The Role of Contrast-Enhanced Mammography

Outline

- Background: Breast Cancer Facts
- Contrast Enhanced Mammography (CEM): Procedural Definitions, Reporting
- Pre-Screening Requirements for CEM and Operational Workflow
- Clinical Indications, Benefits of CEM, Brief Data Review
- CEM Cases

Background: Breast Cancer Epidemiology

- Estimated 271,270 new invasive breast cancer cases in women in the US in 2019 and 42,260 breast cancer deaths.1
- 2nd most common cancer diagnosis in women.
- To date, screening mammography is the only breast imaging modality demonstrated to reduce mortality secondary to breast cancer in randomized, controlled clinical trials.
- The sensitivity of screening mammography ranges from 75-85%, often decreasing to 30-50% in patients with dense breasts or patients with BRCA genetic mutation.1

CEM: Procedural Definitions

CEM couples anatomic 2D or 3D Full Field Digital Mammographic (FFDM) imaging with functional imaging derived from contrast enhancement.
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CEM: Procedural Definitions

- "HIGH ENERGY" Above the k-edge of iodine (33 keV)
- "LOW ENERGY" Below the k-edge of iodine (33 keV)
- Subtracted

CEM: Enhancement based upon neovascularity

Lesions which enhance demonstrate neovascularity from tumoral angiogenesis and/or leakage of contrast media into interstitial tissue as a result of immature tumoral vessels (yellow arrow = malignant concordant Invasive Ductal Carcinoma, Grade 1).

CEM: Reporting

- Low energy 2D/3D image interpreted according to BI-RADS lexicon (Breast Imaging-Reporting and Data System)
- Subtracted images report background parenchymal enhancement (BPE) in quartiles similar to MRI:
  - Minimal (0-24%), mild (25 to 49%), moderate (50 to 74%), marked (75-100%) and degree of symmetry of BPE
- Regions of pathologic enhancement designated as a mass or non-mass enhancement

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CEM: Institutional Requirements

- Software upgrade
- Insertion of Copper filter which can be retrofit to existing mammographic systems
- Power injector to administer intravenous contrast

CEM: Institutional Requirements

- Minimal up front capital expenditure to operationalize.
- May be performed on the same unit utilized for screening FFDM (2D/3D) and upright stereotactic guided core biopsy (2D/3D), it is practical in regards to constraints of continually expanding breast imaging centers.

CEM: Institutional Prescreening Requirements (Preprocedural Creatinine)

- "High-risk": Creatinine within 4 weeks of CEM
  - age ≥60, prior renal disease necessitating renal transplant, solitary kidney, renal tumor, active graft, autoimmune diseases, collagen vascular diseases such as lupus, scleroderma, rheumatoid arthritis, hypertension, diabetes, multiple myeloma
  - Outpatient breast centers may utilize single-use iSTAT cartridges

Paralleling institutional CT guidelines: CEM Creatine is greater than 1.6 mg/dL.

CEM: Operational Workflow

CEM is performed irrespective of menstrual cycle timing in premenopausal patients.

Once patient cleared to proceed with CEDM, 22 Gauge antecubital IV placed.

In a seated position, the patient receives weight based (1.5 mL/kg) iodinated contrast agent (Omnipaque 350) via power injector at a rate of 3mL/sec followed by a 10-mL bolus of saline.

CEM: Delay to imaging following contrast injection

Contrast washout from suspicious lesions on CEDM does not parallel Breast MRI, which may be secondary to differences between iodinated contrast and gadolinium.

Breast neoplasms tend to enhance gradually on CEDM, unlike rapid enhancement with washout kinetics which may be discerned on Breast MRI.

Therefore, contrast imaging may be undertaken up to 10-12 minutes following contrast injection without degradation of image quality or contrast enhancement.

Variable delay to imaging following contrast injection:

- Recently diagnosed neoplasm (Preoperative Disease Extent):
  - Lobular neoplasia: 4 minute delay following contrast injection
  - Ductal origin neoplasia: 2 minute delay following injection
- All other indications: Standard 2 minute delay following injection

CASE 1(a). Postmenopausal patient presenting for screening mammogram.

CASE 1(b). Postmenopausal patient presenting for screening mammogram: high density, ellipsoid mass upper outer left breast (2-3:00, posterior depth).

CASE 1(c). Spiculated, high density, 2.2 cm mass noted left breast 2-3:00, posterior depth.
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CASE 1(d). Biopsy reveals malignant concordant left breast Invasive Ductal Carcinoma, Grade 1 with colloid features.

Low-Energy 2D Right CC
Postcontrast Right CC Subtracted View
Low-Energy 2D Left CC
Postcontrast Left CC Subtracted View

Case 1(e). Contrast Enhanced mammography demonstrates faint enhancement within left breast malignant concordant Invasive Ductal Carcinoma with Colloid Features (yellow arrow).

Low-Energy 2D Right MLO
Postcontrast Right MLO Subtracted
Low-Energy 2D Left MLO
Postcontrast Left CC Subtracted View

Case 1(f). Contrast Enhanced mammography demonstrates faint enhancement within left breast malignant concordant Invasive Ductal Carcinoma with Colloid Features (yellow arrow).

Postcontrast Right MLO Subtracted
Right 2D MLO
Left 2D MLO
Postcontrast Left MLO Subtracted

Case 1(g). Contrast Enhanced mammography demonstrates gradual enhancement of Invasive Ductal Carcinoma with Colloid Features (yellow arrow) with increasing delay following contrast injection.

2 MINUTE DELAY
8 MINUTE DELAY
20 MINUTE DELAY

Case 1(h). Wireless localizer placed utilizing sonographic guidance immediately following CEM (same date of service).

Consistently increased patient satisfaction with same day 2nd look US/biopsy and same day wireless localization following CEM encounter.

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CASES: Clinical Indications

- Asymptomatic high risk surveillance
- Preoperative disease extent evaluation: newly diagnosed breast neoplasm
- Axillary metastases, unknown primary
- Postneoadjuvant follow-up evaluation
- Assessment of indeterminate mammographic or sonographic abnormalities
- Assessment of persisting clinical symptoms with negative initial imaging evaluation.

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Benefits of CEM

Lower institutional Costs:
Ease of scheduling. No preauthorization insurance process required for CEM. Billed as Diagnostic Mammogram with contrast (20% total cost of Breast MRI).

Higher Patient Satisfaction:
- Ease of utilization in claustrophobic patients- no need for premedication.
- Upright seated positioning instead of prone positioning.
- Truncated exam time of 8-15 minutes instead of 45-60 minutes.
- Can perform in patients with contraindications to MRI.
- Real time results shared with patients s/p CEM.

Workflow Optimization:
Same day workup of additional lesions detected on CEM (2nd look US). If patient requires additional biopsy, performed on same date of service. If neoplasm solitary, lesion localized on same date.

Limitations of CEM

Increased radiation exposure as compared to FFDM exposure.
Radiation dose for CEDM estimated at 1.2x the dose for conventional digital mammography, with the high energy projections assuming 20% of the dose of conventional mammography.

Limited anatomic visualization in specific cases
- Anatomically far posterior lesions, characterization of chest wall invasion, characterization of subpectoral and internal mammary chain lymphadenopathy.

Performance of CEM compared to conventional mammography

CEM has been described as superior to conventional mammography (1-4).
Jochelson et al.: Index cancer detection for CEDM and MRI= of 96% , index cancer detection for conventional mammography = 81% (2).
Dromain et al.: CEDM sensitivity of 93% versus 78% for conventional mammography (4).
Fallenberg et al.: Index cancer detection of 83% for conventional mammography, 100% for CEDM and 97% for breast MRI, with no significant difference identified between lesion size measurement on Breast MRI and CEDM as compared to final histopathology.

References:
Comparable index cancer detection for CEM as compared to Breast MRI

Breast MRI exhibits less than optimal specificity, with specificity inferior to that even of conventional mammography in multiple reports.

Lee-Felker et al.: 52 women with 120 breast lesions:
- CEM had similar sensitivity to MRI (94% vs 99%).
- CEM had significantly higher PPV than Breast MRI imaging (55% vs 60%).
- CEM had fewer false positives than MRI imaging (5 vs 45 lesions) with high sensitivity for secondary cancer detection as compared to MRI (100% vs 91%, P<0.001 for all results).

Ali-Mucheru et al.: Index cancer detection rate of 98% in CEM, CEM results in prospective change in surgical plan as high as 20%, confirmed to be histopathologically accurate upon final pathologic interrogation.


CEM compared to MRI: Index Cancer Detection

CEM for Screening (Elevated lifetime risk and/or Dense Breasts)

Given superiority of CEDM to conventional mammography, early reports of CEDM utilization for screening in patients with elevated lifetime risk of breast cancer and/or dense breasts.

Fallenberg et al demonstrates that CEM alone and MRI exhibit the biggest benefit for dense breasts, with significant variance in ROC AUCs as compared to conventional mammography (AUC dense: CEM 0.84, MRI 0.86, MG: 0.73; non-dense CEM AUC: 0.85, MRI 0.84, MG: 0.79).


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CASE 2(a). Premenopausal female presenting for screening mammography.
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CASE 2(b). Premenopausal female presenting for screening mammography.

CASE 2(c). Focal asymmetry upper inner right breast middle depth sonographically colocalizes with 0.96 cm solid mass, biopsied, benign concordant stromal fibrosis.

CASE 2(d). 6 month follow up reveals interval growth of previously biopsied benign concordant biopsy. Lesion underwent stereotactic guided core biopsy, high risk benign concordant ADH, later surgically excised.

CASE 2(e). Asymptomatic high risk surveillance status post high risk benign surgical excisional biopsy. Minimal BPE. No pathologic enhancement. BI-RADS 2: BENIGN.

CASE 2(f). Asymptomatic high risk surveillance status post high risk benign surgical excisional biopsy. Minimal BPE. No pathologic enhancement. BI-RADS 2: BENIGN.

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CASE 6: RIGHT breast Invasive Lobular Carcinoma, Grade 1. This mass was mammographically occult and discerned upon screening ultrasound. Postcontrast images demonstrate aggressive, spiculated mass measuring up to 4.3 cm (mass measured only 1.1 cm on index ultrasound evaluation).

CASE 7(a): Premenopausal woman presenting for left breast palpable abnormality (yellow arrow).

CASE 7(b): Diagnostic examination reveals 2.06 cm hypoechoic, avascular mass, biopsied and revealing malignant concordant Invasive Ductal Carcinoma Grade 1.

CASE 7(c): Enhancing left breast Invasive Ductal Carcinoma, measuring 1.6 cm on left CC postcontrast view (2.06 cm on original ultrasound).

CASE 7(d): Enhancing left breast Invasive Ductal Carcinoma, measuring 1.6 cm on left CC postcontrast view (2.06 cm on original ultrasound).

CASE 8(a): Postmenopausal female presents for annual screening mammography.
Case 8(b). Postmenopausal female presents for annual screening mammography—recalled for at least two left breast focal asymmetries (yellow and pink arrows).

CASE 8(c). Spiculated architectural distortion upper outer left breast sonographically represents solid mass, upon biopsy malignant concordant IDC1/DCIS1.

CASE 8(d). CEM demonstrates spiculated mass (pink arrow) corresponding to known IDC1/DCIS1. CEM identifies new spiculated enhancing mass.

Case 8(f). 2nd site biopsied is malignant concordant IDC1/DCIS1. Patient received bracketed BCS with negative margins.

Case 8(g). Perimenopausal patient presenting with new grouped, amorphous microcalcifications, biopsied and revealing malignant concordant Invasive Ductal Carcinoma Grade 2 with admixed DCIS2.
CASE 9(b). CEM reveals longitudinal 4 cm clumped, aggressively enhancing NME corresponding to right breast IDC2/DCIS2 at 6:00 upon background of moderate BPE.

CASE 9(c). Postcontrast Breast MRI reveals longitudinal 4.2 cm clumped, aggressively enhancing NME corresponding to right breast IDC2/DCIS2 at 6:00 upon background of moderate BPE. No other suspicious enhancement identified.

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Case 10(a). Premenopausal patient presenting for right axillary palpable abnormality (radiopaque marker/yellow arrow).

2D Right MLO 2D Right CC View 2D Left CC View 2D Left MLO View

Case 10(b). Right axillary palpable abnormality sonographically colocalizes with pathologically enlarged right axillary lymph node. Upon biopsy, axillary nodal metastasis is identified.

Subtracted Right MLO View
Low Energy 2D Right MLO View
Subtracted Left MLO View

Case 10(c). CEDM demonstrates multiple, aggressively enhancing masses within the right breast (pink arrows).
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CASE 11(a): 10 cm palpable spiculated, high density mass upper outer quadrant right breast (denoted by yellow arrows).
No mammographic evidence malignancy contralateral unaffected left breast.

CASE 11(b): Diagnostic ultrasound images demonstrated longitudinally extensive 10 cm hypoechoic breast mass at the 10:00 axis, 6 cm FN (IDC) with a pathologic right axillary lymph node within low right axilla, 13 cm FN (axillary nodal metastasis).

Figure 11(c): Postcontrast axial T1 breast MRI images demonstrate longitudinally extensive Invasive Ductal Carcinoma 11 cm upper outer right breast extending to the nipple areolar complex (yellow arrows) with associated nodal metastatic disease (blue arrows).
CASE 11(d). Complete radiographic postneoadjuvant treatment response. No residual pathologic enhancement within the upper outer quadrant is identified. There is interval resolution dermal thickening of the right breast.

In conclusion...

- CEM is a highly sensitive, practical, breast imaging modality coupling morphologic lesion depiction with functional imaging at a fraction of the cost of breast MRI.
- CEM is expeditiously interpreted by radiologists, with substantial inter-reader agreement independent of radiology reader experience level and ease of interpretation additionally by breast surgical colleagues.
- CEM offers more efficient image acquisition and higher specificity than breast MRI imaging, which can routinely shorten time to final diagnostic resolution and result in improved patient satisfaction with potentially decreased unnecessary downstream resource utilization.