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ORIGINAL ARTICLE

Comparison Between Contrast-Enhanced Digital Mammography and Dynamic Contrast-Enhanced MRI in the Evaluation of Breast Cancer

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Abstract

Background: **The main purpose of this study was to compare between contrast-enhanced digital mammography (CEDM) and contrast-enhanced MRI (CEMRI) with histopathological results and to compare the sensitivity, specificity, and positive and negative predictive values for both imaging modalities.**

Objective: **The aim was to evaluate the diagnostic accuracy in comparison between CEDM and CEMRI in the assessment of breast cancer.**

Patients and methods: **Forty-four patients who were suspected of having breast abnormalities by clinical examination; 22 patients underwent CEDM and the other 22 patients underwent CEMRI using histopathologic results. The sensitivity and specificity as well as predictive values are obtained for each modality and comparison was done.**

Results: **In this study, the sensitivity of CEMRI (92.86%) was higher than CEDM (84.62%), and the specificity of CEDM (88.9%) is slightly higher than CEMRI (87.5%). Positive predictive values are nearly the same for both imaging modalities (92.86 for CEMRI and 91.67% in CEDM) and negative predictive values are higher in CEMRI (87.5%) than CEDM (80%).**

Conclusion: **There is no significant difference between sensitivity and specificity in both CEDM and CEMRI.**

Keywords: Breast cancer, Contrast-enhanced digital mammography, Dynamic contrast-enhanced MRI

1. Introduction

Digital mammography (DM) is the standard technique in the detection of breast cancer in screening programs. But, several obstacles are present due to the decreased contrast between tumors and the surrounding tissue.[1]

Contrast-enhanced MRI (CEMRI) is considered to be the gold standard imaging for the detection of suspicious breast lesions, staging, and follow-up.[2]

The sensitivity of contrast-enhanced MRI ranges from 79 to 98% in the detection of cancer breast.[3] But several limitations for this imaging modality are present due to expensiveness, longer duration, claustrophobia, its contraindication, and limited availability.[4]

CEMRI has a lower hand to DM in the item of specificity.[1]

Contrast-enhanced digital mammography (CEDM) consists of high-energy and low-energy radiographic exposure that comes after iodinated contrast media injection. This results in a low-energy image; in comparison to mammography a combined image, both low-energy and high-energy images, will show contrast agent uptake by breast lesions. Similar to MRI, contrast uptake is prominent in malignant lesions, which enhances the detection of cancerous lesions.[5]

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The main aim of this study was to retrospectively make a comparison of the diagnostic performance of CEDM with that of CEMRI in the diagnosis of breast cancer using parameters, including sensitivity, specificity, and positive predictive value (PPV) and negative predictive value (NPV).

2. Patients and methods

2.1. Patients

This prospective study was performed on 44 female patients with clinical suspicion to have breast lesions; 22 of them randomly underwent CEDM and the other 22 patients underwent CEMRI.

This study was conducted at hospitals of the Ministry of Health in Egypt.

The age of the participants ranged from 18 to 72 years.

2.2. Inclusion criteria

Female patients included in the study with suspected breast lesions with CEDM and CEMRI procedures, followed by histopathological confirmation, which was performed between September 2020 and April 2022. Before the examinations, blood urea and creatinine levels and estimated glomerular filtration rate were determined.

2.3. Exclusion criteria

Exclusion criteria were decreased estimated glomerular filtration rate below 30 ml/min, iodinated or gadolinium-based contrast agent allergic reaction, claustrophobia, implanted pacemakers or metallic implants, and pregnant females.

2.4. CEDM protocol

CEDM is done with a dual-energy system produced by GE Healthcare (Chalfont St-Giles, UK): A series of high-energy and low-energy images are acquired after contrast agent administration with compressed breast, producing a low-dose image as well as a recombined postprocessing image that pronounces the contrast medium distribution.[6]

The examinations use an option called automatic exposure, according to the density and thickness of the compressed breast.[7]

After that an iodinated contrast agent intravenous injection of omnipaque 350 mg/ml was done with a dose of 1.5 ml/kg of body weight. The breast is compressed for the mediolateral oblique projection 2 min after contrast agent injection, and then decompression was done and then 2 min later the breast is compressed again for the craniocaudal projection (CC).[6]

2.5. MRI protocol

An MRI scanner is used (GE-Signa 1.5 T), equipped with phased array coils. The acquired sequences was T1-weighted and T2-weighted with an acquisition taken before the injection of contrast agent and the next seven acquisitions are taken after the gadolinium contrast agent administration and diffusion-weighted image sequence with b values of 0 and 600 mm/s^2 were set.[6]

Sensitivity and specificity as well as PPV and NPV of CEDM and CEMRI were assessed.

2.6. Statistical analysis

Recorded data were analyzed using the Statistical Package for the Social Sciences.

The following tests were done: χ^2-test of significance was used to compare proportions between qualitative parameters.

Diagnostic performance evaluation: sensitivity, specificity, PPV, NPV, and accuracy.

The P value was considered significant as the following: probability (P value): P value less than 0.05 was considered significant; P value less than 0.001 was considered as highly significant; and P value greater than 0.05 was considered insignificant.

3. Results

Eight female patients out of 44 cases have a negative history for breastfeeding and 36 out of 44 cases have a history of positive history for breastfeeding.

Twenty-eight patients out of 44 cases have a positive family history of breast cancer and 16 out of 44 cases have a negative family history or indeterminate history of breast cancer.

Twenty-two cases were complaining from the right breast complaint and 22 cases were complaining from the left side.

Twenty-seven out of 44 cases are confirmed to be malignant and 17 out of 44 cases were benign (Table 1).

Table 1. The total number of benign and malignant breast lesions.

Final pathological diagnosis	*N* (%)
Benign	17 (38.64)
Malignant	27 (61.36)
Total	44 (100)

3.1. Histological classification of cases

Pathological diagnosis of the malignant lesions were 17 cases diagnosed as IDC, five cases diagnosed as invasive mammary carcinoma (IMC), three cases were DCIS, and two cases were ILC (Table 2).

The final diagnosis of benign lesions was eight cases diagnosed as fibroadenoma, five cases diagnosed as mastitis, three cases diagnosed as abscesses, and one case was found to be an intramammary lymph node (Table 3).

3.2. Imaging findings

3.2.1. Mammographic

DM followed by CEDM was done for 22 female patients:

American College of Radiology (ACR) of the 22 patients were 10 cases have an ACR a, nine cases have ACR b, two cases were ACR c, and one case was ACR d.

3.2.2. Contrast-enhanced digital mammography enhancement

The enhancement pattern is either mass enhancement or nonmass enhancement.

Mass enhancement was characterized according to the shape (oval, rounded, and irregular), margin (circumscribed, obscured, microlobulated, indistinct, or speculated), or internal enhancement: homogeneous, heterogeneous, or rim enhancement.

Nonmass enhancement is further divided according to the distribution pattern into diffuse, linear, segmental, or regional.

In our study, 21 cases have variable degrees of enhancement while one case showed no enhancement pattern.

Eighteen out of 21 enhanced lesions were found to be of mass enhancement and three cases were of nonmass enhancement (Table 4).

Nonmass enhanced lesions are divided into one segmental nonmass enhanced lesion diagnosed pathologically as malignant (IMC) and two diffuse nonmass enhancement lesions, one diagnosed as granulomatous mastitis and the other diagnosed as DCIS.

Table 3. Final diagnosis of benign breast lesions.

Final pathological diagnosis	*N* (%)
Fibroadenoma	8 (47)
Mastitis	5 (29.4)
Abscess	3 (17.7)
Intramammary lymph node	1 (5.9)

With pathological finding correlation two cases of NME were malignant and one case was benign.

The 18 mass-enhanced lesions show by shape 12 masses have an irregular shape and six masses have a regular shape.

By margin, nine masses were indistinct, two masses were speculated, and seven masses were circumscribed.

By enhancement pattern, nine cases were heterogeneously enhanced lesions, six have homogeneous enhancement, and three cases have ring enhancement.

With pathological finding correlation, there were 18 mass-enhancing lesions, 11 of them were malignant and seven of them were benign.

The mass lesion having an irregular shape and indistinct or speculated margin with heterogeneous enhancement and nonmass enhancement with linear, segmental, or regional distribution are highly characteristic of malignancy, while rim enhancement and diffuse nonmass enhancement are considered to be of benign criteria.

Rim enhancement and diffuse nonmass enhancement are considered benign criteria; however, they are seen in both benign and malignant lesions.

Enhanced axillary lymph nodes were observed in 15 cases.

There were 10 out of 22 cases (45.5%) diagnosed as benign by CEDM, eight of them (80%) were benign (true negative) by pathology, and two of them (20%) were malignant proved by pathology (false negative) (one case had rim enhancement and the other case had diffuse nonmass enhancement).

There were 12 out of 22 cases (54.5%) diagnosed as malignant by CEDM. There were 11 of them (91.7%) diagnosed as malignant by pathology (true positive). There was one case (8.3%) diagnosed as benign proven by pathology (false positive) (Table 5).

Table 2. Final diagnosis of malignant lesions.

Final pathological diagnosis	*N* (%)
Invasive duct carcinoma	17 (63)
Invasive mammary carcinoma	5 (18.5)
Ductal carcinoma in situ	3 (11.1)
Invasive lobular carcinoma	2 (7.4)

Table 4. Enhancement pattern by contrast-enhanced digital mammography.

Enhancement pattern	*N* (%)
Mass enhancement	18 (85.7)
Nonmass enhancement	3 (14.3)
Total	21 (100)

Table 5. Analysis of false-positive and false-negative entities with contrast-enhanced digital mammography.

False diagnosis	Pathological diagnosis	Number of cases
False negative	Ductal carcinoma in situ (DCIS)	2
False positive	Granulomatous mastitis	1

In our study, the calculated sensitivity of CEDM was 84.6%, specificity was 88.9%, while the PPV was 91.7% and the NPV was 80.0%.

3.2.3. Contrast-enhanced MRI

CEMRI was done for 22 female patients and shows:

ACR of the 22 patients were six cases have ACR a; three cases have ACR b; six cases were ACR c; and seven cases were ACR d.

3.2.4. Dynamic MRI enhancement

The enhancement pattern is either mass enhancement or nonmass enhancement.

Mass enhancement was characterized according to shape (oval, rounded, irregular), margin (circumscribed, not circumscribed), and mass enhancement characteristics as being homogeneous, heterogeneous, rim enhancement, or dark internal septations.

Nonmass enhancement is further divided according to the pattern of distribution into focal, diffuse, segmental, linear, regional, and multiple regions.

In our study, 20 cases have variable degrees of enhancement while two cases show no enhancement pattern.

One case out of two nonenhancing cases is found to be malignant by pathology (DCIS) and one case is diagnosed as benign (mastitis).

Thirteen out of 20 enhanced lesions were found to be of mass enhancement and seven cases have nonmass enhancement (Table 6).

Nonmass enhanced lesions are divided into two focal, two linear, and three segmental nonmass enhancement.

With pathological finding correlation six out of seven NME were proven pathologically to be malignant and one of the NME taking the focal pattern of enhancement was proven to be benign (mastitis) (false positive).

The 13 mass-enhanced lesions show: by shape six masses have irregular shapes and seven masses have regular shapes.

Table 6. Enhancement pattern by contrast-enhanced MRI.

Enhancement pattern	*N* (%)
Mass enhancement	13 (65)
Nonmass enhancement	7 (35)
Total	20 (100)

Table 7. Analysis of false-positive and false-negative entities with contrast-enhanced MRI.

False diagnosis	Pathological diagnosis	*N*
False negative	Ductal carcinoma in situ (DCIS)	1
False positive	Mastitis	1

By margin seven masses were circumscribed and six masses were not circumscribed.

By enhancement pattern seven cases were heterogeneously enhanced lesions, five had homogeneous enhancement, and one had rim enhancement.

With pathological finding correlation, seven out of 13 mass-enhancing lesions were malignant and six of them were benign.

The mass lesion having an irregular shape and not circumscribed margin with heterogeneous enhancement and nonmass enhancement with linear, focal, or regional distribution are highly characteristic of malignancy.

The mass lesion having a regular shape, circumscribed margin, and homogeneous, ring or dark internal septation enhancement patterns are characteristic of benignity.

Focal nonmass enhancement was seen in both benign and malignant lesions.

Rim enhancement is seen in benign lesions (abscess).

Enhanced axillary lymph nodes were observed in eight cases.

There were eight out of 22 cases (36.4%) diagnosed as benign by CEMRI, seven of them (87.5%) were benign (true negative) by pathology and one of them (12.5%) was malignant proved by pathology (false negative) (nonenhancing lesion).

There were 14 out of 22 cases (63.6%) diagnosed as malignant by CEMRI. There were 13 of them (92.9%) diagnosed as malignant by pathology (true positive). There was one case (7.1%) diagnosed as benign proven by pathology (false positive) (mastitis) (Table 7).

In our study, the calculated sensitivity of CEMRI was 92.9%, specificity was 87.5%, while the PPV was 92.9%, and NPV was 87.5%.

Table 8. Association between CEDM compared with pathology 'Gold standard'.

	Pathology [*n* (%)]			χ^2	*P* value
	Malignant	Benign	Total		
CEDM					
Malignant	11 (84.6)	1 (11.1)	12 (54.5)		
Benign	2 (15.4)	8 (88.9)	10 (45.5)	8.814	0.003*
Total	13 (100.0)	9 (100.0)	22 (100.0)		

CEDM, contrast-enhanced digital mammography.

Table 9. Association between CEMRI compared with pathology 'gold standard'.

	Pathology [*n* (%)]			χ^2	*P* value
	Malignant	Benign	Total		
CEMRI					
Malignant	13 (92.9)	1 (12.5)	14 (63.6)		
Benign	1 (7.1)	7 (87.5)	8 (36.4)	10.946	<0.001**
Total	14 (100.0)	8 (100.0)	22 (100.0)		

CEMRI, contrast-enhanced MRI.

In our study, the sensitivity of CEMRI was higher than CEDM and both have nearly the same specificity that was slightly higher in CEDM.

PPVs are nearly the same for both imaging modalities and NPVs are higher in CEMRI than CEDM (Table 8).

This table shows a highly statistically significant relationship between CEDM compared with pathology 'gold standard', with *P* value of 0.003 and Kappa agreement being of substantial agreement ($\kappa = 0.723$) (Table 9).

Kappa agreement ($\kappa = 0.723$)

This table shows a highly statistically significant relation between CEMRI compared with pathology 'Gold standard', with a *P* of less than 0.001 and Kappa agreement being in almost perfect agreement ($\kappa = 0.804$) (Table 10).

This table shows high accuracy in CEMRI compared with CEDM, but insignificant with *P* value ($P > 0.05$) (Fig. 1).

Table 10. Comparison between results of CEDM and results of CEMRI.

	CEDM (%)	CEMRI (%)
Sensitivity	84.6	92.9
Specificity	88.9	87.5
PPV	91.7	92.9
NPV	80.0	87.5
Accuracy	86.4	90.9
χ^2	0.370	
P value	0.985	

CEDM, contrast-enhanced digital mammography; CEMRI, contrast-enhanced MRI; PPV, positive predictive value; NPV, negative predictive value.

4. Case 1

4.1. Clinical background

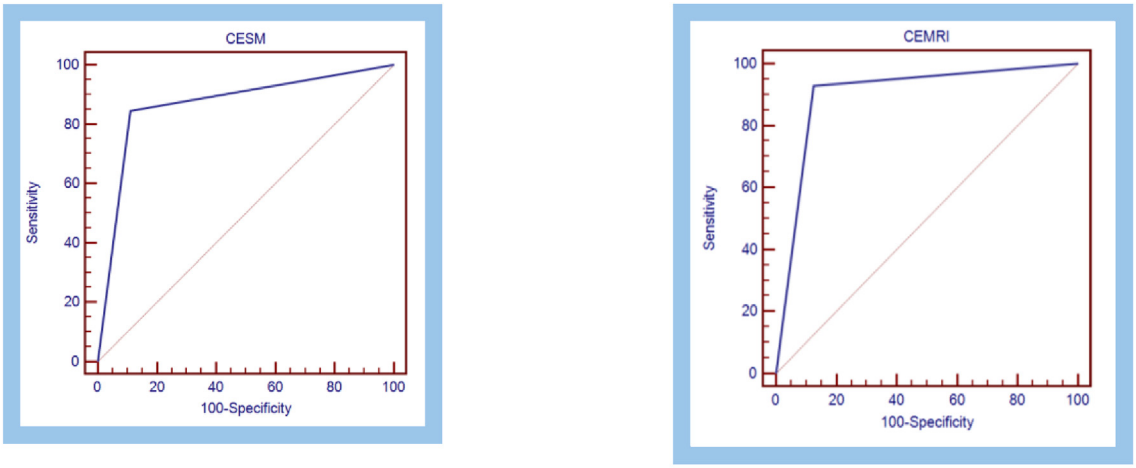
A 55-year-old female patient complaining of a left breast lump.

4.2. By CEDM

Mediolateral oblique and CC views of the left breast show a left upper outer quadrant (UOQ) mass lesion with avid heterogeneous contrast enhancement.

4.3. Pathological diagnosis

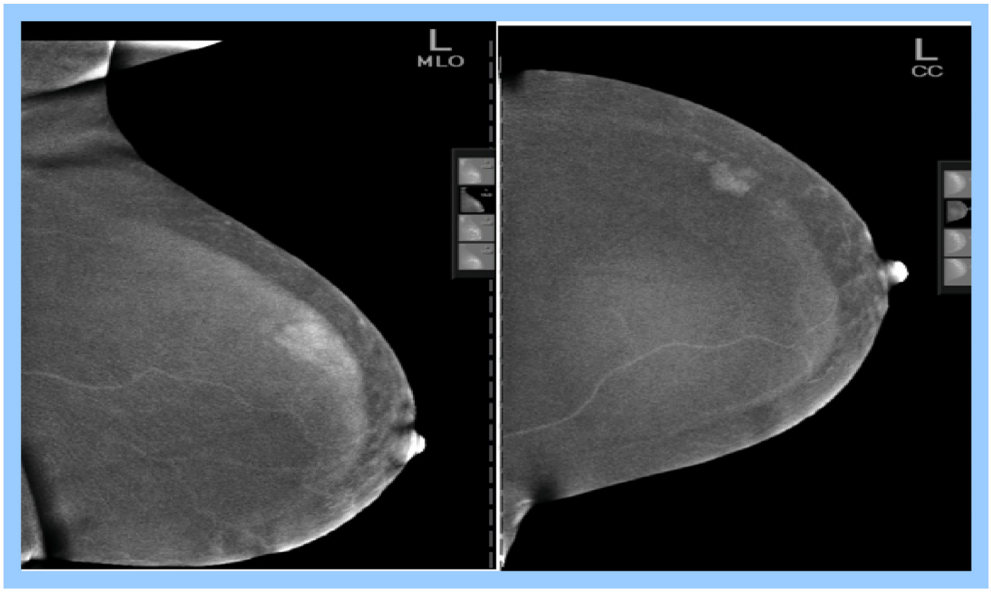
Invasive ductal carcinoma.



(a) ROC curve, CEDM sensitivity, and specificity

(b) ROC curve, CEDM sensitivity, and specificity

Fig. 1. Receiver operating characteristic (ROC) curves for the two techniques. Area under the curve (AUC) for CEMRI (0.909) was higher than AUC for CEDM (0.684), but this difference was not significant (P > 0.05).



5. Case 2

5.1. Clinical background

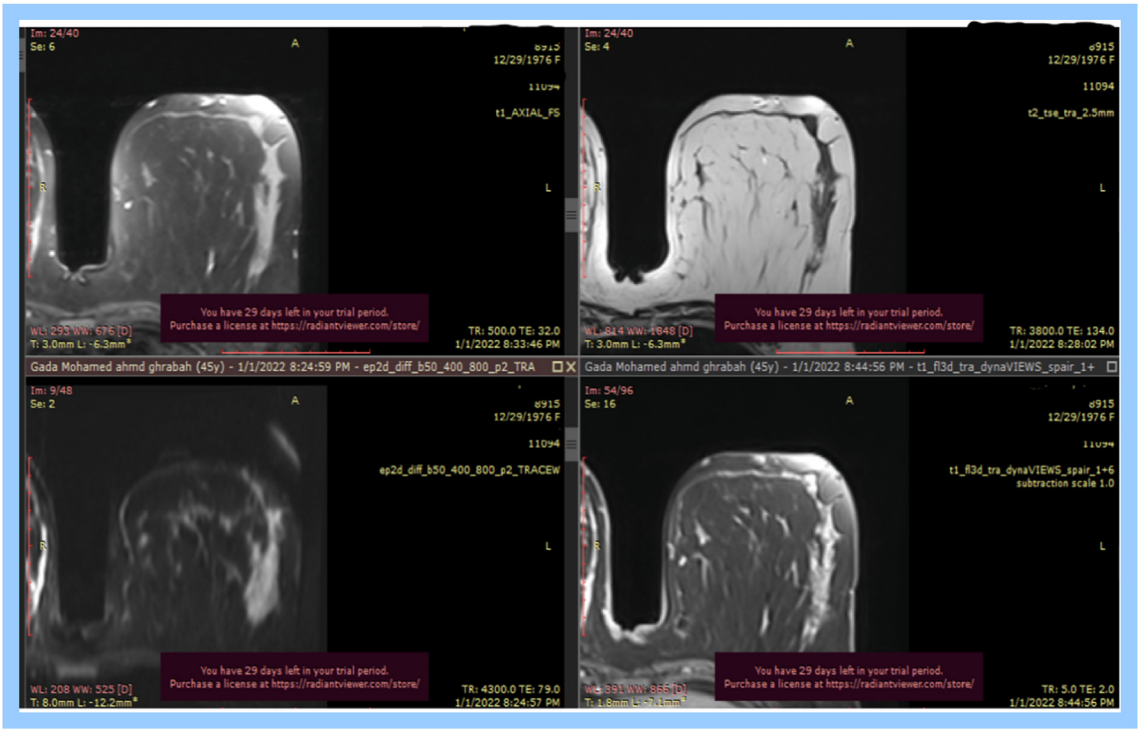
A 40-year-old-female patient complaining of a left breast lump.

5.2. By MRI

T1, T2, DWI, and dynamic postcontrast study showing the left lower outer quadrant linear clumped nonmass enhancement.

5.3. Pathological diagnosis

Invasive ductal carcinoma.



6. Discussion

The gold standard imaging modality for cancer breast detection and staging is breast MRI; however, it is limited by expensiveness, longer duration, and limited availability. CEDM is a relatively new technique that overcomes the limitations of breast MRI.[8]

CEDM can be done for patients who have contraindications to BMRI. CEDM is more comfortable being an efficient and accessible alternative to BRMI. CEDM can be done as a daily easy method for the diagnosis and when other modalities such as ultrasound and conventional DM are inconclusive for suspicious findings.[8]

Studies by Diekmann and Bick,[9] which were biopsy-proven carcinomas, showed enhancement of all cases of carcinoma by CEDM. As CEDM has acquired popularity, additional studies have been done and compare CEDM to conventional imaging modalities.

Both CEDM and DCE-MRI have common features. For acquiring good quality image, an administration of contrast media is essential to improve the diagnostic accuracy, aiming for an accurate morphological assessment. And so on, an accurate morphological assessment should be associated with standard morphology descriptors that pronounce the differentiation between malignant and benign breast lesions.[10]

In line with our study, Iotti et al.[7] have shown that CEDM can characterize tumors in even both breasts in the standard positions (mediolateral oblique and CC views) after injection of an intravenous contrast medium.[6] The results of their study have shown that CEDM nearly has an identical or higher sensitivity and better specificity when put in comparison with ultrasound and DM for breast cancer detection.[7]

Our data is consistent with that of Jochelson and colleagues that CEDM is more practical showing a higher diagnostic rate of cancer breast than DM alone and it can compete MRI in the item of specificity. They showed a higher specificity of CEDM in comparison to MRI.[11]

The mass lesion having an irregular shape with speculated or irregular margins and showing heterogeneous enhancement and also nonmass enhancement with a focal, segmental, or ductal distribution and showing heterogeneous or clumped internal enhancement pattern are suggestive of malignant descriptors. The mass lesion having a rounded or oval shape with homogeneous enhancement are suggestive of benign descriptors; however, malignancy could not be ruled out.[11]

Invasive lobular carcinoma and ductal carcinoma in situ are breast malignancies that may be commonly missed by an MRI. The reason for such a finding is mainly due to the absence of neoangiogenesis in DCIS that results in nonspecific or even no enhancement in MRI.[5]

Larger studies by Fallenberg and colleagues[5,7,11-14] have shown the sensitivity and specificity of CEDM in comparison to FFDM. Older studies have shown the superiority of CEDM over FFDM for the detection of breast cancer, even equaling the results of breast MRI.[14]

Fallenberg et al.[5] reported a comparative study between MRI and MMG CEDM. They determined that malignant breast lesions were noted in 66 of 80 cases on MMG, 80/80 on CEDM, and 77/79 on MRI.

As CEDM seems to be a good modality elevating the sensitivity of MG, with a diagnostic accuracy competing MRI, it is also improving the determination of size and staging. The best imaging modality comes in correlation with histological confirmation as a gold standard in terms of determination of lesion size. CEDM is found to be the best modality; MRI and MG come after as both imaging modalities that underestimate the size and extent of breast lesions compared with CEDM. Our results confirm the results of earlier studies comparing the different imaging modalities in measuring the lesion size and its detection. Wasif et al.[15] found that breast MRI is considered to have more accuracy than mammography in estimating the primary breast cancer size.

Nowadays, the most sensitive imaging modality for detection, estimating size, and staging of breast cancer is breast MRI. Breast MRI often is not available to women, however, due to lack of technology or inadequate health insurance coverage. The present study considers that as breast MRI, CEDM could have a diagnostic value for breast cancer detection, estimation of its size, and even multifocality.[16]

The study has several limitations as it consisted of a small patient number. Further larger studies are essential for conclusions about both techniques and to show that CEDM can compete with CEMRI and the individual roles in routine clinical practice.

Another limitation was invasiveness during the procedure in the form of contrast agent injection, which is not acceptable for a population-based screening program.

6.1. Conclusion

In conclusion, this study explains better diagnostic values of CEDM and MRI in terms of lesion detection and estimating the size of the lesion. CEDM seems to be a suitable alternative to MRI in various obstacles that reduce the chance of the patient to

undergo MRI. In our study the sensitivity of CEMRI was higher than CEDM and both have nearly the same specificity that was slightly higher in CEDM. PPVs are nearly the same for both imaging modalities and NPVs are higher in CEMRI than CEDM.

Conflict of interest

None declared.

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