



**FULL RESEARCH ARTICLE** 

# A descending enhancement pattern on CEM is associated with invasive breast cancer: the first Mexican experience

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## **ABSTRACT**

Introduction: There are few studies on the quantitative analysis and enhancement pattern of breast lesions on contrastenhanced mammography (CEM). We performed a quantitative analysis and defined CEM enhancement patterns of malignant, benign with upgrade potential (BWUP), and benign breast lesions with a histopathologic correlation. Materials and Methods: A retrospective cross-sectional study of women with breast lesions showing CEM enhancement patterns was conducted with a confirmed histopathologic diagnosis. The quantitative CEM parameters were the contrast-to-noise ratio (CNR), the percentage signal ratio between the enhanced lesion and background (%RS), and the relative signal difference (RSD). The enhancement patterns analyzed were ascending, steady, and descending. Results: A total of 32 women with a mean age of 53.5 ± 11.1 (range 33-75) years with 36 breast lesions assessed by CEM were included. Histopathologic diagnoses were infiltrating breast carcinoma (n = 13, 36.1%), breast carcinoma in situ (n = 2, 5.5%), BWUP (n = 4, 11.1%), and benign breast lesions (n = 17, 11.1%), and benign breast lesions (n = 17, 11.1%). 47.2%). The ascending pattern was found in 16 (44.4%) of the 36 lesions, the descending enhancement pattern in 15 (41.7%), and the steady pattern in 5 (13.9%). The descending enhancement pattern was significantly more frequent in infiltrating breast carcinomas (n = 9, 60.0%) (p = 0.018), while carcinoma in situ (n = 2) showed an ascending pattern (p = ns). Benign and BWUP lesions were more likely to show an ascending pattern (n = 9 and n = 3, respectively) (p = ns). Conclusion: This is the first study in Mexico to present a quantitative analysis and enhancement patterns to better characterize breast lesions in CEM. The descending enhancement pattern provides useful information for predicting invasive breast cancer.

Keywords: Contrast-enhanced mammography. Recombined images. Quantitative CEM values. Breast cancer. Infiltrating breast carcinoma.

## INTRODUCTION

Contrast-enhanced mammography (CEM) increases diagnostic accuracy in detecting breast cancer with higher specificity and similar sensitivity (93-100%) to conventional mammography and magnetic resonance imaging<sup>1,2</sup>. CEM allows the assessment of the morphology and physiological characteristics of the breast lesion by contrast enhancement<sup>3</sup>. Malignant lesions have immature vascular proliferation and increased microvascular permeability that allow the contrast agent to accumulate in and around the malignant tumor4.

Some malignant, benign with upgrade potential (BWUP), and benign lesions may have similar imaging features<sup>5</sup>. The first version of the BI-RADS<sup>®</sup> lexicon for CEM included only subjective qualitative descriptors of

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defined internal enhancement patterns, extent of lesion enhancement, asymmetry enhancement, and conspicuity<sup>6,7</sup>. Interestingly, a quantitative assessment of enhancement in low-energy and recombined images can improve the diagnostic performance of CEM. Few quantitative analyses of CEM have shown an association between increased enhancement and breast malignancy<sup>8-10</sup>. Moreover, contrast kinetics have been evaluated and categorized into three patterns: ascending, steady, and descending8. The descending pattern has been associated with an increased likelihood of breast malignancy<sup>8-10</sup>. It is crucial to differentiate breast carcinomas from benign breast lesions to improve the diagnostic performance of CEM<sup>10</sup>. Quantitative analysis of CEM enhancement can help differentiate malignant, BUWP, and benign breast lesions. This study focused on the quantitative analysis and CEM enhancement patterns with a histopathologic correlation of malignant, BWUP, and benign breast lesions.

#### MATERIALS AND METHODS

This retrospective cross-sectional study was conducted from September 2015 to June 2023 at the Centro de Imagenologia Integral IMAX in Tampico, Tamaulipas, Mexico. Women with breast lesions on CEM and diagnosis confirmed by histopathology were included. Exclusion criteria were the lack of a histopathology report or incomplete imaging studies. Informed consent was not required for this retrospective data analysis obtained during routine medical care. The Institutional Research Ethics Committee and the Research Committee approved the study.

# Study development and variables

CEM was performed in patients with clinically or ultrasonographically suspected breast lesions of malignancy. Patients with a breast lesion with enhancement on CEM and histopathologic confirmation of their diagnosis were identified in the institutional database. The first version of the BI-RADS® lexicon for CEM was used to describe subjective qualitative descriptors that define internal enhancement patterns, extent of lesion enhancement, asymmetric enhancement, and conspicuity<sup>6</sup>.

# **Quantitative CEM parameters**

Contrast-to-noise ratio (CNR) is the difference in signal between lesion enhancement and background<sup>10</sup>:

$$CNR = \frac{LS - BS}{SD}$$

where LS is the lesion signal with the maximum pixel value in the region of interest (ROI) of the breast lesion<sup>10</sup>; BS is the background signal with the mean pixel value of the signal in the ROI of the background<sup>10</sup>; and SD is the standard deviation (pixels).

Percentage signal difference between enhancing lesion and background (%RS):

$$\%RS = \frac{LS - BS \times 100}{BS}$$

Relative signal difference (RSD) of the enhancement pattern:

$$RSD = \frac{CNR MLO - CNR CC \times 100}{CNR CC}$$

*CNR\_MLO:* CNR in the mediolateral oblique (MLO) projection.

CNR\_CC: CNR in the caudal cranial (CC) projection.

# **CEM** enhancement patterns

Two acquisition time points, the relative enhancement at early (CC view) and late (MLO view) net enhancement on the CEM, were recorded and classified as follows<sup>10</sup>:

Ascending pattern: The intensity of the enhancement showed a continuous increase state with an RSD > 10%<sup>10</sup>. Enhancement increased by more than 10% from the early to the late phase<sup>8</sup>.

Steady pattern: The enhancement intensity showed no notable difference between the two projections, with the absolute RSD value within 10%<sup>10</sup>. The enhancement changed within 10%<sup>8</sup>.

Descending pattern: The intensity of the enhancement is weaker in the latter position than in the former with an RSD  $\leq 10\%^{10}$ . Enhancement decreased by more than  $10\%^8$ .

# Image acquisition and analysis

# CONTRAST-ENHANCED MAMMOGRAPHY (CEM)

The CEM technique was performed with SenoBright<sup>TM</sup> (GE Medical Systems, Buc, France) equipment<sup>7</sup>. A peripheral intravenous line was placed in the antecubital fossa, and 1.5 mL/kg of an iodinated contrast

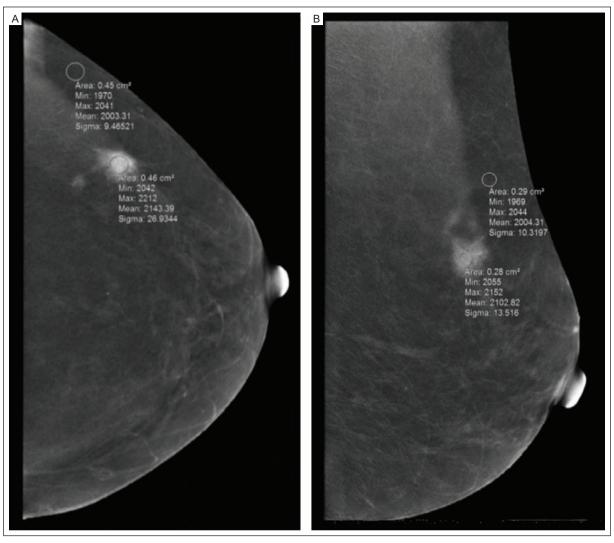


Figure 1. Quantitative measurement of the enhancement of breast lesions on CEM. A: RC CC view. B: RC MLO view shows an irregular, spiculated lesion with homogeneous internal enhancement and high conspicuity. The ROI was placed on the enhanced breast lesion and background area. The quantitative CNR was 15.7 in the CC view and 9.5 in the MLO view. A descending enhancement pattern was seen with an RSD value of -41.7%.

CC: craniocaudal view; CEM: contrast-enhanced mammography; CNR: contrast-to-noise ratio; MLO: mediolateral oblique; RC: recombined; ROI: region of interest; RSD: relative signal difference.

agent was administered at a rate of 3 mL/s (Omnipaque<sup>™</sup> 300, GE Healthcare, Carrigtwohill Co. Cork, Ireland). The patient was positioned for two standard CC and MLO mammography projections of each breast at least 90 s after the injection. The CC and MLO projections of both breasts were performed with a delay of 2 min between each projection of the same breast. It started with the right breast and continued with the left breast. Images were obtained from the Picture Archiving and Communication System (PACS) (Synapse 5™, Fujifilm Medical Systems U.S.A., Inc.).

All CEM examinations were analyzed by the same breast radiologist (DPM) with 31 years of experience on a SecurView workstation (Hologic, Inc. Danbury, CT. USA) with 5 MP medical-grade monitors (BARCO, Kortrijk, Belgium). The region of interest (ROI) of the lesion with enhancement was recorded with the mean value of the calculated enhancement. A second ROI similar to the first was placed in an area without enhancement. Figure 1 illustrates the quantitative measure of the CEM signal values. The ROI was placed over the enhanced area of the lesion and the background area with pixel measurement to

Infiltrating breast carcinoma	n (%)
Infiltrating ductal carcinoma	8 (61.5)
Infiltrating lobular carcinoma	2 (15.4)
Infiltrating ductal-lobular carcinoma	3 (23.1)
Total	13 (100)
In situ breast carcinoma	n (%)
Ductal carcinoma in situ	1 (50.0)
Ductal lobular carcinoma in situ	1 (50.0)
Total	2 (100)
BWUP	n (%)
Atypical ductal hyperplasia	3 (75.0)
Lobular carcinoma in situ	1 (25.0)
Total	4 (100)
Benign breast lesion	n (%)
Fibroadenoma	6 (35.3)
Complex fibroadenoma	2 (11.8)
Sclerosing adenosis	3 (17.6)
Fat necrosis	1 (5.9)
Mastitis/abscess	4 (23.5)
Fibrosis	1 (5.9)
Total	17 (100)

BWUP: benign with upgrade potential; CEM: contrast enhanced mammography.

calculate the CNR and evaluate the enhancement intensity. The RSD was calculated to assess the enhancement pattern. The ROIs of the background were as close as possible to the fatty components of the breast background and away from the enhanced lesion or the enhanced breast parenchymal tissue. ROI sizes varied according to the homogeneity of the pixel values between the lesion and noise areas. ROI values were evaluated separately for CC and MLO projections.

#### **Ultrasound**

LOGIC<sup>TM</sup> ultrasound (US) equipment (General Electric, Boston, MA, USA) with a linear multifrequency transducer of 10–16 MHz was used. The US grayscale and color Doppler images were stored in a PACS.

Breast US features were reported according to the BI-RADS<sup>11</sup>. The US findings of three clinical cases are shown in the figures presented.

# Breast biopsy

Breast biopsies were performed with a 14-gauge Bard<sup>TM</sup> needle (Bard Care, Covington, GA, USA) using the Bard Magnum System<sup>TM</sup>. A pathologist (KGA) blinded to the patient's imaging findings and with 11 years of experience evaluated the biopsies and reported the histopathologic diagnosis.

# Statistical analysis

A descriptive analysis of the numerical and categorical variables was performed. The mean, SD, minimum and maximum of CNR, %RS, and RSD were calculated. The association of the enhancement patterns (ascending, descending, or steady) with the histopathologic diagnosis was evaluated with the chi-square test with a significance of  $p \le 0.05$ . Statistical analysis was performed with SPSS version 25 (IBM Corp., Armonk, NY. USA).

# **RESULTS**

A total of 32 women with 36 breast masses with CEM enhancement were included. Two lesions were found in four patients. The mean ( $\pm$ SD) age was 53.5  $\pm$  11.1 (range 33–75) years. Table 1 shows the histopathologic diagnoses: infiltrating breast carcinoma (n = 13, 36.1%), breast carcinoma in situ (n = 2, 5.5%), BWUP (n = 4, 11.1%), and benign lesions (n = 17, 47.2%).

# Quantitative analysis of CEM enhancement

The quantitative CNR and %RS values of CEM enhancement of the 36 breast lesions in relation to histopathologic diagnosis are shown in Table 2. The highest mean value of CNR\_CC and %RS\_CC corresponded to infiltrating carcinoma (6.5  $\pm$  3.3 and 3.7  $\pm$  1.9, respectively). In contrast, CNR and %RS in the MLO projection had comparable values between malignant, BWUP, and benign breast lesions.

# Enhancement pattern of CEM

The quantitative RSD values of CEM enhancement are shown in Table 3. Infiltrating breast carcinomas had a mean RSD of  $-22.8 \pm 39.7$ , corresponding to a

Table 2. Quantitative CNR and %RS values of CEM enhancement in relation to histopathologic diagnosis in 36 breast lesions

Description	n	Mean ± SD	Minimum	Maximum
CNR_CC				
Infiltrating breast carcinoma	13	6.5 ± 3.3	2.7	15.4
In situ breast carcinoma	2	2.7 ± 1.1	1.8	3.5
BWUP	4	$3.2 \pm 0.5$	2.7	3.8
Benign breast lesions	17	4.9 ± 1.9	3.2	10.6
Total	36			
%RS_CC				
Infiltrating breast carcinoma	13	3.7 ± 1.9	1.4	7.5
In situ breast carcinoma	2	1.9 ± 1.0	1.1	2.6
BWUP	4	2.2 ± 0.6	1.9	3.1
Benign breast lesions	17	2.9 ± 2.4	1.4	12.0
Total	36			
CNR_ML0				
Infiltrating breast carcinoma	13	4.5 ± 2.2	1.1	9.0
In situ breast carcinoma	2	4.2 ± 1.8	2.9	5.6
BWUP	4	4.4 ± 1.1	3.2	6.0
Benign breast lesions	17	5.0 ± 3.2	0.2	12.5
Total	36			
%RS_ML0				
Infiltrating breast carcinoma	13	2.9 ± 1.4	0.7	5.7
In situ breast carcinoma	2	2.6 ± 1.3	1.6	3.6
BWUP	4	3.4 ± 1.8	1.7	5.9
Benign breast lesions	17	2.7 ± 1.9	0.1	8.2
Total	36			

CEM: contrast enhanced mammography; CNR: contrast to noise ratio; %RS: percentage signal difference between enhancement lesion and background; CC: craniocaudal; MLO: medio-lateral oblique; BWUP: benign with upgrade potential; SD: standard deviation.

descending enhancement pattern. Carcinoma in situ had a mean RSD of 6.1  $\pm$  2.0, corresponding to a steady pattern, while benign lesions had an RSD of 13.1  $\pm$  72.0, corresponding to an ascending pattern. BWUP lesions had a mean RSD of 41.7  $\pm$  41.4, corresponding to an ascending pattern.

The enhancement pattern of breast lesions in CEM and its relationship to histopathologic diagnosis is shown in Table 4. The ascending pattern was found in 16 (44.4%) of 36 breast lesions, the descending enhancement pattern in 15 (41.7%), and the stable pattern in 5 (13.9%). The descending pattern was significantly

more frequent in infiltrating breast carcinomas (n = 9, 60.0%) (p = 0.018). The ascending pattern was more frequent in in situ carcinoma (n = 2, 100%), BWUP lesions (n = 3, 75%), and benign lesions (n = 9, 56.3%).

Figure 2 shows a 48-year-old woman with a palpable mass in the retroareolar region of the left breast. The CEM shows a focal asymmetry in the retroareolar region with heterogeneous internal enhancement. The quantitative CNR was 8.5 in the CC view and 6.7 in the MLO view. A descending enhancement pattern was detected with an RSD value of –20.9%. The histopathologic diagnosis was an infiltrating ductal lobular carcinoma.

Table 3. Quantitative RSD values of CEM enhancement in relation to histopathologic diagnosis in 36 breast lesions

Diagnosis	(n = 36)	Mean ± SD	Minimum	Maximum
Infiltrating breast carcinoma	13	$-22.8 \pm 39.7$	-76.5	58.0
In situ breast carcinoma	2	$6.1 \pm 2.0$	58.6	61.5
BWUP	4	41.7 ± 41.4	-17.2	71.5
Benign breast lesions	17	13.1 ± 72.0	-98.4	223.3

CEM: contrast enhanced mammography; RSD: relative signal difference; CC: craniocaudal; MLO: medio-lateral oblique; BWUP: benign with upgrade potential; SD: standard deviation.

Table 4. Enhancement patterns on CEM and their relationship with the histopathologic diagnosis in 36 breast lesions

Diagnosis	Ascending pattern n (%)	Steady pattern n (%)	Descending pattern n (%)	<i>p</i> -value
Infiltrating breast carcinoma	2 (12.5)	2 (40.0)	9 (60.0)	0.018
In situ breast carcinoma	2 (12.5)	0	0	0.619
BWUP	3 (18.7)	0	1 (6.7)	0.633
Benign breast lesions	9 (56.3)	3 (60.0)	5 (33.3)	0.393
Total	16 (100)	5 (100)	15 (100)	0.101

CEM: contrast enhanced mammography; BWUP: benign with upgrade potential.

Figure 3 shows the CEM of an asymptomatic 60-year-old woman with a nonmass lesion in the upper outer quadrant and heterogeneous internal enhancement with moderately conspicuous in the upper quadrant. The quantitative CNR was 7.2 in the CC view and 3.2 in the MLO view. A descending enhancement pattern was detected with an RSD of -55.6%. The histopathologic diagnosis was an infiltrating ductal lobular carcinoma.

Figure 4 shows the CEM of an asymptomatic 46-yearold woman with focal asymmetry in the upper inner quadrant, with a heterogeneous internal enhancement pattern. The mammographic lesion is fully enhanced with high conspicuity. The quantitative CNR was 4.7 in the CC view and 6.2 in the MLO view. An ascending enhancement pattern was detected with an RSD value of 32.0%. The histopathologic diagnosis was fibroadenoma.

#### DISCUSSION

A significant association between the descending pattern of enhancement in CEM and invasive breast cancer was found in this study. We also observed that the ascending pattern was associated with benign breast lesions and BWUP. The descending enhancement pattern in CEM is useful for predicting invasive breast cancer.

Few reports show that malignant breast lesions are more likely to have a descending enhancement pattern8,10; thus, assessment of the enhancement pattern on CEM becomes relevant in identifying malignant breast cancer. In a study of 145 breast lesions in 131 patients, Liu et al.10 reported that 22 (51.2%) of 43 malignant lesions had a descending pattern with a mean RSD of -9.7 and 26 (25.5%) of 102 benign lesions had ascending enhancement with a mean RSD of 11.0% (p < 0.001). In contrast, 48 (47.1%) showed no enhancement. These results are comparable with our study in which 9 (60.0%) of 15 descending pattern lesions were infiltrating carcinomas with a mean RSD of -22.8%, while 9 (56.2%) of 16 lesions with an ascending pattern were benign, with a mean RSD of 13.1%. We believe that the differences in the mean quantitative RSD values between our results (-22.8%) and the results (-9.7%) of Liu et al.10 are because their population included infiltrating (n = 26) and non-infiltrating carcinomas (n = 17). In contrast, our population included only infiltrating carcinomas (n = 13) with a more pronounced descending

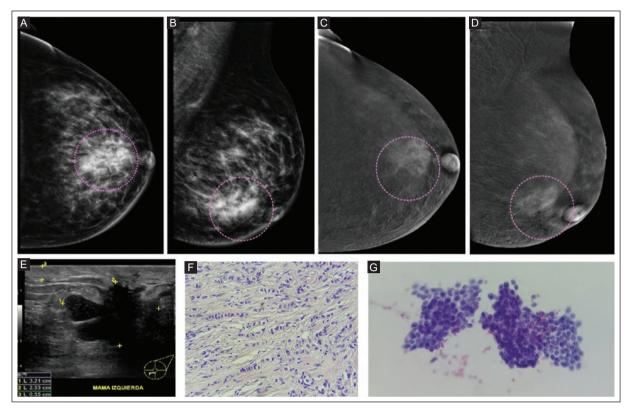


Figure 2. CEM of a 48-year-old woman with a palpable mass in the retroareolar region of the left breast. A: LE CC view. B: LE MLO view showing breast type C and with retroareolar focal asymmetry (circle). The contralateral breast has no abnormal imaging findings (not shown). C: RC CC view. D: RC MLO view with asymmetry in the retroareolar region and heterogeneous internal enhancement. The mammographic lesion is completely enhanced with moderate conspicuity. The measurements in pixels in the CC view were as follows: LS of 2091.46, BS of 1985.76, SD of 12.399 with ROI 1.1 cm², and MLO with LS of 2070.51, BS of 1985.68, SD of 12.58 with ROI 1.1 cm². The quantitative CNR was 8.5 in the CC view and 6.7 in the MLO view. A descending enhancement pattern was detected with an RSD value of -20.9%. E: Breast US in grayscale, in an anti-radial plane, showing an irregular, parallel mass with an indistinct margin, hypoechoic with posterior acoustic shadowing causing skin retraction and thickening (5 mm). F: CNB H&E 40×: infiltrating epithelial malignant neoplasm composed of medium-sized cells arranged in "Indian file" and some in ducts. G: CNB H&E 40×: smear with malignant epithelial cells and lymphocytes. The histopathologic diagnosis was an infiltrating ductal lobular carcinoma.

BS: background signal; CC: craniocaudal view; CEM: contrast enhanced mammography; CNB: core needle biopsy; CNR: contrast-to-noise ratio; MLO: mediolateral oblique; LE: low energy; LS: lesion signal; RC: recombined; ROI: H&E hematoxylin and eosin; RSD: relative signal difference; SD: standard deviation; US: ultrasound.

pattern. In CEM, malignant lesions tend to show enhancement washout (descending pattern), and most benign lesions show non-enhancing or persistent enhancement (ascending pattern). In terms of enhancement patterns, a large proportion of malignant lesions show descending patterns. In contrast, most benign lesions do not show enhancing or ascending patterns, which is a finding that may help distinguish benign and malignant breast lesions.

CEM enhancement can be found in malignant, BWUP, and benign breast lesions<sup>12</sup>. Rudnicki et al.<sup>9</sup> examined 120 (61.5%) infiltrating carcinomas, 16 (8.2%) non-infiltrating carcinomas, and 59 (30.3%) benign lesions in 167 patients with 195 breast lesions. Only 13

(6.7%) did not show enhancement (benign). They found a significant difference in %RS between infiltrating and non-infiltrating carcinomas and between infiltrating and benign lesions, with no significant difference between benign and non-infiltrating breast carcinomas. Enhancement was similar in the CC and MLO projections. The mean %RS values correlated with the type of enhancement lesion, with infiltrating carcinomas having the highest values and benign lesions having the lowest values. Liu et al. demonstrated that enhancement quantified by CNR was significantly higher in malignant lesions than in benign lesions (p < 0.001). In contrast, the difference between infiltrating and non-infiltrating malignant lesions was insignificant.

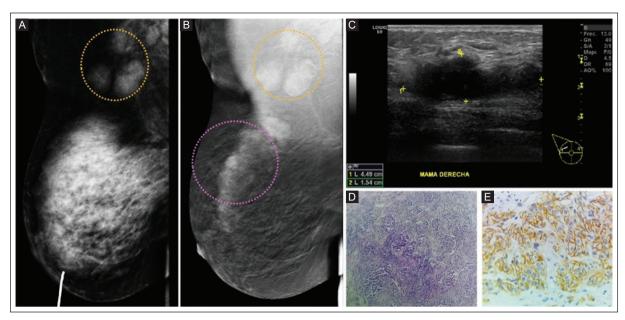


Figure 3. CEM in an asymptomatic 60-year-old woman. A: LE MLO view showing breast type D and lymph nodes with loss of morphology and fatty hilum (yellow circle). B: RC MLO view with no mass lesion in the upper outer quadrant and heterogeneous internal enhancement pattern with moderate conspicuity in the upper quadrant. Lymph nodes with enhancement (yellow circle). The measurements in pixels in the CC view were as follows: LS of 2081.31, BS of 2016.92, SD of 8.89 with ROI 0.64 cm² and MLO with LS of 2113.46, BS of 2029.03, SD of 26.27 with ROI 0.64 cm². The quantitative CNR was 7.2 in the CC view and 3.2 in the MLO view. A descending enhancement pattern was detected with an RSD of –55.6%. C: Breast US in grayscale, antiradial axis, showing an irregular, parallel, spiculated, hypoechoic mass with posterior acoustic enhancement. D: CNB H&E 40×: infiltrating epithelial malignant neoplasm composed of medium-sized cells arranged in "Indian file" and some in ducts. E: CNB H&E 20×: infiltrating epithelial malignant neoplasm composed of medium-sized cells. Immunohistochemistry HER 2/neu positive with membrane staining in more than 10% of the cells. The histopathologic diagnosis was an infiltrating ductal lobular carcinoma.

BS: background signal; CC: craniocaudal view; CEM: contrast enhanced mammography; CNB: core needle biopsy; CNR: contrast-to-noise ratio; H&E: hematoxylin and eosin; LE: low energy; RC: recombined; LS: lesion signal; MLO: mediolateral oblique; RSD: relative signal difference; SD: standard deviation; US: ultrasound.

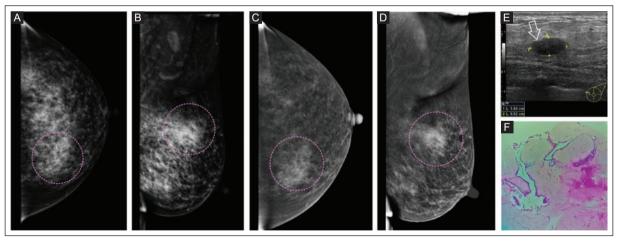


Figure 4. CEM in an asymptomatic 46-year-old woman. A: LE CC view. B: LE MLO view with focal asymmetry in the upper inner quadrant (circle) with a heterogeneous internal enhancement pattern. The contralateral breast has no abnormal imaging findings (not shown). C: RC CC view. D: RC MLO view with focal asymmetry in the upper inner quadrant, with heterogeneous internal enhancement. The mammographic lesion is completely enhanced, with high conspicuity. The measurements in pixels in the CC view were as follows: LS of 2067.41, BS of 1686.87, SD of 17.02 with ROI 0.78 cm² and MLO view with LS of 2118.26, BS of 2014.05, SD of 16.68 with ROI 0.78 cm². The quantitative CNR was 4.7 in the CC view and 6.2 in the MLO view. An ascending enhancement pattern was detected with an RSD value of 32.0%. E: breast US in grayscale, antiradial axis, showing an oval, parallel, circumscribed, hypoechoic mass (hollow arrow). F: CNB H&E 40×: biphasic neoplasm composed of ductal proliferation in a largely fibrous stroma. The histopathologic diagnosis was fibroadenoma.

BS: background signal; CC: craniocaudal view; CEM: contrast enhanced mammography; CNB: core needle biopsy; CNR: contrast-to-noise ratio; H&E: hematoxylin and eosin; LE: low-energy; LS: lesion signal; MLO: mediolateral oblique; RC: recombined; RSD: relative signal difference; SD: standard deviation; US: ultrasound.

The enhancement of infiltrating carcinomas (n = 26) showed a CNR\_CC of 7.6 and a CNR\_MLO of 6.4. Our study found comparable results in infiltrating carcinomas (n = 13) with a CNR\_CC of 6.5, which was higher than in benign lesions with a CNR\_CC of 4.9. In contrast, the CNR\_MLO showed comparable values between malignant and benign lesions (4.5 and 5.0, respectively). Quantitative CNR and %RS enhancement analysis in CEM provides useful information for predicting breast malignancy<sup>8-10</sup>.

The strengths of the study were the evaluation of images in two projections, which allowed the acquisition of data in both early and late stages and facilitated understanding of the enhancement pattern in CEM in malignant, BWUP, and benign breast lesions. In addition, all cases were confirmed by histologic analysis. Limitations were the small sample size, the retrospective analysis, and the fact that this is a single-center study. We excluded lesions that did not show enhancement, which precludes a specific comparison with the results of other studies that included these lesions.

## CONCLUSION

The descending pattern of enhancement in CEM showed a significant association with infiltrating breast cancer, whereas the ascending pattern was more common in benign breast lesions and BWUP. Although both benign and malignant breast lesions may show some enhancement, the pattern proves to be a feature that allows adequate characterization of malignant lesions. Quantitative analysis of patterns of CEM enhancement features is feasible for clinical practice<sup>10</sup>. The need for a larger number of multicenter patient studies is evident to determine the role of quantitative analysis of CEM enhancement in accurately distinguishing malignant and benign breast lesions.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

#### Ethical disclosures

**Protection of Individuals.** This study complied with the Declaration of Helsinki (1964) and its amendments.

**Confidentiality of Data.** The authors declare that they followed their center's protocol for sharing patient data.

Right to privacy and informed consent. Informed consent was not required for this observational study of information collected during routine clinical care.

Use of artificial intelligence. The authors did not use generative artificial intelligence to prepare this manuscript and/or create tables, figures, or figure legends.

#### **REFERENCES**

- Zamora K, Allen E, Hermecz B. Contrast mammography in clinical practice: Current uses and potential diagnostic dilemmas. Clin Imaging. 2021;71(1):126-135. doi:10.1016/j.clinimag.2020.11.002.
- Sogani J, Mango V, Keating D, Sung J, Jochelson M. Contrast-enhanced mammography: past, present and future. Clin Imaging. 2021;69: 269-279. doi:10.1016/j.clinimag.2020.09.003.
- Jochelson MS, Lobbes MBI. Contrast-enhanced Mammography: State of the Art. Radiology. 2021;299(1):36-48. doi: 10.1148/radiol.2021201948.
- Sensakovi W, Carnahan M, Czaplicki C, Fahrenholtz S, Panda A, Zhou Y, et al. Contrast-enhanced Mammography: How Does It Work? Radiographics. 2021;41(3):829-839. doi.org/10.1148/rg.2021200167.
- Cho SH, Park SH. Mimickers of breast malignancy on breast sonography. J Ultrasound Med. 2013;32(11):2029-2036. doi: 10.7863/ultra.32. 11.2029.
- Lee C, Phillips J, Sung J, Lewin J, Newell M. Breast Imaging Reporting and Data System: ACR BI-RADS breast imaging atlas. Contrast Enhanced Mammography (CEM) (A supplement to ACR BI-RADS® Mammography 2013). 5th Edition. Reston: American College of Radiology, 2022.
- Perez-Montemayor DF, Rios-Rodriguez TA, Garcia-Alvarez KG. Clinical application of the first version of the BI-RADS lexicon for contrast enhanced mammography: a pictorial essay. J Mex Fed Radiol Imaging. 2023;2(1):61-71. doi: 10.24875/jmexfri.m23000042.
- Deng CY, Juan YH, Cheung YO, Lin YC, Lo YF, Lin G, et al. Quantitative analysis of enhanced malignant and benign lesions on contrast-enhanced spectral mammography. Sci Rep. 2018;91(10):9807. doi:10.1259/bjr. 20170605.
- Rudnicki W, Heinze S, Niemiec J, Kojs Z, Sas-Korczynska B, Hendrick E, et al. Correlation between quantitative assessment between contrast enhancement in contrast-enhanced spectral mammography (CESM) and histopathology-preliminary results. Eur Radiol. 2019;29(11):6220-6226. doi:10.1007/s00330-019-06232-6.
- Liu Y, Zhao S, Huang J, Zhang X, Qin Y, Zhong H, et al. Quantitative Analysis of Enhancement Intensity and Patterns on Contrast-enhanced Spectral Mammography. Sci Rep. 2020;10(1):9807. doi: 10.1038/s41598-020-66501-z.
- Mendelson EB, Böhm-Vélez M, Berg WA, Whitman GJ, Feldman MI, Madjar H. ACR BI-RADS® Ultrasound. In: ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. Reston, VA, American College of Radiology; 2013.
- Corona-Gonzalez CB, Gonzalez-Ulloa BE, Perez-Montemayor DF, Juarez-Lopez GE. High diagnostic performance of architectural distortion enhancement on CEM for predicting malignant breast lesions. J Mex Fed Radiol Imaging. 2023;2(3):172-183. doi: 10.24875/JMEXFRI. M23000053.