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Agenda:

- Definition of contrast enhanced digital mammography
- Clinical applications
- Considerations for implementing CEDM
- Contrast-contraindications/bloodwork testing
- Injection rates/volumes
- Dual Energy Imaging
- CEDM procedure
- Case examples
- Reimbursement

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Contrast Mammography- AKA

- 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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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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What is Contrast Enhanced Mammography?

- Approved by the FDA in 2011 for adjunct use in a diagnostic setting
- **Contrast-enhanced mammography (CEM) uses a dual-energy technique performed after the IV administration of iodinated contrast agent to identify abnormalities on the basis of angiogenesis, as well as morphologic features and density.**
- The physiologic information provided by CEM is similar to that provided by breast MRI, without the added time or expense of conventional breast MRI protocols. The combination of morphologic and physiologic information provided by CEM has been shown to provide superior sensitivity and specificity in diagnosing breast cancer when compared with digital mammography alone
- 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

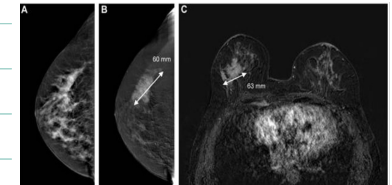
Lobbes MBI, Lalji U, Houwers J, et al. Contrast-enhanced spectral mammography in patients referred from the breast cancer screening programme. *Eur Radiol* 2014; 24:1668-1676

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Clinical Applications

Alternative to Breast MRI

- Evaluate difficult to interpret mammograms¹
- Screening women with elevated risk for breast cancer¹
- Patients contraindicated for MRI²
- Monitor effectiveness of drug therapy³
- Identify potential undetected malignancies¹



¹ Lewin et al. Contrast Mammography Reveals Hard-to-Find Cancers. *RSNA Press Release*. 30th September 2003.

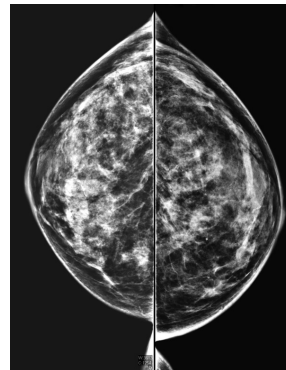
² Weinstein SP, Localio AR, Conant EF, Rosen M, Thomas KM, Schnall MD. Multimodality screening of high-risk women: a prospective cohort study. *J Clin Oncol*. 2009 Dec 20;27(36):6124-8. doi: 10.1200/JCO.2009.24.4277. Epub 2009 Nov 2.

³ <http://www.acr.org/-/media/2a0eb28eb59041e2825179sub72ef624.pdf>

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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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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,

Key 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 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)

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Author Affiliations

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

Tools Share

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 \pm 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

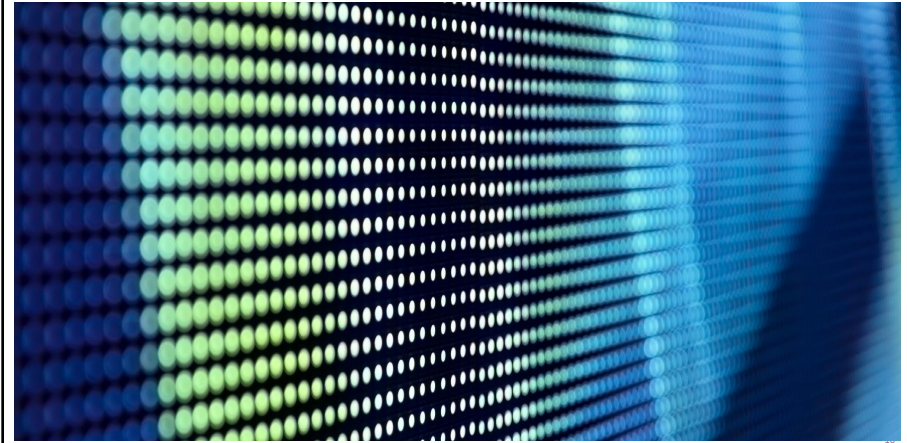
In an asymptomatic study sample, CEM was noninferior to full MRI and AB MRI and was superior to digital mammography.

Clinical trial registration no. NCT03482557 and NCT02275871

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Dual Energy Imaging and Image Processing



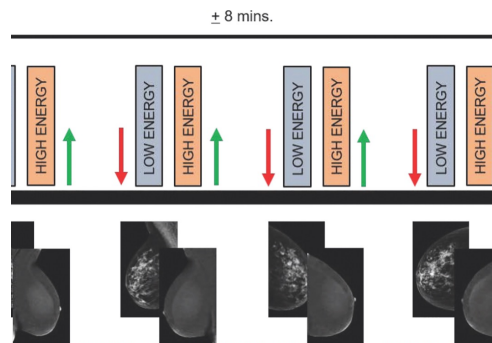
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Dual Energy Imaging

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?

- > Dual Imaging- LE (~28-33 KV) and HE (~45-49 KV)

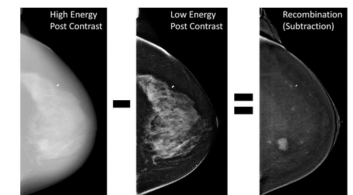
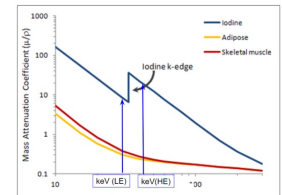
- > **K-edge** is a sudden increase in x-ray absorption occurring when the energy of the X-rays is just above the binding energy of the k-shell electrons of the absorbing atom. The 'k-edge' of iodine 33.2 keV

What?????

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

- > By using X-ray beams just above and below this K-edge, radiologists can highlight areas of the contrast agent, making abnormal tissues like tumors stand out more clearly.

- > **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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Contrast Enhanced Breast Imaging

- **MRI**- uses gadolinium as a contrast agent
- **CEM**- 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. CEM

Comparison of MR to CEM	MRI with Gd contrast	CEM 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 microcalcs		*
Scheduling based on a women's menstrual cycle	*	

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Comparison of MRI vs. CEM

Contraindications	MRI with Gd contrast	CEM 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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Things to consider.....

Implementation



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Equipment requirements to perform CEDM

- 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

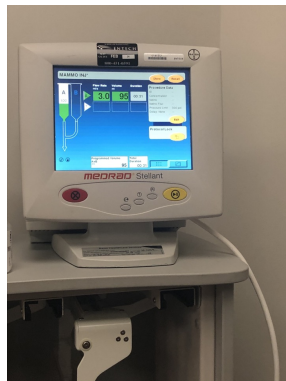
- Vendor specific training on using the CEDM software and the procedure
- Staff member to review patient history (can be a nurse, technologist, or another staff member)
 - review medications
 - any prior history of contrast reactions
 - ask about renal disease
 - Menstruating patients may have exam scheduled 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. (Covington, et al., 2018)
 - ACR has a contrast reaction quick guide that can be kept in the mammography room
- Patients are often monitored for contrast reactions in the department for about 15 mins after the procedure.

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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)**
- Check for any signs of contrast extravasation
- After a **delay of 2 minutes** from the end of the injection, the patient is positioned for 2 standard mammography views (craniocaudal 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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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

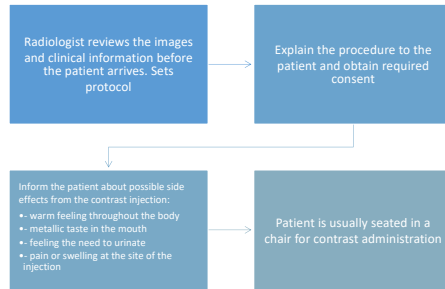
➤ **Metformin**

Patients taking metformin (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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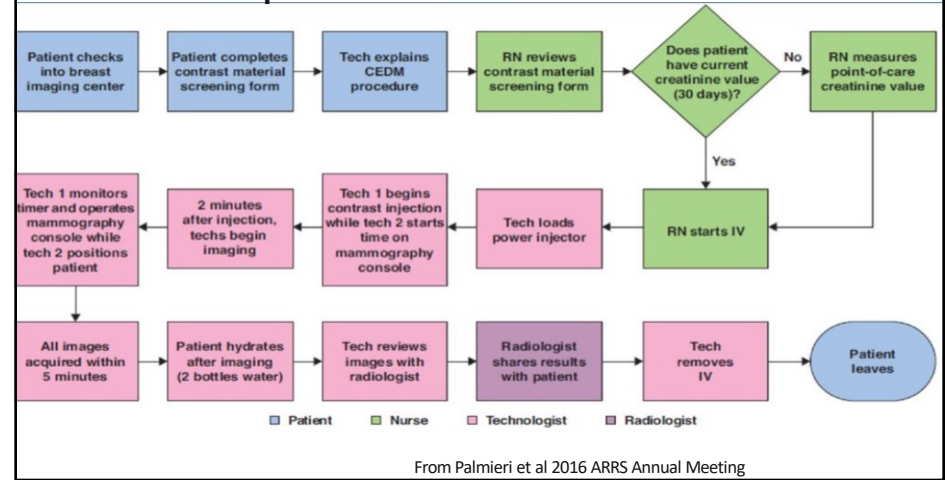
Procedure Steps

Before the exam starts



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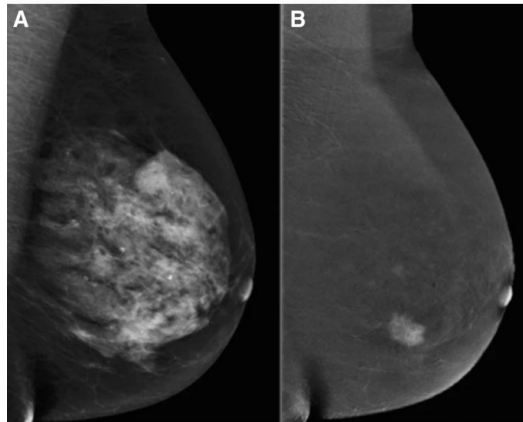
Workflow-Example



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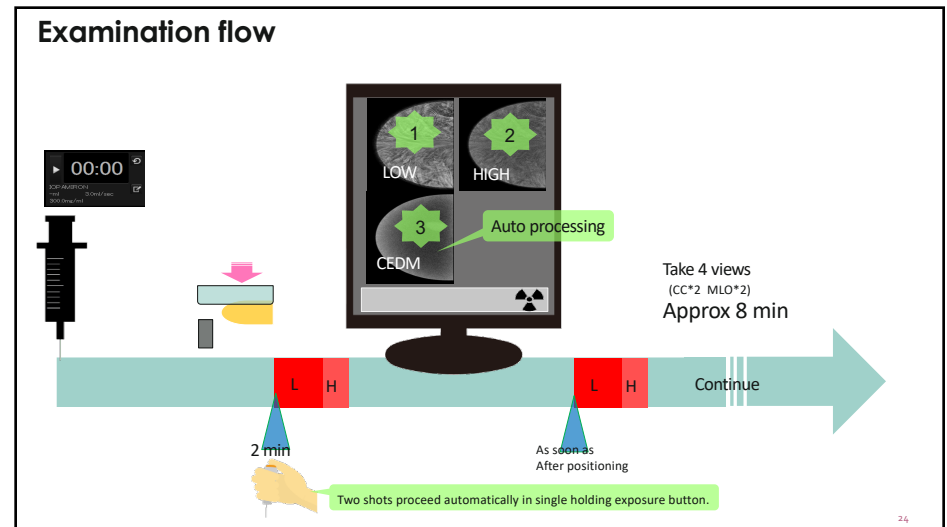
Dual Energy Imaging: Protocol

- The appropriate left or right breast is compressed in either the CC or MLO view
- Imaging is typically performed on both breasts. Order of breasts and projections is determined by the site.
- Commonly the side of interest is imaged first (ipsilateral) when the contrast agent is at its highest concentration followed by the contralateral breast.



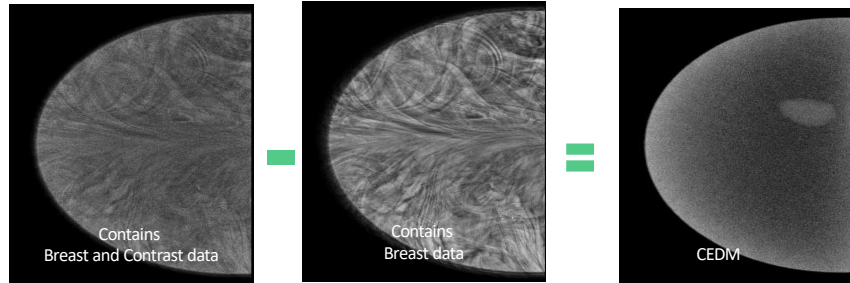
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Examination flow



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Examination flow



HIGH KV (45 - 47 kV)
with Cu filter

LOW KV (26 - 31 kV)
with Rh filter

Energy subtraction

This image is used as a 2D

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The collage shows three scenes from the CEDM procedure. The top left photo shows a patient sitting in a chair. The top middle photo shows a technician standing by a table with a patient. The top right photo shows a technician adjusting a device on a patient's arm. The bottom right photo shows a patient with a breast pad on her chest, looking surprised. A small inset image shows a breast pad with text: 'MORE FLEXIBLE! (vs. Standard Breast Pads)', 'SAFE AND COMFORT FABRIC', and 'FAST ABSORPTION'. The text 'My CEDM Procedure' is overlaid on the bottom left of the collage.

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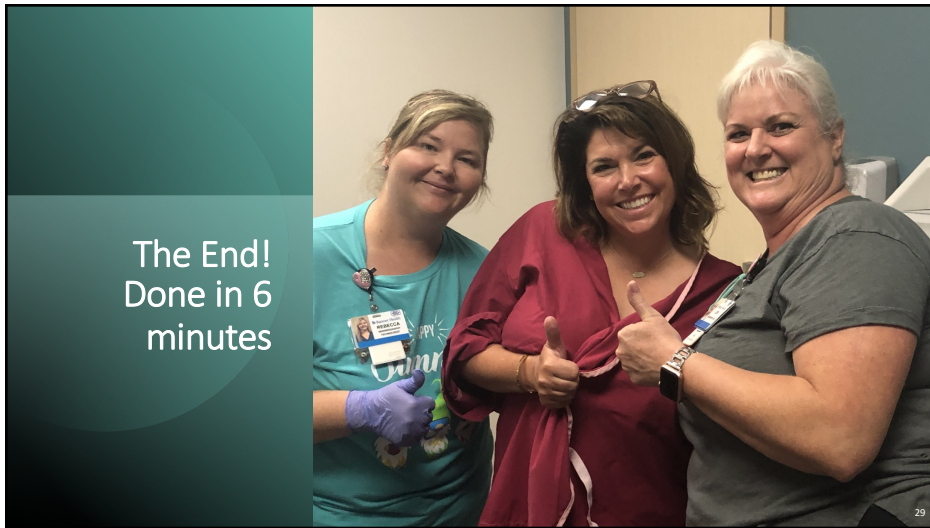
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After the Procedure

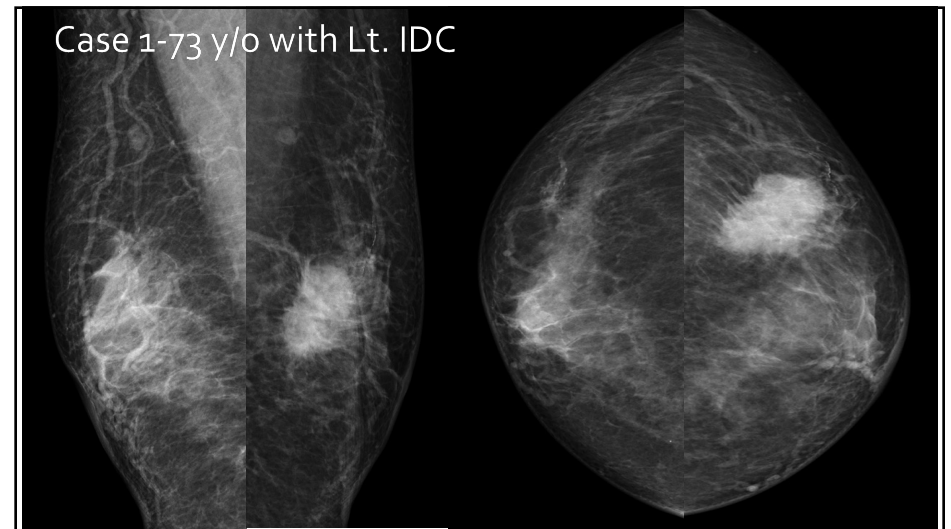
- Remove IV from patients' arm
- Check for any signs of contrast extravasation
 - -swelling
 - -stinging or burning
 - -tightness
- Contrast Reactions- mild reactions generally don't require any medical treatment, but vitals should be checked, and the patient monitored for ~30 mins.
- Mild allergic-like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

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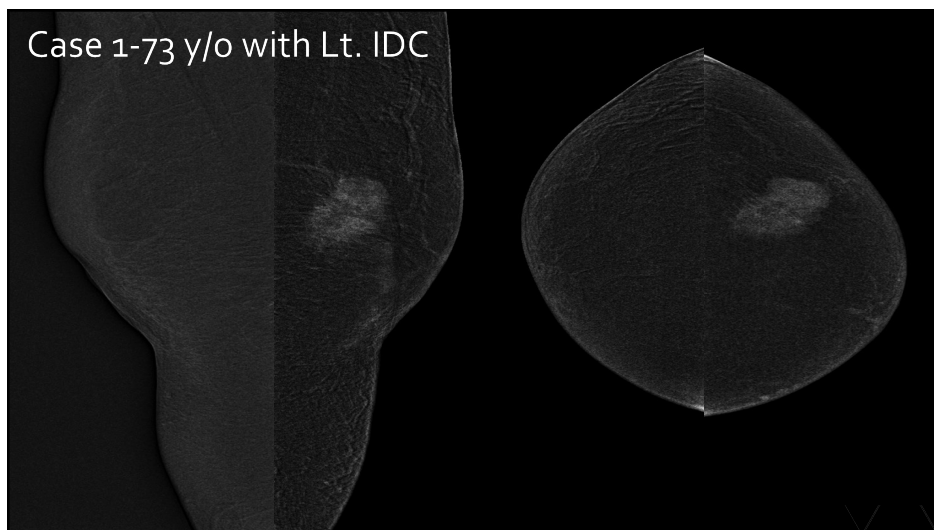
Case Studies

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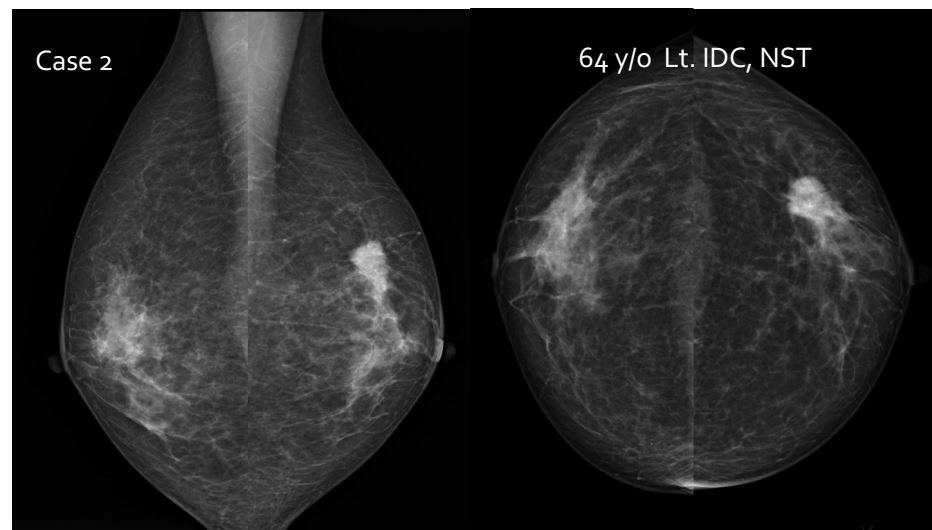
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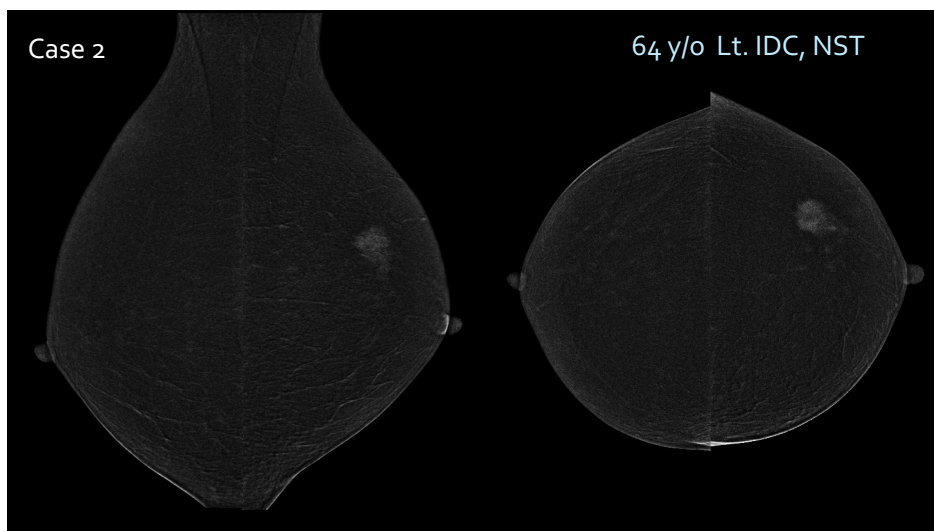
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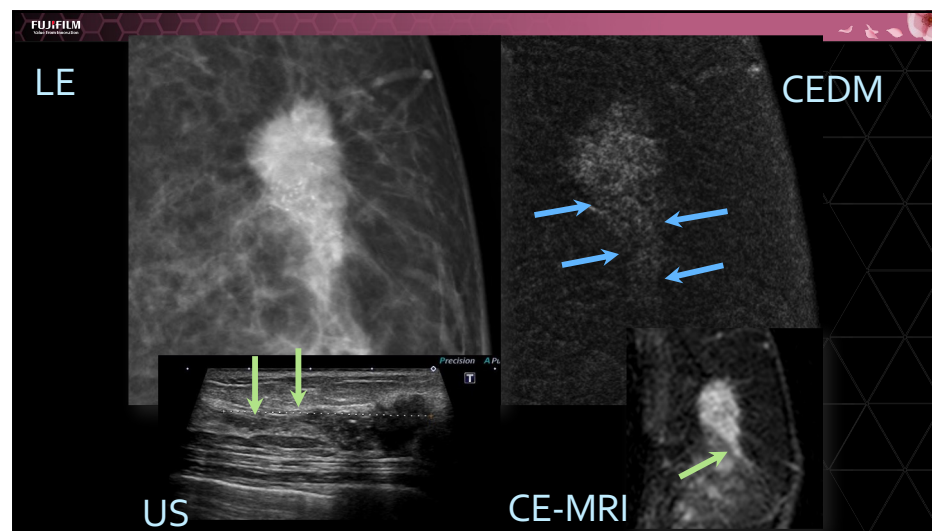
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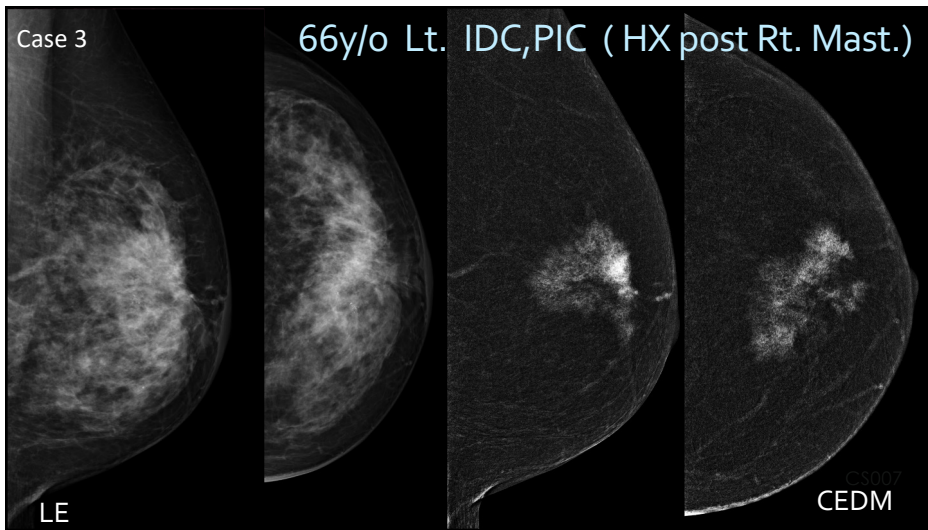
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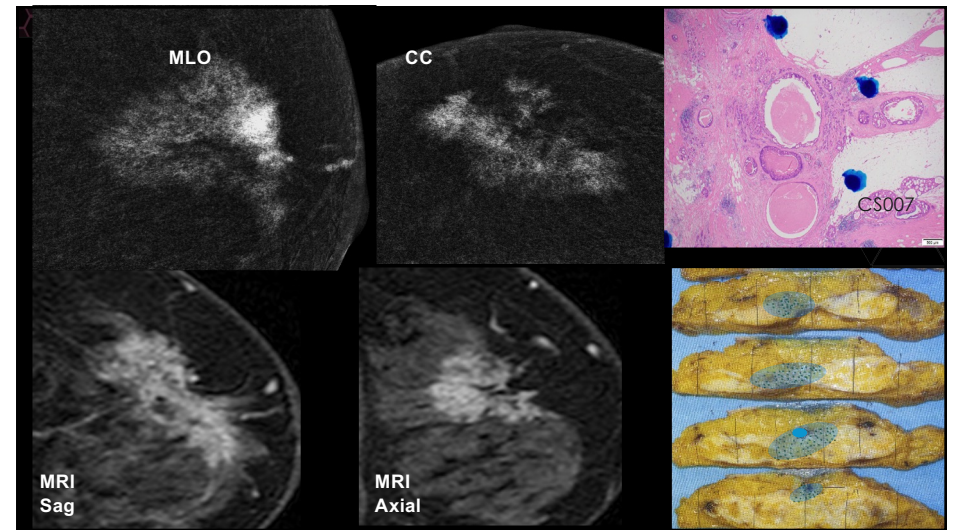
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Reimbursement

- CEDM is billed as a **Diagnostic Breast Imaging Contrast Examination** with 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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Breast Imaging: Contrast-Enhanced Mammography

Coding and Medicare 2024 Global, Professional and Payment

Global and Professional Payment
 Contrast Enhanced Mammography can be reported with either 76499 and Q9967 without a code for a mammography procedure OR codes 96374 and Q9967 in addition to the primary mammography code 77065 or 77066.

CPT Code	Description	Site of Service	RUV ¹	2024 National Unadjusted Medicare Rate ²
96374	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug	Global (office/Freestanding) Professional (Facility)	1.10 N/A	\$36.02 N/A
76499	Unlisted diagnostic radiographic procedure	Global (office/Freestanding) Professional (Facility)	N/A N/A	Determined by contractors Determined by contractors
Q9967	Low osmolar contrast material, 300-399 mg/ml iodine concentration, per ml	Global (office/Freestanding) Professional (Facility)	N/A N/A	\$0.131/ml N/A

Facility Payment
 When contrast is utilized with mammography, it could be reported with either (1) 96374 and Q9967 in addition to the primary procedure code (i.e., 77065 or 77066); or (2) 76499 and Q9967 without a code for a mammography procedure.

CPT Code	Description	Site of Service	APC ³	Status Indicator ⁴	2024 National Unadjusted Medicare Rate ⁵
96374	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug	Hospital	5693	5 ⁶	\$204.43
76499	Unlisted diagnostic radiographic procedure	Hospital	5521	Q1 ⁶	\$86.67
Q9967	Low osmolar contrast material, 300-399 mg/ml iodine concentration, per ml	Hospital	NA	N/A	N/A

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Summary

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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