

Multiparametric comparison of low-energy contrast-enhanced mammography and full-field digital mammography for image quality and lesion conspicuity using EUREF standards and Likert scoring

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ABSTRACT

Purpose: To determine whether low-energy (LE) images acquired during contrast-enhanced mammography (CEM) are diagnostically and technically comparable to full-field digital mammography (FFDM) using standardised image quality and lesion conspicuity metrics.

Materials and Methods: In this retrospective study, 268 women (mean age: 44.6 years) who underwent both FFDM and CEM imaging, were included. Three blinded radiologists independently assessed the FFDM and LE-CEM images using 20-point EUREF (European Reference Organisation for Quality Assured Breast Screening and Diagnostic Services) criteria and 5-point Likert scale for image quality, lesion conspicuity, margin clarity, and diagnostic adequacy. An analysis of the additional lesion detection rate was done. Additionally, technical metrics including posterior nipple line (PNL), compressed breast thickness (CBT), and average glandular dose (AGD) were also recorded. Statistical analysis included Wilcoxon signed-rank, McNemar's test, intraclass correlation coefficient (ICC), and Fleiss' kappa.

Results: LE images scored significantly higher than FFDM in 11 of 20 EUREF parameters ($p < 0.05$) and were non-inferior in the remaining. Median Likert scores were significantly higher for LE images across all lesion parameters, including conspicuity against background (5 vs. 4), margin clarity (5 vs. 4), and overall lesion visibility (5 vs. 4) (all $p < 0.001$). LE images detected significantly more lesions per patient (0.557 vs. 0.314; $p < 0.001$) with excellent inter-reader agreement ($\kappa > 0.80$). PNL and CBT showed near-perfect positional reproducibility (ICC > 0.98), and all AGD values remained within EUREF safety limits.

Conclusion: LE-CEM images match or rather exceed FFDM in image quality, lesion detection, and diagnostic adequacy, while maintaining technical reproducibility. These findings support omitting additional FFDM exposure in patients with indications for CEM, thereby reducing radiation dose and streamlining the workflow.

Introduction

Breast cancer remains a leading cause of cancer-related morbidity and mortality among women worldwide. Full-field digital mammography (FFDM) is the cornerstone of early detection, but its diagnostic yield diminishes significantly in dense breast tissue, with sensitivity as low as 50%.¹ Contrast-enhanced mammography (CEM) augments conventional mammography by integrating functional imaging via intravenous iodinated contrast. It improves lesion conspicuity with results comparable to MRI, while offering cost-efficiency and greater patient acceptability.²⁻⁷ The technique employs a dual-energy acquisition protocol per view optimised for iodine detection, comprising of a

low-energy (LE) image at 26-31 kVp, and a high-energy (HE) image at 45-49 kVp.^{2,3} These images are processed to generate a recombined (RC) image that highlights regions of contrast enhancement.

The LE component of CEM, acquired below the K-edge of iodine (33 keV), is theoretically unaffected by the presence of contrast agent due to negligible photoelectric interactions at these energies, rendering it morphologically similar to FFDM.⁸⁻¹⁰ However, despite this similarity, patients undergoing CEM often undergo a prior FFDM in the current clinical workflow. Given the rising concerns about cumulative radiation dose, especially in repeated follow-up scenarios, it becomes essential to reassess the necessity of each imaging step. The As Low As Reasonably Achievable (ALARA) principle supports such efforts by encouraging the

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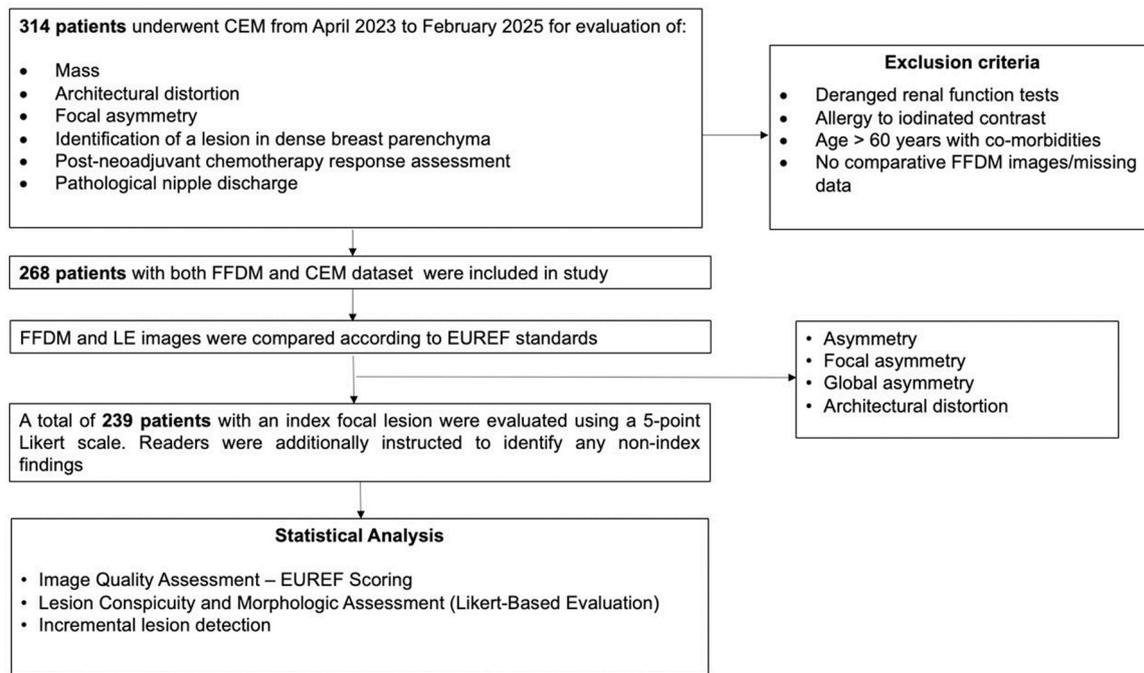


Fig. 1. Flow design of the study. CEM-Contrast enhanced mammography, EUREF- European Reference Organization for Quality Assured Breast Screening and Diagnostic Services, FFDM-Full Field Digital Mammography, US-Ultrasonography.

elimination of avoidable exposures without compromising diagnostic performance.

A few preliminary studies have suggested that LE-CEM images may be diagnostically equivalent to standard FFDM, but these have been limited by small sample sizes, inconsistent acquisition protocols, and reliance on unidimensional assessment tools. The objective evidence comparing the diagnostic adequacy of LE-CEM images with FFDM remains limited.⁸⁻¹¹

The purpose of this study was to address this gap and conduct a comprehensive, blinded, multiparametric comparison of LE-CEM and FFDM images acquired on the same mammography unit. Using EUREF 20-point quality criteria, Likert-based lesion scoring, and reader-level diagnostic concordance, the study aims to determine whether low-energy images are technically and diagnostically comparable to FFDM images. If proven non-inferior, LE images may eliminate the need for routine FFDM in CEM workflows, reducing radiation dose, improving patient comfort, and streamlining resource utilisation.

Materials and methods

This single-center observational study was conducted by retrieving data of patients acquired between April 2023 and February 2025 from the Picture Archiving and Communication System (PACS). The institutional ethics committee approved the study, and the need for informed consent was waived in view of the retrospective study design. (Fig. 1)

Participant selection

Inclusion criteria

Women who underwent both FFDM and CEM for the following clinical indications were included:

- Evaluation of mass, architectural distortion or focal asymmetry
- Identification of a lesion in dense breast parenchyma
- Post-neoadjuvant chemotherapy response assessment
- Patients with pathological nipple discharge with no localizing pathology found on FFDM or ultrasound

Exclusion criteria

- Deranged renal function tests
- Known allergy to iodinated contrast
- Age > 60 years with significant co-morbidities
- Missing data or no comparative CEM or FFDM images

The mean time between FFDM at the time of referral and CEM was 11 days (SD 7 days) with no interim interventions. Relevant demographic data, findings from supplementary radiological investigations, and histopathological results were also recorded.

Imaging protocol

All imaging was performed using a single Hologic Selenia Dimensions unit (Bedford, MA, USA) with I-View contrast upgrade. FFDM was acquired in standard craniocaudal (CC) and mediolateral oblique (MLO) views for each breast. For CEM, intravenous iodinated contrast (Iohexol 300 mg/mL) was administered at a dose of 1.5 mL/kg (max 120 mL), using a power injector at 3 mL/s, followed by a 20 mL saline flush. Image acquisition commenced 2 minutes following the contrast injection. The sequence of acquisition was CC affected breast → CC unaffected breast → MLO affected breast → MLO unaffected breast. The LE and HE images were acquired simultaneously and completed within 8 minutes of contrast injection.

Image analysis

Three experienced breast radiologists (V.S., D.G., and P.T.) independently reviewed image datasets following a blinded, randomised, and time-separated protocol to minimise interpretive bias. The LE and FFDM image sets were anonymised and reviewed in distinct sessions, separated by a washout period of at least six weeks to reduce reader recall bias. Readers were blinded to the type of imaging modality (LE/FFDM), clinical data, and histopathologic outcomes.

For each case, another radiologist (B.N.) pre-annotated the index lesion (largest and most conspicuous) on both CC and MLO views for LE-CEM as well as FFDM images. These annotations were visible to the

readers during image review and were used solely to localize the lesion of interest. No additional clinical, imaging, or histopathological information was provided during scoring. These datasets were then presented to the readers randomly, without revealing the imaging modality (LE or FFDM image). All assessments were performed using 5-megapixel Barco diagnostic-grade monitors under standardised ambient lighting. Radiologists were not permitted to alter window width or level settings while scoring the images. The readers reviewed ten test cases each to familiarise themselves with the interpretation strategy. Discrepancies in scoring were resolved by consensus, with the lowest score favoured when consensus could not be reached.

Scoring and evaluation metrics

Image quality assessment

European Reference Organisation for Quality Assured Breast Screening and Diagnostic Services (EUREF) Criteria¹²

Both FDM and LE images were assessed using the EUREF image criteria across 20 parameters, including visualization of parenchyma, skin line, retroglandular clarity, sharpness, contrast, presence of noise, and visibility of calcifications.¹² Each parameter was scored on a 5-point ordinal scale (1 = Very Poor to 5 = Excellent).^{6,12}

Lesion conspicuity and morphologic assessment (Likert-based evaluation)

Cases with focal lesions like masses and architectural distortions ($n = 239$), were scored for lesion conspicuity. The analysis of the pre-annotated index lesion was based on its margin clarity, conspicuity relative to the surrounding parenchyma, and overall lesion visibility. Each characteristic was scored using a 5-point Likert scale, where 1 represented poor quality and 5 represented excellent quality.¹¹ Inter-reader agreement was measured via Fleiss' Kappa; consistency across modalities was assessed using intraclass correlation coefficients (ICC) and Bland–Altman analysis.

Incremental lesion detection

Each reader independently assessed the number of additional non-index masses (distinct from the pre-annotated index lesion) on FFDM and LE images. The additional non-index findings were considered true positives if a corresponding correlate was identified on either the recombined image or on ultrasound, and false positives if no imaging correlate was present. Paired lesion detection counts between FFDM and LE were compared using the Wilcoxon signed-rank test. McNemar's test assessed discordant binary lesion detection (≥ 1 vs. 0) using the recombined image-ultrasound composite as the reference standard. Inter-reader agreement was measured via Fleiss' Kappa. Statistical significance was defined as $p < 0.05$.

Technical reproducibility metrics

For each patient, posterior nipple line (PNL) distance and compressed breast thickness (CBT) were extracted from DICOM headers to evaluate positional consistency. Average Glandular Dose (AGD) was compared between FFDM and LE acquisitions. Intraclass correlation coefficients (ICC) assessed reproducibility, and dose comparisons were analyzed using paired t-tests and Wilcoxon signed-rank tests stratified by CBT.

Reader responses were entered in an Excel sheet directly and subsequently used for analysis.

Statistical analyses

Statistical analysis was performed using IBM SPSS Statistics v22.0. For ordinal data (EUREF, Likert scores), Wilcoxon signed-rank tests were

Table 1

Distribution of final histopathological diagnoses among study participants.

Diagnosis	Number of Cases (n)	Percentage (%)
Invasive breast cancer	167	62.23%
Ductal carcinoma in situ (DCIS)	16	6.0%
Fibroadenoma	57	21.3%
Phyllodes tumor	15	5.6%
Granulomatous mastitis	8	3.0%
Intraductal papillary neoplasm	5	1.9%
Total	268	100%

used to assess paired differences. Proportional data were compared using McNemar's test. Interobserver agreement was quantified with Fleiss' Kappa and ICC. AGD differences were stratified by CBT and analyzed using paired t-tests. All p-values < 0.05 were considered statistically significant.

Results

A total of 268 women (mean age: 44.6 ± 8.9 years; range: 30–76 years) were included. Each underwent both FFDM and LE-CEM imaging. Among them, 167 patients (62.3 %) were diagnosed with invasive carcinoma, 16 (6.0 %) with ductal carcinoma in situ (DCIS), and 85 (31.7 %) had benign lesions such as fibroadenoma, phyllodes tumor, granulomatous mastitis, or papilloma (Table 1).

Comparative image quality (EUREF) results

Using the 20-point EUREF quality criteria, LE images scored significantly higher than FFDM in 11 parameters ($p < 0.05$), particularly in skin line visibility, vascular detail in dense parenchyma, contrast in white/dark areas, and depiction of Cooper's ligaments. In the remaining 9 criteria—including microcalcification visibility—there was no statistically significant difference ($p > 0.05$). The proportion of "excellent" (score = 5) ratings was higher in LE (82.9–98.4 %) than FFDM (72.1–98.3 %) (Table 2), (Fig. 2).

Lesion assessment (Likert scoring)

Among the 239 cases with focal index lesions, LE images consistently outperformed FFDM across all diagnostic metrics: (Table 3)

- **Cancer Visibility:** The median grade for LE images was 5 compared to the FFDM median grade of 4 ($p < 0.001$). There was almost perfect interobserver agreement for visibility of lesion on LE images ($\kappa = 0.86$) and for FFDM images ($\kappa = 0.81$).
- **Confidence in Margins:** The median grade for LE images was 5, while that of FFDM images was 4 ($p < 0.001$). There was almost perfect interobserver agreement for margin confidence on LE images ($\kappa = 0.83$) and substantial interobserver agreement for FFDM images ($\kappa = 0.75$).
- **Conspicuity of Cancer Compared to Tissue Density:** The median grade for LE and FFDM images was 5 and 4, respectively ($p < 0.001$). There was substantial to almost perfect interobserver agreement for lesion conspicuity on LE and FFDM images ($\kappa = 0.88$ and $\kappa = 0.77$, respectively).

Incremental lesion detection

The average number of lesions detected per patient was consistently higher on LE images (0.552) compared to FFDM (0.351), with a statistically significant difference ($p < 0.001$, Wilcoxon test). McNemar's test showed a significantly higher number of cases where lesions were identified on LE but missed on FFDM ($p < 0.001$). No substantial FFDM-only detections were observed. Interobserver agreement for both modalities remained excellent, with LE exhibiting slightly higher agreement (FFDM: $\kappa = 0.848$, LE: $\kappa = 0.898$) (Tables 4, 5).

Table 2
Comparative assessment of ‘Image Quality’ between low energy (LE) and full-field digital mammography (FFDM) using EUREF criteria (N = 268).

Imaging Attributes (N=268)	LE maximum 5 score (%)	FFDM maximum 5 score (%)	McNemar <i>p</i> -value	Median LE score	Median FFDM score	Wilcoxon <i>p</i> -value
Delineation of skin line	94.4	84.5	0.0055	5	4	<0.001
Visibility of vascular structures within the dense parenchyma	87.2	72.6	0.0017	5	4	<0.001
Sharp demarcation of pectoral muscle	95.2	92.6	0.3492	5	5	0.115
Good visualization of the Cooper’s ligaments and vascular structures in the subcutaneous and pre pectoral area	97.6	90.4	0.0090	5	5	0.001
Reviewer satisfaction with the visibility of microcalcifications (n=96)	82.9	84.2	0.8534	5	5	0.219
Reviewer satisfaction with the representation of microcalcifications (n=96)	82.9	84.2	0.8534	5	5	0.219
Sufficient contrast in the dark areas	96.8	92.1	0.0769	5	5	<0.001
Sufficient contrast in the white areas	91.3	76	0.0004	5	4	<0.001
Glandular tissue sufficiently white	97.2	90.9	0.0217	5	5	0.002
Background sufficiently dark	98.4	88.8	0.0007	5	5	<0.001
Consistency of image acquisition	94.3	96.9	0.2747	5	5	0.136
No disturbing noise in the dark areas	97.6	98.3	0.6704	5	5	0.1817
No disturbing noise in the white areas	96.9	95.7	0.5838	5	5	0.182
Absence of artefacts	94.9	97.6	0.2207	5	5	0.133
Distinct contrast in high-density structures	96.7	72.1	<0.0001	5	4	<0.001
Distinct contrast in low-density structures	98.3	88.7	0.0008	5	5	<0.001
Overall contrast sufficiency	96.7	90.7	0.0333	5	5	<0.001
Image sharpness and spatial resolution	95.1	92.6	0.3699	5	5	0.08
Reviewer satisfaction with opacity depiction	94.4	85.2	0.0088	5	5	0.001
Overall diagnostic satisfaction with image quality	93.6	88.7	0.1371	5	5	0.156

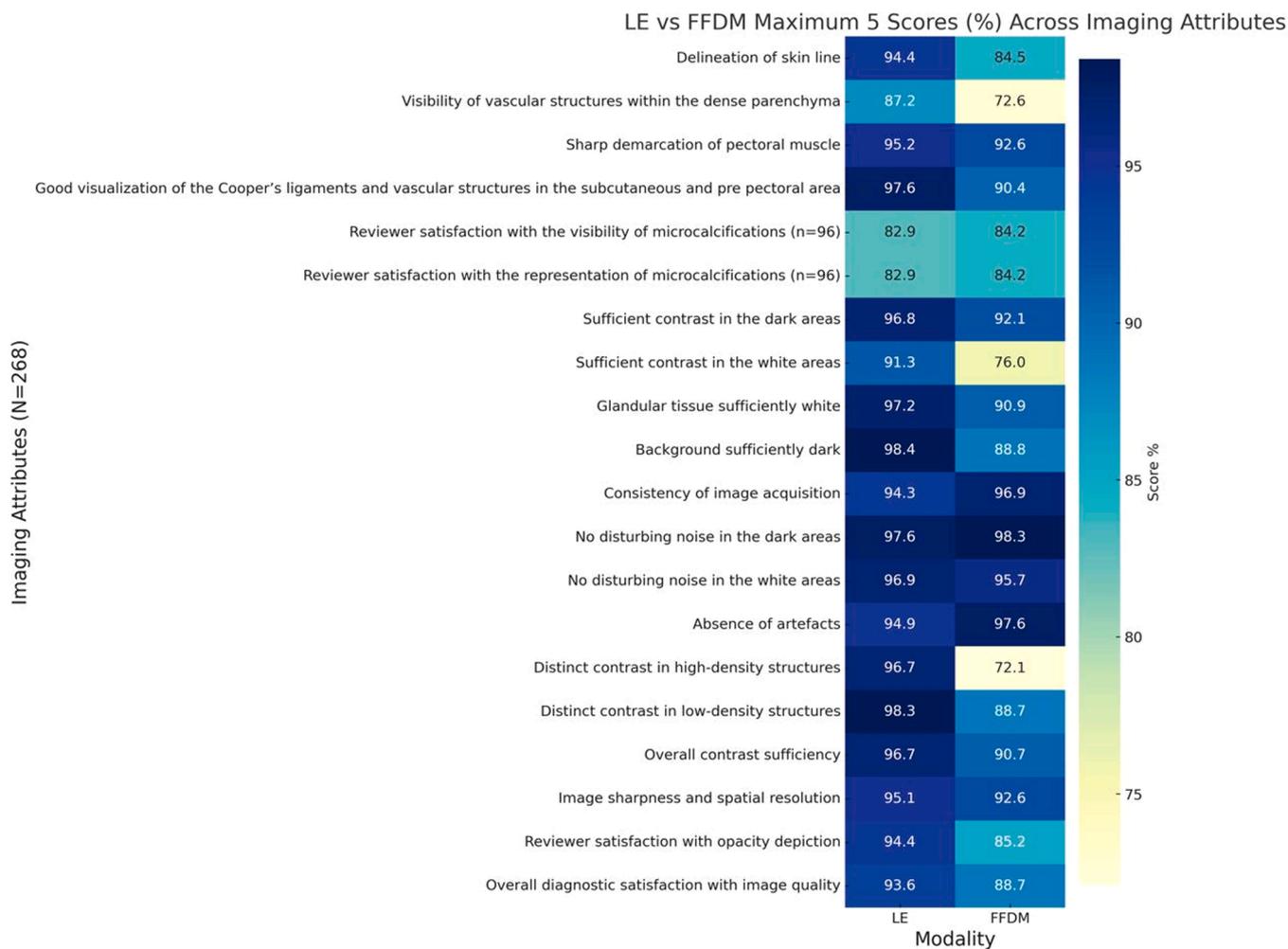


Fig. 2. Comparison of Image Quality Scores Between Low-Energy (LE) Contrast-Enhanced Mammography and Full-Field Digital Mammography (FFDM) Across EUREF imaging attributes.

Table 3
Comparison of ‘Lesion Visibility’ on low energy (LE) and full-field digital mammography (FFDM) using Likert Scale (n = 239 lesions).

Criteria	LE median	FFDM median	p-value	LE interobserver agreement	FFDM interobserver agreement
Visibility of finding	5	4	<0.001	0.86	0.81
Margin confidence	5	4	<0.001	0.83	0.75
Conspicuity of finding compared to tissue density	5	4	<0.001	0.88	0.77

Table 4
Comparison of ‘Non-Index Additional Lesion Detection’ between full-field digital mammography (FFDM) and low-energy (LE) images across three independent readers (R1, R2, R3).

Reader	FFDM+/LE-	FFDM-/LE+	Mean FFDM Lesions	Mean LE Lesions	Wilcoxon p-value
R1	0	36	0.351±0.74	0.552±0.85	<0.001
R2	1	29	0.351±0.75	0.527±0.85	<0.001
R3	0	34	0.356±0.75	0.548±0.86	<0.001

Table 5
Lesion-wise detailed analysis of the ‘Non-Index Additional Lesion Detection’ between full-field digital mammography (FFDM) and low-energy (LE) images with ultrasound and recombined image as reference standard (n=159) across three independent readers (R1, R2, R3).

Reader	Modality	True Positive	False Positive	False Negative	Sensitivity
R1	FFDM	84	0	75	52.8%
R1	LE	132	0	27	83.0%
R2	FFDM	84	1	75	52.8%
R2	LE	126	1	33	79.2%
R3	FFDM	85	1	74	53.5%
R3	LE	131	1	28	82.4%

Table 6
Comparison of ‘Technical Parameters’ and ‘Average Glandular Dose’ (AGD) between low energy (LE) and full-field digital mammography (FFDM) images. (N = 268) PNL: posterior nipple line, CBT: compressed breast thickness.

Image Type	PNL (cm) Mean± SD	CBT (mm) Mean± SD	AGD (mGY)
FFDM	10.43 ± 0.98	56.49 ± 10.89	2.132 ± 0.628
LE	10.47 ± 1.00	56.75 ± 10.03	2.372 ± 0.989
p value	0.0741	0.83	0.0102

Technical reproducibility metrics

- PNL distance in the LE images (n = 268) had a mean of 10.47 cm ± 1.00 and a median of 10.5 cm (range 7.7–13.9). PNL distance in FFDM images had a mean of 10.43 cm ± 0.98. and a median of 10.5 cm (range 7.8–13.7). There was no statistically significant difference in PNL distance between the two modalities (p = 0.0741). The mean signed difference (LE-FFDM) was 0.047 cm, and the mean absolute difference was 0.275 cm. In 98.1 % of cases, the PNL difference was within the 1.0 cm EUREF acceptability margin. The ICC for PNL was 0.983, indicating almost perfect agreement. The 95 % limits of

agreement ranged from -0.79 cm to +0.89 cm, centered around zero.

- No significant difference was observed in CBT between LE (mean: 56.75 ± 10.03 mm) and FFDM (mean: 56.49 ± 10.89 mm); p = 0.83.
- The mean AGD was slightly higher for LE (2.372 ± 0.989 mGy) compared to FFDM (2.132 ± 0.628 mGy), with a statistically significant difference (p = 0.0102). However, in matched-pair analysis stratified by CBT, the difference was no longer significant (p = 0.81). All AGD values remained within the EUREF-recommended safety limits (Table 6).¹²

Discussion

CEM is being increasingly integrated into breast imaging workflows, offering diagnostic benefits akin to MRI with superior accessibility and cost-efficiency.³ The latest American College of Radiology guidelines suggest that CEM can be considered for supplemental screening in high-risk women and in those with dense breast tissue when MRI is contraindicated or not feasible.^{3,13-15} Although LE images in CEM appear morphologically similar to FFDM, they are acquired under fundamentally different technical and clinical conditions. LE images are obtained immediately following intravenous iodinated contrast administration as part of the dual-energy CEM protocol. They utilise lower tube voltages (typically 26–31 kVp), selected to fall just below the K-edge of iodine (33.2 keV), thereby suppressing contrast enhancement and preserving anatomical detail. FFDM involves single-energy exposures, typically without contrast, acquired at kVp values of 28–32 kVp. In addition, LE images are captured using detector systems that are specifically calibrated for dual-energy acquisition. These systems incorporate advanced image processing algorithms optimised for later subtraction HE images, to generate recombined contrast maps.¹²⁻¹⁴

Despite increasing clinical adoption of CEM, only a handful of studies have compared the quality and diagnostic performance of LE to FFDM images, with limited sample size, heterogeneity in acquisitions and focus on isolated technical or visual parameters without a comprehensive framework.⁸⁻¹¹ Our study addresses this critical gap by conducting a methodical multiparametric comparative evaluation of LE versus FFDM images on the largest number of patients reported so far. Also, no study has till date has been inclusive of both EUREF criteria and Likert scale in the same patient cohort.

In our study, LE images demonstrated superiority over FFDM in 11 out of 20 image quality criteria defined by the EUREF standards.¹² These included critical parameters such as visualization of the skin line, vascular structures within dense parenchyma, Cooper’s ligaments, contrast in both dark and white areas, and representation of opacities, among others. In the remaining 9 criteria, there was no statistically significant difference between the two modalities, establishing the non-inferiority of LE imaging in those domains. (Fig. 3) These results are concordant with smaller studies by Lalji et al. and Francescone et al., which also reported comparable or superior LE image quality.^{8,10} Importantly, our results showed that LE and FFDM images performed comparably in depicting microcalcifications, with no significant difference in visibility and representation scores. This is a key observation, as microcalcifications are often subtle and the only markers of early-stage malignancies such as ductal carcinoma in situ (DCIS). In a study by Lalji et al. LE performed superior to FFDM in depicting microcalcification.⁸ A critical methodological difference, however, lies in the image acquisition protocol: Lalji et al. compared LE and FFDM images acquired on separate mammography systems, potentially introducing inter-device variability. In contrast, our study employed a unified single mammography system acquisition platform for both LE and FFDM images, ensuring technical consistency and enhancing the internal validity of our comparative analysis.

In addition, LE images consistently outperformed FFDM across all key parameters—lesion visibility, margin confidence, and conspicuity relative to background parenchyma, when evaluation was done using

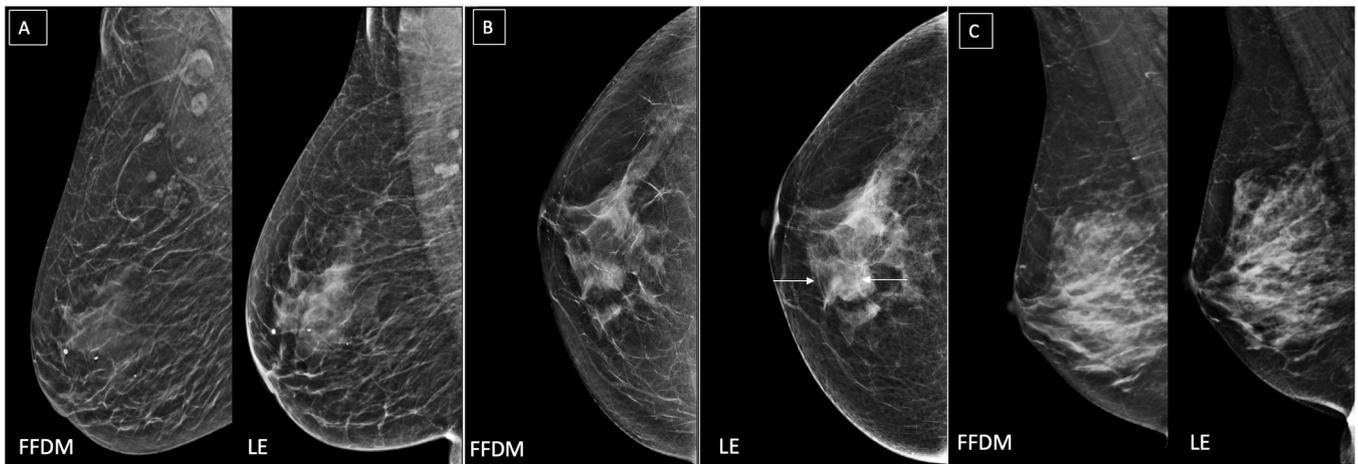


Fig. 3. EUREF-based qualitative comparison of image quality between Full-Field Digital Mammography (FFDM, left) and Low-Energy (LE, right) contrast-enhanced mammography images in three different patients (A–C). (A) The LE image demonstrates sharp visualisation of the pectoralis muscle, well-defined skin line, and glandular tissue that appears sufficiently white; aligning with the EUREF-defined standards for anatomical delineation and tissue contrast. FFDM, in comparison, demonstrates reduced edge sharpness and lower parenchymal clarity. (B) Vascular structures within the dense parenchyma are visible on the LE image (white arrows), a feature that is less appreciable on FFDM. The LE image also meets EUREF benchmarks for subcutaneous structural detail and contrast in dark regions. (C) LE image demonstrates superior contrast in both dark and white regions, with minimal disturbing noise and excellent background suppression. This results in enhanced overall contrast and sharpness of the image, outperforming FFDM in overall interpretability.



Fig. 4. Mediolateral oblique (MLO) views of the right breast in a 53-year-old patient with biopsy-proven invasive ductal carcinoma, (A) Full-Field Digital Mammography (FFDM), (B) Low-Energy (LE) and (C) Recombined (RC) contrast-enhanced mammography images. On FFDM (A), the mass appears as a dense opacity with suboptimal margin definition and a lack of differentiation from adjacent glandular tissue, reducing overall conspicuity. The background lacks sufficient darkness, impacting the visibility of the mass. In contrast, the LE image (B) demonstrates sharper visualisation of the mass margins, sufficient contrast in both dark and white areas, and a clearly delineated pectoralis muscle and subcutaneous anatomy, including vascular structures and Cooper's ligaments. The glandular tissue appears sufficiently white, and the background is appropriately dark, improving overall contrast and sharpness. The mass is more conspicuous, with enhanced representation of morphology (Likert score 5 vs 3). The RC image (C) confirms heterogeneous enhancement of the mass with high conspicuity.

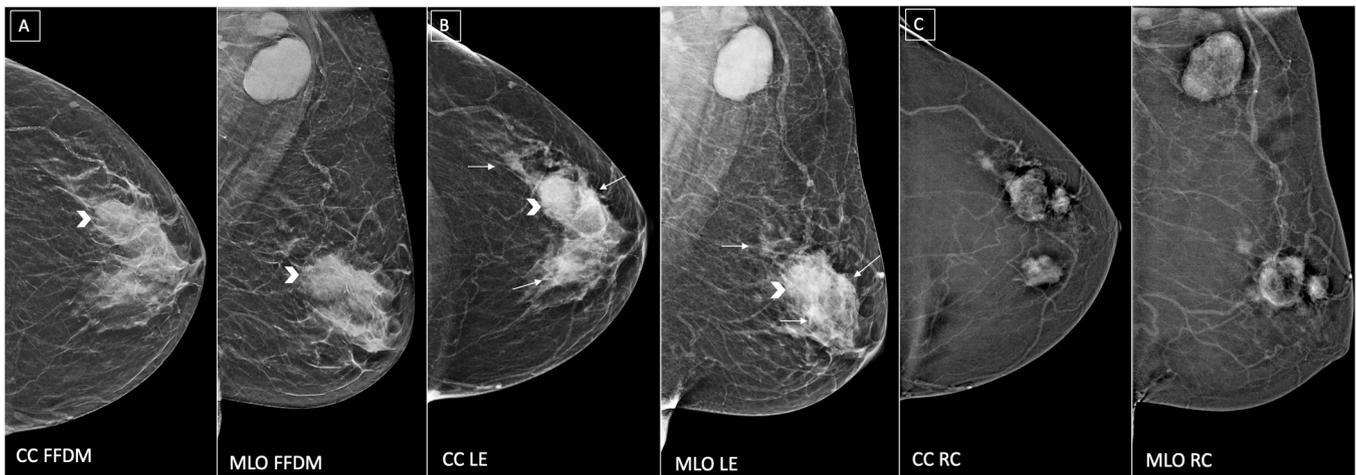


Fig. 5. Craniocaudal (CC) and mediolateral oblique (MLO) views of the left breast in a patient with biopsy-proven invasive ductal carcinoma, acquired in an ACR B density breast using (A) Full-Field Digital Mammography (FFDM), (B) Low-Energy (LE), and (C) Recombined (RC) contrast-enhanced mammography images. On FFDM (A), a dense, irregular mass with indistinct margins is seen in the upper lateral quadrant (white arrowhead). In comparison, LE images (B) show sharper margin delineation and markedly improved mass–parenchyma contrast (Likert 5 vs 3), which enables readers to identify additional masses (white arrows). RC images (C) demonstrate avid heterogeneous enhancement of all masses, confirming multifocality. This case highlights the superior diagnostic performance of LE images over FFDM in detecting multifocal malignant masses and accurately assessing the extent of the disease.

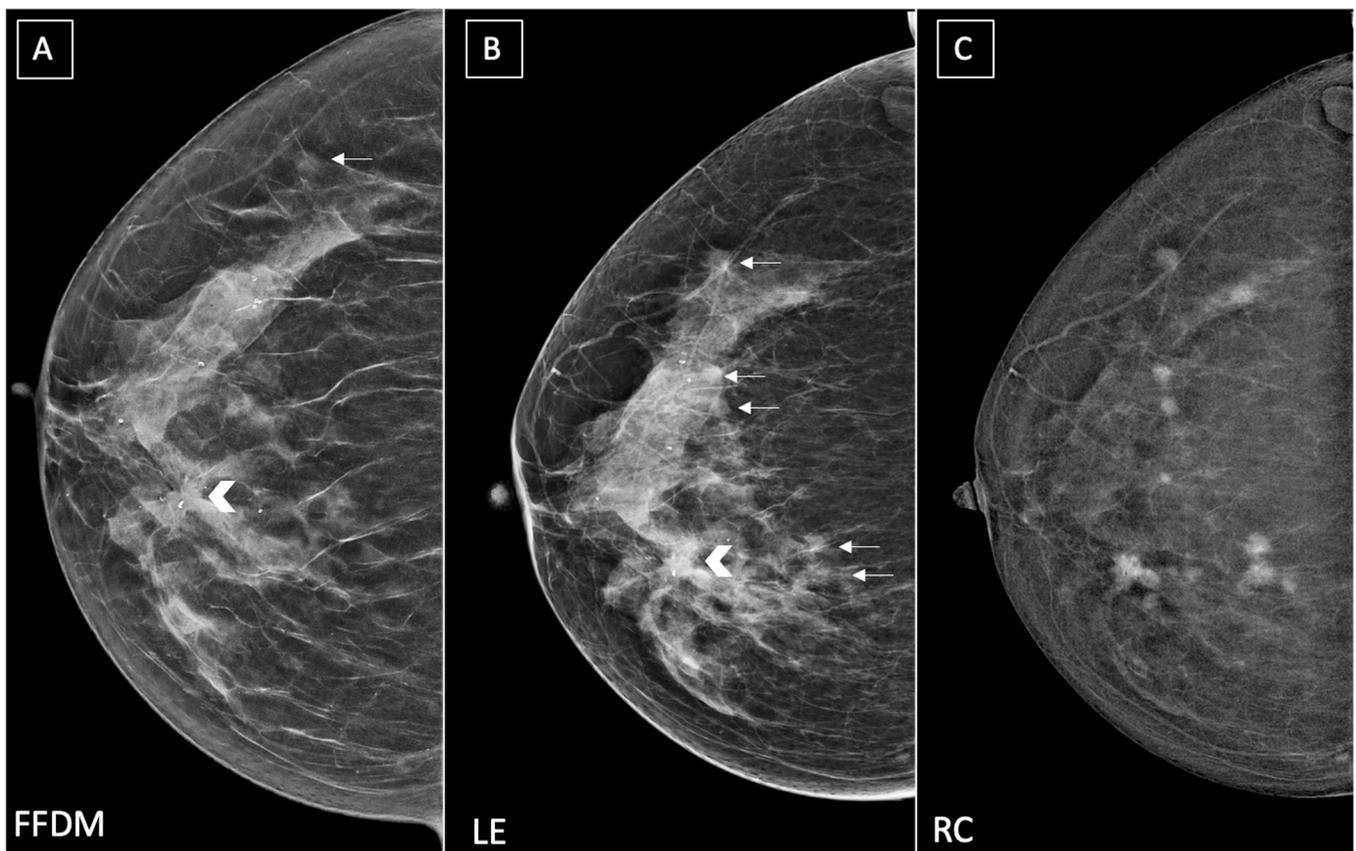


Fig. 6. Craniocaudal (CC) views of the right breast in a patient with breast metastasis from lung carcinoma. (A) Full-Field Digital Mammography (FFDM), (B) Low-Energy (LE) and (C) Recombined (RC) contrast-enhanced mammography images. On FFDM (A), an irregular mass with indistinct margins is seen in the medial breast (arrowhead), and another smaller mass is visualised in the lateral quadrant (arrow). In comparison, LE images (B) show markedly improved mass–parenchyma contrast, with sharper delineation of the mass margins in the medial breast (Likert 5 vs 3), also enabling the identification of four additional masses (arrows). RC images (C) demonstrate avid heterogeneous enhancement of all the masses. This case highlights the superior diagnostic performance of LE over FFDM in detecting multifocality.

Likert scale. All three radiologists consistently rated LE higher across these domains, with inter-reader agreement also marginally improved in LE image assessment. (Fig. 4) These findings agree with the results of

Konstantopoulos et al., who similarly reported enhanced lesion depiction on LE images.¹¹ However, our study was conducted as a fully blinded assessment, ensuring reader masking to the modality, and was

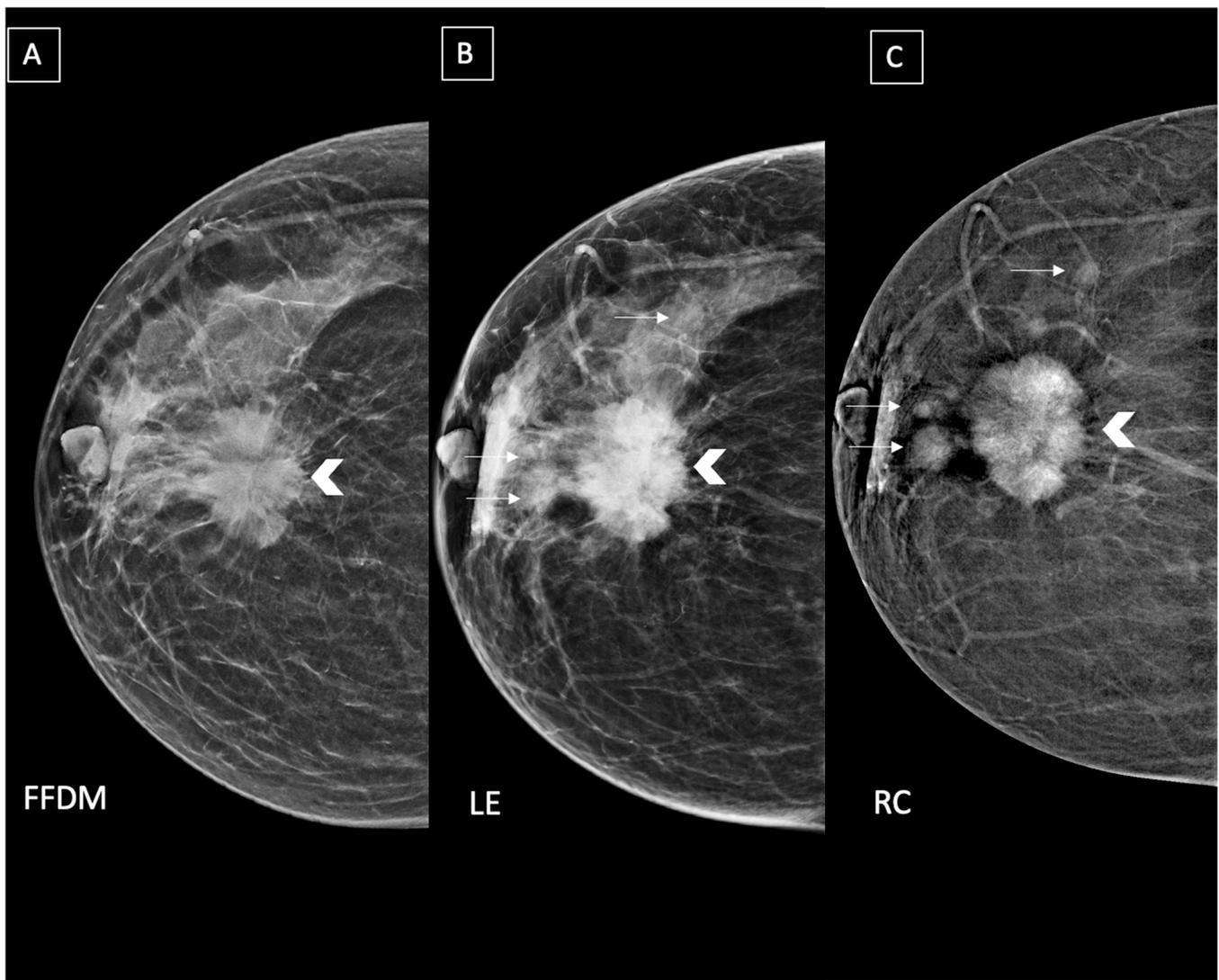


Fig. 7. Craniocaudal (CC) views of the right breast in a patient with biopsy-proven invasive ductal carcinoma, acquired in an ACR B density breast using (A) Full-Field Digital Mammography (FFDM), (B) Low-Energy (LE) and (C) Recombined (RC) contrast-enhanced mammography images. On FFDM (A), a dense, irregular mass is seen in the central breast (arrowhead). No other mass is conspicuous. In comparison, LE images (B) show markedly improved mass-parenchyma contrast, with sharper margin delineation of the primary mass (Likert 5 vs 4) and identification of two additional satellite nodules (arrows) anterior to the mass. RC images (C) demonstrate avid heterogeneous enhancement of the mass as well as the satellite nodules, confirming multifocality. This case highlights the superior conspicuity of masses on LE image in comparison to FFDM image.

based on a substantially larger sample size, ensuring a more rigorous assessment.

A key novel aspect of this study is the objective and blinded comparative evaluation of the number of lesions detected on LE and FFDM images. LE images detected more non-index lesions per patient, without an increase in false positives. This diagnostic advantage may stem from enhanced parenchymal contrast or reduced background noise in LE images. Fig. 5-8 These findings support the argument that LE images not only match but may enhance lesion detection capability, especially in dense breast populations. Additionally, the slightly improved inter-reader agreement on LE suggests that the improved lesion visibility on LE images facilitates more consistent interpretation.

Technical reproducibility and positioning consistency are critical determinants of diagnostic reliability. CBT and PNL distance are established surrogates for assessing the technical reproducibility and adequacy of mammographic positioning. In our cohort, both PNL and CBT, showed near-perfect correlation between LE and FFDM images. These findings meet EUREF-defined quality assurance thresholds and reinforce the reliability of LE images for clinical interpretation.¹² Our results are

consistent with those reported by Lalji et al.⁸ and Francescone et al.¹⁰ who demonstrated that the introduction of iodinated contrast and dual-energy acquisition in contrast-enhanced mammography does not compromise fundamental positioning or compression parameters. While our study observed a broader PNL variation, likely reflecting greater sample size, ethnic variability and clinical heterogeneity, overall consistency in image acquisition was preserved.

LE images demonstrated a marginally higher mean AGD compared to FFDM (2.372 vs. 2.132 mGy), however, at constant CBT through matched-pair analysis, this difference was no longer significant ($p = 0.81$), suggesting that the observed dose variation was primarily influenced by anatomical factors. Importantly, AGD values remained within EUREF safety limits in all patients.

Our results have direct implications for diagnostic efficiency and patient safety. Eliminating a FFDM exposure prior to CEM could reduce cumulative radiation exposure, shorten imaging, improve patient comfort and streamline radiology workflows. This aligns with ALARA principles and growing emphasis on value-based imaging.

This study has a few limitations. First, it was conducted at a single

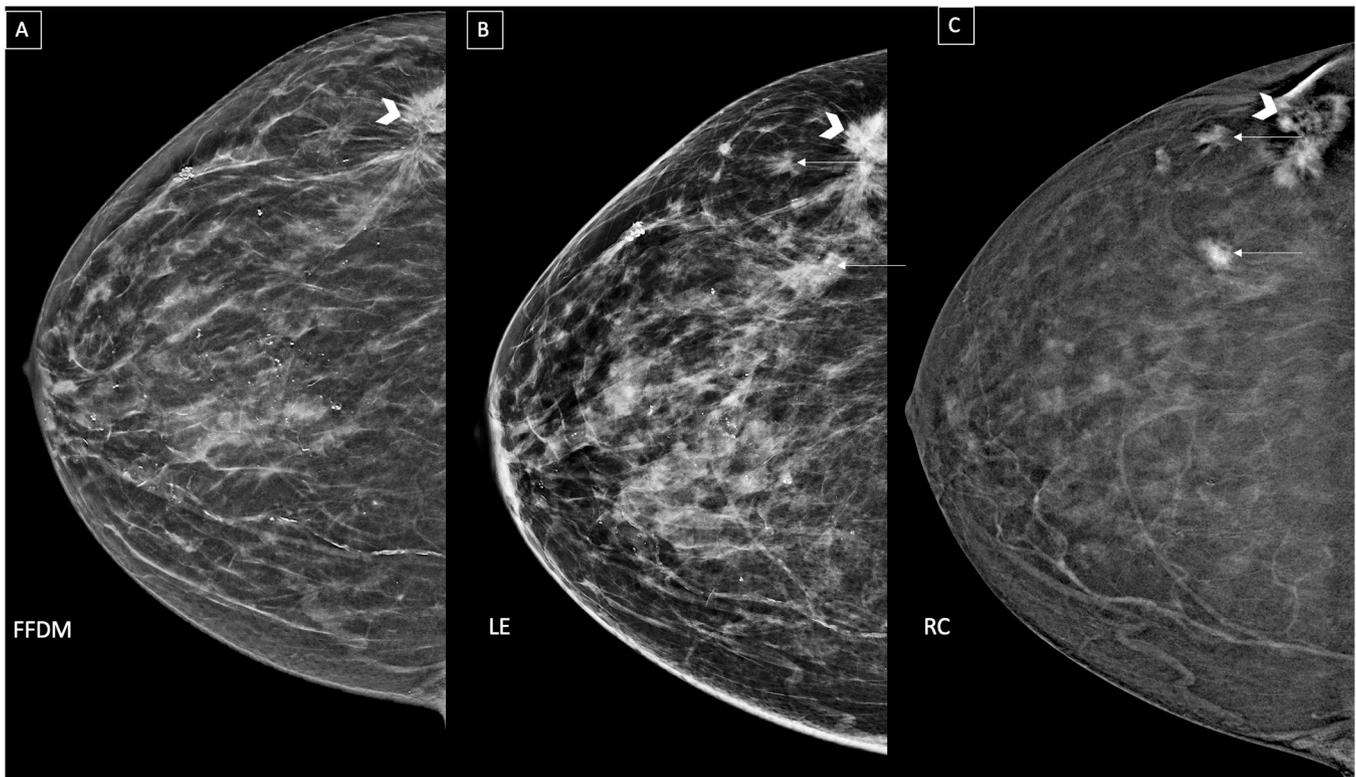


Fig. 8. Craniocaudal (CC) views of the right breast in a patient with biopsy-proven invasive ductal carcinoma, acquired in an ACR B density breast using (A) Full-Field Digital Mammography (FFDM), (B) Low-Energy (LE) and (C) Recombined (RC) contrast-enhanced mammography images. On FFDM (A), a dense, irregular mass with spiculated margins is seen in the lateral breast (arrowhead). No other masses are appreciable. LE images (B) demonstrate improved mass–parenchyma contrast, sharper margins of the primary spiculated mass, and visualisation of two additional satellite nodules (arrows) anterior and medial to the mass. Readers rated this with a higher Likert score (5 vs 3). RC images (C) demonstrate avid heterogeneous enhancement of all masses, including the satellite nodules, confirming multifocality. This case highlights the superior anatomical detailing as well as lesion detection performance of LE over FFDM images in detecting multifocality and accurately assessing disease extent in dense breast tissue.

centre using a single vendor platform, which may limit generalizability. Second, is the retrospective design and the limited sample size of the study. However, the observations of this study may pave way for future researchers conducting prospective studies as it has highlighted that LE images are analogous to/ even outdo FFDM images in several key parameters, emphasizing that FFDM can be omitted if a direct indication for CEM exists. Third limitation is that although the mean time between FFDM and CEM acquisitions was ~11 days, minor interval changes cannot be ruled out, though technical reproducibility metrics support consistency. Regulatory approval and further multicentre studies are required to validate the findings.

Conclusion

Our study demonstrates that low energy contrast-enhanced mammography (LE-CEM) images are non-inferior, and in several key metrics, superior to full-field digital mammography (FFDM) images, while maintaining technical reproducibility and acceptable radiation doses. There is also a better representation of lesions in LE images with higher detection rates and strong interobserver agreement. The depiction of microcalcifications is also comparable between the two, with no statistically significant difference. These findings collectively endorse the feasibility of omitting a prior FFDM in patients with indications for CEM. Eliminating FFDM in this context can reduce cumulative radiation dose, streamline the workflow, and improve patient comfort, advocating for a shift in standard breast imaging protocols. Further multicentre studies are recommended to validate these findings.

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Declaration of competing interest

The authors declare that they have no competing financial interests.

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References

- Carney PA, Miglioretti DL, Yankaskas BC, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. *Ann Intern Med.* 2003;138:168–175. <https://doi.org/10.7326/0003-4819-138-3-200302040-00008>.
- Lalji U, Lobbes M. Contrast-enhanced dual-energy mammography: a promising new imaging tool in breast cancer detection. *Womens Health (L).* 2014;10:289–298. <https://doi.org/10.2217/whe.14.18>.
- Singla DV, DP T, Garg DD. Contrast enhanced mammography - revisiting structured reporting with special focus on suggested modifications. *Curr Probl Diagn Radiol.* 2025. <https://doi.org/10.1067/j.cpradiol.2025.04.010>. S0363-0188(25)00076-3.
- Blum KS, Rubbert C, Mathys B, et al. Use of contrast-enhanced spectral mammography for intramammary cancer staging: preliminary results. *Acad Radiol.* 2014;21:1363–1369. <https://doi.org/10.1016/j.acra.2014.06.012>.
- Luczyńska E, Heinze-Paluchowska S, Dyczek S. Contrast-enhanced spectral mammography: comparison with conventional mammography and histopathology

- in 152 women. *Korean J Radiol.* 2014;15:689–696. <https://doi.org/10.3348/kjr.2014.15.6.689>.
6. Jochelson MS, Dershaw DD, Sung JS, et al. Bilateral contrast-enhanced dual-energy digital mammography: feasibility and comparison with conventional digital mammography and MR imaging in women with known breast carcinoma. *Radiology.* 2013;266:743–751. <https://doi.org/10.1148/radiol.12121084>.
 7. Blum KS, Antoch G, Mohrmann S, et al. Use of low-energy contrast-enhanced spectral mammography (CESM) as diagnostic mammography-proof of concept. *Radiography.* 2015;21:352–358. <https://doi.org/10.1016/j.radi.2015.02.005>.
 8. Lalji UC, Jeukens CR, Houben I. Evaluation of low-energy contrast-enhanced spectral mammography images by comparing them to full-field digital mammography using EUREF image quality criteria. *Eur Radiol.* 2015;25:2813–2820. <https://doi.org/10.1007/s00330-015-3695-2>.
 9. Fallenberg EM, Dromain C, Diekmann F, et al. Contrast-enhanced spectral mammography: does mammography provide additional clinical benefits or can some radiation exposure be avoided? *Breast Cancer Res Treat.* 2014;146:371–381. <https://doi.org/10.1007/s10549-014-3023-6>.
 10. Francescone MA, Jochelson MS, Dershaw DD, et al. Low energy mammogram obtained in contrast-enhanced digital mammography (CEDM) is comparable to routine full-field digital mammography (FFDM). *Eur J Radiol.* 2014;83:1350–1355. <https://doi.org/10.1016/j.ejrad.2014.05.015>.
 11. Konstantopoulos C, Mehta TS, Brook A, et al. Cancer conspicuity on low-energy images of contrast-enhanced mammography compared with 2D mammography. *J Breast Imaging.* 2022;4:31–38. <https://doi.org/10.1093/jbi/wbab085>.
 12. EUREF European Guidelines - EUREF. *European Reference Organization for Quality Assured Breast Screening and Diagnostic Services. European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis.* Fourth edition Supplements; 2013. available at <http://www.euref.org/european-guidelines>.
 13. Mainiero MB, Moy L, Baron P, et al. ACR appropriateness criteria® breast cancer screening. *J Am Coll Radiol.* 2017;14:S383–S390. <https://doi.org/10.1016/j.jacr.2017.08.044>.
 14. Singla DV, Garg DD, Bhavith. Optimizing contrast enhanced mammography: a comprehensive review of artefacts, causes, and remedies. *Curr Probl Diagn Radiol.* 2025. <https://doi.org/10.1067/j.cpradiol.2025.05.001>. S0363-0188(25)00091-X.
 15. Covington MF. Contrast-enhanced mammography implementation, performance, and use for supplemental breast cancer screening. *Radiol Clin North Am.* 2021;59:113–128. <https://doi.org/10.1016/j.rcl.2020.08.006>.