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RESEARCH

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Lesion conspicuity and contrast kinetics as predictors to differentiate benign and malignant breast lesions in contrast-enhanced mammogram

Porkodi Dharmalingam[1*†] and Devimeenal Jagannathan[1†]

Abstract

Background Contrast-enhanced mammography (CEM) is a recently developed, cost-effective imaging technique that offers both anatomical and functional breast imaging. Lesion conspicuity, a newly introduced lexicon in the ACR BIRADS supplementary atlas on CEM (2022), lacks sufficient data to correlate with malignancy likelihood. The feasibility of assessing contrast kinetics with CEM remains uncertain, and there is a scarcity of available data. Our research aims to address these gaps.

Results Two radiologists, blinded to pathological reports, independently evaluated 504 CEM enhanced breast lesions with histopathology reports, out of which 176 were benign and 328 were malignant. Subjective qualitative assessment of lesion conspicuity and contrast kinetics was done for each enhancing lesion. The lesion conspicuity was classified as low, moderate, or high. The kinetic behavior of each lesion was categorized into either persistent, plateau, or washout. The distribution of lesion conspicuity among benign and malignant lesions, respectively, was as follows: for low conspicuity, 74.4% versus 25.6%; for moderate conspicuity, 30.6% versus 69.4%; and for high conspicuity, 8.4% versus 91.6%. Regarding contrast kinetics and their distribution between benign and malignant lesions, persistent kinetics was detected in 95.6% compared to 4.4%, plateau kinetics in 43.4% versus 56.6%, and washout kinetics in 3.5% versus 96.5%. Statistically significant differences in distribution between benign and malignant lesions were observed for both lexicons ($P < 0.001$). The inter-observer agreement for lesion conspicuity (kappa = 0.97) and contrast kinetics (kappa = 0.92) was deemed excellent.

Conclusion The addition of lesion conspicuity and contrast kinetics as lexicons in CEM could enhance its diagnostic accuracy.

Keywords Contrast-enhanced mammogram, Lesion conspicuity, Contrast kinetics, Breast malignancy

Background

Contrast-enhanced mammography (CEM) represents a modern approach to breast imaging, merging the advantages of digital mammography with the application of intravenous contrast agents. The intravenous contrast agents used in CEM and contrast-enhanced magnetic resonance imaging (CE-MRI) enlighten the area of neo-angiogenesis in malignant lesions, By offering functional imaging capabilities, CEM and CE-MRI

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demonstrate heightened sensitivity and specificity compared to the purely anatomical imaging provided by standard mammograms or ultrasonography (USG). But, CE-MRI has the disadvantage of high false positive rates, limited availability of dedicated breast coil, and high cost. Additionally, MRI scans are not feasible for individuals with severe claustrophobia, morbid obesity (due to table weight limitations), or those with pacemakers, metallic foreign bodies, or aneurysmal clips. In contrast, CEM presents a patient-friendly and cost-effective alternative to CE-MRI, offering quicker imaging and interpretation time [1–3].

There was no separate lexicon for CEM in the 5th edition of the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BIRADS) published in 2013, hence lexicon for CE-MRI was used [4]. In response to CEM's increasing potential as an imaging technique, ACR released a dedicated supplementary atlas for CEM in 2022 [5]. Apart from describing morphology and internal enhancement that are more or less similar to CE-MRI, the supplement on CEM has introduced a newer descriptor specific to CEM, namely lesion conspicuity**.** Lesion conspicuity refers to the intensity of enhancement in comparison with the background parenchymal enhancement (BPE). It may be categorized as low, moderate, or high. These classifications are subjective and qualitative in nature. Low conspicuity indicates enhancement comparable to or slightly exceeding BPE, whereas high conspicuity suggests enhancement significantly surpassing BPE. Moderate conspicuity falls between low and high levels of conspicuity. The ACR BIRADS atlas for CEM highlights the absence of data correlating lesion conspicuity with the likelihood of malignancy. The inclusion of conspicuity term in the lexicon is intended to facilitate future research in this area [5].

CE-MRI aids in the characterization of enhancing breast lesions through early enhancement assessment and dynamic kinetic curve analysis. Three contrast kinetics types exist: Type 1 shows persistent enhancement, often benign; Type 2 exhibits a plateau pattern, with intermediate malignancy probability; and Type 3, washout kinetics, indicates malignancy. The difference between CEM kinetics and CE-MRI kinetics is that in CE-MRI, dynamic contrast enhancement is assessed at several different points simultaneously in both breasts, and software for quantitative assessment is widely available, whereas in CEM, contrast kinetics is evaluated at a specific time interval based on the predetermined planning of affected breast [6, 7]. The objectives of the study are to evaluate the feasibility of using lesion conspicuity as a descriptor to differentiate between enhancing benign and malignant lesions and to assess the feasibility of contrast kinetics with CEM in characterizing breast lesions within our institutional workflow setup, which has limited imaging protocols.

Methods

Study population

We obtained approval from the Institutional Ethical Committee before conducting the study. Informed written consent was obtained from all participants before performing a CEM scan. We retrospectively selected patients for whom CEM was done between July 2019 and January 2022. The study was conducted at a tertiary care teaching institute, which resulted in an enrichment of malignant lesions compared to the normal population. Additionally, the analysis was performed exclusively on enhancing breast lesions, leading to a higher prevalence of malignancy within the study population.

Inclusion criteria

- Patients who underwent CEM before surgery or biopsy and had a pathologically proven diagnosis of breast lesions and had at least 1 year of imaging follow-up.
- All enhancing lesions were included irrespective of their features on digital breast tomosynthesis (DBT), as well as their enhancing morphology in CEM such as mass enhancement (451 lesions) and non-mass enhancement (53 lesions).

Exclusion criteria

- Non-enhancing lesions in CEM.
- Malignant lesions without a pathological report.
- Benign lesions with neither a pathological report nor a 1-year follow- up.
- Lesions for which a delayed image was not acquired or was unavailable.

Finally, after exclusions, 504 lesions met the inclusion criteria (Fig. 1). The final number of study participants was 492, of whom 479 had a single lesion and 12 had multiple lesions. Among those with multiple lesions, 6 had two lesions on the same side, 5 had single lesions on each breast, and 1 participant had triple lesions.

Imaging workup and interpretation

CEM was performed using the Hologic–Selenia Dimensions 3D tomosynthesis unit. Ultrasonography (USG) of both breast was done for all patients before CEM and second look USG after CEM in a few cases. Digital breast tomosynthesis (DBT) was performed on all patients for screening or diagnostic purposes, and CEM

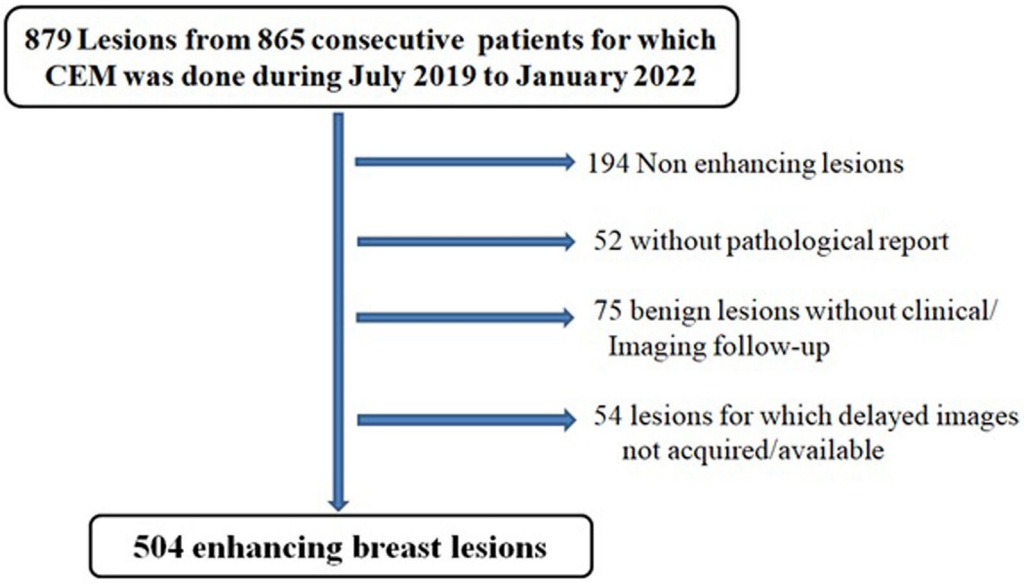

Fig. 1 Patient Selection flow chart

was performed on indicated patients. Prior to CEM, the affected side and the optimal view for lesion identification were documented using DBT and USG.

For CEM, a peripheral intravenous cannula was placed in the antecubital or forearm vein preferably with an 18-G needle. The position was verified through manual injection of a 10 ml saline bolus. Using a Medradplus single-head pressure injector, 1.5 ml/kg body weight of low osmolar, nonionic, iodinated contrast [Iohexol-350 mg of iodine/ml] was injected at a rate of 3 ml/sec with the patient in a sitting position. The patient was also monitored for contrast reaction. After 120 s, imaging commenced with a cranio-caudal (CC) view of the affected breast (2 min), followed by a CC view of the contralateral breast (3 min), and mediolateral oblique (MLO) views of the affected breast (4 min), and contralateral breast (5 min), respectively, completing within 6 min of contrast injection. In cases of enhancing lesions, a delayed CC view of the affected breast was acquired at 8 min [1, 3]. In some cases, where the lesion was more clearly identified in the mediolateral oblique (MLO) view of DBT, CEM imaging commenced with a 2-min MLO view of the affected breast, followed by the MLO view of the contralateral breast (3 min), a cranio-caudal (CC) view of the affected breast (4 min), and then a CC view of the contralateral breast (5 min). In these instances, delayed imaging was performed in the MLO view (8 min).

The CEM mode automatically collected a low-energy (LE) image at 28–32 kVp and a high-energy image at 45–49 kVp. For each low and high-energy pair, subtraction was performed automatically, generating a recombinant (RC) image that maximized the conspicuity of contrast uptake in the lesion. The low-energy and RC images were then sent to the workstation for image interpretation [1, 3, 5].

Two radiologists with more than 20 years of experience in breast imaging, blinded to the pathological report, independently analyzed the lesion conspicuity and contrast kinetics of each lesion twice at 2 different time intervals (at least 2 weeks apart) on the same monitor in the same grayscale settings, and findings were recorded. The second reading of each radiologist was taken for calculating diagnostic indices. In cases of disparity in findings between the two, a third radiologist independently analyzed and noted the findings. Two concordant findings were considered as final and were correlated with histopathological examination (HPE).

Lesion conspicuity was analyzed in comparison with BPE in 2- to 4-min images and categorized as low, moderate, or high. In the case of large heterogeneously enhancing lesion, the maximum intensity of enhancement is considered for lesion conspicuity.

Contrast kinetics was observed by analyzing images taken at early (2 min) and delayed (8 min) phases of the same view. They were classified as follows: persistent kinetics (exhibiting slow progressive enhancement in the delayed phase compared to the early image), plateau kinetics (where the intensity of contrast enhancement at the delayed image remains the same as that of initial image), or washout kinetics (showing a decrease in contrast intensity at the delayed image compared to the early image). In the case of large heterogeneously enhancing

lesions, the difference in intensity across the major part of the lesion was considered in assessing contrast kinetics (Figs. 2, 3, 4, 5, 6).

Data collection and statistical analysis

General demographic information of patients, as well as the laterality of the breast lesion, and background parenchymal enhancement were recorded. The assessment of lesion conspicuity and contrast kinetics by the radiologists were recorded. Based on the histopathological results obtained from the core biopsy or excision biopsy, the lesions were segregated into benign or malignant categories. All benign cases had imaging or clinical follow-up for at least 1 year. All data were entered in an Excel sheet and presented as frequency and percentage. Categorical variables were compared using the Pearson chi-square test. Kappa statistics was used to assess inter-observer variability. Cross tabs were created to find the sensitivity and specificity. MedCalc's Diagnostic test evaluation calculator was used to estimate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for lesion conspicuity and contrast kinetics. Significance was defined by P values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc.,Chicago, IL).

Results

The general features of the study population and histopathological distribution of the lesions are listed in Table 1.

Distribution of each level of lesion conspicuity and 3 types of contrast kinetics among malignant and benign

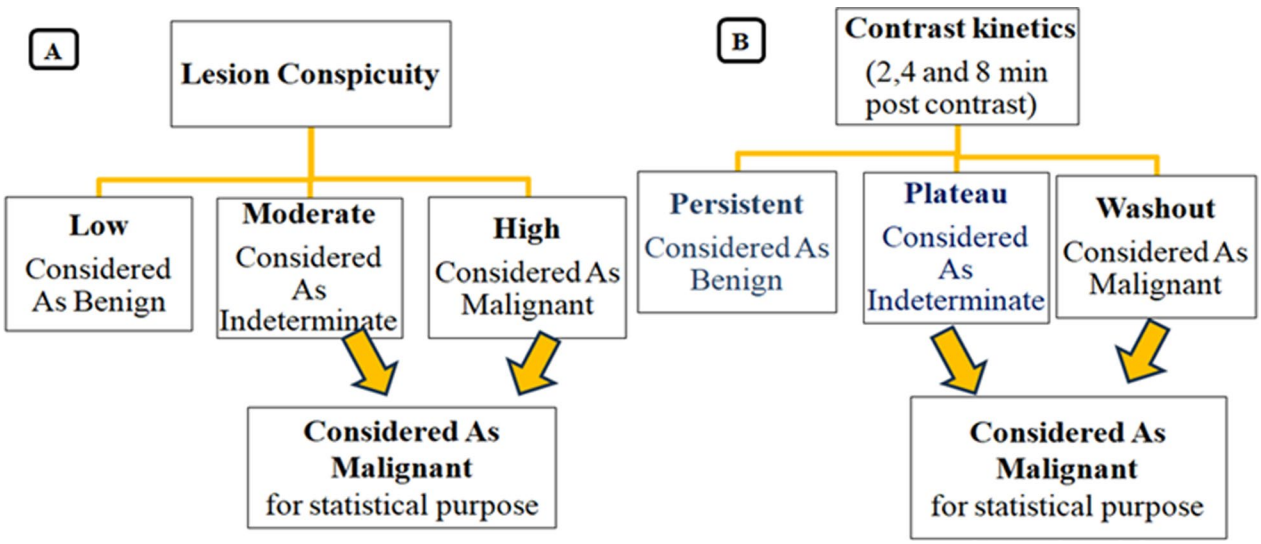

Fig. 2 Interpretation of CEM features: **A** lesion conspicuity; **B** contrast kinetics

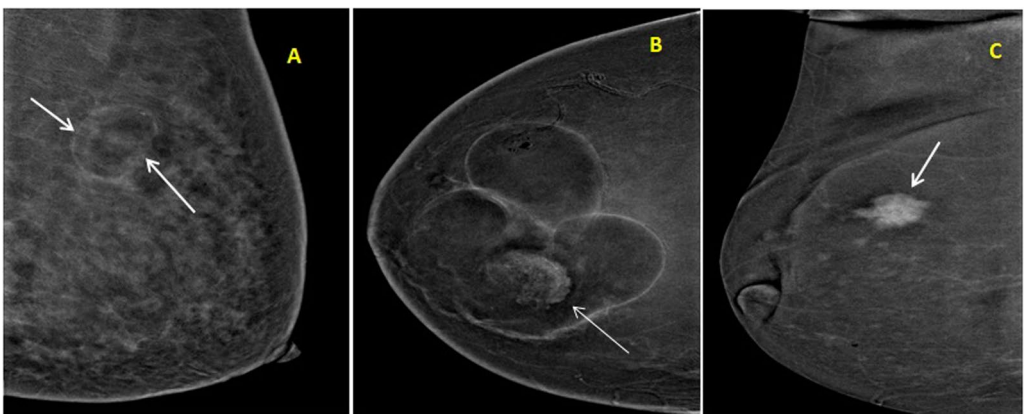

Fig. 3 Lesion Conspicuity: **A** low (HPE report:low-grade mucinous carcinoma); **B** moderate (HPE report:encapsulated papillary carcinoma without invasion); **C** high (HPE report: invasive ductal carcinoma-no special type)

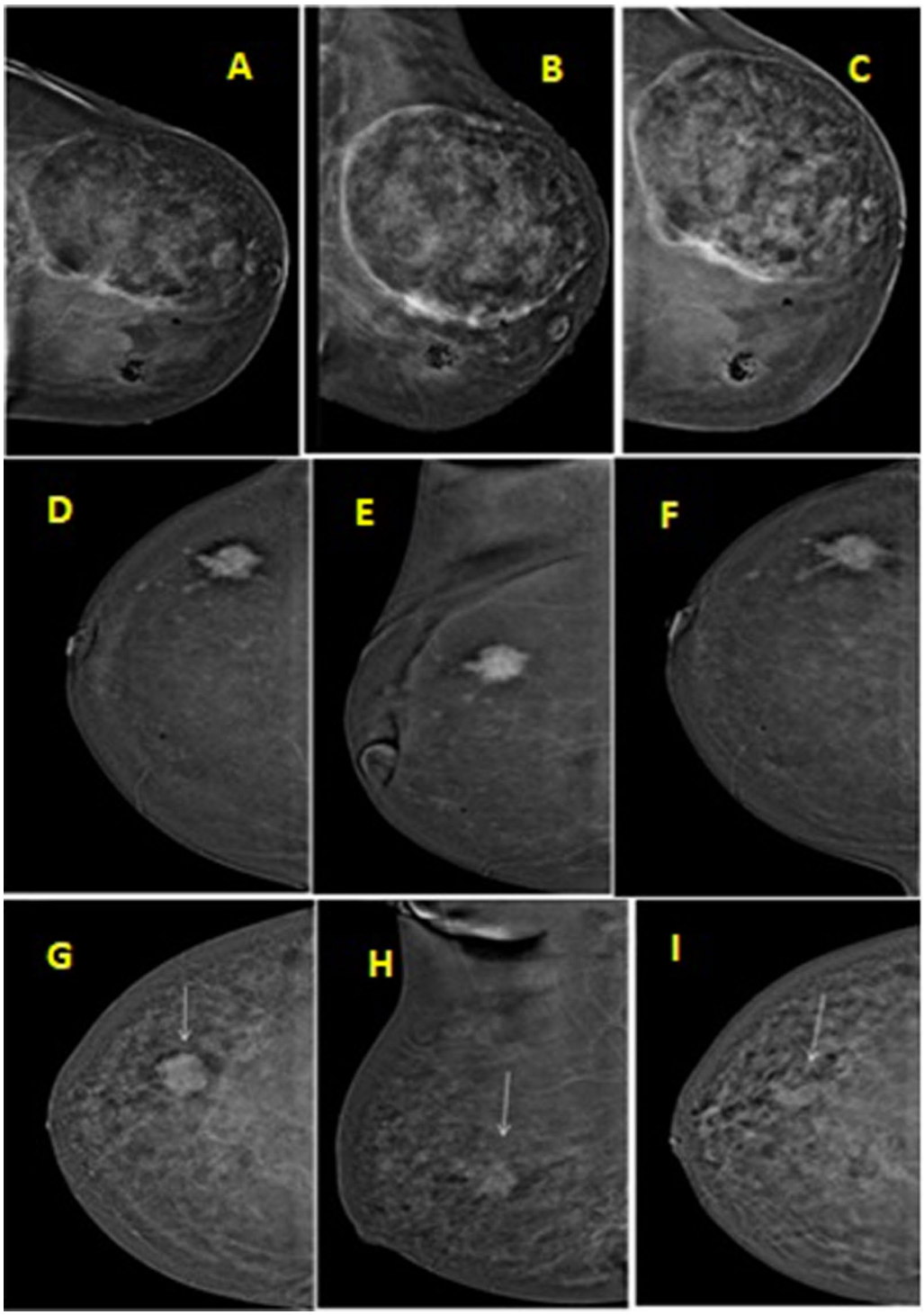

Fig. 4 **A**–**C** Persistent contrast kinetics-post-contrast images at **A** 2-min CC view; **B** 4-min MLO view; **C** 8-min CC view. The intensity of enhancement of the lesion at 8-min image is more than the intensity at 2 min. (HPE report: benign phyllodes). **D**–**F** plateau contrast kinetics-post-contrast images at **D** 2-min CC view; **E** 4-min MLO view; **F** 8-min CC view. The intensity of enhancement of the lesion at 8-min image is same as that of the intensity at 2 min. (HPE report: invasive ductal carcinoma-no special type). **G**–**I** Washout contrast kinetics-post-contrast images at **G** 2-min CC view; **H** 4-min MLO view; **I** 8-min CC view. The intensity of enhancement of the lesion at 8-min image is less than that of the intensity at 2 min. (HPE report: invasive ductal carcinoma-not otherwise specified)

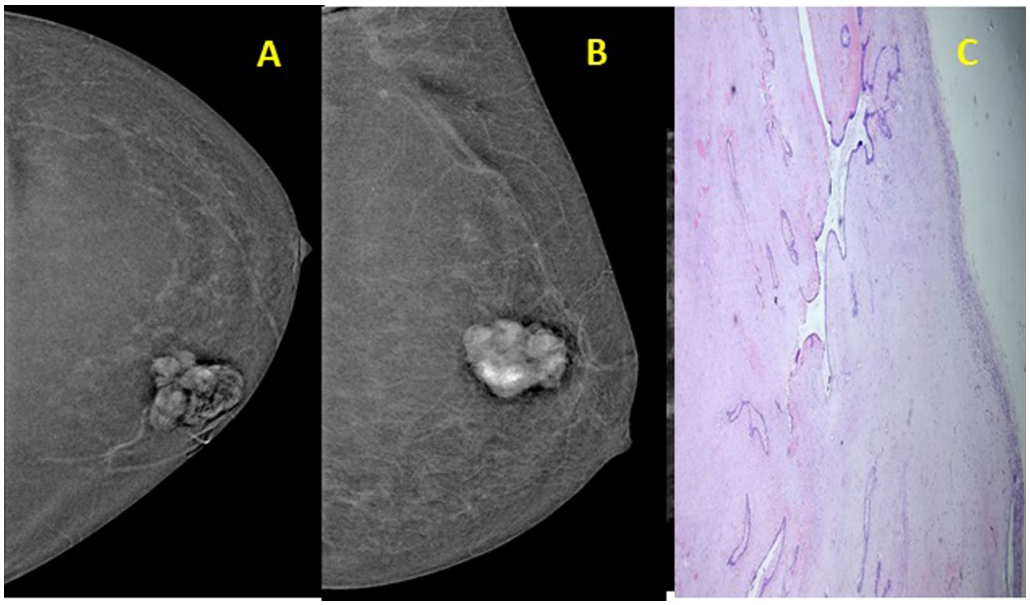

Fig. 5 48y/F with complaints of LB lump for 2 months. **A** Post-contrast 2-min CC view shows heterogeneously enhancing mass lesion with non-enhancing septae and macrolobular margins with *low conspicuity* lesion; **B** 4-min MLO view shows progressive increase in intensity of enhancement—*persistent kinetics*; **C** HPE: fibroadenoma

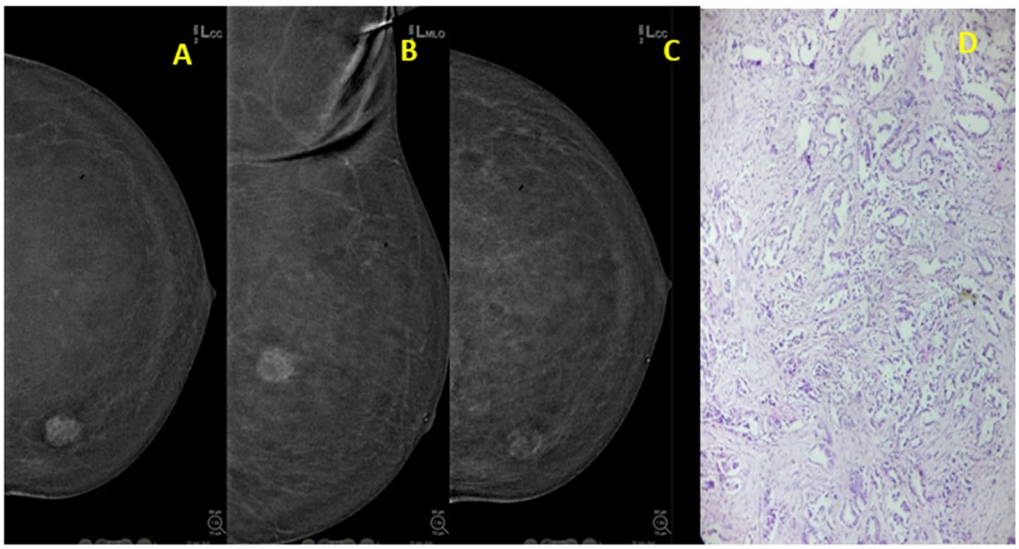

Fig. 6 53y/F with complaints of painless lump in LB for 15 days. **A** Post-contrast 2-min CC view shows irregular heterogeneously enhancing mass lesion with with *moderate conspicuity*; **B** Post-contrast 4-min MLO view; **C** Post-contrast 8-min CC view shows decrease in intensity of enhancement—*washout kinetics*; **C** HPE: IDC-NOS, grade 2

lesions with respect to the two observers are listed in Table 2.

Inter-observer agreement for subjective assessment of lesion conspicuity between the two readers was a near-perfect agreement with a kappa value of 0.969. The *p*-value for lesion conspicuity among benign and malignant lesions was < 0.0001 for both observers and was found to be statistically significant.

Table 3 illustrates the correlation of lesion conspicuity and contrast kinetics (as observed cumulatively) with respect to HPE.

Table 1 The general features of the study population and histopathological distribution of the lesions

1. Age	Years
Mean	50.5
Range	20 to 93
2. Lesion laterality	Number (%)
Left Breast	274(54.4)
Right Breast	230(45.6)
3. Mean tumor size	Centimeters
Malignant	2.37 ± 1.32
Benign	1.35 ±.37
4. Background Parenchymal Enhancement	Number (%)
Minimal	287(57.2)
Mild	109(21.7)
Moderate	84(16.7)
Marked	22(4.4)
5. Pathology Report	Number (%)
a. Malignant Lesions	328 (65.1)
Invasive Breast carcinoma–NST	304
Papillary carcinoma	5
Mucinous carcinoma	3
Malignant phyllodes tumors	2
Lobular carcinoma	1
Metastatic carcinoma	1
Ductal carcinoma in situ	10
Poorly differentiated malignancy	2
b. Benign Lesions	176 (34.9)
Fibroadenoma	61
Cyst (simple/complicated)	36
Benign phyllodes tumor	11
Intramammary lymph node	2
Fibrocystic change without atypia	29
Inflammatory/granulomatous lesions	20
Fibroadenolipoma	3
Postoperative seroma	2
Benign papilloma	11
Benign adenomyoepithelioma	1

In our study, the lesion conspicuity demonstrates a sensitivity of 89.6%, specificity of 57.4%, positive predictive value (PPV) of 79.7%, negative predictive value (NPV) of 74.8%, diagnostic accuracy of 78.4%, a positive likelihood ratio of > 1 (2.1) and a negative likelihood ratio of < 1 (0.18).

Inter-observer agreement for subjective assessment of contrast kinetics between the two observers showed near-perfect agreement, with a kappa value of 0.924. The p-value for contrast kinetics among benign and malignant lesions was < 0.0001 for both observers and was found to be statistically significant.

In this study, the contrast kinetics demonstrates a sensitivity of 98.2%, specificity of 74.4%, positive predictive value (PPV) of 87.7%, negative predictive value (NPV of 95.6%, diagnostic accuracy of 89.9%, a positive likelihood ratio of > 1 (3.8) and a negative likelihood ratio of < 1 (0.02) (Fig. 7).

In our study, we observed that low conspicuity malignant lesions (total number, $N=35$) were mainly invasive ductal carcinoma (63%), Ductal Carcinoma in situ (DCIS) (29%), mucinous carcinoma (5.7%), and one case of lobular carcinoma. Among the high conspicuity benign lesions ($N=14$), inflammatory lesions (57%), fibroadenomas (28.6%), and benign papillomas (14.3%) were the most common. We noted persistent kinetics in 6 malignant lesions, primarily in DCIS (66.7%), followed by mucinous carcinoma (33.3%), lobular carcinoma (16.7%), and one case of invasive ductal carcinoma grade 1. Washout kinetics were observed in 10 benign lesions, predominantly in inflammatory lesions (80%), followed by one case of benign phyllodes and a benign intraductal papilloma.

Discussion

CEM, like CE-MRI, offers functional imaging due to the usage of IV contrast agents. It has been proven to be a cost-effective, patient-friendly, and newer problem-solving tool in the breast imaging armamentarium [2]. Many studies have shown that the sensitivity of CEM is equivalent to that of CE-MRI and specificity more than that of CE-MRI. CEM also has the advantage of picking up micro-calcifications in the low-energy image and thereby diagnosis of DCIS and early malignancies can be done [2]. Assessment of morphology of enhancing lesions in RC images in correlation with low-energy images helps in the characterization of breast lesions. The amount of perfusion and capillary permeability in malignant lesions differs from that of benign lesions [6]. Hence, assessment of intensity of enhancement of lesions at early phase and delayed kinetics will also aid in the characterization of breast lesions both in CE-MRI and CEM [8]. Compared to CE-MRI, CEM has certain limitations: sequential imaging involves radiation; simultaneous assessment of both breasts is not possible; software for quantitative assessment is not widely available in CEM with most of the vendors.

Deng C-Y et al. analyzed quantitative enhancement at 2- to 3-min and 3- to 6-min images in CEM and concluded that malignancies have distinctive stronger enhancement and depressed relative enhancement compared to benign lesions [8]. The qualitative method assessment employed in our study yielded diagnostic accuracy comparable to that of quantitative assessment. (82.3% compared to 78.4% in our study). In their study,

Table 2 Distribution of each level of lesion conspicuity and 3 types of contrast kinetics among malignant and benign lesions with respect to the two observers

CEM feature		Histopathological examination (HPE)				*P* value
		Malignant		Benign		
		Count	Row N %	Count	Row N %	
Lesion conspicuity						
Observer 1	Low(Benign)	34	25.6	99	74.4	< 0.0001
	Moderate(Intermediate)	143	69.4	63	30.6	
	High(Malignant)	151	91.5	14	8.5	
Observer 2	Low(Benign)	35	25.2	101	74.8	< 0.0001
	Moderate(Intermediate)	138	69.3	61	30.7	
	High(Malignant)	155	91.7	14	8.3	
Contrast kinetics						
Observer 1	Persistent(Benign)	6	4.4	130	95.6%	< 0.0001
	Plateau(Intermediate)	47	56.6	36	43.4	
	Washout(Malignant)	275	96.5	10	3.5	
Observer 2	Persistent(Benign)	7	5.3	124	94.7	< 0.0001
	Plateau(Intermediate)	49	54.4	41	45.6	
	Washout(Malignant)	272	96.1	11	3.9	

Table 3 Illustrates the correlation of lesion conspicuity and contrast kinetics (as observed cumulatively) with respect to HPE

CEM feature		Histopathology		Total
		Malignant	Benign	
Lesion conspicuity	Malignant	294 (TP)	75 (FP)	369
	Benign	34 (FN)	101 (TN)	135
	Total	328	176	504
Contrast kinetics	Malignant	322 (TP)	45 (FP)	367
	Benign	6 (FN)	131 (TN)	137
	Total	328	176	504

TP-True Positive; FP-False Positive; FN- False Negative; TN-true Negative

they compared contrast kinetics in CC and MLO views, which could potentially influence the enhancement results because of differences in the shape and density of the lesion in different views [8]. In our study, we ensured that the 2-min and 8-min images were captured from the same view to minimize the riskof misinterpretation.

Rudnicki et al. analyzed the qualitative assessment of Signal intensity of 107 breast lesions in CEM. They correlated it with MRI kinetics and found it to be statistically significant [9]. The proportionate distribution of weak, moderate, and strong enhancement among benign and

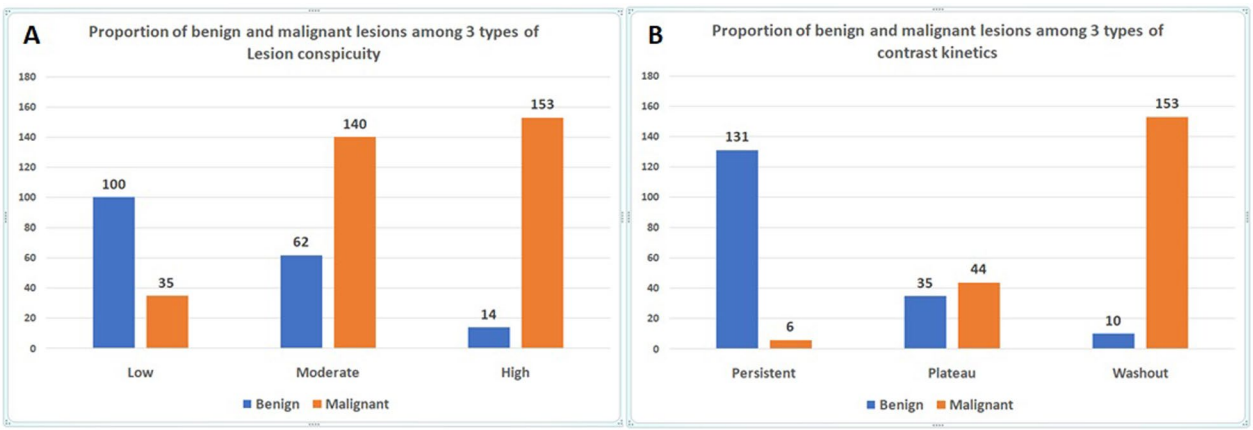

Fig. 7 Bar chart showing proportion of CEM features among benign and malignant lesions. **A** Lesion conspicuity. **B** Contrast kinetics

malignant lesions in their study aligns closely with our own findings.

Yongbin and colleagues conducted a quantitative assessment of the enhancement of 299 lesions in CEM, revealing that malignant lesions exhibited a higher intensity of enhancement compared to benign ones [10]. In our study, we found that 91.6% of lesions with high conspicuity were malignant, while only 8.4% of benign lesions showed similar high conspicuity, aligning with the results of Yongbin et al.

Huang J-S et al. conducted a qualitative assessment of contrast kinetics in CEM for the affected side using a single MLO view at 2, 3, 4, 7, and 10 min, involving 148 lesions. They discovered that a washout kinetic pattern was significantly linked to malignant lesions within the 2–4-min and 2–10-min frames [11]. Our study, which employed a lower radiation dose, also demonstrated that 96.5% of cases with washout kinetics were associated with malignant lesions.

Weimin Xu et al. analyzed the quantitative enhancement of 111 lesions in 3 phases of CEM and concluded that the addition of quantitative analysis of enhancement between two consecutive phases to the morphological assessment of enhancement has great potential in the characterization of breast lesions [12].

Luca Nicosia and colleagues conducted an analysis on 381 lesions in contrast-enhanced mammography (CEM), revealing that lesion conspicuity (LC) exhibited commendable efficacy in predicting malignancy [13]. Their study yielded a sensitivity of 91.9% (in contrast to 89.6% in our investigation) and a specificity of 67.2% (compared to 57.4% inour study). They also noted a notable association between LC and the receptor status of malignant lesions. However, in our study, we did not explore this correlation or investigate receptor status.

Na Li et al. investigated the correlation between various CEM features and different molecular types of breast cancer in 313 patients and found that no correlation existed between lesion conspicuity and molecular type of breast cancer [14].

Prema Subramanian et al. compared the kinetic pattern of 123 lesions in qualitative CEM with quantitative CE-MRI and concluded that the addition of a delayed post-contrast image at 8 min for CEM kinetic analysis showed almost perfect agreement with quantitative CE-MRI kinetics [15].

Compared to the above studies, our study is a larger study with more reliability because of the reduced margin of error associated with a larger sample size. Our study involves a limited imaging sequence with less radiation protocol to analyze contrast kinetics than the above studies. Since the average glandular dose with CC view is less than that of MLO view [16], we prefer to acquire a 2-min CC view, 4-min MLO view, and an 8-min delayed CC view of diseased breast for evaluating contrast kinetics, except in two instances where lesions were located posteriorly. In these cases, the visibility of the lesion was clearer on the MLO view compared to the CC view in the standard mammogram.

Studies indicate that CEM radiomic features can effectively distinguish malignant lesions regardless of background parenchymal enhancement. This method shows promise for the noninvasive differentiation of tumors by invasiveness, hormone receptor status, and tumor grade [17–19]. Dominique and colleagues demonstrated that deep learning analysis on CESM could identify histoprognostic markers, such as estrogen receptor and triple-negative receptor status, providing rapid prognostic and predictive information [20]. Similarly, the future application of radiomics and deep learning analysis in CEM could aid in the analysis of lesion conspicuity and contrast kinetics.

Our study has certain limitations: quantitative assessment of the intensity of enhancement in CEM would be preferable for evaluating lesion conspicuity and contrast kinetics. However, as of now, software for quantitative enhancement assessment in CEM is not widely available. Consequently, our study relied on qualitative assessment, potentially introducing subjective bias and limiting the direct application of the study's findings. To mitigate this limitation to some extent, two observers independently assessed the data at different time intervals in our study. The second limitation pertains to the potential impact of patient-related factors and differences among technologists on the acquisition time and protocol. However, we endeavored to alleviate this limitation by diligently following our institutional workflow protocol. Furthermore, our machine automatically adapts the compression force according to the breast thickness observed in each view. A third limitation is the inability to analyze the combined performance of lesion conspicuity and contrast kinetics, as these lexicons serve as independent predictors. Some lesions with low conspicuity exhibited washout kinetics, while those with high conspicuity demonstrated persistent kinetics, precluding the assessment of combined performance.

Conclusions

The sensitivity in detecting malignant lesions using both contrast kinetics and lesion conspicuity as independent predictors in this study is notably high. Therefore, the addition of these two lexicons to routine morphological assessment could enhance the diagnostic accuracy of CEM, particularly for cases with equivocal findings in morphological assessment. Additionally, this study protocol offers

the advantage of utilizing limited imaging sequences with reduced radiation dose to evaluate contrast kinetics.

Abbreviations

CEM	Contrast-enhanced mammography
ACR BIRADS	American college of radiology breast imaging reporting and data system
LC	Lesion conspicuity
CK	Contrast kinetics
CC view	Cranio-caudal view
MLO view	Medio-lateral oblique view
DBT	Digital breast tomosynthesis
USG	Ultrasonography
CEMRI	Contrast-enhanced magnetic resonance imaging
BPE	Background parenchymal enhancement
HPE	Histopathological examination
PPV	Positive predictive value
NPV	Negative predictive value

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Author contributions
PD has contributed in designing the study, acquisition and interpretation of the data and drafting. DJ has contributed in interpretation of the image and acquisition of the data. Both authors, PD and DJ of this paper, have read and approved the final version submitted. The contents of this manuscript have not been copyrighted or published previously. The contents of this manuscript are not now under consideration for publication elsewhere. The contents of this manuscript will not be copyrighted, submitted or published elsewhere, while acceptance by the Journal is under consideration. There are no directly related manuscripts or abstracts, published or unpublished, by any authors of this paper. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated or analyzed during the study are not publically available to maintain the anonymity, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was taken from the Government Kilpauk Medical College institutional ethics committee, (ECR/1385/Inst/TN/2020, IEC protocol number 896/2023). As ours is a retrospective observational study, informed consent was waived off by the review board of Kilpauk Medical College.

Consent for publication
Not applicable as we have not used any personally identifiable data including biomedical, clinical and biometric data.

Competing interests
The authors declare that they have no competing interests. We herewith declare that we have no actual, potential or perceived conflict of interest in relation to the subject matter or material discussed in this article being submitted.

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