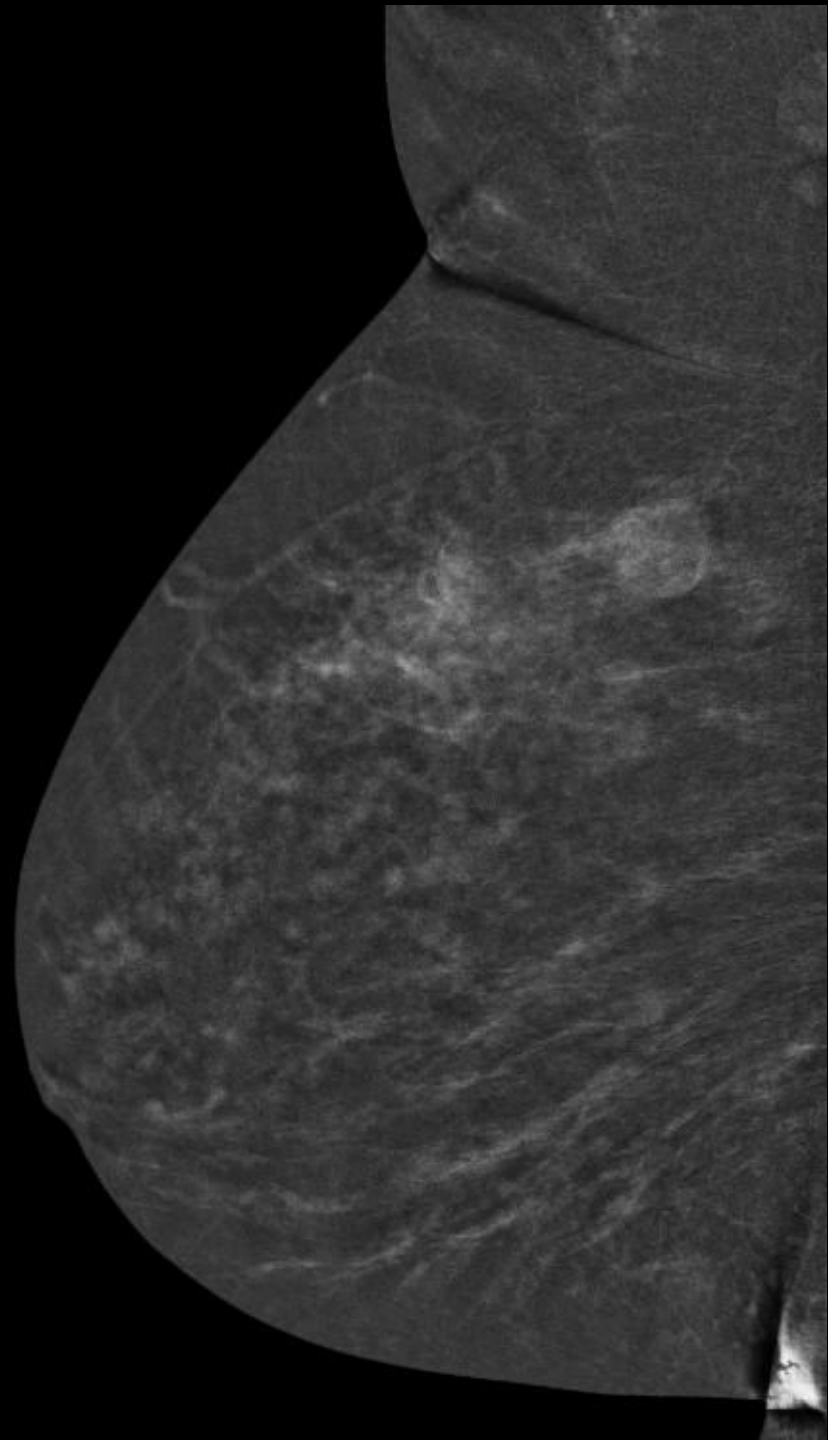
## First study w/ bilateral CEDM

- Mammography 42/52 (81%)
- CESM 50/52 (96%)
- MRI 50/52 (96%)

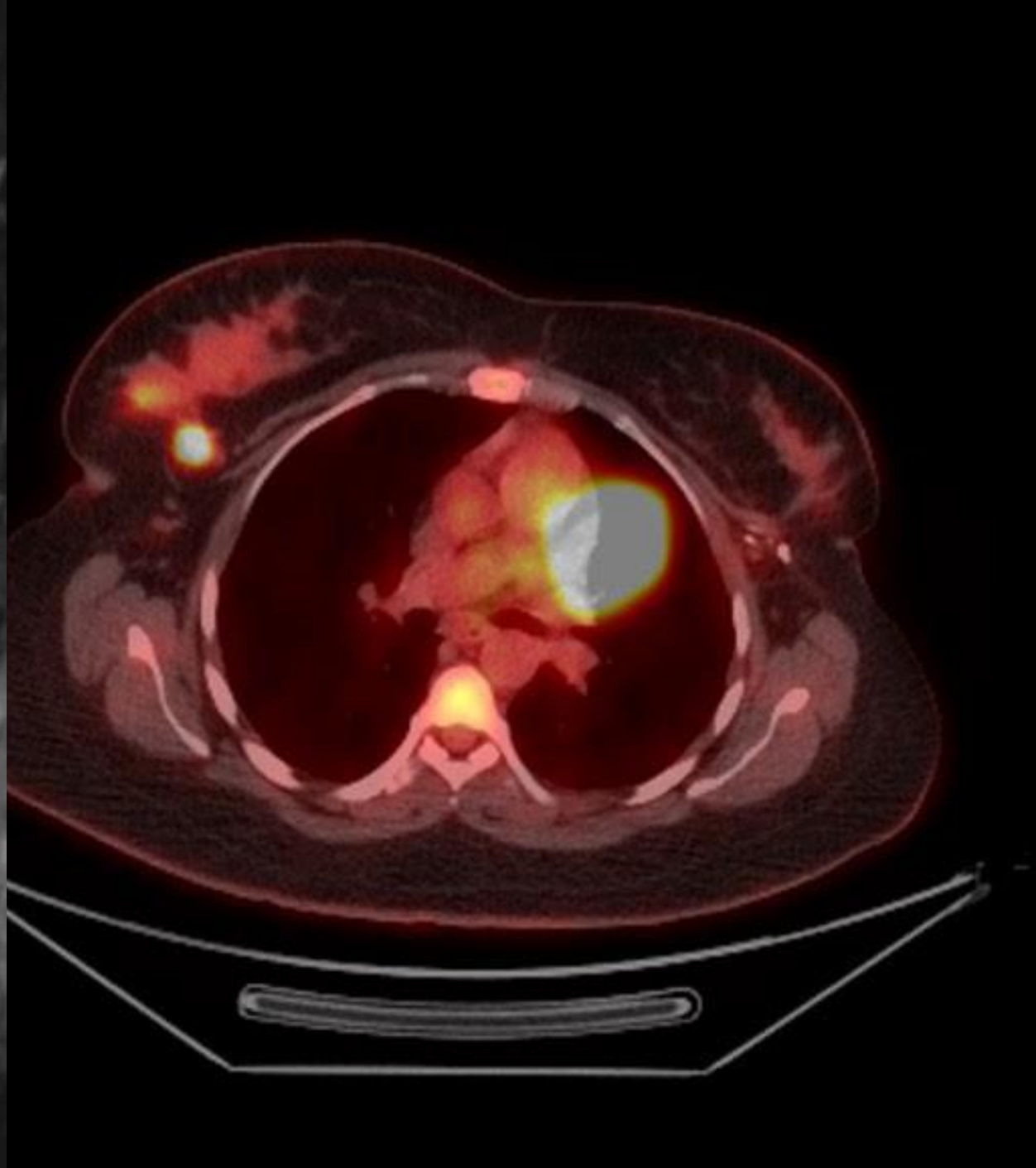
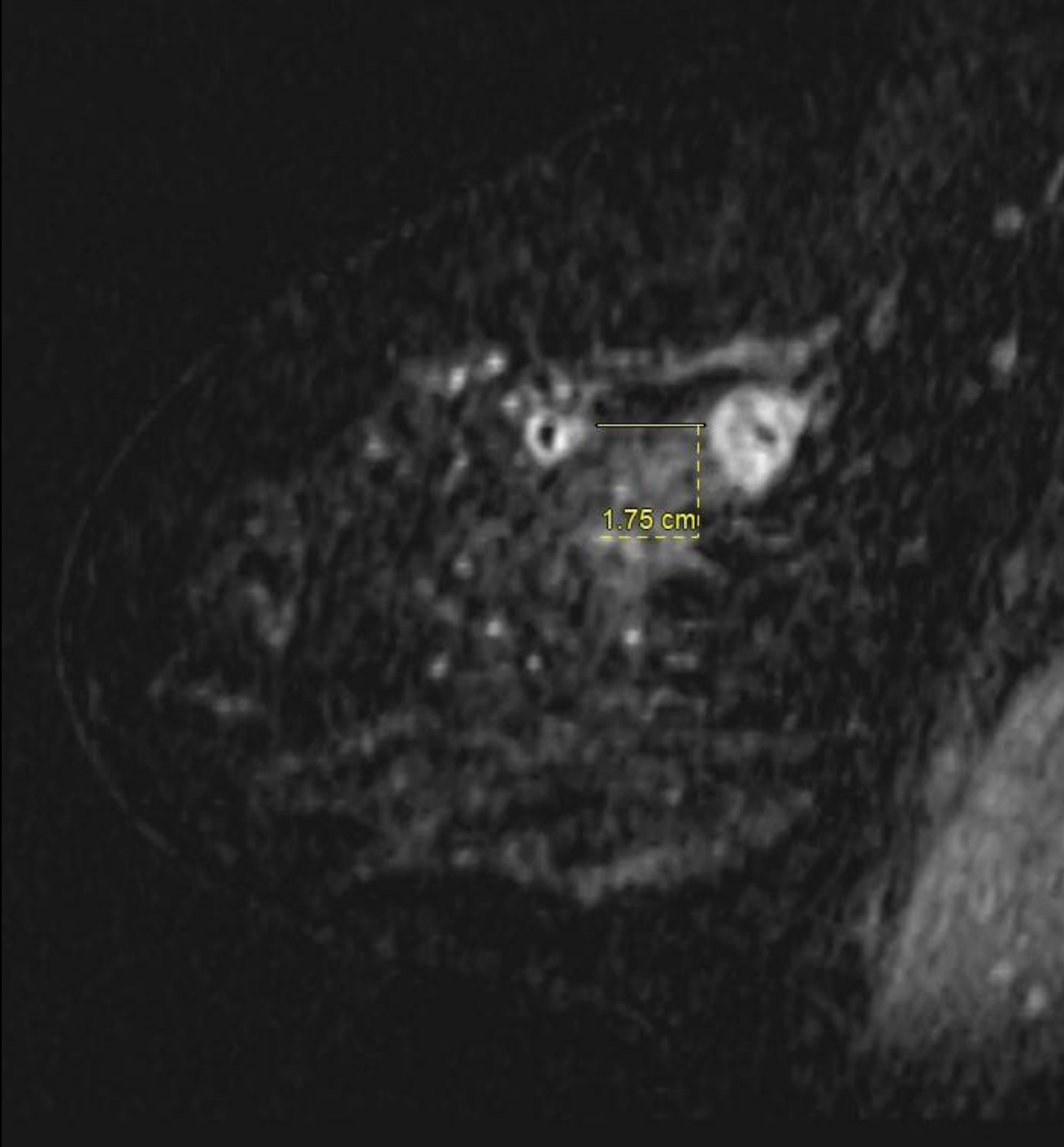
Based in part on this work CEDM received FDA approval











**Follow up after neoadjuvant Rx**

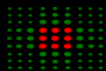
# CEM vs MRI for NAC

- N = 46 **prospective** study
- Studies interpreted blinded to each other
- Both slightly underestimated residual tumor size
- CESM predicted pCR better than MRI (Lin's coefficient 0.81 vs 0.59).
- CESM vs MRI CR: sensitivity: 100% vs 87%  
specificity: 84% vs 60%

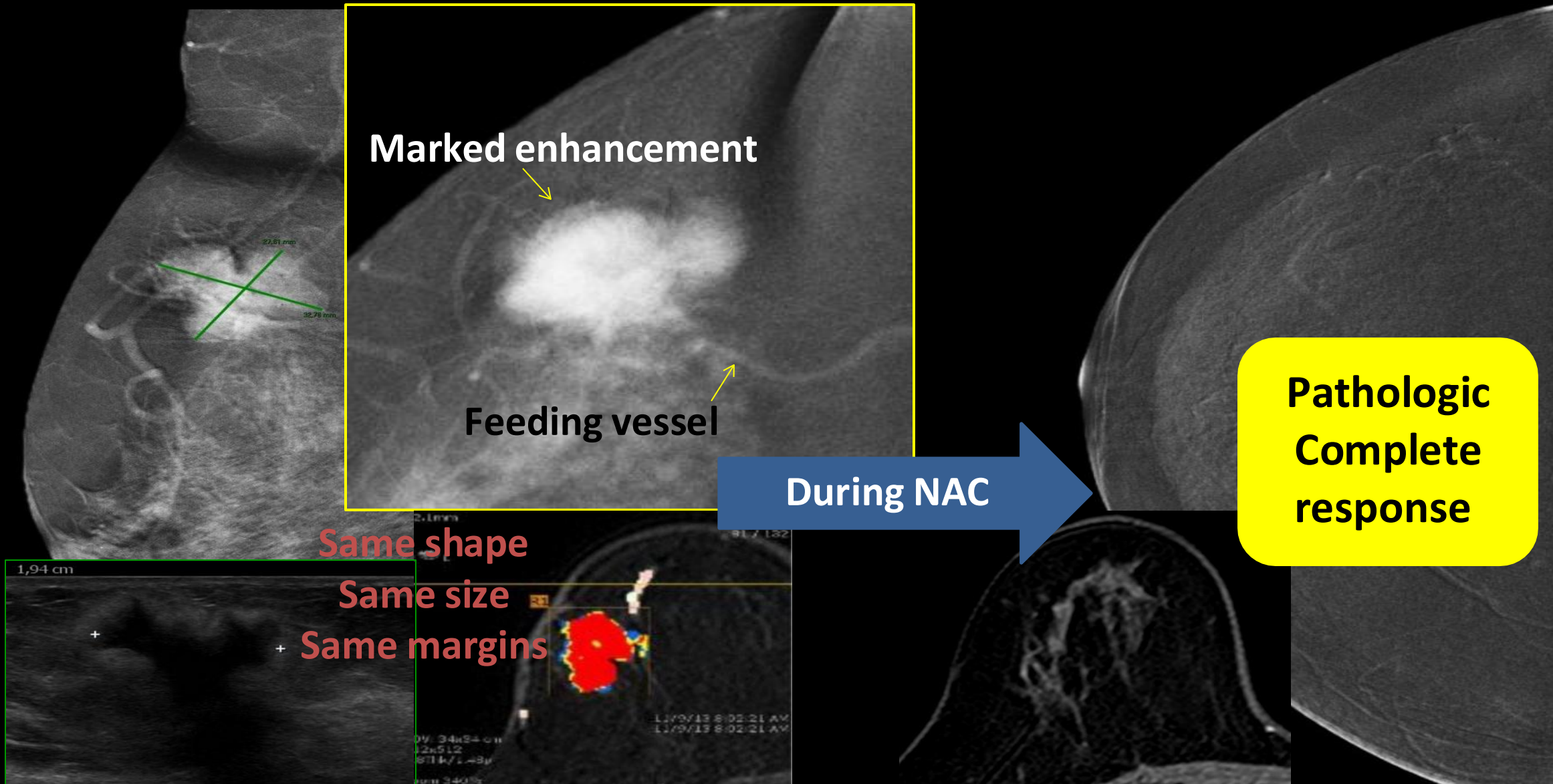
# CEM vs MRI for NAC

- **N=65 retrospective**
- **CESM & MRI read blinded to each other**
- **CESM sensitivity 95% vs 95% MRI**
- **CESM specificity 66.7% vs 68.9% MRI**
- **CESM PPV 55.9% vs 57.6% MRI**
- **CESM NPV 96.7% vs 96.9% MRI**

Patel et al Ann Surg Oncol 2018



44-year-old w/ 3 cm IDC & DCIS



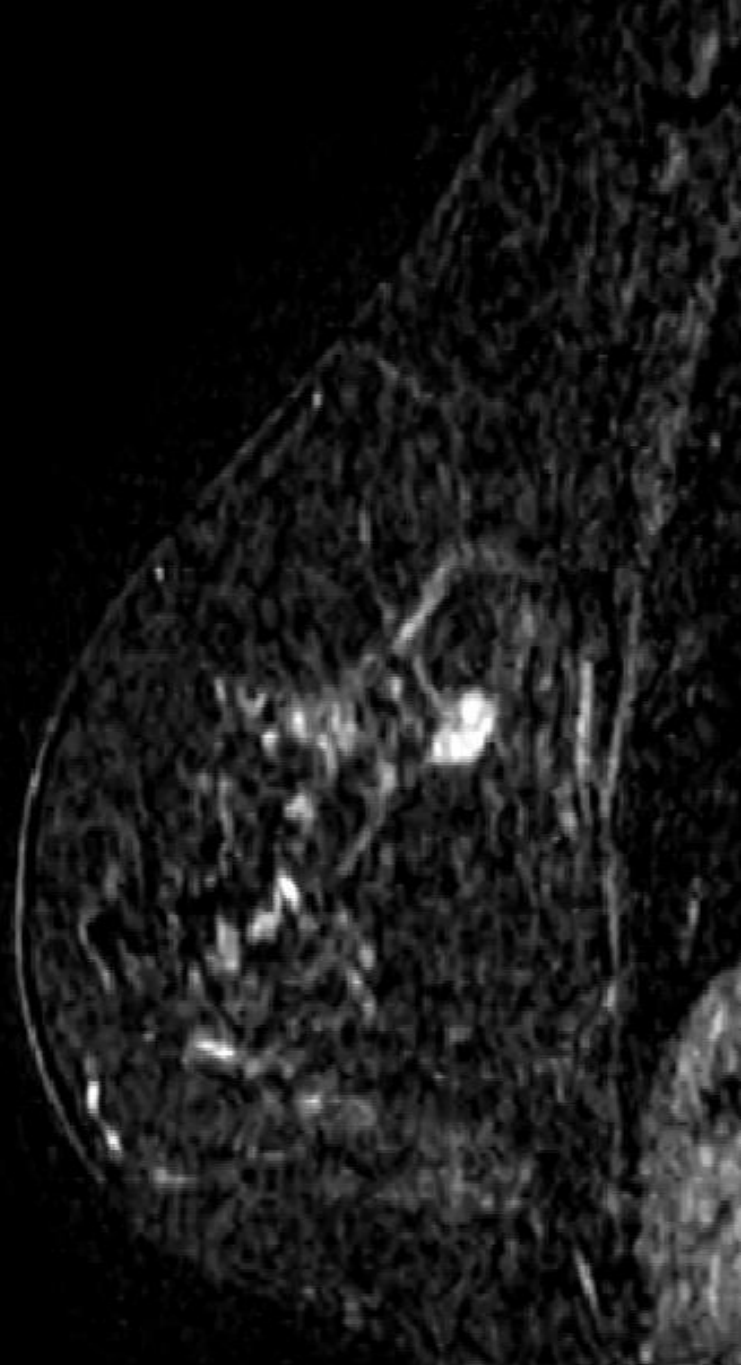
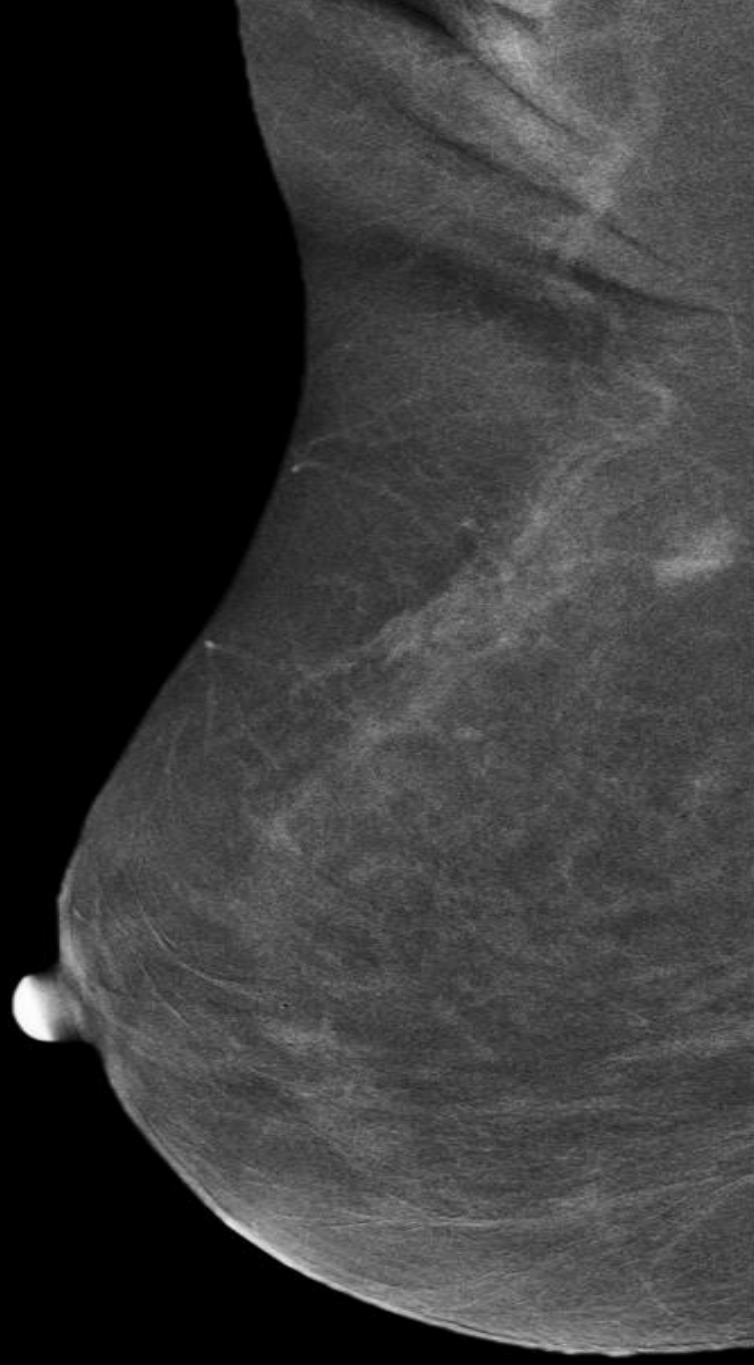
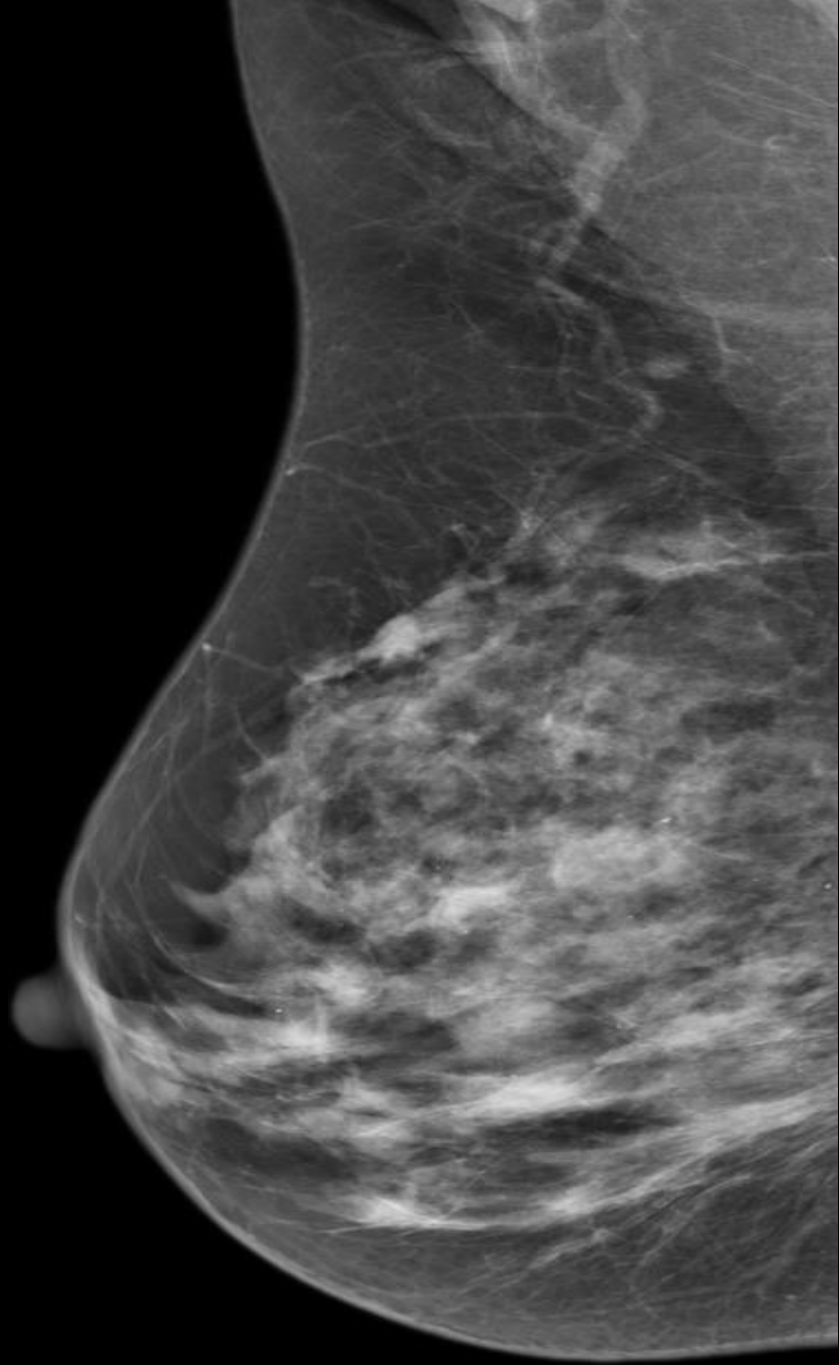
# CEM vs MRI prospective trial

**N=307 : prospective blinded study**

- **3 cancers detected first year**
  - **Mammo: 0 cancers**
  - **CEDM: 2 ILC**
  - **MRI: 2 ILC, 1 DCIS**
- **1 year follow- up:**
  - Cancers: 2 imaging detected (no symptomatic interval cancers)**

**Funding- Norton/BCRF**





## **CEM for screening (prevalence)**

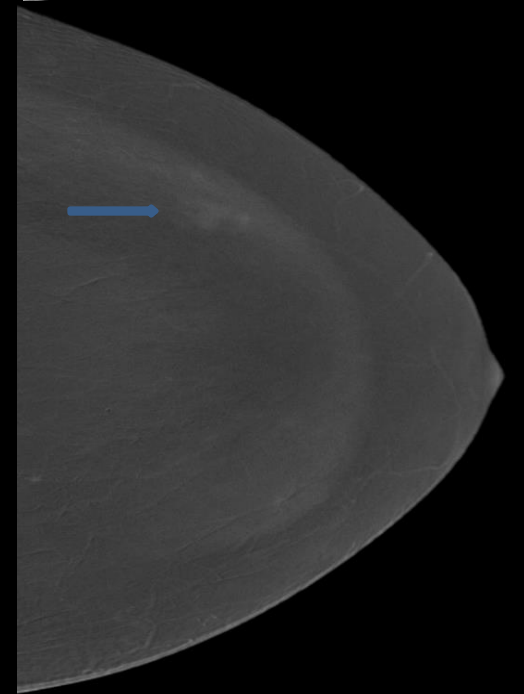
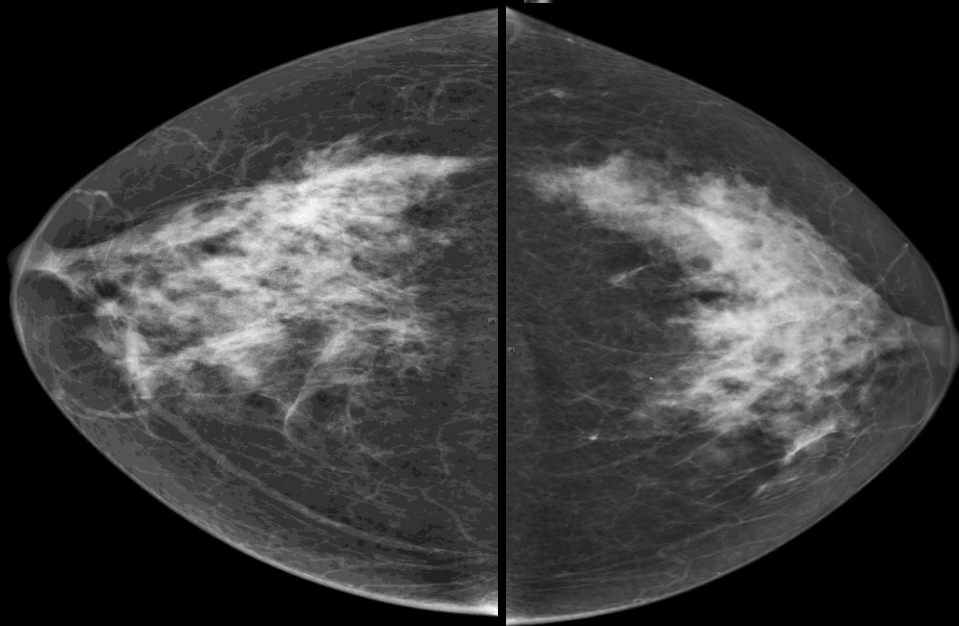
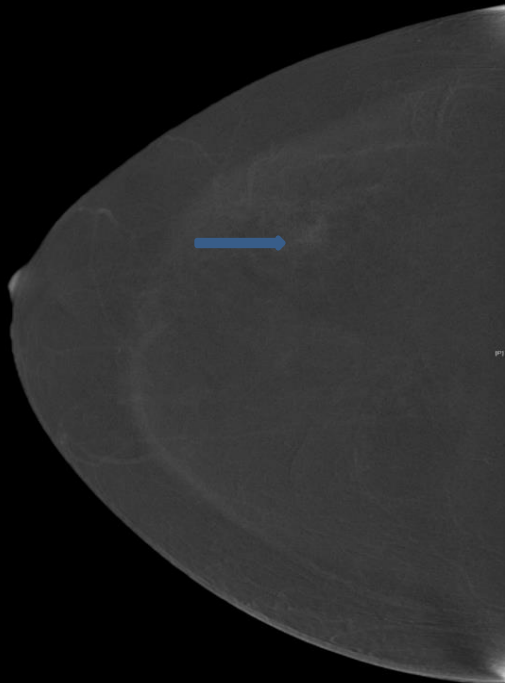
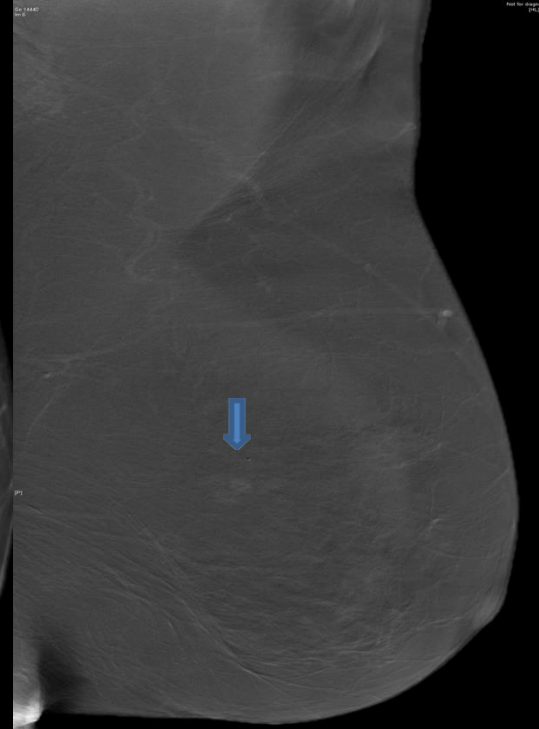
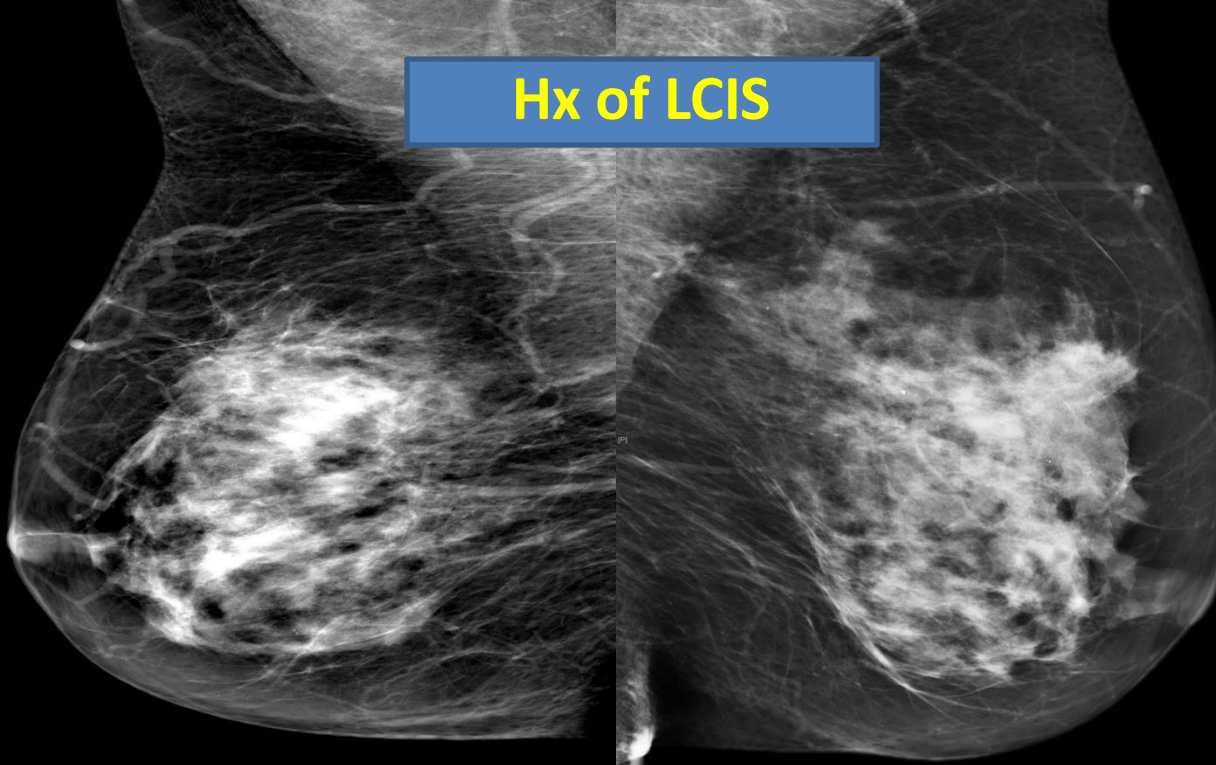
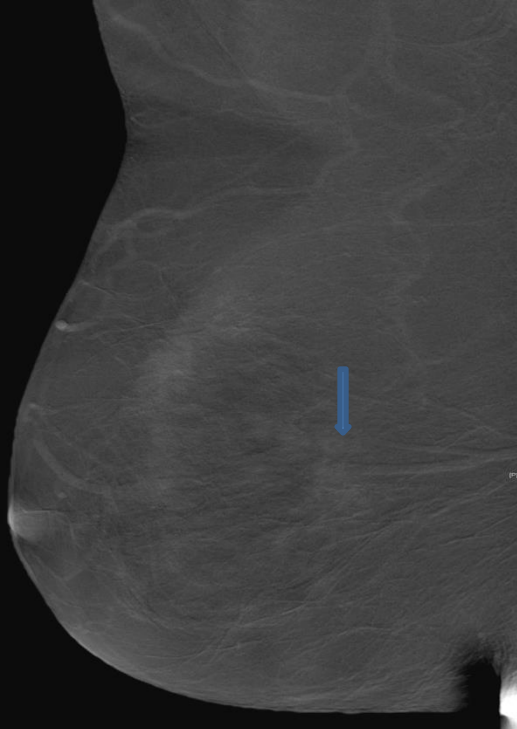
- **N=904 baseline CEM's**
- **Retrospective study**
- **77% dense breasts; > 90% other risk factors**
- **Detected 15 cancers in 14 women**
- **Cancer detection rate 15.5/1000**



## **CEM for screening (incidence)**

- **N= 2990/938 women**
- **32 cancers: CDR9/1000**
- **Recall rates and biopsy recommendations decreased w/ availability of prior studies**

Hx of LCIS



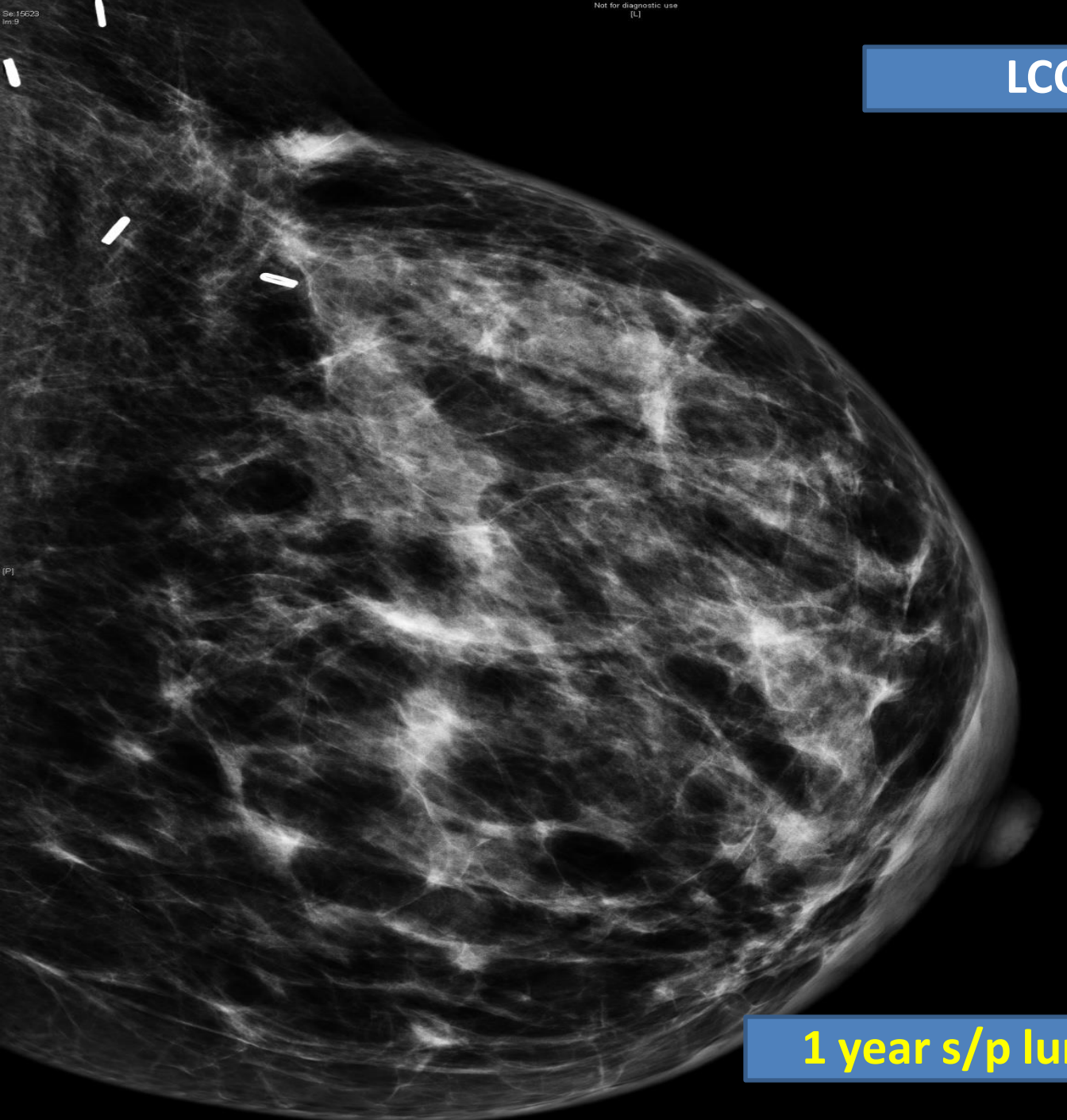
# T. van Nijnatten... Jochelson et al BJR open 2019

Enhancement	ILC (n=22)	IDC (n=22)	P-value
<b><i>Reader 1</i></b>			
Weak (%)	7 (32)	1 (5)	0.046
Moderate (%)	10 (45)	10 (45)	1.000
Strong (%)	5 (23)	11 (50)	0.060
<b><i>Reader 2</i></b>			
Weak (%)	5 (23)	1 (5)	0.185
Moderate (%)	8 (36)	5 (22)	0.322
Strong (%)	9 (41)	16 (73)	0.033
<b><i>Reader 3</i></b>			
Weak (%)	8 (36)	4 (18)	0.310
Moderate (%)	6 (28)	10 (46)	0.210
Strong (%)	8 (36)	8 (36)	1.000

# Contrast-Enhanced mammography for screening women after breast conserving surgery

- N=971 exams in 541 asymptomatic patients
- 21 cancers
- 6/21 (28.6%) seen on routine mammo
- Additional 9 (42.9%) detected only on post contrast images
- Cancer detection rate: mammo alone **6.2/1000**; CEM **15.4/1000**
- PPV 42.9%





# **CMIST: Contrast Enhanced Mammography Screening Trial**

**Comstock chair; Sung & Jochelson co-chairs**

- **CEM vs DBT for screening ~ 2000 pts**
- **Multicenter prospective trial**
- **Women 40-74 w/ dense breasts scheduled for DBT**
- **Both academic & private centers**
- **To compare of CEM to DBT at baseline & one year follow up**

**If we do screening CEM,**

**Do we need screening ultrasound?**

# CEDM for breast cancer screening

- N=611, retrospective study c/w mammo
- Intermediate risk & dense breasts
- Sensitivity: CEDM 90.5% vs 52.4%. P = 0.008
- Specificity: CEDM 76.1% vs 90.5%
- **Adjunct ultrasound showed 73 additional lesions: all false positive when not enhancing**

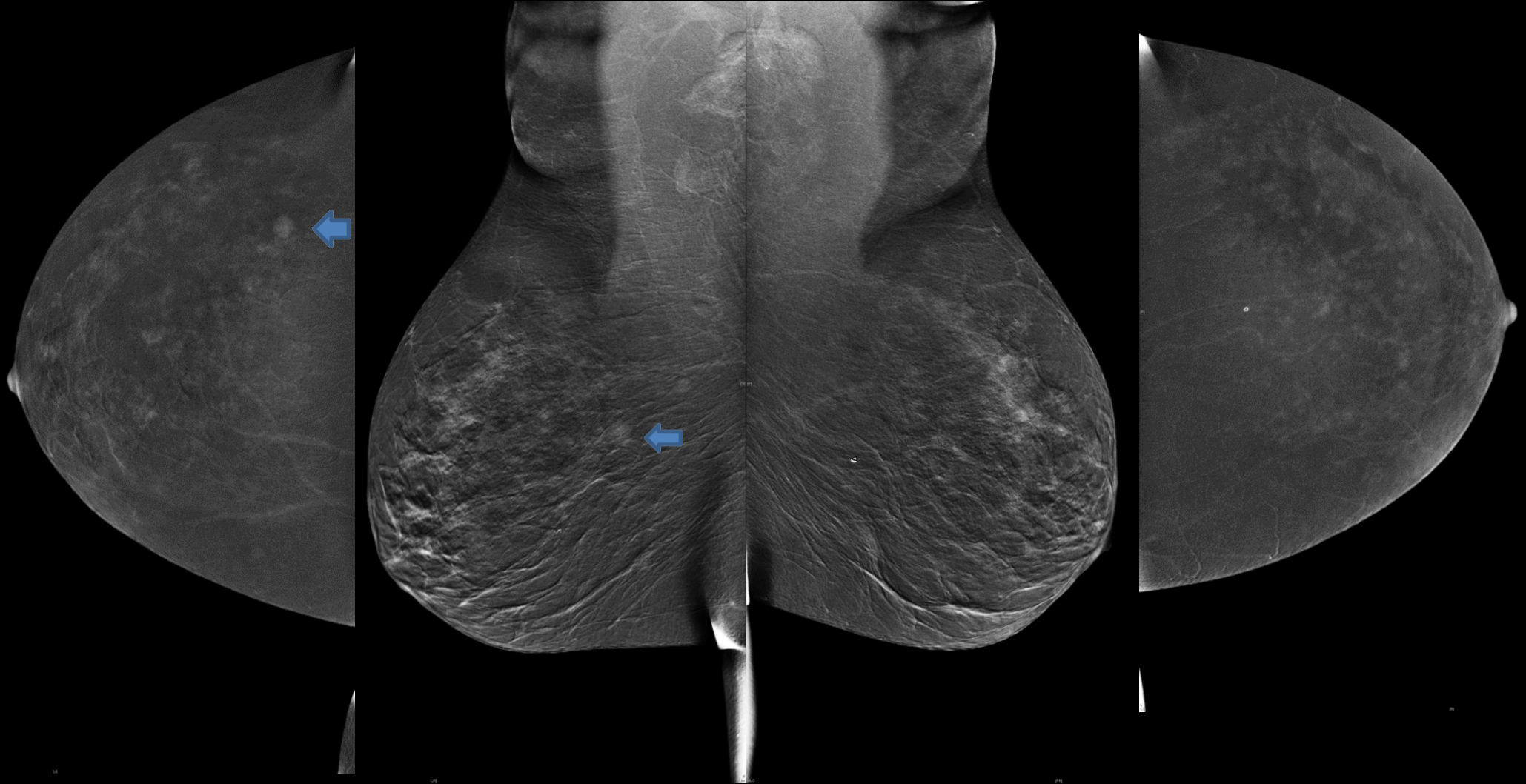


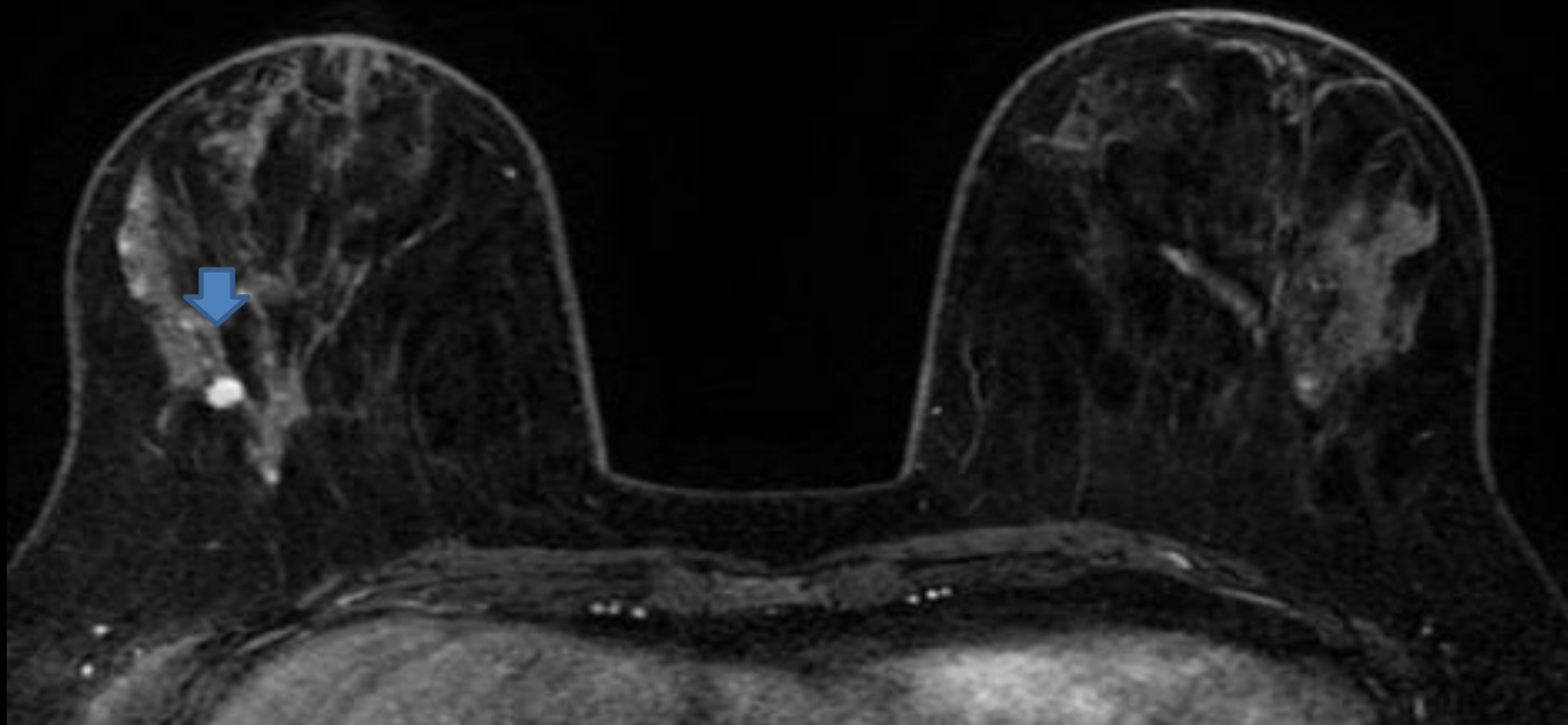
# CEM vs mammo + screening US (MSKCC)

- **N=468 prospective trial**
- **10 cancers in 9 women**
- **Cancer Detection Rate 19/1000**
- **9 cancers detected on CEM**
- **1 interval cancer**
- **No cancer found on ultrasound not seen on CEM**

# False negative ultrasound







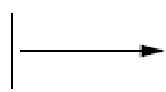
# BPE w/ Contrast Mammography

- N=516: 82% for screening
- 53/516 breast cancer
- BPE associated w/ breast density
- **Women w/ increased BPE: increased odds for breast ca:  $p < 0.001$**

### SCREENING OR SYMPTOM CATEGORY<sup>a</sup> SCREENING/FOLLOW-UP

#### Increased Risk:

Lifetime risk  $\geq 20\%$  as defined by models that are largely dependent on family history<sup>g,h,i</sup>

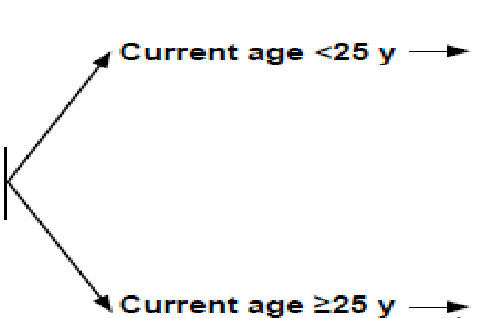


- Clinical encounter<sup>b,c,d,e,k</sup> every 6–12 mo
  - ▶ To begin when identified as being at increased risk, but not prior to age 21 y
  - ▶ Consider referral to a genetic counselor or other health professional with expertise and experience in cancer genetics, if not already done
  - ▶ Consider referral to a breast specialist as appropriate
- Annual screening<sup>b</sup> mammogram,<sup>m</sup> consider tomosynthesis<sup>o</sup>
  - ▶ To begin 10 years prior to when the youngest family member was diagnosed with breast cancer, not prior to age 30 y or age 40 y (whichever comes first)
- Recommend annual breast MRI<sup>p</sup>
  - ▶ To begin 10 years prior to when the youngest family member was diagnosed with breast cancer, not prior to age 25 y<sup>q</sup> or age 40 y (whichever comes first)
  - ▶ Consider contrast-enhanced mammography<sup>b</sup> or whole breast ultrasound<sup>b</sup> for those who qualify for but cannot undergo MRI
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
- Breast awareness<sup>l</sup>

OR



Thoracic RT between the ages of 10 and 30 y



- Annual clinical encounter<sup>b,c,d,e,k</sup>
    - ▶ Beginning 8 y after RT
  - Breast awareness<sup>l</sup>
- 
- Clinical encounter<sup>b,c,d,e,k</sup> every 6–12 mo
    - ▶ Begin 8 y after RT
  - Annual screening<sup>b</sup> mammogram,<sup>m</sup> consider tomosynthesis<sup>o</sup>
    - ▶ Begin 8 y after RT but not prior to age 30 y
  - Recommend annual breast MRI<sup>p</sup>
    - ▶ Begin 8 y after RT but not prior to age 25 y
    - ▶ Consider contrast-enhanced mammography<sup>b</sup> or whole breast ultrasound<sup>b</sup> for those who qualify for but cannot undergo MRI
  - Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
  - Breast awareness<sup>l</sup>

Note: All recommendations are category 2A unless otherwise indicated.  
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

**BREAST SCREENING CONSIDERATIONS**

- Individuals should undergo breast cancer risk assessment by age 25 and be counseled regarding potential benefits, risks, and limitations of breast screening in the context of their risk stratification. Shared decision-making is encouraged based on a patient's values and preferences ([See Discussion](#)).
- Adequate clinical breast exams include the following: upright and supine position during inspection, and palpation of all components of the breast (lateral-medial: from mid-axillary line to sternum; cephalad-caudad: from clavicle to inframammary ridge), axilla, and clavicular lymph node basins. Time spent on the palpable portion of the exam is associated with increased detection of palpable abnormalities. Clock/quadrant location and distance from nipple facilitate geographic correlation with imaging findings.
- Consider severe comorbid conditions limiting life expectancy (eg,  $\leq 10$  years) and whether therapeutic interventions are planned.
- Upper age limit for mammographic screening is not yet established.
- For individuals with mammographically dense breast tissue (heterogeneously or extremely dense breast tissue), recommend counseling on the risks and benefits of supplemental screening.
- Dense breasts limit the sensitivity of mammography. Mammographically dense breast tissue is associated with an increased risk for breast cancer.
- Handheld or automated ultrasound can increase cancer detection rates in individuals with dense breast tissue, but may increase recall and increase benign breast biopsies.
- Multiple studies show that tomosynthesis can decrease call back rates and improve cancer detection. Of note, most studies used double the dose of radiation. This is still within the federal guidelines for radiation dosage for mammography. The radiation dose can be minimized by using synthesized 2-D reconstruction.
- Contrast-enhanced mammography is also an emerging efficacious option for higher risk breast cancer screening.
- While there is emerging evidence that molecular imaging (breast-specific gamma imaging, sestamibi scan, or positron emission mammography) as screening procedures may improve detection, whole-body effective radiation dose with these tests is substantially higher than that of mammography.
- Current evidence does not support the routine use of thermography or ductal lavage as screening procedures.
- In high-risk settings, based on current evidence and considering the FDA safety announcement<sup>1</sup> (gadolinium-based contrast agents) we continue to recommend annual MRI in select populations after shared decision-making. Breast cancer screening MRI may also increase recall and increase benign breast biopsies.
- Abbreviated MRI used to replace traditional MRI is undergoing active investigation.

<sup>1</sup>FDA Drug Safety Communication: FDA identifies no harmful effects to date with brain retention of gadolinium-based contrast agents for MRIs; review to continue: <https://www.fda.gov/Drugs/DrugSafety/ucm559007.htm>.

Note: All recommendations are category 2A unless otherwise indicated.  
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

[Continued](#)



# CONCLUSIONS

- **CEM is a useful option for supplemental imaging**
- **One can upgrade your existing mammo units in certain situations**
- **Starting a program takes a team but there are many before you who can give advice**
- **The indications for CEM are like those for MRI**
- **The learning curve for reading is not steep if you already read mammo and MRI**
- **While work-flow is an issue, there are efficiencies you can adopt**

**DON'T LET FEAR OF REACTIONS GET TO YOU- YOU CAN DO IT!!**