



Contrast-enhanced spectral mammography features of invasive ductal carcinoma and invasive lobular carcinoma

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PURPOSE

This study aimed to characterize and compare contrast-enhanced spectral mammography (CEM) features of invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) according to the American College of Radiology Breast Imaging Reporting and Data System for Contrast-Enhanced Mammography (ACR BI-RADS CEM) lexicon.

METHODS

This retrospective study included patients with pathologically confirmed breast cancer who underwent pretreatment CEM between July 2023 and May 2025. Low-energy (LE) and recombined (RC) images were reviewed in consensus by two radiologists blinded to clinical, histopathologic subtype, and other pathological results. Imaging findings were categorized according to the ACR BI-RADS CEM lexicon. Associations between histologic subtype and CEM features were analyzed using binary logistic regression with odds ratios and 95% confidence intervals. A P value < 0.05 was considered significant.

RESULTS

Of 361 lesions, 312 (86.4%) were IDC and 49 (13.6%) were ILC. The mean age was 53 years in the IDC group and 51 years in the ILC group. Molecular subtype, tumor grade, Ki-67 index, and tumor focality differed significantly between groups (all $P < 0.05$). ILC was more frequently Luminal A, lower grade, and associated with lower Ki-67 levels, whereas IDC more often demonstrated a triple-negative phenotype and grade 3 tumors. Multifocality was significantly more common in ILC. On LE images, oval/round mass shape ($P = 0.028$) and mass-associated microcalcifications ($P = 0.027$) were significantly less frequent in ILC than in IDC. On RC images, significant differences were observed in enhancement type ($P = 0.016$), internal enhancement pattern ($P = 0.013$), extent of enhancement ($P < 0.001$), and enhancement kinetics ($P = 0.013$). Enhancement conspicuity was similar between groups ($P = 0.796$). Mass enhancement and rim-enhancement patterns were more common in IDC, whereas non-mass enhancement, enhancement extending beyond the mass, and regional enhancement were more frequent in ILC. Washout kinetics were significantly less likely in ILC than in IDC, and persistent kinetics were more frequent in ILC.

CONCLUSION

IDC and ILC demonstrate distinct CEM imaging features, particularly in enhancement type, internal enhancement pattern, extent, and kinetics. These findings may contribute to the preoperative characterization of breast cancer histologic subtype on CEM.

CLINICAL SIGNIFICANCE

CEM may provide clinically useful morphologic and functional information for distinguishing ILC from IDC before treatment. Because ILC is often less conspicuous on conventional imaging, recognizing characteristic CEM features—such as enhancement type, pattern, extent, and kinetics—may improve detection and characterization.

KEYWORDS

Invasive ductal carcinoma, invasive lobular carcinoma, breast cancer, contrast-enhanced mammography, contrast-enhanced spectral mammography

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Breast cancer remains the most frequently diagnosed malignancy in women worldwide and a leading cause of cancer-related mortality. Its marked histopathologic heterogeneity has important implications for imaging, diagnosis, and clinical management. Among invasive breast cancers, invasive ductal carcinoma (IDC) is the most common subtype and typically presents as a discrete mass. Invasive lobular carcinoma (ILC), the second most common subtype and accounting for approximately 10%–15% of cases, is biologically and radiologically distinct.^{1,2} Loss of E-cadherin expression drives its characteristic dis cohesive growth, with tumor cells infiltrating the stroma in single-file strands or subtle linear patterns rather than forming a well-circumscribed mass. This infiltrative behavior often renders ILC less conspicuous on conventional imaging, contributes to delayed detection, and complicates accurate preoperative assessment. Compared with IDC, ILC is more likely to be multifocal/multicentric and underestimated in size at diagnosis, all of which may adversely affect surgical planning and oncologic outcomes.^{3,4}

Contrast-enhanced spectral mammography (CEM) is an increasingly adopted breast imaging technique that integrates the morphologic detail of mammography with functional information derived from iodinated contrast enhancement.⁵⁻⁸ By combining low-energy (LE) images with recombined (RC) images that highlight tumor vascularity, CEM improves lesion conspicuity and has demonstrated superior cancer detection compared with full-field digital mammography and digital breast tomosynthesis, particularly in women with dense breast tissue.^{7,9} In selected settings, its diagnostic performance approaches that of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) while offering advantages in accessibility, acquisition time, and cost.^{9,10}

Despite increasing evidence supporting CEM for breast cancer detection and staging, subtype-specific imaging data remain limited, particularly regarding differentiation between IDC and ILC. In addition, the RC imaging characteristics of ILC are poorly defined, and its CEM appearances have not been comprehensively described using the American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS) 5th edition CEM lexicon. Defining the imaging signatures of these biologically distinct entities may improve interpretive confidence, enhance preoperative characterization, and ultimately support more tailored patient management.

Accordingly, this study aims to characterize the CEM features of IDC and ILC according to the BI-RADS lexicon and to compare their appearances on LE and RC images.

Methods

Study design and patient population

This retrospective study was approved by the Akdeniz University Ethics Committee (approval number: TBAEK-473; date: May 29, 2025), and the requirement for informed consent was waived.

In the university clinical practice, CEM is performed instead of conventional mammography in patients presenting with a palpable mass, spontaneous nipple discharge, or nipple retraction when targeted ultrasonography of the area of concern demonstrates suspicious findings. All eligible patients underwent CEM before the initiation of any treatment.

Consecutive patients with histopathologically confirmed breast cancer were retrospectively identified from the institutional radiology database between July 2023 and May 2025 by an independent radiology as-

sistant who did not participate in image interpretation. A total of 408 patients were initially identified. Patients were excluded if they had received neoadjuvant chemotherapy, radiotherapy, immunotherapy, or breast surgery before CEM (n = 10); additional exclusion criteria were pregnancy or lactation (n = 3); contraindications to iodinated contrast media, including a history of severe contrast reaction or renal dysfunction (n = 0); lesions located outside the CEM field of view (n = 8); non-diagnostic or poor-quality CEM images (n = 8); presence of breast implants (n = 5); and tumors with mixed histology (n = 13). After applying these criteria, 47 patients were excluded, and the final study cohort comprised 361 patients with breast cancer. The study flowchart is presented in Figure 1.

Contrast-enhanced spectral mammography acquisition

CEM examinations were performed using a dual-energy mammography system (Giotto Class; IMS Giotto, Sagittario, Sasso Marconi, Bologna, Italy). Prior to imaging, iohexol (Omnipaque 350 mgI/mL; GE, Shanghai, China) was administered intravenously at a dose of 1.5 mL/kg using a power injector at an injection rate of 3 mL/s. Approximately 2 minutes after contrast administration, LE and high-energy (HE) craniocaudal (CC) and mediolateral oblique (MLO) projections were acquired sequentially, beginning with the clinically suspicious breast. RC images were generated by subtracting LE from HE images. Delayed images were obtained approximately 8 minutes after contrast injection. The total examination time did not exceed 10 minutes. Exposure parameters were automatically adjusted according to breast thickness and density using automatic exposure control. Tube voltage ranged from 26 to 31 kVp for LE acquisitions and from 45 to 49 kVp for HE acquisitions.

Main points

- Invasive lobular carcinoma (ILC) more frequently presented as non-mass enhancement with regional or beyond-lesion extension than invasive ductal carcinoma (IDC).
- IDC more commonly showed mass-like enhancement with a rim-enhancement pattern and washout kinetics.
- Microcalcifications did not differ significantly between IDC and ILC overall. However, on multivariate analysis, mass-associated microcalcifications were significantly less common in ILC than in IDC.

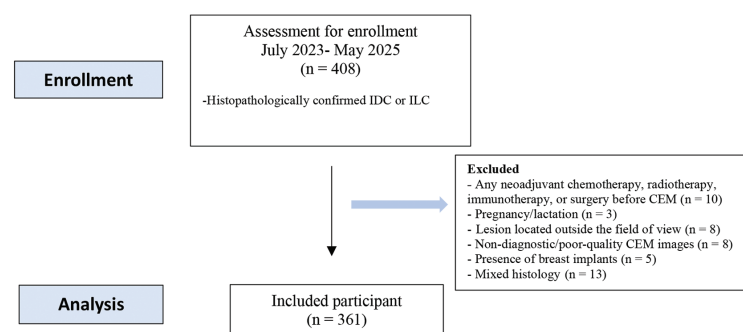


Figure 1. Enrollment of patients in the study. IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; CEM, contrast-enhanced spectral mammography.

Image interpretation

The imaging descriptors were obtained from a retrospective, study-specific review of the original anonymized CEM images, not from routine clinical CEM reports. Two radiologists with 15 and 5 years of experience reviewed the examinations in consensus on a mammography workstation using standardized descriptors. Although they were aware that the cohort included patients with pathologically proven breast cancer, they were blinded to the detailed original CEM reports, clinical information, and pathology reports, including such details as histopathological type, tumor grade, estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67 status.

For each patient, only one breast cancer lesion was included in the analysis. In patients with multifocal or multicentric disease, the index lesion was defined as the largest lesion visible on CEM that could be matched with a histopathologically confirmed malignant lesion. Index lesion size was measured as the maximum diameter on RC CC or MLO CEM images.

Imaging features were recorded using the ACR BI-RADS CEM lexicon (5th edition, 2022 supplement).¹¹ Breast composition was assessed on LE images and categorized as almost entirely fatty (type A), scattered fibroglandular density (type B), heterogeneously dense (type C), or extremely dense (type D). Background parenchymal enhancement (BPE), defined as normal enhancement of fibroglandular tissue, was evaluated on RC images and graded as minimal, mild, moderate, or marked. Imaging findings were recorded in three categories: findings visible only on LE images, findings seen on LE images with corresponding enhancement on RC images, and findings visible only on RC images. Final CEM interpretation required assessment of both LE and RC images.

On LE images, findings included mass, asymmetry, architectural distortion, and microcalcifications. Masses were described according to shape (oval/round or irregular), margins (circumscribed, obscured/indistinct, irregular, or spiculated), and density (low, equal, or high). Although not in the formal ACR BI-RADS CEM lexicon, microcalcifications were classified in this study as either isolated or mass-associated. Associated findings, including nipple retraction, skin retraction, skin thickening, trabecular thickening, and axillary lymphadenopathy, were also documented.

On RC images, enhancement characteristics were assessed as follows:

- **Enhancement type and internal pattern:**

- **Mass enhancement:** Internal enhancement pattern classified as homogeneous, heterogeneous, or rim enhancement.

- **Non-mass enhancement (NME):** Enhancement without a discrete space-occupying mass, with internal enhancement described as homogeneous, heterogeneous, or clumped.

- **Enhancement conspicuity:** A CEM-specific descriptor reflecting lesion enhancement intensity relative to background parenchyma, categorized as low, moderate, or high.

- **Extension of enhancement:** For masses, enhancement extent was recorded as partial, complete, extending beyond the lesion, or absent; for NME, distribution was classified as focal, linear, segmental, regional, or diffuse.

- **Delayed enhancement kinetics:** Although not included in the formal ACR BI-RADS CEM lexicon, delayed RC images were visually assessed using MRI-like kinetic descriptors: persistent, plateau, and washout kinetics. Lesion enhancement intensity changes were compared between the CC views obtained in the early and late phases. An increase in enhancement intensity from early to late CC images was classified as a persistent pattern, no change as plateau, and a decrease in intensity as washout kinetics.

Histopathological assessment

Histopathological diagnosis was established by core needle biopsy or vacuum-assisted breast biopsy. All biopsy specimens were fixed in formalin and embedded in paraffin according to standard institutional protocols. Histopathological evaluation was performed centrally at the study institution by experienced breast pathologists who were blinded to the CEM findings, in accordance with the 2012 World Health Organization Classification of Tumours of the Breast.¹²

Tumor characteristics were assessed on hematoxylin and eosin-stained sections. Histological tumor type, tumor grade, ER status, PR status, HER2 status, and Ki-67 proliferation index were recorded for all patients. Breast cancers were categorized into molecular subtypes based on ER, PR, HER2 expression, and Ki-67 level as follows: Luminal A tumors were defined as ER-positive, PR-pos-

itive or PR-negative, HER2-negative, and Ki-67 < 20%; Luminal B tumors were defined as ER-positive, PR-positive or PR-negative, HER2-positive or HER2-negative, and Ki-67 ≥ 20%; HER2-enriched tumors were defined as ER-negative, PR-negative, HER2-positive, with any Ki-67 level; and triple-negative tumors were defined as ER-negative, PR-negative, HER2-negative, with any Ki-67 level.

Statistical analysis

All analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using the Shapiro-Wilk test. Descriptive statistics are presented as mean ± standard deviation and median with minimum–maximum values for continuous variables and as frequency (n) and percentage (%) for categorical variables. For comparisons between two groups, the Mann-Whitney U test was used for continuous variables that were not normally distributed. The categorical variables were analyzed by the chi-square or Fisher's exact test. Post-hoc pairwise comparisons of proportions were performed using the Z test with Bonferroni correction. Binary logistic regression analysis was performed to analyze the correlation between histologic subtypes and CEM imaging characteristics. Variables that were statistically significant in the univariate analysis were included in the multivariable model, including oval/round tumor shape, mass-associated microcalcifications, mass enhancement, and washout kinetics. Factors with significant individual effects in the univariate analysis were further evaluated in the multivariable model to assess their combined effects. Effect estimates are reported as odds ratios (ORs) with 95% confidence intervals (CIs). A *P* value < 0.05 was considered statistically significant.

Results

A total of 361 breast lesions were analyzed, including 312 (86.4%) IDC and 49 (13.6%) ILC. The mean patient age was 53 years (range, 25–88 years) in the IDC group and 51 years (range, 37–79 years) in the ILC group. Index lesion size was not significantly different between IDC and ILC lesions, with mean sizes of 22.9 ± 14.4 mm (range, 7–51 mm) and 17.8 ± 11.4 mm (range, 11–38 mm), respectively (*P* = 0.541). In contrast, tumor focality showed a statistically significant association with histological subtype (*P* = 0.004). IDC lesions most commonly presented as unifocal disease (65.7%), whereas ILC lesions more frequently demonstrated multifocal

disease (44.9%). The clinical and biological tumor characteristics according to histological subtype are summarized in Table 1.

Molecular subtype distribution, tumor grade, and Ki-67 proliferation index differed significantly between IDC and ILC groups ($P < 0.001$, $P = 0.011$, and $P = 0.010$, respectively). In post-hoc analyses, Luminal A tumors were significantly more frequent in the ILC group than in the IDC group (71.4% vs. 44.2%), whereas triple-negative tumors were more frequent in the IDC group (13.5% vs. 2%). HER2-enriched tumors were identified in 7.1% of IDC cases, whereas no HER2-enriched tumors were observed in the ILC group. Tumor grade also varied according to histological subtype. Grade 3 tumors were more frequently observed in IDC than in ILC (19.6% vs. 4.1%), whereas grade 1 tumors were more common in ILC than in IDC (32.7% vs. 22.4%). Regarding proliferative activity, low Ki-67 levels (0%–20%) were significantly more frequent in ILC than in IDC (75.5% vs. 50.3%), whereas no significant differences were observed between the groups for the other Ki-67 categories.

No statistically significant difference was found in the distribution of breast composition and BPE according to histological subtypes ($P = 0.674$ and $P = 0.535$).

Imaging findings on CEM LE images, described according to the ACR BI-RADS CEM lexicon, are presented in Table 2. Corresponding findings on RC images are presented in Table 3. Histologic subtype was not significantly associated with the presence of architectural distortion, asymmetry, microcalcifications, or mass on LE images (all $P > 0.05$). Mass shape differed significantly between subtypes ($P = 0.004$). Although irregular morphology was the most common appearance in both groups, multivariate analysis showed that oval/round masses were significantly less likely to be associated with ILC than with IDC (6.1% vs. 28.5%; OR: 0.232, 95% CI: 0.063–0.857; $P = 0.028$). Mass margins and density did not differ significantly between IDC and ILC ($P = 0.118$ and $P = 0.455$). The presentation of isolated microcalcifications did not differ significantly between IDC and ILC ($P = 0.399$). In contrast, multivariate analysis showed that mass-associated microcalcifications were significantly less likely to occur in ILC than in IDC (12.2% vs. 26.0%; OR: 0.354, 95% CI: 0.141–0.890; $P = 0.027$). No significant association was found between histologic subtype and nipple retraction, skin retraction, skin thickening, trabecular thickening, or axillary lymphadenopathy (all $P > 0.05$).

Table 1. Patients and tumor biological characteristics by histologic group

	IDC n = 312 (%)	ILC n = 49 (%)	P
Size (mm)	22.9 (7–51)	17.8 (11–38)	0.541
Age	53 (25–88)	51 (37–79)	0.911
Premenopausal	132 (42.3)	21 (42.9)	0.942
Postmenopausal	180 (57.7)	28 (57.1)	
Focality			
Unifocal	205 (65.7)	20 (40.8)	0.004
Multifocal (MF)	71 (22.8)	22 (44.9)	
Multicentric (MC)	4 (1.3)	0 (0)	
MF + MC	32 (10.3)	7 (14.3)	
Molecular subtypes			
Luminal A	138 (44.2)	35 (71.4)	< 0.001
Luminal B	110 (35.3)	13 (26.5)	
HER2-enriched	22 (7.1)	0 (0)	
Triple-negative	42 (13.5)	1 (2)	
Grade			
1	70 (22.4)	16 (32.7)	0.011
2	181 (58)	31 (63.3)	
3	61 (19.6)	2 (4.1)	
Ki-67			
0–20	157 (50.3)	37 (75.5)	0.010
20–40	80 (25.6)	8 (16.3)	
40–60	44 (14.1)	3 (6.1)	
> 60	31 (9.9)	1 (2)	

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2.

Table 2. Descriptive variables of low-energy images of contrast-enhanced spectral mammography of IDC and ILC

	IDC n = 312 (%)	ILC n = 49 (%)	P
On low-energy images			
Breast composition			
Almost entirely fatty	40 (12.8)	5 (10.2)	0.674
Scattered fibroglandular density	97 (31.1)	15 (30.6)	
Heterogeneously dense	142 (45.5)	21 (42.9)	
Extremely dense	33 (10.6)	8 (16.3)	
Architectural distortion			
No	296 (94.9)	44 (89.8)	0.182
Yes	16 (5.1)	5 (10.2)	
Asymmetry			
No	294 (94.2)	42 (85.7)	0.061
Yes	18 (5.8)	7 (14.3)	
Microcalcifications			
No	204 (65.4)	108 (34.6)	
Yes	108 (34.5)	8 (16.3)	
-Only microcalcifications	27 (8.6)	2 (4.1)	0.399
-Mass-associated microcalcifications	81 (26)	6 (12.2)	0.037

	IDC n = 312 (%)	ILC n = 49 (%)	P
Mass			
No	81 (26)	17 (34.7)	0.201
Yes	231 (74)	32 (65.3)	
-Mass shape			
Oval/round	89 (28.5)	3 (6.1)	0.004
Irregular	142 (45.5)	29 (59.2)	
-Mass margins			
Circumscribed	10 (3.2)	0 (0)	0.118
Irregular/microlobulated	87 (27.9)	7 (14.3)	
Spiculated	100 (32.1)	21 (42.9)	
Obscured/indistinct	34 (10.9)	4 (8.2)	
-Mass density			
Low	10 (3.2)	0 (0)	0.455
Equal	99 (31.7)	16 (32.7)	
High	122 (38.8)	16 (32.7)	
Associated findings			
-Nipple retraction			
No	294 (94.2)	42 (85.7)	0.061
Yes	18 (5.8)	7 (14.3)	
-Skin retraction			
No	289 (92.6)	43 (87.8)	0.257
Yes	23 (7.4)	6 (12.2)	
-Skin thickening			
No	295 (94.6)	49 (100)	0.144
Yes	17 (5.4)	0 (0)	
-Trabecular thickening			
No	303 (97.1)	48 (98)	1.000
Yes	9 (2.9)	1 (2)	
-Axillary adenopathy			
No	279 (89.4)	45 (91.8)	0.801
Yes	33 (10.6)	4 (8.2)	

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

Enhancement type differed significantly between subtypes ($P = 0.016$). In the univariate analysis, mass enhancement was significantly less likely to be associated with ILC than IDC (71.4% vs. 85.3%; OR: 0.432, 95% CI: 0.216–0.866; $P = 0.018$), whereas NME was more frequently observed in ILC (28.6% vs. 14.7%). Internal enhancement patterns also differed significantly between groups ($P = 0.013$): rim enhancement was more common in IDC than ILC (18.6% vs. 6.1%). NME most commonly demonstrated a heterogeneous pattern in both IDC and ILC. Enhancement conspicuity did not differ significantly between IDC and ILC ($P = 0.796$). The extent of enhancement showed a significant association with histologic subtype ($P < 0.001$). Total

mass enhancement was more common in IDC than in ILC (57.4% vs. 28.6%), and extension beyond the mass enhancement (13.5% vs. 28.6%) and regional enhancement (1.0% vs. 16.3%) were more frequently observed in ILC. Enhancement pattern and extent of enhancement were not included in the multivariable model because they were highly correlated with other independent variables, resulting in multicollinearity and separation issues. The final multivariable model was statistically significant (χ^2 : 25.577, $P < 0.001$), although the included factors explained only a limited proportion of the variation in histological subtypes (Nagelkerke R^2 : 0.125). Enhancement kinetics also differed significantly between subtypes ($P = 0.013$). IDC

most commonly exhibited washout kinetics (55.1%), whereas ILC more frequently showed persistent kinetics (20.4%). In the multivariate analysis, washout kinetics were significantly less likely to be associated with ILC than IDC (34.7% vs. 55.1%; OR: 0.359, 95% CI: 0.139–0.929; $P = 0.035$). Figures 2 and 3 illustrate tumor cases of ILC and IDC, respectively.

Discussion

In this study, we provide a comprehensive CEM-based imaging comparison of ILC and IDC and identify imaging features that may support subtype-specific preoperative assessment. In our study cohort, ILC accounted for 13.6% of included cases, which is within the 10%–15% proportion reported in the literature.² In accordance with its established pathological profile, ILC was more frequently associated with low histologic grade, hormone receptor positivity, HER2 negativity, and a predominantly Luminal A molecular subtype.^{13–15}

CEM demonstrated significant differences between IDC and ILC across multiple imaging characteristics, including tumor focality, mass shape, microcalcifications, enhancement type, internal enhancement pattern, extent of enhancement, and enhancement kinetics. Although many of these findings are consistent with previous mammography and MRI studies, the novelty of our study is demonstrating these subtype-related differences specifically on CEM, an imaging technique that combines morphologic information from LE images with functional information related to tumor vascularity from RC images. In this respect, CEM may provide a practical “one-stop” assessment by integrating mammographic and contrast-enhancement features in a single, widely applicable examination, particularly in settings where MRI availability is limited, contraindicated, or less feasible. These results support the potential role of CEM not only in lesion detection but also in subtype-specific characterization.

The literature indicates that ILC may be mammographically occult in up to 30% of cases.^{2,16} When detectable, ILC most commonly manifests as a spiculated or indistinct mass that is iso- or hypodense relative to the surrounding parenchyma; architectural distortion is the next most frequent presentation, whereas asymmetry is less commonly observed.^{16–18} In the present analysis, most of the reported imaging findings are broadly consistent with the established biological and radiological characteristics of IDC and

Table 3. Descriptive variables of recombined images of contrast-enhanced spectral mammography of IDC and ILC

	IDC n = 312 (%)	ILC n = 49 (%)	P
On recombined images			
Background parenchymal enhancement			
Minimal	228 (73.1)	32 (65.3)	0.535
Low	61 (19.6)	12 (24.5)	
Moderate	16 (5.1)	4 (8.2)	
Marked	7 (2.2)	1 (2)	
Enhancement type			
Mass	266 (85.3)	35 (71.4)	0.016 0.013
-Internal homogeneous	80 (25.6)	8 (16.3)	
-Internal heterogeneous	128 (41)	24 (49)	
-Rim	58 (18.6)	3 (6.1)	
Non-mass	46 (14.7)	14 (28.6)	0.143
-Homogeneous	1 (0.3)	0 (0)	
-Heterogeneous	44 (14)	12 (24.5)	
-Clumped	1 (0.3)	2 (4)	
Conspicuity			
Low	53 (17)	15 (30.6)	0.796
Moderate	109 (34.9)	8 (16.3)	
High	150 (48.1)	26 (53.1)	
Extent of enhancement			
Mass	266 (85.3)	35 (71.4)	0.016 < 0.001
-Partial	45 (14.4)	7 (14.3)	
-Total	179 (57.4)	14 (28.6)	
-Extension beyond the lesion	42 (13.5)	14 (28.6)	
-None	0 (0)	0 (0)	< 0.001
Non-mass	46 (14.7)	14 (28.6)	
-Focal	20 (6.4)	3 (6.1)	
-Linear	5 (1.6)	0 (0)	
-Segmental	9 (2.9)	2 (4.1)	
-Regional	3 (1)	8 (16.3)	
-Diffuse	9 (2.9)	1 (2)	
Kinetics			
Persistent	30 (9.6)	10 (20.4)	0.013
Plateau	110 (35.3)	22 (44.9)	
Washout	172 (55.1)	17 (34.7)	
IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.			

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

ILC and therefore primarily reinforce existing evidence. Although irregular masses predominated in both IDC and ILC, oval/round masses were observed more frequently in IDC and were rarely identified in ILC.^{16,18,19} Cserni et al.²⁰ reported that microcalcifications are uncommon in pure ILC and are more frequently associated with mixed IDC/ILC tumors.

The RC images provide greater discriminatory value than LE imaging alone. Distinct

enhancement patterns may reflect the different growth characteristics of IDC and ILC. Mass-like enhancement was more common in IDC, whereas ILC more frequently showed NME, often with enhancement extending beyond the lesion or regional NME. These findings are consistent with the infiltrative growth pattern of ILC and its propensity for multifocal or multicentric spread.^{1-4,21,22} Although data specifically focusing on ILC remain relatively limited, CEM has been shown to be useful for breast cancer staging and

assessment of disease extent, suggesting a potential role in preoperative evaluation of ILC.⁹ Previous studies have identified heterogeneous and rim enhancement as suspicious features indicative of malignancy;^{23,24} however, their relationship with IDC and ILC has not been well characterized. In our study, rim enhancement was observed more frequently in IDC. Prior reports indicate that rim enhancement is more commonly associated with biologically aggressive tumors, particularly triple-negative breast cancers (TNBCs), likely reflecting peripheral tumor angiogenesis and relatively poor central perfusion with central necrosis.^{25,26} This association may be explained, at least in part, by the significantly higher frequency of the TNBC subtype among IDC cases than among ILC cases in our cohort (13.5% vs. 2%, $P < 0.001$).

Enhancement kinetics are routinely used on DCE-MRI to characterize breast lesions and help differentiate benign from malignant tumors. In general, benign lesions on DCE-MRI tend to demonstrate persistent kinetics, whereas malignant lesions more often show washout; however, a plateau kinetics pattern may be observed in both benign and malignant lesions. CEM can depict not only morphologic abnormalities but also contrast uptake related to tumor vascularity; however, unlike DCE-MRI, it does not provide continuous dynamic acquisition. Accordingly, kinetic assessment is not currently included in the formal BI-RADS CEM lexicon, and the use of DCE-MRI-like kinetic descriptors—such as persistent, plateau, or washout patterns—on delayed CEM images should be regarded as exploratory. Only a few studies have described enhancement intensity changes between early and delayed RC CEM images.^{27,28} In our analysis, these changes appeared potentially useful for subtype differentiation, with IDC more frequently exhibiting a washout pattern and ILC more often showing persistent enhancement. These findings may reflect differences in tumor perfusion and vascular characteristics. Yetkin et al.²⁹ reported that washout kinetics may be associated with immature tumor vasculature and increased vascular permeability, leading to rapid contrast uptake followed by subsequent clearance from the tumor. In contrast, persistent enhancement or less intense enhancement may be observed in lesions with lower angiogenic activity or smaller tumor burden. However, these findings should be interpreted with caution. In the present study, kinetic assessment was based on visual comparison of enhancement intensity between early and delayed RC CEM images

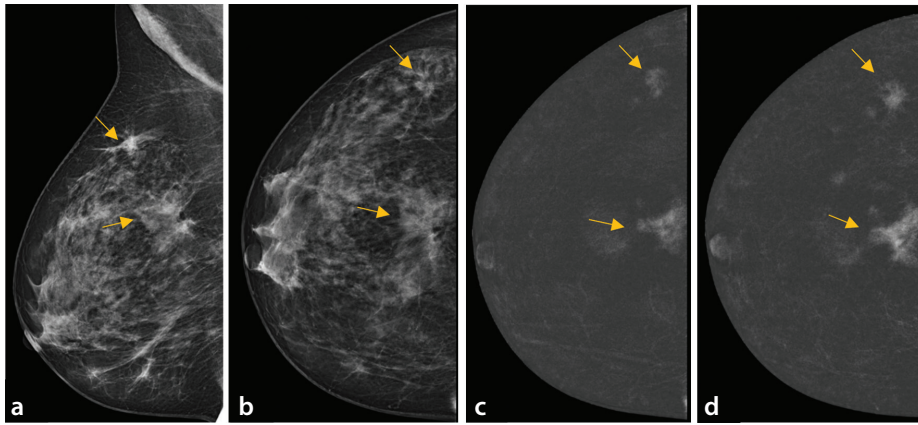


Figure 2. A 47-year-old woman diagnosed with invasive lobular carcinoma of the right breast (ER 10%, PR 90%, HER2-negative, Ki-67 10%, grade 2) exhibited multifocal and multicentric disease (arrows). Low-energy craniocaudal (a) and mediolateral oblique (b) images demonstrate architectural distortion. Recombined early (c) and delayed (d) CC views of contrast-enhanced spectral mammography show mass and non-mass heterogeneous enhancement, with enhancement extending beyond the lesions and progressive kinetics on delayed imaging. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CC, craniocaudal.

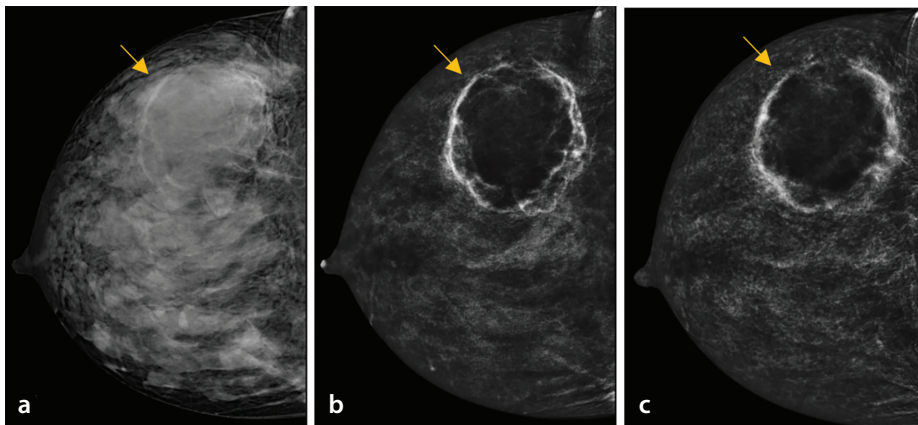


Figure 3. A 43-year-old woman with invasive ductal carcinoma of the right breast (ER-negative, PR-negative, HER2-negative, Ki-67 60%, grade 3) presenting as a mass (arrows). Low-energy (a) and recombined (b, c) craniocaudal CEM images demonstrate a round mass with obscured/indistinct margins. The lesion shows rim enhancement with washout kinetics on the delayed imaging. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CEM, contrast-enhanced spectral mammography.

rather than on standardized quantitative measurements. This approach is inherently subjective and may be influenced by image acquisition timing, breast compression, BPE, lesion size, technical parameters, and reader experience. Moreover, the reproducibility of delayed CEM kinetic interpretation has not been sufficiently established, and there is currently no universally accepted threshold or validated method for defining washout, plateau, or persistent enhancement on CEM. Therefore, although enhancement intensity changes on delayed CEM images may provide additional information, they should not be used as a standalone criterion for lesion characterization.

The literature has shown that stronger enhancement is more frequently observed

in malignant than in benign breast mass lesions.^{27,30,31} However, enhancement intensity alone is not specific for malignancy. Phillips et al.³² reported that some benign entities, including adenosis, fibroadenoma, and mastitis, may demonstrate moderate or marked enhancement, whereas some malignant lesions, particularly ductal carcinoma *in situ*, may show no or only subtle enhancement. Therefore, enhancement conspicuity on CEM should not be interpreted as a direct marker of malignancy or histologic subtype alone. Enhancement conspicuity may be associated with a combination of histopathologic and biological factors, such as histologic grade, hormone receptor and HER2 status, and Ki-67 proliferation index. Consistent with this concept, Marzogi et al.³³ showed that more

aggressive breast cancers, which typically have higher proliferative activity and metastatic potential, tend to exhibit stronger enhancement than less proliferative tumors. Previous studies have also reported that ILC more commonly demonstrates weaker enhancement than IDC, highlighting that weakly enhancing lesions may still be malignant, particularly in the setting of ILC.^{21,33} In our study, enhancement conspicuity did not differ significantly between IDC and ILC; however, weak enhancement was observed in approximately 30% of ILC cases and 17% of IDC cases. This finding suggests that the absence of strong enhancement should not be used to exclude malignancy or to underestimate disease, especially in patients with ILC. In addition, several studies have shown that lesion conspicuity is influenced by lesion size and enhancement pattern.³⁴⁻³⁶ Larger lesions and mass-type enhancement generally tend to be more conspicuous, whereas NME is more often associated with lower conspicuity. In our study, lesion size did not differ significantly between IDC and ILC, suggesting that the observed imaging differences are unlikely to be primarily attributable to tumor size imbalance. Taken together, these findings suggest that conspicuity alone may be insufficient for differentiating breast cancer subtypes. A combined assessment including enhancement type, internal enhancement pattern, lesion extent, and kinetic features is likely to provide more informative imaging characterization.

This study has several limitations. First, its retrospective, single-center design, relatively small sample size, and uneven distribution of histologic subtypes may have reduced statistical power for subgroup analyses and limited the generalizability of the findings. In particular, the number of less common ILC cases was relatively small ($n = 49$), which may have affected the reliability of subtype-specific comparisons. Therefore, prospective multicenter studies with larger and more balanced cohorts are needed to validate these results. Second, because this was a single-center retrospective cohort, the findings may reflect local patient characteristics, imaging protocols, referral patterns, and reader experience. As a result, the applicability of our results to other institutions, different CEM systems, and broader patient populations may be limited. Third, the absence of pathological tumor size measurements limited our ability to evaluate the potential influence of lesion size on subtype-related CEM findings, including enhancement pattern, lesion conspicuity, and extent of enhance-

ment. Future studies should include both imaging-based and tumor size measurements and assess their effects using multivariable analyses to determine whether CEM features are independently associated with histologic subtype. Fourth, molecular subtype may have been a potential confounder, as CEM features can be influenced by both histologic subtype and molecular tumor characteristics. Because of the limited sample size and uneven subtype distribution, multivariable adjustment for molecular subtype was not feasible. Therefore, some observed differences in CEM features may partly reflect underlying molecular heterogeneity rather than histologic subtype alone. Consistently, the low Nagelkerke R^2 value (0.125) indicates that the model explained only a small proportion of subtype variability. Fifth, the assessment of lesion conspicuity, enhancement extent, and enhancement kinetics was based on qualitative visual interpretation rather than quantitative enhancement parameters. The lack of objective quantitative measurements may have reduced measurement precision and introduced subjectivity into image interpretation. Sixth, interobserver agreement analysis was not performed. Although all images were interpreted in consensus by experienced radiologists, the absence of a formal agreement assessment is a limitation, particularly because interpretation of enhancement characteristics may vary according to reader experience. Finally, CEM features may intrinsically overlap among different breast pathologies, which may limit the ability of CEM alone to distinguish histologic subtypes. These limitations should be considered when interpreting the conclusions of this study.

In conclusion, CEM shows meaningful subtype-specific imaging differences between IDC and ILC, particularly in tumor shape, mass-associated microcalcifications, enhancement pattern and extent of enhancement, and enhancement kinetics. These findings align with known tumor biology: ILC more often presents with multifocality, non-mass with regional enhancement, enhancement beyond the lesion, and persistent kinetics, whereas IDC more commonly appears as a mass with rim enhancement and washout kinetics. These differences are clinically meaningful and may help radiologists improve CEM interpretation and preoperative assessment. Further prospective studies are needed to clarify the role of CEM-based subtype-specific features in treatment planning and patient management.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

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