

# Contrast Enhanced Digital Mammography

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FUJIFILM Value from Innovation  
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1. Understand the clinical indications and applications of contrast enhanced digital mammography (CEDM)
2. Compare CEDM and MRI applications
3. Review considerations for implementing CEDM while analyzing CEDM case studies

Learning Outcomes

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## Contrast Mammography

- CEDM is Contrast Enhanced Digital Mammography
- CEM is Contrast Enhanced Mammography
- CESM is Contrast Enhanced Spectral Mammography
- CE2D is Contrast Enhanced 2D Mammography
- CE3D is Contrast Enhanced 3D Mammography

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## POLL

Are you performing Contrast Mammography at your site?

1. YES
2. NO

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## What is Contrast Enhanced Digital Mammography?

A study by Lobbes et al. [1] showed a sensitivity of 100%, specificity of 87.7%, positive predictive value of 76.2%, and negative predictive value of 100% for CEM in the diagnostic mammogram

Lobbes MBI, Lalji U, Houwers J, et al. Contrast-enhanced spectral mammography in patients referred from the breast cancer screening programme. *Eur Radiol* 2014; 24:1668-1676

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## Why do we need contrast? How does it work?

- Increased vascularity is associated with tumor development
- Imaging with contrast, helps in the detection of the formation of blood vessels (angiogenesis)
- New capillary growth "feeds" the cancerous tumor so that it can thrive and grow.

Source: Time Magazine, May 1998

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## Dual Energy Imaging

Two exposures are made in rapid sequence:

1. Low kV (normal mammogram technical factors)
2. High kV (~45-49kV, Cu filter)
3. High kV-Low kV = subtraction image with contrast visible

\*\*\* Imaging window ends after ~8 minutes due to contrast redistribution

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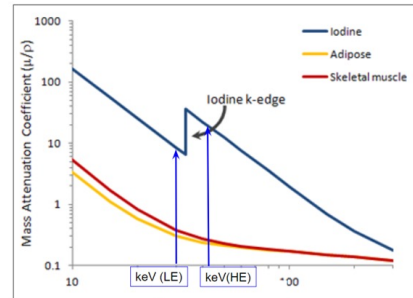
## What is K-edge?

- **K-edge** is a sudden increase in x-ray absorption occurring when the energy of the X-rays is just above the binding energy of the k-shell electrons of the absorbing atom. The 'k-edge' of iodine is 33.2 keV

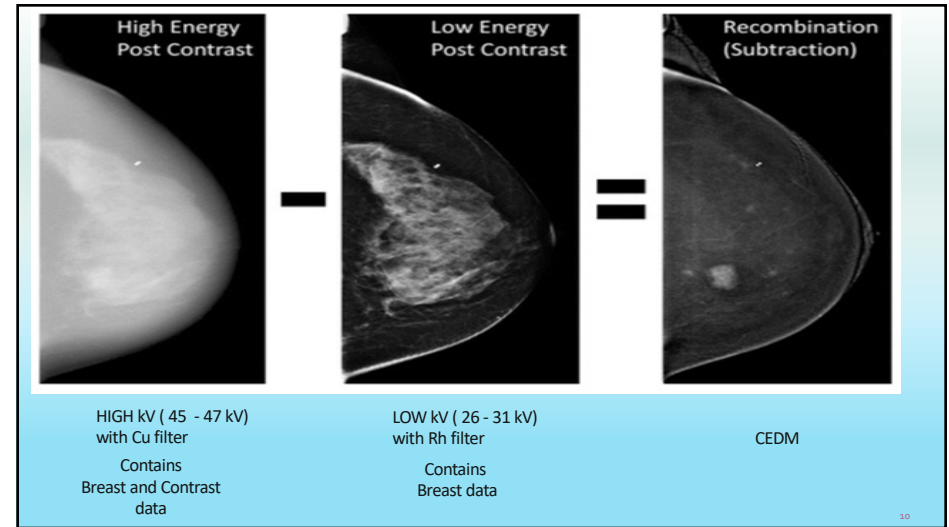
What?????

- The k-edge of iodine is a certain energy level where iodine absorbs X-rays very well.

**K-edge in CEDM helps target the energy level that makes iodine show up best on the image, enhancing the visibility of areas of interest**



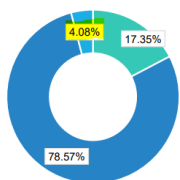
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The U.S. mammography market (by type) has been dominated by the digital breast tomosynthesis segment, which held 78.57% of the market share in 2023. **However, the contrast enhanced mammography segment is expected to be the fastest-growing**, with a CAGR of 15.64% in the forecast period 2024-2030. **This dominance is due to its superior contrast capabilities, effectiveness in high-risk patients, and its potential as a faster and more cost-effective alternative to breast MRI**

U.S. Mammography Market (2023)

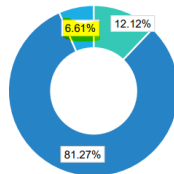


• 2D Mammography

• DBT/3D Mammography

• Contrast Enhanced Mammography

U.S. Mammography Market (2030)



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## Adoption

CEDM reflects steady growth, driven by its **demonstrated effectiveness in improving breast cancer detection and diagnosis**. As technological improvements continue and CEDM becomes more accessible, its role in breast imaging is expected to expand further, **potentially becoming a routine part of breast cancer care in combination with other imaging modalities**.

## Future Outlook

As the demand for more accurate breast cancer detection methods grows, Contrast-Enhanced Digital Mammography (CEDM) is expected to gain wider adoption, **particularly where MRI is inaccessible**. Ongoing improvements in contrast agents and image-processing technologies will likely enhance its diagnostic capabilities. **CEDM may also see more use as part of personalized breast cancer screening strategies tailored to individual risk factors and breast density**

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## Health Disparities in Canada

Average wait time for a screening mammogram was 4 weeks with most hospitals at 8+ weeks.

**Trillium Health Partners - Credit Valley Hospital**  
 Appointment Wait Time: 8+ weeks  
 42.5 KM Wheelchair Accessible English, French  
 Address: 2200 Eglinton Ave. West, Mississauga, ON L5M 2N1  
 Phone Number: 905-813-2731  
 Toll-Free: 1-800-668-9304  
 Hours +

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## MRI Wait times in Ontario

Patients with emergency conditions (Priority 1) are seen immediately and are not included in wait times data. Priority levels 2, 3, and 4 are determined by surgeons, specialists, and other health care providers, based on clinical evidence, to guide treatment decisions and improve patient access and outcomes. To learn about your priority level, please consult with your health care provider.

**Priority 4 patients** should be scanned within a target time of **28 Days**

**Priority 3 patients** should be scanned within a target time of **10 Days**

**Priority 2 patients** should be scanned within a target time of **2 Days**

**Ontario Provincial Average**

Overall Wait MRI: 31% Patients scanned within target time

Priority	Waited on average
Priority 4 Patients	102 Days
Priority 3 Patients	29 Days
Priority 2 Patients	3 Days

[+ Show time-trend data](#)

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## Women with breast cancer receive different care depending on where they live in Canada

Authors say that knowing the differences in treatment and acute care use for women with breast cancer across Canada will help to identify opportunities for learning and improvement.

Study looked at de-identified health records for more than 50,000 women newly diagnosed with stage I to III breast cancer who underwent surgery in **British Columbia, Manitoba, Ontario and Nova Scotia**. The women were followed for six months after the initial treatment and subsequent care (adjuvant or neoadjuvant chemotherapy, or no additional treatment).



A similar proportion of patients underwent **lumpectomy** across all provinces (67.2% - 71.2%).

**Mastectomy** was more common in **Nova Scotia** than in other provinces (51.7% vs. 33.3% - 36.9%).

**Chemotherapy** was most likely in **Ontario** (46.4%), and least likely in **Nova Scotia** (38%).

**Radiotherapy** was more common in **British Columbia** (70.3%) and **Ontario** (64%) than in **Manitoba** (56.3%) or **Nova Scotia** (55.2%).

The proportion of women who received chemotherapy and were **hospitalized** was highest in **British Columbia** (26.7%) and lowest in **Ontario** (6.4%).

The proportion of women who received chemotherapy and had **at least one ER visit** was highest in **Ontario** (36.1%) and lowest in **British Columbia** (16%).

The proportion of women who received chemotherapy and had **at least one ER visit that led to hospitalization** was similar across all provinces (13.9% - 16.8%).

Powis M et al. *Curr. Oncol.* 2019.

ICES Data. Discovery. Better Health. ices.on.ca



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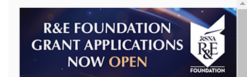
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energies just above and just below the k edge of iodine, both the traditional low-energy (LE) image and the iodine-enhanced image can be obtained from a single relatively short compression. In the initial protocol, temporal subtraction CEM was compared with dual-energy subtraction CEM techniques for mediolateral oblique views only in patients who were scheduled for biopsy. While both techniques facilitated contrast material uptake in the lesions, the dual-energy technique generated superior image quality owing to a lack of misregistration artifact and improved compression (8).

Since the initial feasibility study,

**Teaching Point** additional studies have demonstrated that CEM, alone or in combination with standard mammography, is as accurate as MRI for lesion detection. Compared with MRI, CEM has demonstrated lower sensitivity but higher specificity, particularly in patients with dense breast tissue (11). Furthermore, the information acquired from CEM images has been found to be especially useful in addressing inconclusive screening studies (12), shows promise for possible improvement in high-risk screening populations (12,13), and enables assessment of neoadjuvant systemic therapy responses (13,14).

With the performance of CEM being similar to that of MRI, studies to investigate applications of CEM for multiple indications that were historically reserved for MRI continue to be performed. Current research is focused on the radiomic features embedded in CEM images (15-17) and the development of contrast-enhanced digital breast tomosynthesis in the clinical arena (18).



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**Comparison of Contrast-enhanced Mammography with MRI Utilizing an Enriched Reader Study: A Breast Cancer Study (CONTRAST Trial)**

Jordana Phillips, Fejas S. Mehta, Leah H. Portnow, Michael D. C. Fishman, Zheng Zhang, Etta D. Pisano

Published Online: Nov 14 2023 | <https://doi.org/10.1148/radiol.230530>

**Abstract**

Contrast-enhanced mammography had noninferior performance to full breast MRI and abbreviated breast MRI and superior performance to digital mammography in terms of reader average area under the receiver operating characteristic curve in an asymptomatic study sample.

**Results**

The study included 132 case sets (14 negative, 74 benign, and 44 malignant); all female participants; mean age, 54 years ± 12 (SD). The mean areas under the receiver operating characteristic curve (AUCs) for digital mammography, CEM, AB MRI, and full MRI were 0.79, 0.91, 0.89, and 0.91, respectively. CEM was superior to digital mammography ( $P < .001$ ). No evidence of a difference in AUC was found between CEM and AB MRI and MRI.

**Conclusion**

In an asymptomatic study sample, CEM was noninferior to full MRI and AB MRI and was superior to digital mammography.

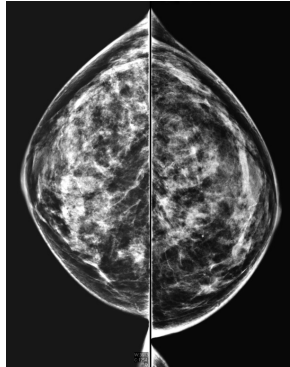
Clinical trial registration no. NCT03482557 and NCT02275871

© RSNA, 2023

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## Benefits of Contrast Mammography

- Fast results, reduces patient anxiety
- Alternative for claustrophobic patients
- Can reduce the number of unnecessary biopsies
- More cost effective than MRI
- Fast exam time/enhanced productivity
- Functional Imaging/Dense Breast Imaging

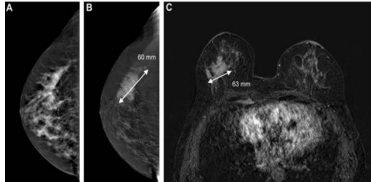


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## Clinical Applications

**Alternative to Breast MRI**

- Evaluate difficult to interpret mammograms<sup>1</sup>
- Screening women with elevated risk for breast cancer<sup>1</sup>
- Patients contraindicated for MRI<sup>2</sup>
- Monitor effectiveness of drug therapy<sup>3</sup>
- Identify potential undetected malignancies<sup>1</sup>



<sup>1</sup> Lewin et al. Contrast Mammography Reveals Hard-to-Find Cancers. RSNA Press Release. 30th September 2023.  
<sup>2</sup> Weinstein SP, Localio AR, Conant EF, Rosen M, Thomas KM, Schnall MD. Multimodality screening of high-risk women: a prospective cohort study. J Clin Oncol. 2009 Dec 20;27(36):6124-8. doi: 10.1200/JCO.2009.24.4277. Epub 2009 Nov 2.  
<sup>3</sup> <http://www.aacr.org/jco/medial/2a0eb28eb59041e2825179afb72ef624.pdf>

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## Contrast Enhanced Breast Imaging

- **MRI-** uses gadolinium as a contrast agent
- **CEDM-** uses an iodine contrast agent (CT contrast)
- **Same principal-** images lesions with higher neovascularity (extracellular contrast leakage)
- **Morphology and physiology**
- **Imaging not affected by breast density**
- **Both have high sensitivity for cancer detection**

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## Comparison of MRI vs. CEDM

Comparison of MRI to CEDM	MRI with Gd contrast	CEDM with Iodine contrast
Standard of care	*	
Image both breasts in one acquisition	*	
Easy to measure kinetics	*	
Risk of adverse reaction to contrast agent	*	*
Image both breasts with 1 injection	*	*
Equipment Cost < \$900k		*
Short procedure time		*
Imaging of microcalcifications		*
Scheduling based on a women's menstrual cycle	*	

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## Contraindication Comparison of MRI vs. CEDM

Contraindications	MRI with Gd contrast	CEDM with Iodine contrast
Allergy to contrast agents	*	*
Claustrophobia	*	
Metallic or electronic implants, shrapnel	*	
Unable to lie prone	*	
Unable to lie still	*	

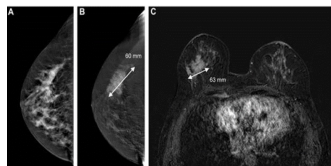
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## Notable limitations to CEDM

The Field of View for CEDM is much smaller than MRI

→ CEDM images do not include an evaluation of the entire axilla

→ CEDM images are unable to assess for chest wall invasion or internal mammary nodal enlargement



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## Contraindications and Renal Function testing

### Before a CEDM procedure:

#### **Creatinine blood test**

Patients older than 70 years of age or have diabetes, will need to have a blood test called a **serum creatinine** before CEDM. This test checks to see how the kidneys are working. Patients will need to have a serum creatinine test within 3 months (12 weeks) before the CEDM procedure

**POC Testing**- Creatinine POC devices allow rapid measurement of creatinine levels and require very small sample volumes. Fingerpick blood collection is often sufficient. The time taken to generate a result varies between 30 seconds and 12 minutes depending on the device used.

- History of previous reaction to iodinated contrast
- Patients who pregnant or breastfeeding
- Patients with poor renal function or kidney disease
- eGFR < 30mL

#### ➤ **Meformin**

Patients taking meformin (a medication for diabetes), may need to stop taking it for 2 days after the test depending on their creatinine results

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## Implementation




Things to consider.....

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## Equipment Requirements

- Vendor specific CEDM software
- Addition of a copper filter
- Power Injector\*
  - hand injection can be done, but using a power injector is the preferred method. This will allow for a consistent flow rate and post injection saline bolus.
- Crash Cart- for possible contrast reactions
- Room set-up
  - mayo stand
  - IV materials
  - Contrast Warmer (optional)
- Equipment to monitor vitals

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## Staff Requirements

- Vendor specific training on using the CEDM software and the procedure
- Staff member to review patient history (can be a nurse, technologist, or another staff member)
  - review medications
  - any prior history of contrast reactions
  - ask about renal disease
  - Menstruating patients may have exam scheduled 7-14 days after last period \*\*Facility dependent
- IV Line can be placed by mammography technologists, nurses, IV team
- A physician must be physically present to evaluate for any contrast reactions.
  - Reactions needing physician involvement are very rare- severe reactions are approximately 4 in 10,000(Covington, et al., 2018)
- Patients are often monitored for contrast reactions in the department for about 15 mins after the procedure.


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## Workflow Procedure Steps

Before the exam starts

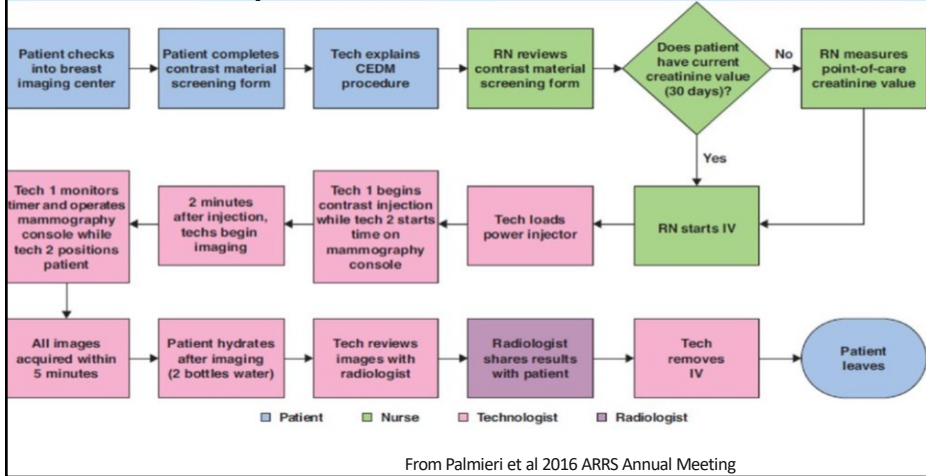
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    graph TD
      A[Radiologist reviews the images and clinical information before the patient arrives. Sets protocol] --> B[Technologist explains the procedure to the patient and obtain required consent]
      B --> C[Technologist examines breasts for any capillary hemangiomas as this will absorb contrast]
      C --> D[Patient is usually seated in a chair for contrast administration]
      D --> E[Inform the patient about possible side effects from the contrast injection:  
• warm feeling throughout the body  
• metallic taste in the mouth  
• feeling the need to urinate  
• pain or swelling at the]
      E --> A
  
```



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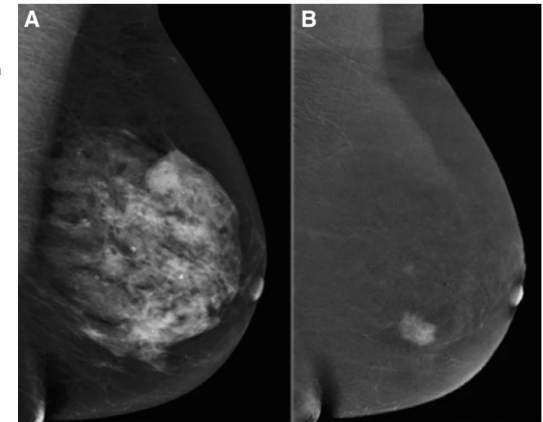
## Workflow-Example



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## Imaging Protocol:

- Imaging is typically performed on both breasts. Order of breasts and projections is determined by the radiologist.
- Commonly the side of interest is imaged first (ipsilateral) when the contrast agent is at its highest concentration followed by the contralateral breast. Typical order: MLO of affected breast-MLO contralateral breast-CC of affected breast and CC non affected side
- Some routines include a delayed MLO image of the affected side
- 3D Images could be done after basic views
- Spot compression views are occasionally performed

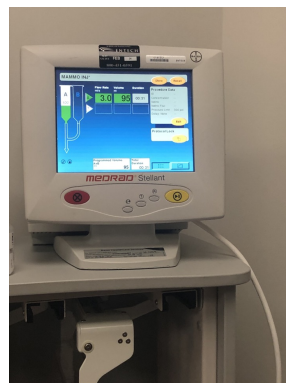


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## Contrast/Rates/Volumes

- To perform a CEDM examination, an IV is placed in the forearm or antecubital vein and a low osmolar iodinated contrast agent is administered at **2cc-3cc/s** using a power injector.
- Contrast agents with iodine concentration between **300 mg/ml and 370 mg/ml** are typically used.
- The volume of contrast is similar to that used for a CT scan, approximately **1.5 cc/kg body weight, typically around 90-150cc** followed by a saline flush (10 or 20cc; facility dependent)
- After a **delay of 2 minutes** from the end of the injection, the patient is positioned for 2 standard mammography views (cranio caudal and mediolateral oblique) of each breast.

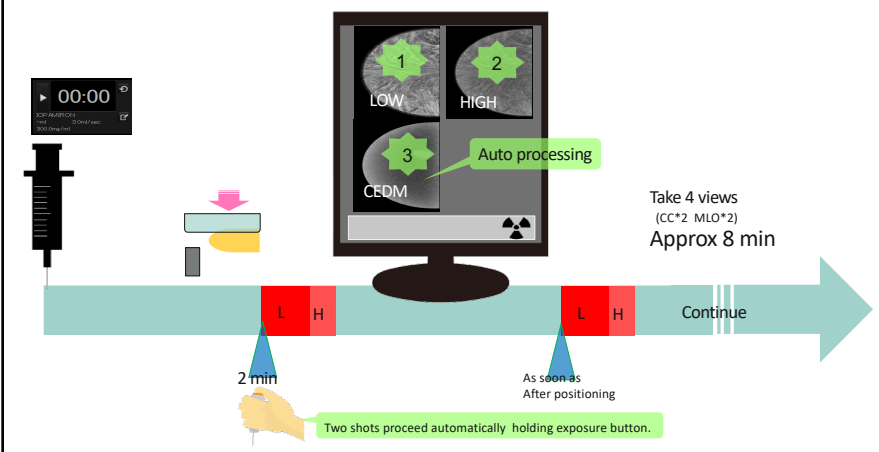


\*\* The patient's breast is not compressed during the contrast injection

John Lewin, MD, Maxine Jochelson, MD: Contrast Enhanced Digital Mammography; SBI White Papers May 1, 2017

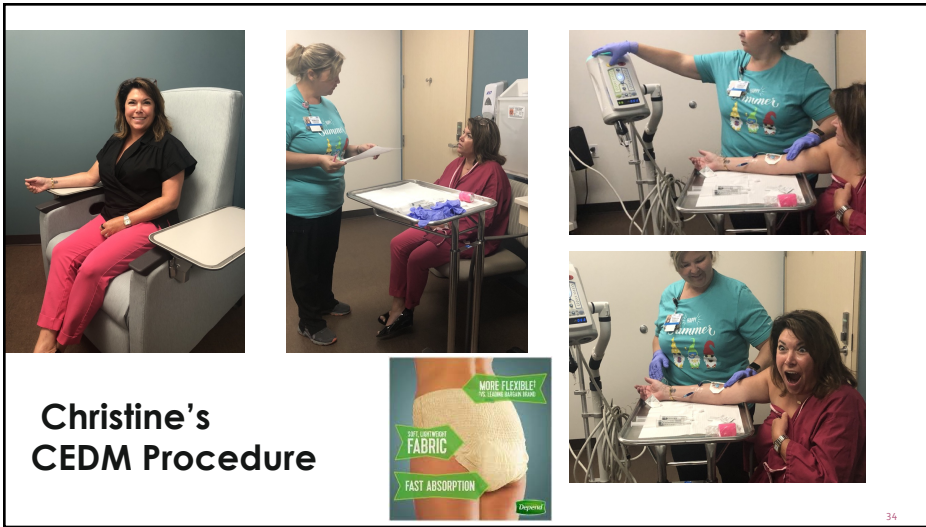
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## Examination flow



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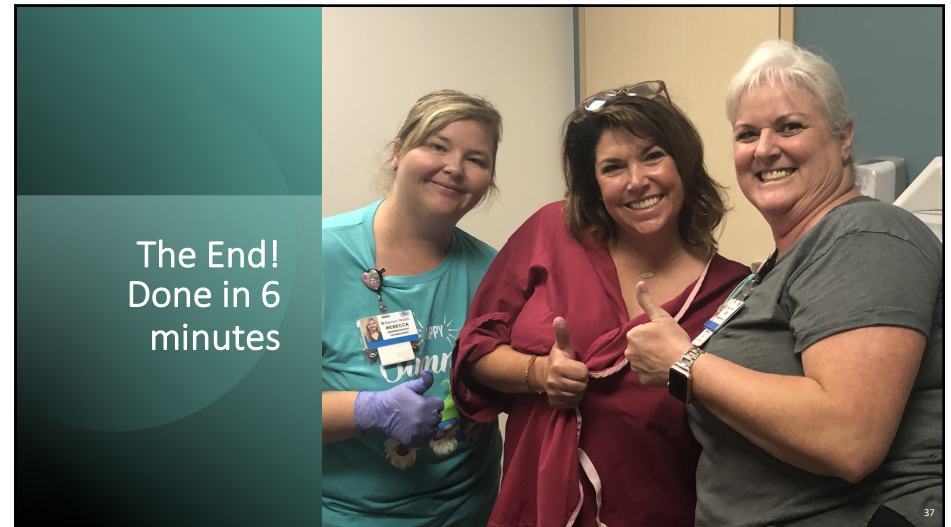
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## After the Procedure

- Remove IV from patients' arm
- Check injection site for any signs of contrast extravasation
  - -swelling
  - - stinging or burning
  - -tightness
- Contrast Reactions- mild reactions generally don't require any medical treatment, but vitals should be checked, and the patient monitored for ~30 mins.
- Mild allergic-like reactions can be treated with an antihistamine.

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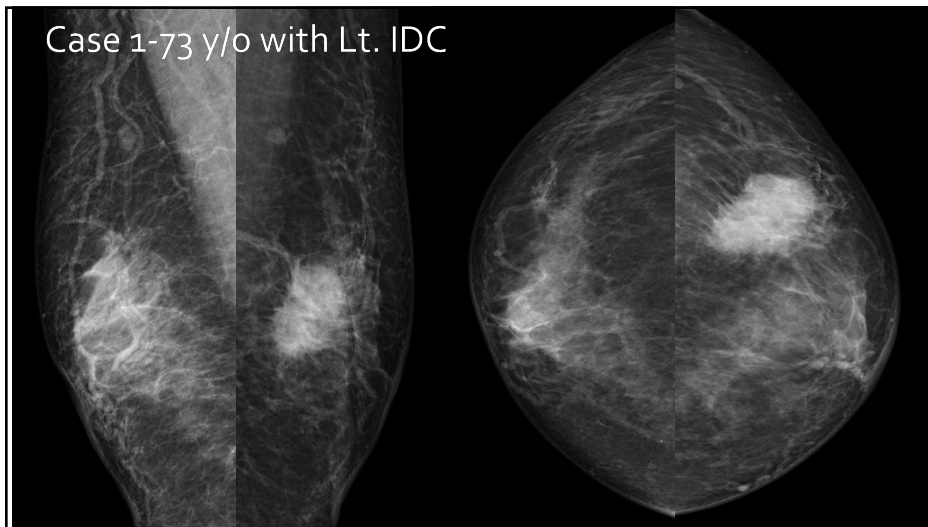
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## Case Studies

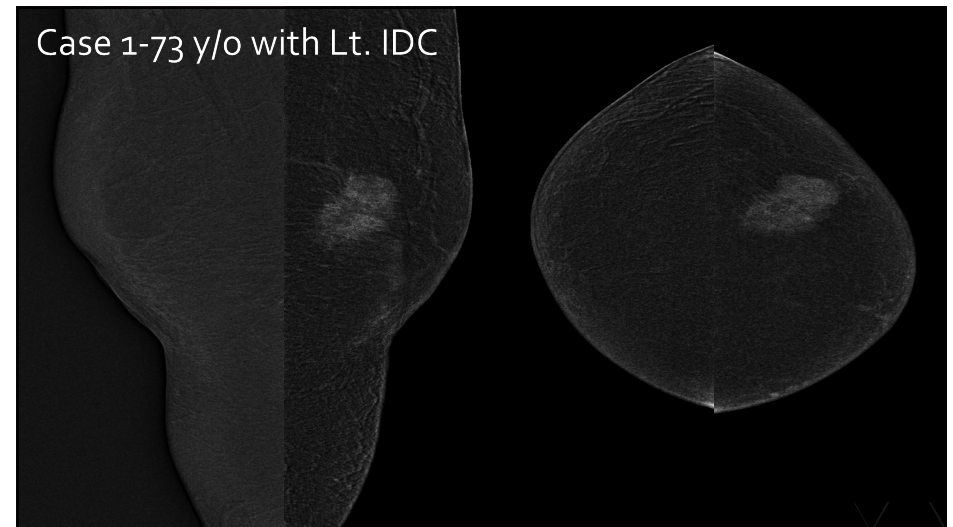


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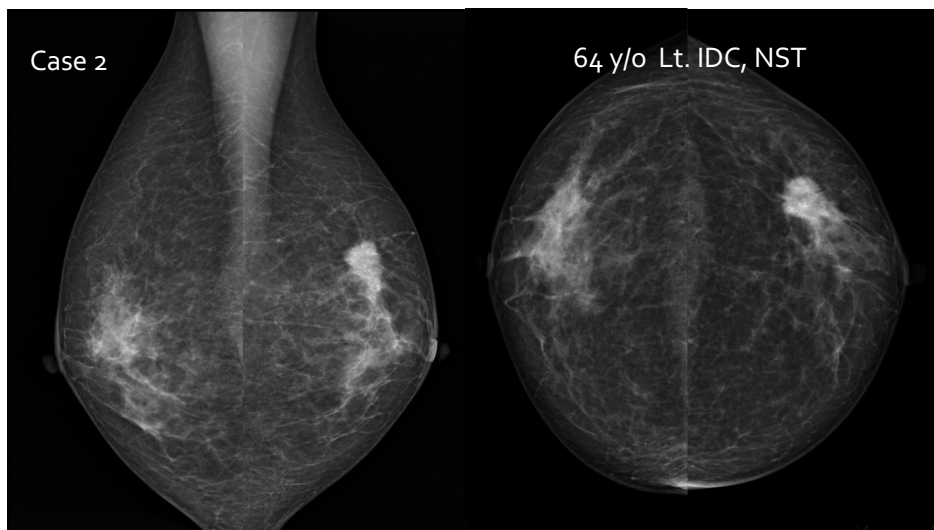
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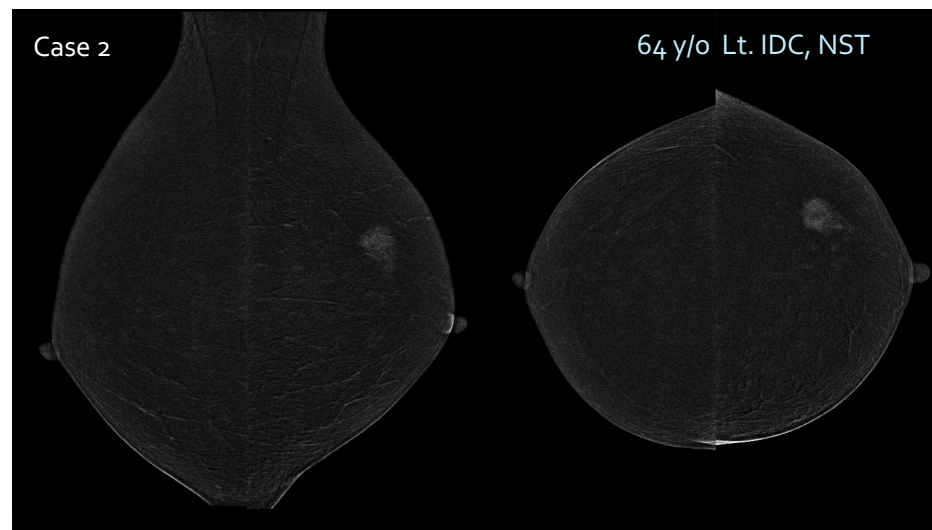
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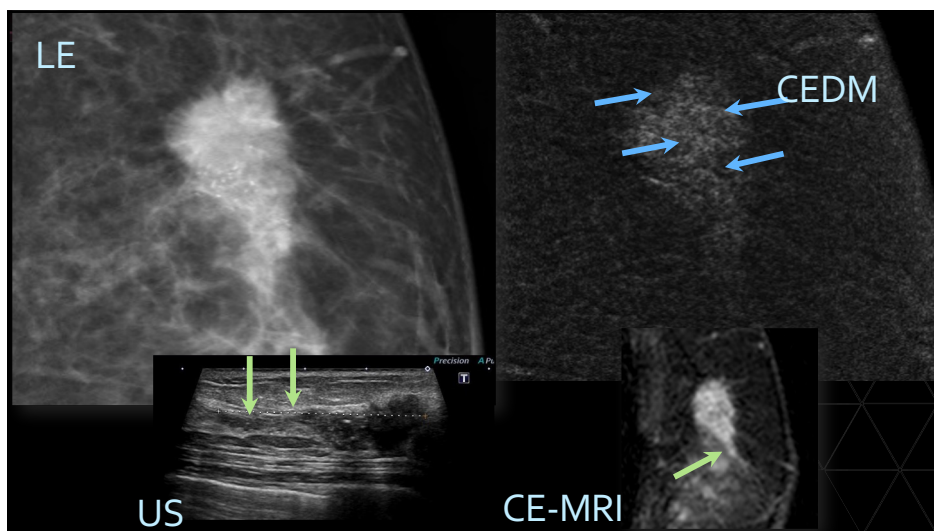
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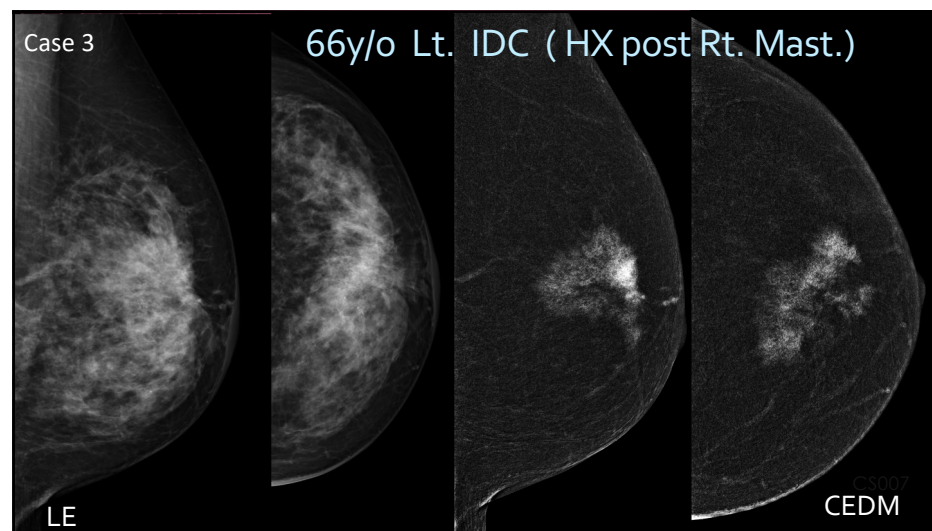
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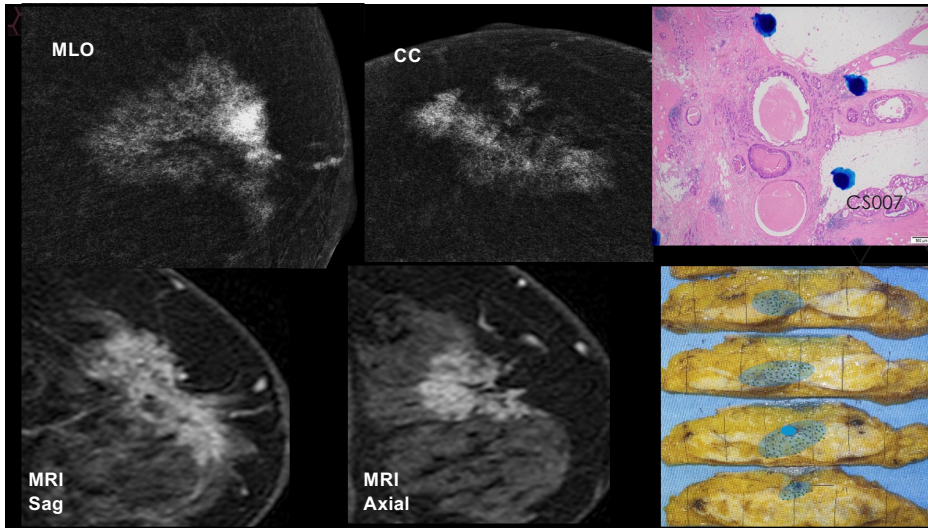
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## Reimbursement

- In the US CEDM is billed as a **Diagnostic** Breast Imaging Contrast Examination with an added charge for intravenous contrast. Even if CEDM is performed for high-risk surveillance in patients with a known genetic predisposition to breast cancer or prior elevated risk benign biopsy, it is billed as Diagnostic Breast Imaging Contrast Examination.

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## Conclusion

### Benefits and clinical indications for CEDM

- Alternative to breast MRI
- Evaluating patients contraindicated for MRI
- More cost effective than breast MRI
- Faster procedure
- Monitor the effectiveness of drug therapies
- Identify potential undetected malignancies

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Thank you

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