Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH

Open Access

Diagnostic accuracy of subjective kinetic assessment of masses in contrast-enhanced mammography in comparison with contrast-enhanced magnetic resonance imaging

Prema Subramaniam[1], Rupa Renganathan[1*], P. Suganya[1] and Adrija Mandal[1]

Abstract

Background Contrast-enhanced MRI (CE MRI) of the breast is currently the most sensitive imaging technique for detecting invasive breast cancer, and it provides both morphologic and functional information through kinetics for characterizing breast masses. Contrast-enhanced mammography (CEM) uses the same principle of neo-angiogenesis to detect early cancers similar to MRI with comparable diagnostic performance. However, there is an important limitation in CEM in characterizing the breast lesions because of the non-availability of kinetic information. To the best of our knowledge, very few studies have assessed the CEM kinetics. In this study, we have evaluated the accuracy of subjective assessment of contrast kinetics in CEM and compared it with the subjective and quantitative kinetic assessment in CE MRI. If the performance of CEM is comparable to MRI, it may add an additional dimension to CEM in characterizing the breast masses in addition to detection.

Results Kinetic information of 123 lesions in 90 patients was analyzed in CEM and MRI. Of these, 26 (21.1%) were benign, 4 (3.3%) were high risk lesions, and 93 (75.6%) were malignant breast lesions. Comparison of subjective and quantitative assessment in CE MRI had almost perfect agreement with a kappa value of 0.816, and both were used as reference standards for comparing CEM kinetics. Comparison of subjective assessment of kinetic patterns in CEM using only CC and MLO views showed moderate agreement with both quantitative (kappa – 0.483) and subjective (0.547) CE MRI kinetics. When the delayed image obtained at 8 min was included for kinetic analysis, CEM kinetics showed substantial to almost perfect agreement with quantitative (kappa – 0.673) and subjective (kappa – 0.855) CE MRI kinetics, respectively.

Conclusion We hope that this study results would encourage the breast radiologist to assess the kinetic information from CEM and use CEM as a single, simple and cost-effective imaging modality in detecting and characterizing breast masses.

Keywords Contrast-enhanced mammography, Kinetics of breast masses, Magnetic resonance imaging, Characterization of breast masses

*Correspondence:
Rupa Renganathan
drrrupa@gmail.com; drrupa@kmchhospitals.com
Full list of author information is available at the end of the article

Background

CE MRI of the breast is currently the most sensitive imaging technique for detecting invasive breast cancer [1]. MRI is also used to characterize the breast lesions as it provides both morphologic and functional information through kinetics [2]. Contrast-enhanced mammography (CEM) uses the same principle of neoangiogenesis to detect early cancers similar to MRI. Recent studies show that CEM has comparable diagnostic performance compared to MRI [3–5]. However, there is an important limitation in CEM in characterizing the breast lesions because of the non-availability of kinetic information. There is no lexicon to describe kinetic properties of enhancing abnormalities in CEM in American College Radiology Breast Imaging Reporting and Data System (ACR-BIRADS) [2]. To the best of our knowledge, very few studies have assessed the CEM kinetics with histopathological correlation [6–10]. There was no study in the literature which had compared the kinetics of CEM and CE MRI. In this study, we have evaluated the accuracy of subjective assessment of contrast kinetics in CEM and compared it with the subjective and quantitative kinetic assessment in CE MRI. If the performance of CEM is comparable to MRI, it may add an additional dimension to CEM in characterizing the breast masses in addition to detection.

Methods

This is a retrospective observational study approved by the institutional review board.

Patients

This study included patients who are 18 years or older with enhancing breast masses and have undergone CEM, CEMRI and biopsy or excision from April 2021 to December 2022 at our institution. We excluded patients with masses which were not visible on CEM, CE MRI or both, when CEM or MRI data were suboptimal and when lesions did not have histopathological confirmation.

During the study period, there were a total of 174 patients with 217 breast masses who have undergone CEM and MRI at our institution. Out of 217 masses, 37 were excluded because they were not biopsied as they were BIRADS CATEGORY 3 masses. Additional 29 masses were excluded because histopathology report was not available; 28 masses were excluded from the study because they were not clearly visible/non-enhancing or kinetic data are not available in one of the modalities. Final study group included 123 lesions in 90 patients. Figure 1 shows the patient flow in our study.

CEM

CEM examinations were performed using the Hologic 3 Dimensions mammography system. All patients with palpable breast masses had a preliminary Ultrasound of the lump of clinical concern and proceeded with CEM directly. The patient with screen detected non-palpable abnormality had CEM following noncontrast mammography.

After obtaining consent, injection of 1.5 ml/kg of nonionic iodinated contrast was injected through an intravenous route. After 2 min of the start of the contrast injection, low energy and high energy images of abnormal breast in CC view (2–3 min), normal breast in CC view (3–4 min), followed by the MLO views of both breasts (4–5 min and 5–6 min) are taken in that order within the maximum time limit of 8 min from the time of start of contrast injection. One additional delayed image is taken at 8 min after the start of injection of contrast in CC or MLO view in which the lesion is best seen. Recombined images are subtraction images of low and high energy images that contain contrast information. Low energy images are used as non-contrast mammograms when direct CEM was performed.

Reader 1 (RR) with 15 years of experience in breast imaging was blinded to the MRI findings, and histopathology evaluated the CEM findings. The amount of background parenchymal enhancement (BPE), conspicuity of the lesion, relative change in density of the lesion from the first view of the breast to the second (CC to MLO) as well as from first CC to delayed image (obtained after 8 min) are noted down.

Relative change in density of the lesion is assessed subjectively comparing early and late images (CC view and MLO view/CC view and delayed image) and categorized as follows:

Type 1: Progressive increase in density of the lesion in delayed view.
Type 2: No changes in density.
Type 3: Relative decrease in density in delayed view.

MRI

MRI breast is performed on a 3T scanner (Siemens SKYRA). Protocol includes: T1 weighted (TIW) axial, inversion recovery (IR) axial, diffusion-weighted imaging (DWI)), postcontrast dynamic T1W imaging with subtraction and maximum intensity projection (MIP) images, delayed T1 fat sat axial images. Dynamic information is derived subjectively from postcontrast dynamic subtraction MIP images and quantitatively

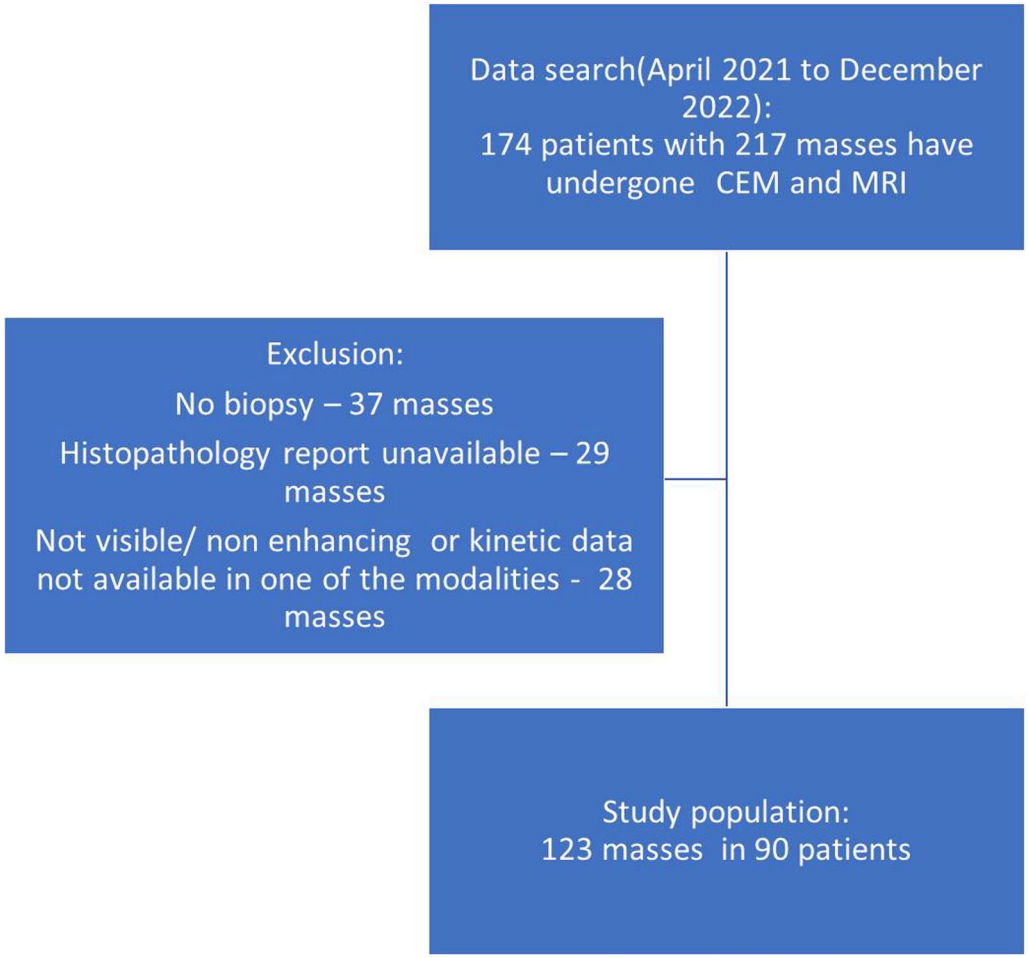

Fig. 1 Patient flow in our study

by plotting the time intensity curves in postcontrast dynamic subtraction images.

Reader 2 (PS) with 6 years of experience in breast imaging was blinded to CEM findings and histopathology evaluated the MRI findings.

The findings that were evaluated are BPE, subjective and quantitative assessment of kinetics. Subjective assessment is carried out from postcontrast subtraction MIP images derived automatically by the system from the dynamic contrast sequences and categorization as:

Type 1: Persistent—progressive increase in intensity,
Type 2: Plateau—no change in signal intensity,
Type 3: Washout—relative decrease in signal intensity.

Quantitative kinetic assessment from time intensity curves is categorized as described in the ACR BIRADS MRI lexicon.

Type 1 (Persistent: > 10% increase in signal intensity after 2 min).
Type 2 (Plateau: < 10% change in signal intensity after 2 min).
Type 3 (Washout: > 10% decrease in intensity after 2 min).

Statistical analysis

The data were entered in excel and were analyzed using SPSS 27 software. Categorical variables were presented as frequency and percentages. Association between the categorical variables was measured using Chi-square test. Kappa statistics was used to measure the association between CEM and MR kinetics, and $P < 0.05$ was considered as statistically significant.

Table 1 Baseline characteristics of the study population

Parameter	Value
Age (years)	
Mean	50.88
Range	25–72
Background parenchymal enhancement—MRI	
Minimal	52 (42.3%)
Mild	45 (36.6%)
Moderate	24 (19.5%)
Marked	2 (1.6%)
Background parenchymal enhancement—CEM	
Minimal	45 (36.6%)
Mild	41 (33.3%)
Moderate	26 (21.1%)
Marked	11 (8.9%)
Conspicuity—CEM	
Low	19 (15.4%)
Moderate	52 (42.3%)
High	52 (42.3%)
Histopathology	
Benign	26 (21.1%)
High risk lesion	4 (3.3%)
Malignancy	93 (75.6%)

Results

Kinetic information of 123 lesions in 90 patients was analyzed in CEM and MRI. Baseline characteristics of the study population are listed in Table 1.

Comparison of subjective assessment using MIP images and quantitative assessment using kinetic curves in MRI had almost perfect agreement with a kappa value of 0.816, and both were used as reference standards for comparing CEM kinetics.

Comparison of subjective assessment of kinetic patterns in CEM using only CC and MLO views showed moderate agreement with both quantitative (kappa − 0.483) and subjective (0.547) MRI kinetics. When the delayed image obtained at 8 min was included for kinetic analysis, CEM kinetics showed substantial to almost perfect agreement with quantitative (kappa − 0.673) and subjective (kappa − 0.855) MRI kinetics, respectively (Figs. 2, 3 and 4).

Table 2 demonstrates the correlation between kinetic patterns in CEM with histopathology. Chi-square analysis showed that CEM kinetics using 8-min delayed images had significant correlation with histopathology ($P < 0.05$).

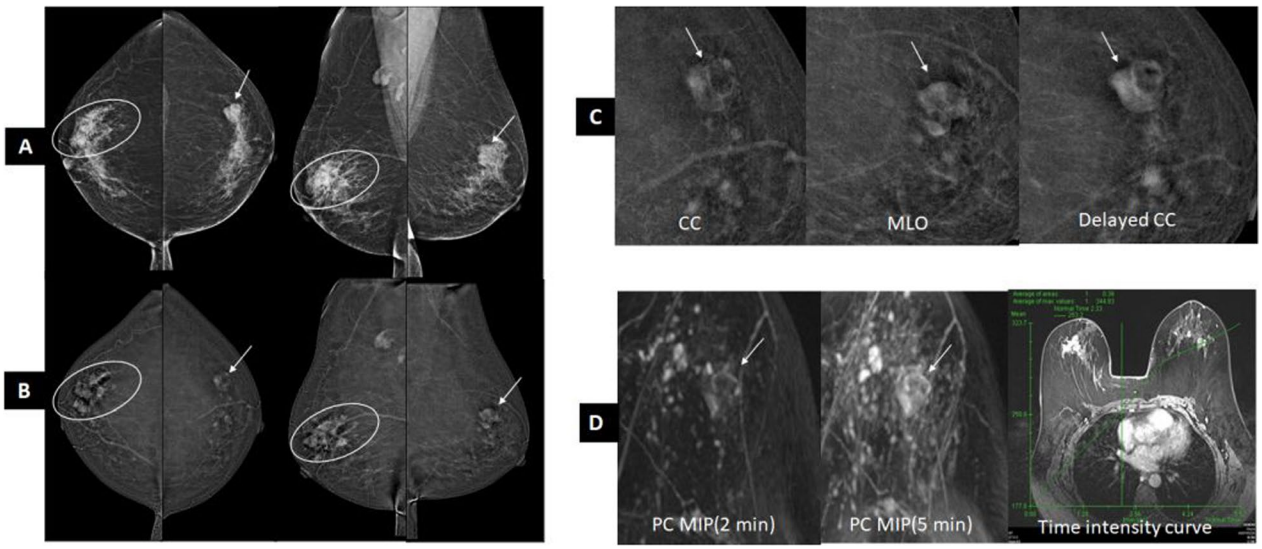

Fig. 2 Images of a 55-year-old lady with a right breast lump: **A** low energy images of both breasts in craniocaudal (CC) and mediolateral oblique (MLO) projections show an irregular mass with indistinct margins in outer central quadrant of right breast (marked by white circles) and an irregular mass with circumscribed margins in left breast (marked by arrows). **B** Postcontrast recombined images of both breasts show heterogeneous enhancement of the masses in both breasts. Right breast **C** postcontrast recombined images of left breast lesion (marked by arrows) show progressive increase in density from CC (2 min) to MLO (4 min) to delayed (8 min) views suggestive of type I kinetics. **D** Postcontrast subtraction maximum intensity projection (MIP) MR images at 2 min and 5 min show progressive increase in density of mass (marked by white arrows) at 5 min consistent with type I kinetics. Time intensity curve confirms the same. Biopsy from the right breast mass was invasive ductal carcinoma, and the left breast mass was fibroadenoma

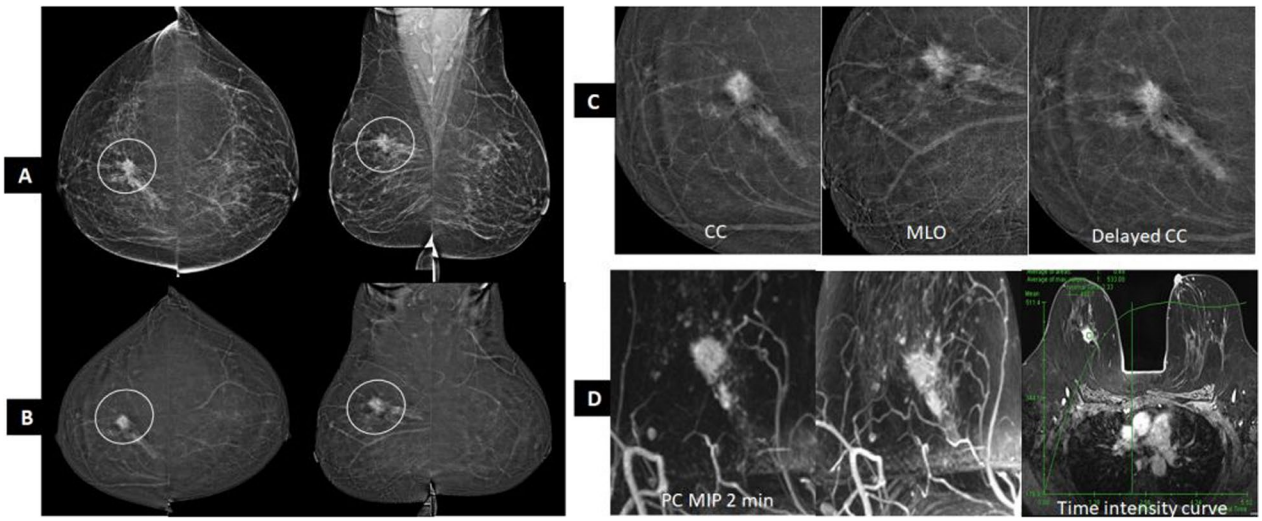

Fig. 3 Images of a 55-year-old lady with a right breast lump. **A** Low energy images of both breasts in craniocaudal (CC) and mediolateral oblique (MLO) projections show an irregular mass with spiculated margins in the upper central quadrant of the right breast (marked by white circle). **B** Postcontrast recombined images of both breasts show heterogeneous enhancement of the right breast mass with high conspicuity. Also note the heterogeneous nonmass enhancement in linear distribution posteromedial to the mass. **C** Postcontrast recombined images of the mass show high density of the lesion in CC image at 2 min with no significant change in density in MLO (4 min) and delayed (8 min) views suggestive of type 2 kinetics. **D** Postcontrast subtraction maximum intensity projection (MIP) MR images at 2 min and at 5 min show early intense enhancement with no significant change in signal intensity at 5 min—consistent with type 2 kinetics. Time intensity curve confirms the same. Biopsy was invasive lobular carcinoma

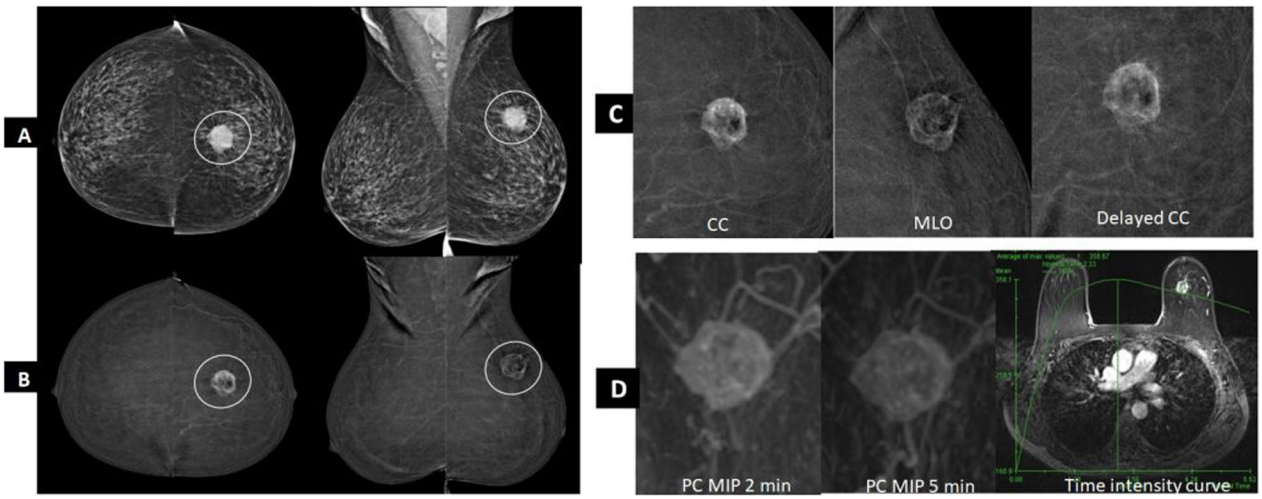

Fig. 4 Images of a 54-year-old lady with a left breast lump. **A** Low energy images of both breasts in craniocaudal (CC) and mediolateral oblique (MLO) projections show a round mass with circumscribed margins in the upper central quadrant of the left breast (marked by white circle). **B** Postcontrast recombined images of both breasts show heterogeneous enhancement of the right breast mass with high conspicuity. **C** Postcontrast recombined images of the mass show high density of the lesion in CC image at 2 min with reduction in density in MLO (4 min) and delayed (8 min) views suggestive of type 3 kinetics. **D** Postcontrast subtraction maximum intensity projection (MIP) MR images at 2 min and at 5 min show early intense enhancement with washout at 5 min—consistent with type 3 (washout) kinetics. Time intensity curve confirms the same. Biopsy was invasive ductal carcinoma

Discussion

CE MRI breast is the most sensitive imaging modality in the detection and characterization of masses because it uses both morphological characteristics and kinetic information from dynamic postcontrast images. Contrast in the MR imaging adds the kinetics information which is unavailable in mammography or ultrasound there by increasing the specificity in differentiating benign and malignant breast lesions [2, 11, 12].

Table 2 Correlation between the type of kinetics using delayed images in CEM with histopathology

Type of kinetics	Benign lesions—30 *n* (%)	Malignant lesions—93 *n* (%)
Type 1	15 (50)	2 (2)
Type 2	12 (40)	21 (23)
Type 3	3 (10)	70 (75)

Kinetic information is quantitatively obtained in MRI from dynamic postcontrast images by plotting the time signal intensity curve. Majority of malignant masses enhance early and intensely within the first 2 min and show rapid washout within 5 min because of leaky capillaries. This is contrary to the majority of benign masses which enhance slowly with progressive increase in signal intensity over time between 2 and 5 min [13, 14]. This difference in the enhancement pattern helps in characterizing the breast masses on MRI.

There are several limitations with CEM in assessing the kinetics. Firstly, CEM involves radiation and so multiple acquisitions would mean incremental increase in radiation. Secondly, simultaneous bilateral imaging is not possible as in MRI. Also, quantitative assessment of kinetics is not currently available in most of the vendors of CEM.

In the past, there were only very few studies that attempted to study CEM kinetics. There have been two studies in the past evaluating CEM enhancement patterns using qualitative assessment.

A study by Rudnicki et al. compared the qualitative assessment of density of masses in CEM with MRI kinetics. They studied the correlation of subjective assessment of signal intensity on CEM with MRI kinetics and found it to be significant [6]. The limitation was that they did not assess the change in density with time in different views and delayed views, i.e., kinetics on CEM.

Qualitative change in density of the masses with time was assessed by Huang J-S et al., who analyzed the subjective change in enhancement at particular time intervals and concluded that kinetic patterns aid in differentiation of benign and malignant breast lesions on CEM [7]. This study had two major limitations; in this study, multiple views of a single breast were acquired in a single projection leading to high radiation dose to one breast and the contralateral breast was not imaged.

There were three studies on the quantitative assessment of enhancement in CEM, and this facility is available only with few vendors. Among the three, two studies in 2018 and 2020 by Deng C-Y et al. and Lv et al., respectively, analyzed the quantitative enhancement (gray scale value) of benign and malignant lesions in CEM and concluded that malignant lesions have a greater degree of enhancement and the difference in enhancement between benign and malignant lesions is statistically significant [8, 9]. Both these studies did not analyze the progressive change in density over time and hence not the kinetic information.

2021 study by Xu et al. analyzed the quantitative enhancement of benign and malignant lesions in CC and MLO views and an additional delayed MLO view and found that significant difference in enhancement pattern in first two consecutive views between benign and malignant lesions and addition of delayed phase added only limited performance improvement [10]. However, this study did not compare with the established and standardized kinetic information from MR imaging.

In our study, we have tried to overcome the above mentioned limitations of CEM in assessing the kinetics in different studies.

In our study, we obtained three views (CC, MLO and delayed CC/MLO views) of the breast with clinical concern instead of obtaining multiple acquisitions. Further, we performed CEM without an additional prior digital mammogram acquisition for all women with a suspicious abnormality by performing a targeted ultrasound.

The kinetic information is obtained from the three views of the same breast which were acquired at 2, 4 and 8 min of CC, MLO and delayed CC/MLO views, respectively. By using this protocol, we get a progressive time delay between the first CC view to first MLO view and the delayed view similar to MRI without losing contrast information from the contralateral breast and also without much additional radiation to the breast.

The next challenge is to compare its diagnostic accuracy with the standardized imaging technique, MRI, to implement the subjective kinetic assessment of CEM into clinical practice.

Experienced breast radiologists can assess the kinetics of breast masses in MRI subjectively when reading the postcontrast dynamic subtraction MIP images in clinical practice. In our study, we compared the subjective and quantitative MRI kinetics and they had almost perfect agreement.

We then compared the CEM kinetics with MRI quantitative and subjective kinetics. To eliminate the bias, two different readers interpreted the CEM kinetics and MRI kinetics separately and we compared both the interpretations. We assessed the subjective CEM kinetics with standard 4 views with MRI parameters, and we had moderate agreement. But when we added

the delayed view obtained at 8 min after the start of the contrast injection, the agreement improved to substantial and near perfect level for subjective and quantitative assessments of MRI, respectively.

Limitations

Our study has few limitations. There can be subjective bias as the kinetic information is obtained subjectively. We eliminated it to a certain extent by using 2 separate readers for assessing the kinetics in CEM and MRI, and also agreement between subjective and quantitative parameters was calculated in MRI and between MRI and CEM. Also there can be variation in the protocols and acquisition times because of patient factors and technologist factors.

Conclusion

To the best of our knowledge, our study is the first in the literature to assess the subjective assessment of kinetics with evaluation of change in density over time in comparison with MRI kinetics overcoming the drawbacks mentioned in the previous studies. There was no significant increase in radiation dose to the patient as we used CEM as the initial study in all diagnostic mammograms with suspicious findings and used low energy images as 2D images thereby avoiding two separate imaging on mammography. By acquiring an additional single delayed image, we calculated the progressive time delay between the views and obtained the kinetic information on CEM which had substantial and near perfect agreement with the standardized imaging, MRI. The contralateral breast is imaged simultaneously for screening without any loss of information.

We are sure that all vendors will provide a technique of calculating the quantitative assessment of enhancement patterns in the near future. We hope this study and the results would encourage the breast radiologist to calculate the kinetic information from CEM by obtaining one additional delayed view and use CEM as a single, simple and cost-effective imaging modality in detecting and characterizing breast masses.

Abbreviations

CEM	Contrast-enhanced mammography
CE MRI	Contrast-enhanced magnetic resonance imaging
CC	Craniocaudal
MLO	Mediolateral oblique
MIP	Maximum intensity projection
BPE	Background parenchymal enhancement
IR	Inversion recovery
TIW	T1 weighted
ACR BIRADS	American College Radiology Breast Imaging Reporting and Data System

Acknowledgements

We would like to acknowledge Dr. Jeevithan Shanmugam, MD, Professor in Community Medicine, KMCH Institute of Health Sciences and Research, for statistical analysis.

Author contributions

All the authors have contributed in conceptualizing and designing the study, retrieval, analysis and interpretation of data. All authors 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.

Funding

No funding was required for the study.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly 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 institutional KMCH ethics committee, Kovai Medical Centre and Hospital limited, (EC/AP/1002/02/2023). As ours is a retrospective observational study, informed consent was waived off by the review board of Kovai Medical Centre and Hospital limited.

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.

Author details

[1]Division of Breast and Women's Imaging, Department of Diagnostic and Interventional Radiology, Kovai Medical Centre and Hospitals, Tamil Nadu, Coimbatore 641014, India.

Received: 30 March 2023 Accepted: 14 May 2023
Published online: 19 May 2023

References

1. Mann RM, Cho N, Moy L (2019) Breast MRI: state of the art. Radiology 292(3):520–536. https://doi.org/10.1148/radiol.2019182947
2. Morris EA, Comstock CE, Lee CH, et al (2013) ACR BI-RADS® magnetic resonance imaging. In: ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. Reston, VA, American College of Radiology
3. Pötsch N, Vatteroni G, Clauser P et al (2022) Contrast-enhanced mammography versus contrast-enhanced breast MRI: a systematic review and meta-analysis. Radiology 305(1):94–103. https://doi.org/10.1148/radiol.212530
4. Xiang W, Rao H, Zhou L (2020) A meta-analysis of contrast-enhanced spectral mammography versus MRI in the diagnosis of breast cancer. Thorac Cancer 11(6):1423–1432. https://doi.org/10.1111/1759-7714.13400
5. Tang S, Xiang C, Yang Q (2020) The diagnostic performance of CESM and CE-MRI in evaluating the pathological response to neoadjuvant therapy in breast cancer: a systematic review and meta-analysis. Br J Radiol 93(1112):20200301. https://doi.org/10.1259/bjr.20200301
6. Rudnicki W, Heinze S, Piegza T et al (2020) Correlation between enhancement intensity in contrast enhancement spectral mammography and

types of kinetic curves in magnetic resonance imaging. Med Sci Monit Int Med J Exp Clin Res 26:e920742. https://doi.org/10.12659/MSM.920742
7. Huang JS, Pan HB, Yang TL et al (2020) Kinetic patterns of benign and malignant breast lesions on contrast enhanced digital mammogram. PLoS ONE 15(9):e0239271. https://doi.org/10.1371/journal.pone.0239271
8. Deng CY, Juan YH, Cheung YC et al (2018) Quantitative analysis of enhanced malignant and benign lesions on contrast-enhanced spectral mammography. Br J Radiol 91(1086):20170605. https://doi.org/10.1259/bjr.20170605
9. Lv Y, Chi X, Sun B et al (2020) Diagnostic value of quantitative gray-scale analysis of contrast-enhanced spectral mammography for benign and malignant breast lesions. J Comput Assist Tomogr 44(3):405–412. https://doi.org/10.1097/RCT.0000000000001019
10. Xu W, Zheng B, Chen W et al (2021) Can the delayed phase of quantitative contrast-enhanced mammography improve the diagnostic performance on breast masses? Quant Imaging Med Surg 11(8):3684–3697. https://doi.org/10.21037/qims-20-1092
11. Macura KJ, Ouwerkerk R, Jacobs MA et al (2006) Patterns of enhancement on breast MR images: interpretation and imaging pitfalls. Radiogr Rev Publ Radiol Soc N Am Inc 26(6):1719. https://doi.org/10.1148/rg.266065025
12. Kuhl CK, Schild HH, Morakkabati N (2005) Dynamic bilateral contrast-enhanced MR imaging of the breast: trade-off between spatial and temporal resolution. Radiology 236(3):789–800. https://doi.org/10.1148/radiol.2363040811
13. Schnall MD, Blume J, Bluemke DA et al (2006) Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. Radiology 238(1):42–53. https://doi.org/10.1148/radiol.2381042117
14. Demartini WB, Kurland BF, Gutierrez RL et al (2011) Probability of malignancy for lesions detected on breast MRI: a predictive model incorporating BI-RADS imaging features and patient characteristics. Eur Radiol 21(8):1609–1617. https://doi.org/10.1007/s00330-011-2094-6

Publisher's Note