



ORIGINAL ARTICLE

Contrast enhanced digital mammography: Is it useful in detecting lesions in edematous breast?



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Abstract *Introduction:* Breast edema can be caused by a variety of pathologic processes of benign or malignant diseases. Contrast enhanced digital mammogram (CEDM) has been shown to improve the probability of malignancy detection when compared with the conventional mammography alone.

Patients and methods: This study was prospectively carried on 34 female patients with breast edema at the female imaging unit of the Radiology Department. The age range was 29–80 years. Bilateral conventional mammography (MX) and contrast-enhanced digital mammographic procedure (CEDM) were performed in approximately 7–10 min and followed by complementary ultrasound (US).

Results: As regards enhancement patterns in our study, noncontrast uptake and diffuse parenchymal uptake were considered as benign and intense contrast uptake is considered malignant and ring enhancement in keeping with both benign and malignant lesions.

The calculated sensitivity and specificity of dual energy contrast enhanced digital mammography were 95%, and 73% respectively, with a positive predictive value (PPV) of 88% and negative predictive value (NPV) of 88%.

Conclusion: Dual-energy contrast-enhanced digital mammography is a useful technique in identification of lesions in mammographically dense edematous breasts and proved to be a useful tool in the follow-up of cases presenting by edema after conservative breast surgery and chemotherapy.

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1. Introduction

The accuracy of mammography is limited in dense breasts where surrounding fibroglandular tissue decreases the

conspicuity of lesions. Even when tumors are detected, the full extent of disease may not be clearly depicted. The primary and metastatic potential of tumors can be directly linked to angiogenesis. Growth beyond a few millimeters in diameter requires the formation of new blood vessels to supply the oxygen and nutrients necessary for survival (1). Tumor angiogenesis factors stimulate formation of abnormal vessels that leak and shunt blood. Therefore, imaging methods with contrast

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medium potentially can aid in the detection and diagnosis of cancer (1).

Breast edema can be caused by a variety of pathologic processes of benign or malignant diseases. It may occur with inflammatory breast carcinoma, lymphatic obstruction, mastitis, lymphoma, post-radiation changes or systemic conditions such as congestive heart failure and nephritic syndrome (1).

The mammographic findings of breast edema are skin thickening and increased parenchymal density with prominent interstitial markings.

On ultrasonography, it presents as marked skin thickening and increased echogenicity of the subcutaneous fat layer with a reticular anechoic structure, which is suggestive of dilated lymphatics (1).

CEDM has been shown to improve the probability of malignancy detection when compared with the conventional mammography alone. CEDM is a useful adjunct to diagnostic mammography and a promising problem-solving tool (2).

Despite the overlap between post treatment changes and tumor recurrence, the two entities can usually be distinguished by the characteristic mammographic appearances of post treatment sequelae and by comparing interval findings on successive studies. Postoperative masses and fluid collections slowly diminish in size and usually resolve by 1 year after surgery. Radiation-induced edema gradually resolves; increasing edema may be due to recurrent cancer. Postsurgical scarring usually appears as a poorly marginated soft-tissue mass with interspersed radiolucent areas. Recurrent cancer is usually seen as a mass with no central radiolucent areas. Pleomorphic and granular microcalcifications are important markers for recurrent cancer and can usually be distinguished from the thick, calcified plaques and elongated dystrophic calcifications associated with scarring.

2. Patients and methods

2.1. Patients

This study was prospectively carried on 34 female patients with breast edema (1) at our female imaging unit. Patients were referred from the outpatient clinics of the internal medicine, surgery and radiotherapy departments. The age range was 29–80 years.

Comprehensive explanations of the procedures were provided for all cases, including the associated risks and contraindications. They agreed with a written consent to undergo the contrast-enhanced digital mammographic examination after performing renal function tests.

The study has been approved by the institutional board.

Inclusion Criteria: 1. Patients presenting by unilateral or bilateral breast edema on conventional imaging (conventional mammography and ultrasound) warranting detection and characterization of breast lesions. 2. Patients who had undergone conservative breast surgery or chemotherapy with newly developed breast edema with suspected residual or recurrent pathology.

Exclusion Criteria: (1) The early post-operative cases or recently treated with radio-therapy, so as to minimize false positive results. (2) Contraindication to IV contrasts material injection, such as: Allergic patients or those known to have history of complications from contrast media such as anaphylactic reaction. (3) Patients with renal failure. (4) Patients with bad general condition. (5) Pregnant females.

All patients were submitted to the following:

- I Clinical history: Full history taking including clinical presentation (complaint), age, family and past medical history.
- II Mammographic, ultrasound and CEDM examination.
- III Pathologic diagnosis: Analysis of obtained biopsies whether by fine-needle aspiration cytology, needle biopsy, excisional biopsy, or by radical surgery, all of which were diagnosed by experienced pathologists in the analysis of breast cancer.

2.2. Contrast agent

The contrast agent used was the nonionic solution (iohexol, Omnipaque 300; Nycomed, Roskilde, Denmark) containing 300 mg of iodine per milliliter, which is commonly used for CT. In our study, we injected 1.5 ml/kg of the agent by hand over a period of approximately 1 min with a maximum of 120 ml.

2.3. Instrumentation

All images were acquired with a production system (Senobright; GE Medical Systems, Milwaukee, Wis). GE Healthcare's new SenoBright Contrast Enhanced Spectral Mammography (CESM) technology was designed to allow the physician to image blood flow through angiography of the breast using a contrast agent and a dual energy acquisition technique.

2.4. Technique

This consisted of high-energy and low-energy digital mammograms obtained after administration of iodinated contrast agent.

Here, the nonionic iodine contrast agent was injected between pre and postcontrast image acquisitions in which the X-ray beam is produced at a relatively high energy, above the K-edge of iodine. The images were subtracted, canceling the soft-tissue contrast that is common to the two images and isolating the iodine signal in the region of angiogenesis.

At first bilateral conventional mammography both cranio-caudal and medio-lateral oblique views were taken. Then typically, the contrast-enhanced digital mammographic procedure was performed in approximately 7–10 min. This included 3 min for placement of the intravenous catheter and contrast injection, 1 min for obtaining the cranio-caudal image for the normal breast, and 3–6 min for acquisition of the rest of images (the cranio-caudal and the medio-lateral oblique projections for the abnormal breast) followed by the medio-lateral oblique view of the normal side.

Finally, the lesions were analyzed by three specialized radiologists for the presence, morphology, and pattern of enhancement.

2.5. Statistics

Using the standard of reference, sensitivity, specificity, and accuracy were calculated (3). In addition, comparison between groups was performed using the unpaired *t* test and McNemar

test. Correlations were sought using the Pearson correlation. A $p < 0.001$ was considered significant.

3. Results

Our study included 34 female patients. Their age ranged from 29 to 80 years, the mean age is about 54.5 years and the median is 49.5.

Two patients had bilateral breast edema while thirty-two patients had unilateral breast edema.

For better statistical analysis and more accurate results, we considered each edematous breast with its ipsilateral axillary lymph nodes as a unit (case), hence giving the total of 36 breasts or “cases”.

Ten patients had underwent conservative breast surgery and axillary evacuation while the rest of patients presented with breast edema (\pm palpable mass) as their first complaint.

Patients’ presentations varied as follows:

- 12/36 patients were presenting with palpable lump as well as the swollen breast.
- For 10/36 patients, breast edema was their first presentation. 4/10 had history of MRM of the contra lateral breast of more than two year duration.
- 10/36 patients underwent conservative breast surgery and axillary evacuation. 5/10 received and ended their chemotherapy and radiotherapy cycles of more than 2 year duration and one came prior to receiving the radiotherapy.
- 4/36 patients received neoadjuvant chemotherapy on follow-up.

All breast lesions detected by CEDM as well as radiologically suspicious axillary lymph nodes were diagnosed pathologically by means of surgery, excisional biopsy, skin punch biopsy, true cut biopsy, or fine needle aspiration cytology.

Cases that proved pathologically of inflammatory or post-operative negative result were considered as benign for statistical analysis.

Sensitivity and specificity were estimated taking the probability of malignancy exhibited as masses or micro-calcific clusters detected by MX, as well as the presence of masses \pm pathological axillary lymph nodes by ultrasound, to be considered as positive results. Comparisons of sensitivity and specificity between MX, US and CEDM were subsequently made.

Eight out of the thirty-six edematous breasts had multiple lesions, diagnosed pathologically as multicentric invasive duct carcinoma; one of which was a postconservative breast surgery recurrence. Of all the multiple lesions detected, only the most dominant or the largest was included in the statistical analysis.

Eleven out of thirty-six edematous breasts were diagnosed pathologically as benign caused edema; including 7 post-operative (\pm radiotherapy) edematous changes, one chronic abscess, one chronic granulomatous mastitis and two acute inflammatory lesions.

The remaining twenty-five were initiated by malignant lesions; either due to primary malignant breast masses or secondary to metastasis to the axillary lymph nodes.

Three out of the ten post-operative edematous breasts showed pathologically proven recurrence; one of them showed multiple lesions (multicentric).

The total numbers of benign and malignant caused breast edema are shown in [Table 1](#)

Detailed description for the number and percentage for each pathological diagnosis of breast edema causative lesion is illustrated in [Table 2](#).

3.1. Imaging findings

Mammography: All cases have a variable degree of breast edema including diffuse increased parenchymal density, coarse trabecular pattern and increased skin thickness.

Twenty cases showed positive mammographic findings in the form of masses \pm micro-calcific clusters. Masses were detected in 10 cases; 3/10 cases had multiple lesions. Masses accompanied by micro-calcific clusters were detected in 6 cases, while increased density with micro-calcific clusters was detected in 4 cases. Dense suspicious axillary lymph nodes were delineated in 2 cases only in addition to breast masses.

Patients according to mammographic examination were 16 benign and 20 malignant (considering negative as benign).

When considering dense irregular masses or micro-calcific clusters as malignant there were 20/36 (55%) edematous breasts diagnosed as malignancy caused edema by digital mammography, out of which 17/20 (85%) confirmed to be malignant by pathology (true positive) and 3/20 (15%) were benign by pathology (false positive).

On the other hand 16/36 (45%) cases diagnosed as benign by digital mammography, out of which 10/16 (62.5%) were benign (true negative) by pathology, and 6/16 (37.5%) were malignant by pathology (false negative) ([Table 3](#)).

The calculated sensitivity of digital mammography hence was 74%, with a specificity of 77%. The PPV and NPV were 85%, and 62.5% respectively ([Fig. 1](#)).

Ultrasound Findings included a variable degree of skin thickening and dilated intradermal lymphatic channels. Masses were detected in 18 cases as follows: 14 cases show irregular infiltrative hypoechoic masses, 2 well circumscribed lesions and 2 complicated cysts.

Seven out of the 14 cases with irregular infiltrative masses exhibited multiplicity (multicentric).

Pathologically enlarged Ipsilateral axillary lymph nodes were detected in 22 cases, of which 2 showed globular configuration; with central preserved fatty hila (proved histologically to be nonspecific inflammatory) while the others showed effaced/lost fatty hila. Only one case showed multiple enlarged axillary lymph nodes with irregular outline.

According to ultrasound examination there were 11 benign and 25 malignant cases.

Three patients showed edematous features of the breast without definite underlying breast lesions only enlarged axillary lymph nodes with effaced/lost fatty hila proved pathologically to be metastatic IDC. Of these, two gave history of

Table 1 Total number of benign and malignant breast lesions causing edema and the final pathologic diagnosis.

Final pathologic diagnosis	No. of cases	Percentage (%)
Benign	11	30.5
Malignant	25	69.5
Total	36	100

Table 2 Total number of cases with final pathologic diagnosis of breast edema causative lesion.

Final pathologic diagnosis	No. of cases	Percentage rev. (%)
Invasive duct carcinoma grade II	19	53
Metastatic axillary Lymph nodes (ductal carcinoma)	3	8
Invasive duct and Lobular carcinoma	3	8
Acute mastitis	2	6
Chronic abscess	1	3
Chronic granulomatous mastitis	1	3
Post therapeutic sequel	7	19
Total	36	100

modified radical mastectomy of the contralateral breast, while the third had the primary breast IDC mass in the contralateral breast in addition to the presenting edematous breast (bilateral breast edema).

Another case showed a plain edematous picture in the absence of any underlying suspicious breast lesion, yet evident ipsilateral enlarged nonspecific axillary lymph nodes, which in turn proved to be periductal mastitis by skin punch biopsy.

On US, 25/36 cases diagnosed as malignant, of which 23 were verified as malignant (true positive), and two were benign by pathology (false positive).

On the other hand, 11/36 were negative by US, of these, eight were true negative and three false negative (Table 4).

The calculated sensitivity of ultrasonography was 88%, with a specificity of 80%. The PPV and NPV were 92% and 73% respectively (Fig. 1).

3.2. CEDM enhancement (Table 5)

Enhancement was observed in 29/36 edematous breasts as follows:

- Intense enhancement was observed in all malignant tumors; 23 were heterogeneous, 1 homogeneous (Fig. 4 (case 3)).
- Contrast uptake was also observed in 5 out of 6 benign related breasts. edema: 3 ring patterns and 2 revealed diffuse increased parenchymal enhancement.

Table 3 Shows analysis of false positive and false negative entities with digital mammography considering mass ± micro calcific clusters as positive results.

False diagnosis	Pathologic diagnosis	No. of cases
False negative	Local recurrence post CBS	1
	Metastatic axillary lymph nodes	3
	Mixed IDC & ILC (Metastatic from contralateral breast after MRM)	1
	Invasive duct carcinoma	1
		6
False positive	Post CBS scar tissue	2
	Granulomatous mastitis	1
		3

Table 4 Shows analysis of false positive and false negative entities with Ultrasound.

False diagnosis	Pathologic diagnosis	No. of cases
False negative	Invasive duct carcinoma	2
	Mixed IDC & ILC	1
		3
False positive	Post CBS scar tissue	2
		2

- Enhancing axillary lymph nodes was observed in four cases; one of which proved to be a metastatic axillary lymph node causing the ipsilateral breast edema.
- Enhancement was absent in seven cases. In two cases, metastatic axillary lymph nodes were the cause of the edema which could not be detected by CEDM (false negative) and one case of benign caused edema proved to be inflammatory periductal mastitis (Fig. 5 (case 4)) and four postoperative cases (Fig. 7 (case 6)).

When considering the different patterns of contrast uptake identified in our study, noncontrast uptake and diffuse parenchymal uptake were considered as benign, while intense contrast uptake as malignant, with a gray zone of ring enhancement observed as both benign and malignant lesions as noted in one of our benign cases that show ring enhancing lesions and proved to be caseating granulomatous mastitis (Fig. 6 (case 5)).

There were 11/36 (31%) cases diagnosed as benign by pathology, 9/11 (82%) of them were benign by contrast mammography, 8 were (true negative) and one case was falsely diagnosed as benign postoperative distortion yet later proved to be recurrence (false negative). 2/11 (27%) were malignant caused edema by contrast and by pathology proved to be benign (false positive).

On the other hand 25/36 (69%) were diagnosed as malignant by pathology, which in turn concurred with the CEDM findings in twenty-two cases (61%) giving true positive findings.

Three out of ten postoperative cases showed pathologically proven recurrence (Fig. 8 (case 7)), one of them was multicentric (Fig. 2 (case 1)).

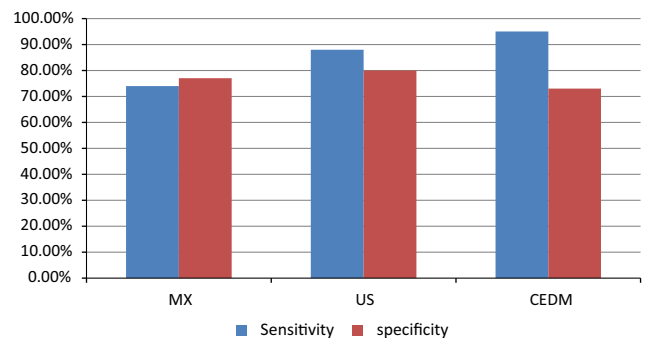


Fig. 1 Bar chart illustrates sensitivity and specificity of MX, US and CEDM in characterization of causative lesion of breast edema.

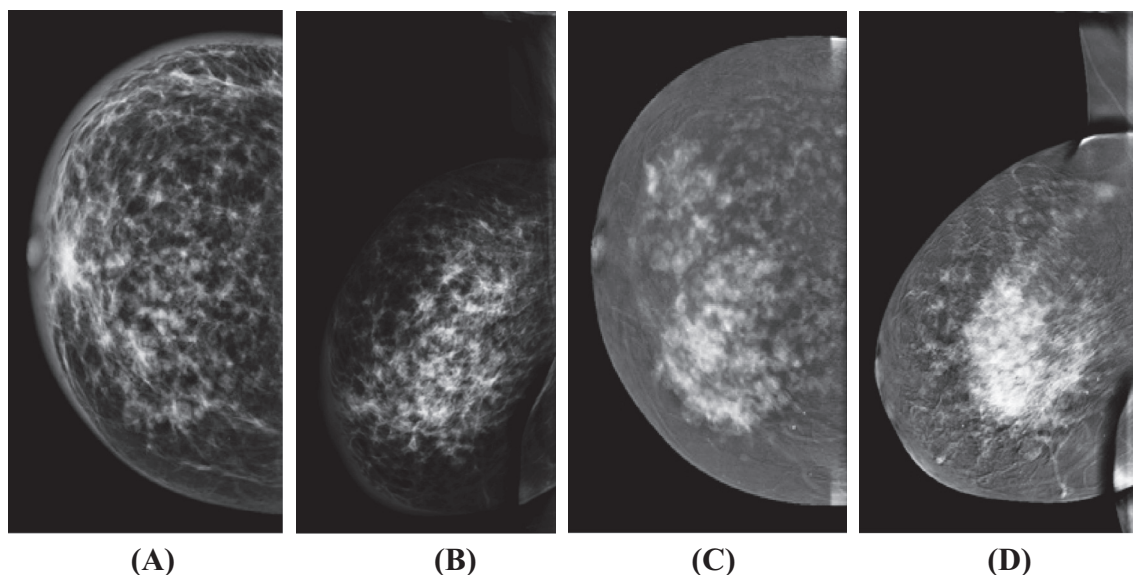


Fig. 2 (case 1): A female patient 47 year-old underwent left MRM, received chemotherapy and now presenting with right breast edema. Digital mammogram Cranio-caudal (CC) and mediolateral oblique (MLO) views of right breast (A&B) showing diffuse parenchymal edema with ill defined densities. Contrast enhanced spectral mammography (CESM) CC & MLO (C&D) multicentric enhancing nodular breast lesions can be clearly delineated. Pathology was mixed invasive ductal and invasive lobular carcinoma.

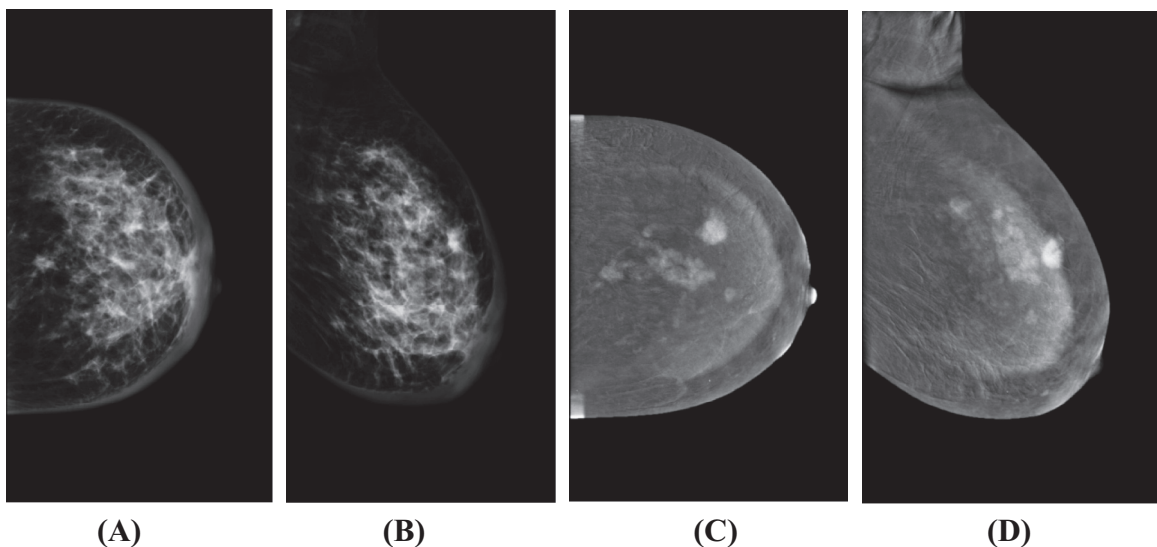


Fig. 3 (case 2): A female patient 48 year-old, complains of diffuse left breast swelling. Digital mammogram CC and MLO (A&B) showing edematous breast with increased density with suspected nodular masses. CESM CC & MLO (C&D) showing multiple enhancing central and UOQ masses. Pathology was left breast invasive ductal carcinoma (IDC) with apocrine features.

Multicentric invasive duct carcinoma was diagnosed pathologically in eight (22%) of our cases (Fig. 3 (case 2)).

The calculated sensitivity of dual energy contrast enhanced digital mammography was 95%, specificity was 73%, while the positive predictive value (PPV) and negative predictive value (NPV) were 88% and 88% respectively (Fig. 1). Among the eight patients with multicentric histologically proven lesions, all were detected by MX (mammography) + CEDM (100%) versus 3 (37.5%) and 7 (87.5%) detected by mammography alone and ultrasound respectively.

4. Discussion

Breast edema can be caused by a variety of pathologic processes of benign or malignant diseases. It may occur with inflammatory breast carcinoma, lymphatic obstruction, mastitis, lymphoma, post-operative and post-radiation changes or systemic conditions such as congestive heart failure and nephritic/nephrotic syndrome (1).

Initial mammography and breast ultrasound examination are the routine investigative modalities utilized for breast

lesions. Unfortunately, the breast edema lowers the sensitivity of the mammography and ultrasonography result frequently in nonspecific findings. In many instances, MRI is done as a complementary study that provides useful information about the causative lesions (1).

Cancers and fibro-glandular tissue show similar X-ray absorption; therefore, tumor enhancement with a contrast medium should improve cancer detection (4).

Contrast-enhanced digital mammography is a new breast imaging technique that aims at demonstrating breast carcinoma angiogenesis. Technical and clinical experience has been acquired and encouraging results have been published during the last few years on CEDM as an adjunct to mammography (5).

Temporal subtraction was first tested with an approach similar to that of breast MRI. These studies have shown the capability of CEDM to depict tumor angiogenesis in invasive breast cancer and have demonstrated contrast uptake in most malignant lesions. The main advantage of temporal subtraction is its ability to analyze the kinetics of time-enhancement curves. Kinetic curve assessment using CEDM, however, has failed to demonstrate clinical relevance. Both benign and malignant breast tumors, evaluated by using a temporal CEDM technique, have shown progressive enhancement.

Table 5 CEDM Pattern of enhancement after contrast injection in masses detected by mammography.

CEDM enhancement pattern	No. of cases	Percentage (%)
Heterogeneous	23	64
Homogeneous	1	3
Ring enhancement	3	8
Diffuse parenchymal enhancement	2	6
No enhancement/no abnormal enhancement	7	19

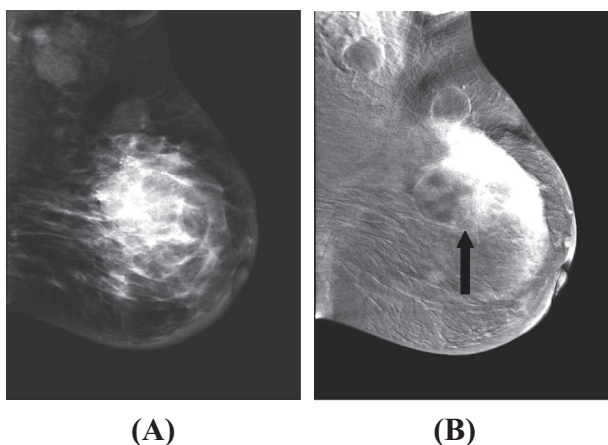


Fig. 4 (case 3): A female patient 39 year-old, complains of diffuse left breast edema and lump. Digital mammogram MLO (A) showing edematous breast with central and axillary increased density. CESM MLO (B) showing multiple cystic lesions with an enhancing soft tissue mass infiltrating one of the cysts (arrowed). Pathology was left breast IDC.

One hypothesis to explain this lack of washout in most cancers depicted with CEDM is that, unlike MRI, CEDM is a two-dimensional projection imaging technique and region-of-interest evaluations are made in a column of breast tissue that is the summation of enhancing tumor and enhancing surrounding normal breast parenchyma (5).

Jong et al. (2003), have performed temporal CEDM on 22 patients with suspect abnormalities found on conventional mammography or ultrasound. The results showed the ability of temporal CEDM to show cancers and suggested a potential to identify cancers in dense breasts (4). Another study carried by Dromain et al. (2006) concluded from a 20-patient study that temporal CEDM has the potential to depict angiogenesis. The study was on patients with malignant findings only, and detected contrast enhancement in 80% of the lesions.

A more extended temporal CEDM study by Diekmann et al. (2007) performed on 75 patients with 85 lesions compared the performance of conventional mammography alone versus temporal CEDM as an adjunct to conventional mammography. The results indicated an improvement in the sensitivity and specificity when adding temporal CEDM to the conventional mammography. However, several limitations affect temporal CEDM: the long examination and breast compression time contribute to patient discomfort and increase the probability of patient motion, generating artifacts on the subtracted images; moreover, only one view per breast can be acquired for a single injection of contrast medium. In addition to this, there has been no proof that the information provided by the contrast agent uptake kinetics is clinically useful. Also no correlation could be found between the contrast enhancement pattern and the malignant nature of the lesion. Hence, it appeared that the diagnostically relevant information was mainly given by the morphology and intensity of the contrast agent uptake (6).

In our study, CEDM examinations were performed using a dual-energy technique.

One preliminary clinical study using the dual-energy technique has been published. Lewin and colleagues (7) examined 26 women (14 with malignant lesions and 12 with benign lesions) scheduled for breast biopsy with a pre- and post-contrast MLO acquisition. Twelve of the 13 invasive carcinomas demonstrated strong or moderate enhancement, and one demonstrated weak enhancement. Five of these invasive cancers were not detected on conventional MX. Of the 12 benign lesions, 10 demonstrated no enhancement and two demonstrated weak enhancement on CEDM images. Lewin's study based on the dual-energy method showed enhancement in 92% of the malignant lesions and in 16.6% of the benign lesions (7). No quantification of the performance of the method was performed in this study, because of the restricted number of recruited patients (3).

Another extended dual energy CEDM performed by Dromain et al. (2011) to assess the diagnostic accuracy of CEDM as an adjunct to mammography versus mammography alone and versus mammography plus ultrasound on 120 women with 142 suspect findings on mammography and/or ultrasound underwent CEDM. There were 80 malignant, 50 benign and 3 pre-cancerous lesions (1 case of atypical hyperplasia and 2 cases of lobular carcinoma in situ). CEDM Enhancement was observed in 74 out of 80 malignant lesions. This study showed that sensitivity was higher for MX + CEDM than it was for MX (93% vs. 78%) with no loss

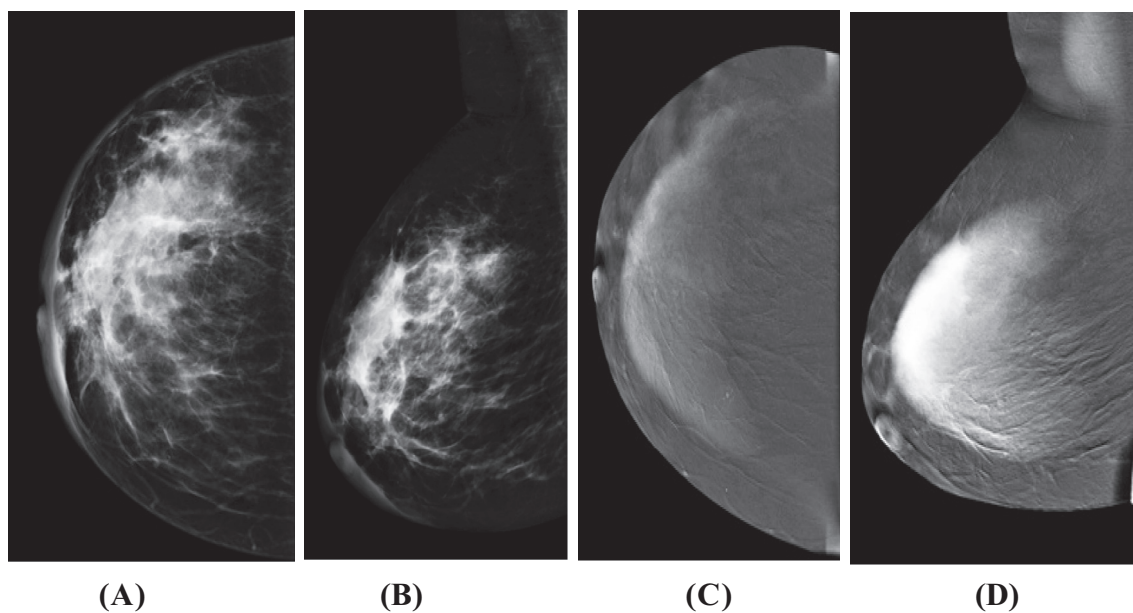


Fig. 5 (case 4): A female patient 44 year-old, complains of diffuse right breast edema, redness and hotness. Digital mammogram CC and MLO (A&B) showing edematous breast with diffuse increased density. CEMM CC & MLO (C&D) showing diffuse parenchymal enhancement with no masses. Pathology was peri-ductal mastitis.

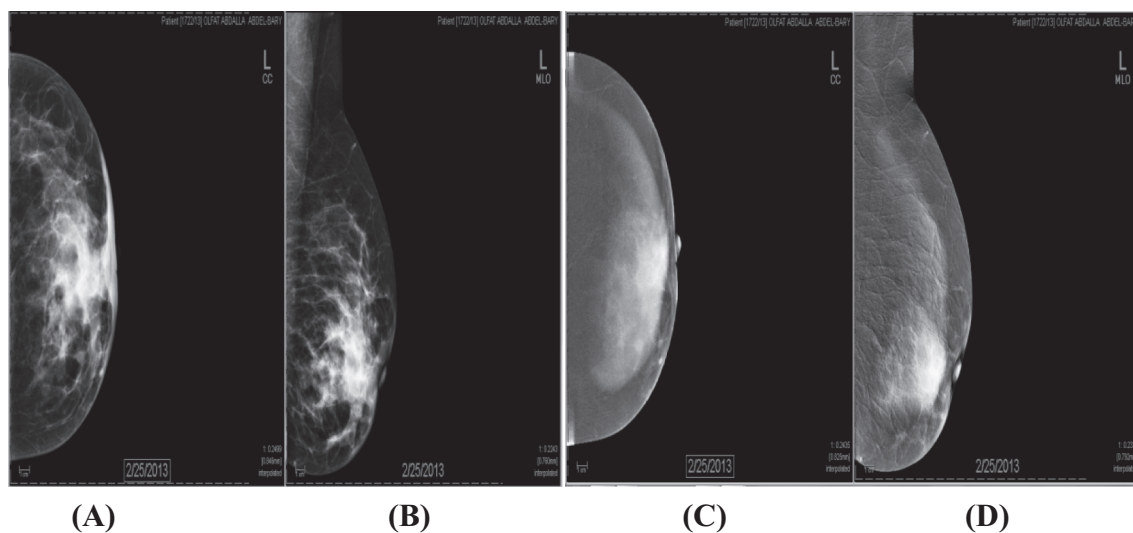


Fig. 6 (case 5): A female patient 37 year-old, complains of left breast edema and lump. Digital mammogram CC and MLO (A&B) showing edematous breast with increased retroareolar density. CEMM CC & MLO (C&D) showing enhancing retroareolar area with ring like or cystic changes seen within. Pathology was noncaseating granulomatous mastitis.

in specificity. Moreover all 23 multifocal lesions were correctly detected by MX + CEDM vs. 16 and 15 lesions by MX and US respectively. Dromain, et al. (2011) confirmed that the initial clinical results show that CEDM has better diagnostic accuracy than mammography alone and combined mammography and ultrasound (3).

In our study, as our inclusion criteria were limited to women with edematous breasts, our results showed significant increase in sensitivity of CEDM compared to MX alone, as it is well known that highly dense breast parenchyma alters the mammographic sensitivity.

Thus concurring with most of the previously published studies for CEDM, for example (3,8), who in turn stated that

the increase in sensitivity of cancer detection with CEDM is highly pronounced in dense breast parenchyma.

We have further demonstrated that by utilizing CEDM, contrast agent uptake was noted in all pathologically proven malignant lesions. Compared with mammography alone, CEDM significantly increased the sensitivity and the specificity, thus allowing a significant reduction in the false negatives.

CEDM is similar in concept to enhanced breast MR imaging and could potentially be applicable in situations in which MR imaging is currently used. Such situations include detection of a primary breast cancer in a woman with a positive axillary lymph node and determination of the extent of disease

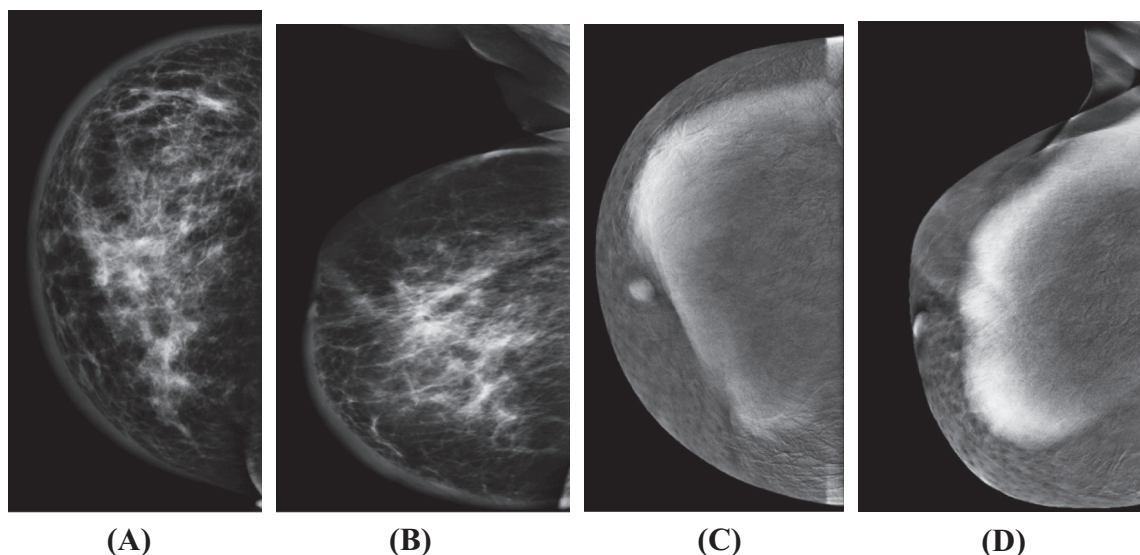


Fig. 7 (case 6): A female patient 52 year-old developed right breast edema after conservative breast surgery. Digital mammogram CC and MLO (A&B) showing edematous breast with increased parenchymatous density and no definite lesions. CESM CC & MLO (C&D) showing no abnormally enhancing areas. Pathology was scar tissue with no recurrence.

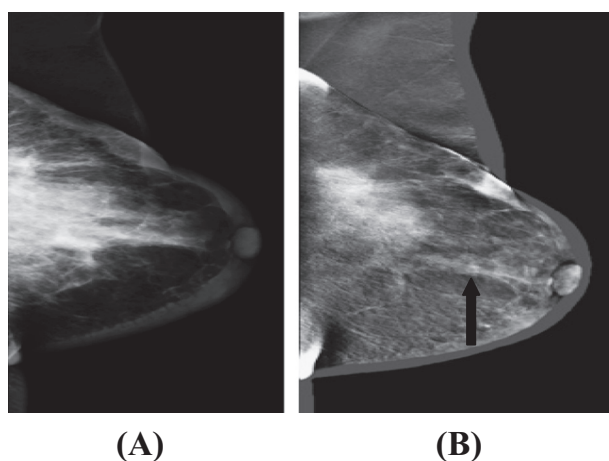


Fig. 8 (case 7): A female patient 49 year-old, underwent CBS 2 years ago for IDC, ended chemo and radiotherapy on follow-up. Digital mammogram MLO (A) showing edematous breast with central increased density. CESM MLO (B) showing central enhancing soft tissue mass with evident intraductal extension (arrowed). Pathology was recurrent IDC.

in cases of known cancer, as well as problem solving in cases of mammographic findings that were not depicted in additional mammograms or US scans (7).

In our study CEDM revealed to be a good negative test for exclusion of the underlying breast lesions in edematous breasts in cases of metastatic axillary lymph nodes, while being a good positive test in delineation of masses obscured by condensed parenchymal tissue. MX alone can detect abnormality in 20/25 malignant breast edema compared to 22/25 detected by CEDM. Two of which were false negative cases owing to edema caused by lymphatic obstruction secondary to nodal metastasis.

Similarly, a study carried by Saad et al. (2012) at the National Cancer Institute, Cairo University included 60

patients with mammographically dense breast parenchyma, of which 14 had edematous breast changes. They noted that there was a significant increase in the detection of lesions and better assessment of the local extent of the disease in these patients with breast edema using CEDM. Of the 14 cases with edematous breast changes, CEDM placed 13 cases in the correct BI-RADS category versus 8 cases with MX alone. More lesions were detected by CEDM than by MX alone or by MX + US. CEDM allowed the diagnosis of multifocal/multi-centric disease in 5 out of the 14 cases, versus 1 and 3 cases by MX alone and US respectively. They conclude that sensitivity was higher for CEDM than it was for MX + US (97.7% vs. 93.2%), while specificity for CEDM was lower than it was for MX + US (50% vs. 75%) (9).

We have managed to demonstrate the level of accuracy of CEDM in detection of multicentric lesions, as CEDM has managed to depict all multicentric lesions in eight patients which were confirmed later by pathological analysis as IDC lesions, thus giving a (100%) detection by MX + CEDM, versus 3 (37.5%) and 7 (87.5%) detected by mammography alone and ultrasound respectively.

In our study, the overall sensitivity of CEDM proved to be 95% vs. 88% for US, while specificity for CEDM was 73% vs. 80% for US.

Axillary lymphadenopathies are the single most important prognostic factor for operable breast cancer. Ultrasound is more accurate than both the physical examination and mammography in identifying metastatic axillary lymph nodes (10).

Benign lymph nodes usually present regular, oval or strip shape on the ultrasonic images, and hyperechoic medulla surrounded by the hypoechoic cortex. Longitudinal/transverse axis ratio (The L/T ratio) of the benign lymph nodes is usually above 2. The L/T ratio of the malignant ones is commonly below 2. In most of the malignant lymph nodes, the medulla echo becomes narrow and sometimes disappears (11).

As the metastatic axillary lymph nodes are important frequent causes of breast edema, utilizing ultrasound in our study revealed a higher sensitivity for detection of axillary nodal

pathology as well as higher specificity particularly in evaluation of axillary lymph nodes regarding sonographic evidence of malignant nodal invasion such as their morphological changes as well as preservation or effacement of their hyperechoic medulla.

In our study axillary nodal pathology was detected by US in 22 cases, and 20/22 showed suspicious malignant invasion which proved pathologically to be metastatic. However, only 2 cases showed suspicious criteria on MX alone, in comparison with the delineation of abnormal enhancement of axillary LNs in 4 cases, by CEDM.

CEDM could be used to monitor the response to chemotherapy. Treatment for women presenting with locally advanced breast cancer includes neoadjuvant chemotherapy with a decrease in tumor size obtained in as many as 91% of patients. Shrinkage or disappearance of the tumor after neoadjuvant chemotherapy predicts a good outcome. CEDM with its ability to demonstrate both morphology and tumor enhancement could be beneficial in the assessment of treatment response. However, its accuracy of determination of the chemotherapeutic response should be evaluated since underestimation of tumor response may be caused by the presence of therapy-induced enhancing lesions, such as fibrosis, necrosis and inflammation (12).

Our study has shown that CEDM allowed an accurate size evaluation of residual active tumoral tissue in two cases of postneoadjuvant chemotherapy with available data of the histological size of lesions after MRM.

As postulated by previous studies, CEDM can be used in the assessment of residual and recurrent disease. Indeed, the diagnosis of residual and recurrent disease is often difficult because of post-surgical and post-radiation changes (12).

This has been consistent with our findings, as CEDM has been perceived as substantially aiding in differentiation of recurrent enhancing tumoral tissue, from scar tissue in post-operative edematous breasts, with higher specificity compared to MX + US.

Advantages of contrast-enhanced digital mammography, which may point to its potential for wider use, compared to MRI, include its relatively low cost and it being less time consuming. The higher resolution guaranteed by the mammography system used is another point in favor of contrast mammography (8).

Dual-energy CEDM presents the unique ability to bring functional information in bilateral examinations of the breast with potentially only one contrast agent injection. It offers an immediate availability in the mammography suite without new appointment and without loss of time. Furthermore, no special training of the technologist is needed for positioning the patient and for the acquisition of images. Dual-energy CEDM examination is well accepted by patients, pleased to have a complete assessment without remaining questionable findings at the end of the day. It is a fast imaging technique that provides a direct correlation with conventional mammograms. In addition, subtracted CEDM images are very easy and fast to interpret by the radiologists and to understand by the oncologist and the surgeons (13). CESM may also be a useful guide for biopsy and accurately detects lesions in mammographically dense breasts (14).

5. Conclusion

Dual-energy contrast-enhanced digital mammography is a useful technique in identification of lesions in mammographically dense edematous breasts and capable of demonstrating lesions that are not visible by standard mammography. It serves as a promising means of follow-up of cases presenting by edema after conservative breast surgery and chemotherapy.

Conflict of interest

Authors have no conflict of interest.

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