

REVIEW

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Contrast-enhanced mammography in comparison with dynamic contrast-enhanced MRI: which modality is appropriate for whom?

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Abstract

Background: Dynamic contrast-enhanced MRI (DCE-MRI) is a revolution regarding screening and diagnosis of breast cancer. Yet, sometimes it is not the appropriate choice of imaging since the examination needs to be scheduled and may take place in another department. Contrast-enhanced mammography (CEM) is contrast-based digital mammogram, and consequently, it has emerged as a potential and promising replacer to DCE-MRI.

Main body of the abstract: There is a frequently asked question during the multidisciplinary breast cancer tumor boards is: which modality is more appropriate to be used in each clinical scenario? This article provided a detailed understanding of these two modalities in order to achieve a successful implementation of them into the clinical practice. Which modality to start with, in the context of the *detection* (screening) followed by characterization or *diagnosis* of the identified lesions? What is the appropriate application of both modalities in *local staging* and *follow-up*? All of these issues would be discussed in this article.

Short conclusion: MRI is a safe tool for breast imaging and has a superior diagnostic performance compared to CEM. However, CEM is getting close: this lies in its accessibility, short-time procedure, requirement of less training and feasibility to standardize.

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

Background

In the past few years, the volume of breast imaging modalities has grown exponentially and has undergone profound transformation, and thus, implementing a sound practice has become a real challenge [1]. At present, the challenge in breast imaging is not only about how to diagnose the causes behind breast symptoms, but it is also about how to apply the best practice to do so.

The success of breast imaging is the ability to choose the most appropriate imaging modality for the patient

and this modality has to be convenient, fast and cost-effective at the same time.

The introduction of dynamic contrast-enhanced MRI (DCE-MRI) has long been considered a breakthrough in breast imaging. DCE-MRI had provided an enhanced morphology and functional information of the breast which yielded a sensitivity of 95–100% when compared to ultrasound and mammography as reported in large-scale multicenter trials [1–3]. Despite the reported high diagnostic performance, DCE-MRI has limitations [4, 5], while breast MRI is the most sensitive method for diagnosis of breast cancer; however, its use in the setting of the clinical practice is often hampered by the idea that the MRI examination has its own schedule, and probably takes place in another department. This

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may postpone the final diagnosis and the management of the patients, and accordingly, affect the prognosis.

Contrast-enhanced mammography is an advanced application of the digital mammogram that uses contrast material and so it has emerged as a strong competitor to DCE-MRI [6–8]. The attractiveness of CEM lies behind its availability, as the patient diagnostic work-up is accomplished on the same day by using the same machine. Another important advantage of CEM is the better patient tolerance and preference when compared to MRI according to surveys that compared both modalities [4, 5].

There is a growing body of evidence that enhances the contribution of CEM as an alternative to DCE-MRI in some situations of breast cancer and this has sparked a controversy among the radiologists and the clinicians. In spite of the abundance of literature discussing both modalities individually or in comparison, there is a lack of consensus about their appropriate use.

In this manuscript, a brief account of the technique of CEM and DCE-MRI will be discussed and then summarized in Table 1 with the stress on the main advantages and drawbacks of each one of them. The controversy in the use of these modalities with regard to the *detection* (screening), *diagnosis* (characterization), *local staging* and *follow-up* will be also deliberated in detail.

Technique of CEM and DCE-MRI: advantages and drawbacks

CEM and DCE-MRI each one of them is dedicated to improve lesion conspicuity and diagnostic performance. This takes place with the aid of intravenous injection of a contrast media to highlight areas of abnormal angiogenesis in the breast lesions.

In MRI, the patient lies *prone* and multi-planar imaging is performed before and after contrast injection (gadolinium gadopentate). *Dynamic* post-contrast sequences are taken after the injection of the contrast agent for duration up to 8 min. The subtraction images are obtained by subtracting the *pre-contrast* images from the *post-contrast* ones [9].

Contrast-enhanced mammography is performed in the *erect* position. The two conventional mammography views of each breast are taken after a 3-min wait following a single injection of the contrast agent (iohexol, 350 mg I/mL). *No further dynamic* sequences are obtained. There is a pair of low- and high-energy images which is obtained during a single compression in the standard cranio-caudal and medio-lateral oblique views. A re-combined image is obtained as a result of subtracting the *post-contrast* low- and high-energy images to produce an image with adequate background subtraction, and consequently, maximizes the conspicuity of the enhancing breast lesions.

Table 1 Comparison between the strengths and the drawbacks of the contrast-based techniques used for breast imaging

	Contrast mammography	MRI protocol
Contrast	IV water soluble 1.5–2 mL/kg	IV Gadolinium Gadopentate 0.1 mmol/kg
Patient position	Erect	Prone
Sequences/positions	A pair of low- and high-energy images in the standard CC and MLO views	Pre-contrast T1 and T2WI Post-contrast dynamic and subtraction sequences
Dynamic sequences	No	Yes
Subtraction	Post-contrast low from high-energy images	Pre- from post-contrast images
Additional mammogram needed	No	Yes
Exam time	7–10 min	10–20 min
Interpretation time	Faster than MRI	10 min
Irradiation exposure	Yes	No
Contraindications	Pregnancy Renal impairment Allergy to contrast medium	Pregnancy Renal impairment Claustrophobia Unable to lie prone Incompatible devices Body weight Allergy with known anaphylactic shock (less common than CEM)
Risk from contrast	Allergy	No reported significant risk
Incorporation into daily practice	Yes	No
Cost	Low cost	Higher cost (as the used contrast media is expensive, the printed number of films is higher, the duration of the machine exhaustion is longer and an additional cost of mammogram may be needed)

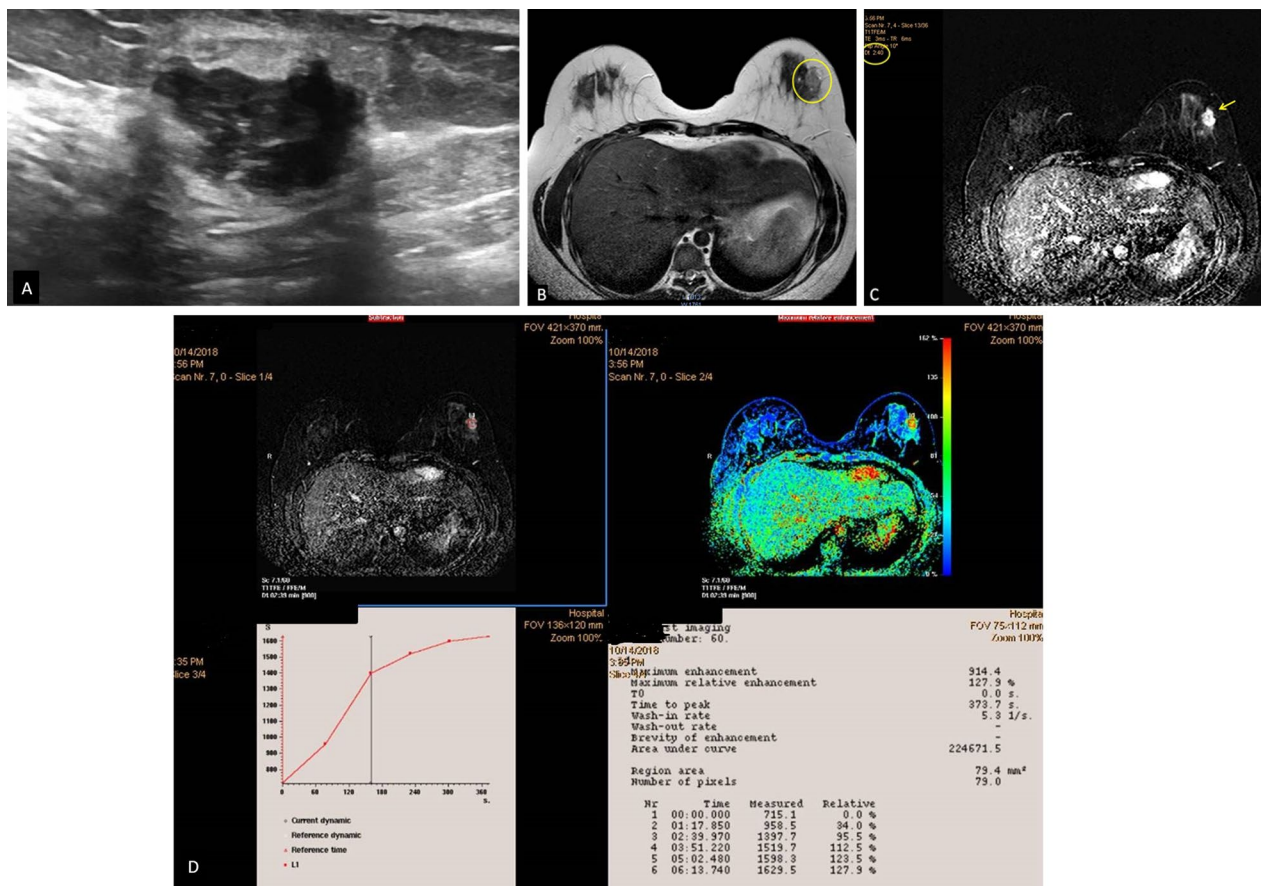


Fig. 1 Young patient, high risk, 31 years old. **a** Ultrasound gray scale image that displayed an oval-shaped solid mass with suspicious infiltrative presentation and irregular borders and accordingly was given as BI-RADS 4 category. **b** Pre-contrast T2-weighted MR image that displayed lower outer solid breast mass (circle). **c** Post-contrast subtraction image (taken at 2 min.40 s, post-injection of contrast, circle) that showed suspicious early and heterogeneous contrast uptake of the left breast mass (arrow). According to the morphology descriptors of the MR images, the mass was irregular and showed intense contrast uptake; these criteria rendered the mass to be suspicious of malignancy (BI-RADS 4) and biopsy was requested. **d** The time/signal intensity curve showed type I pattern presented with early peak of the contrast uptake with a corresponding high signal intensity percentage of 96%. Examination of the removed specimen after surgery revealed an intracanalicular fibroadenoma surrounded with fibrofatty tissue with no evidence of malignancy

Contrast-enhanced mammography is less time-consuming, with a relatively lower cost than DCE-MRI. Patel et al. [8] stated that CEM is a cost-effective modality that could be an alternate to MRI. They stated that CEM can reduce both the direct and the indirect cost of the examination. The review discussed the marked reduction in the equipment (reaching up to 53%) and the staffing (reaching 59%) costs for CEM as compared to breast MRI. They calculated the cost of screening according to the Medicare rates, and they had found that the cost of screening with MRI is fourfolds higher than the cost of screening with CEM. Also, that screening with MRI mandates an additional regular digital mammogram which is not the case with CEM. In CEM, the low energy images serve as a substitute to the regular mammogram.

The classic MRI acquisition takes approximately 30 min, whereas CEM requires about 7–10 min. The latter examination is better tolerated by patients being due to its short procedure time, and the less probability of claustrophobia from the device [4, 5, 8].

MRI also requires a longer interpretation time of the scanned images than CEM [8, 10].

All these factors have rendered CEM to be easily incorporated into the daily workflow [11].

To overcome the above-mentioned MRI limitations, the abbreviated MRI protocol was introduced by Kuhl et al. [11]. The rationale behind the abbreviated protocols is to decrease the cost of MR technique, the acquisition time of the images (3 min) and the interpretation time (3 s). This eventually enhances the feasibility of MRI and

improves the patients' and physicians' acceptance to the idea of using MRI in the context of screening for breast cancer. According to Kuhl et al. [11], the diagnostic performance of the abbreviated protocol was equivalent to the full diagnostic protocol.

One major disadvantage of CEM is that the estimated radiation dose to the patient may be up to 81% higher than that for the standard 2D digital mammography. This varies according to the breast tissue thickness and density; however, the dose still remains within the permissible range [12–14]. Moreover, the risk of a severe adverse reaction to the used contrast medium in CEM is much higher (0.2–0.4%) as compared to gadolinium (0.001–0.01%) [15, 16].

Table 1 shows the summary of the variations of the technique, advantages and drawbacks of the CEM and the classic as well as the abbreviated MR protocols.

*Screening/detection

According to the recommendations of the *American College of Radiology* (ACR), the screening of the breast cancer should be tailored according to the individual's risk category. In general, the female population can be categorized into *average*, *moderate* and *high risk* [17].

Average-risk women have no specific risk of developing breast cancer (lifetime risk < 15%). *Moderate-risk* women are those with a lifetime risk of between 15 and 20%. They include women with biopsy results of an atypical epithelial proliferation, women with a personal history

of breast cancer, and women with heterogeneously or extremely dense breasts. *High-risk* women are defined as those with a lifetime risk for the development of breast cancer of 20–25% higher than the general population, and they include females with a genetic predisposition or those who have received mantle radiation between the ages of 10 to 30 years of age [18–20].

The high sensitivity of MRI as compared to mammography comes on the expense of a relatively low specificity with a consequent increase in patient anxiety and an increase in the number of recall rates and unnecessary biopsies. The reason for its low specificity is because of the overlap of contrast uptake by both benign and malignant mass lesions, Fig. 1.

On the other side, microcalcifications that constitute approximately 31% of identified lesions on screening mammogram and also low grade invasive cancers can be missed on MRI [21, 22]. In a study performed by Bennani-Baity et al. [22], 10% of the false negative MRI results were microcalcifications identified only on mammogram Fig. 2.

Up-to-date, there is no sufficient data to define the appropriate indications of CEM [23]. The use of CEM as a potential alternative to screening with breast MRI has been discussed in several studies as both modalities provide the same kind of information needed for breast imaging, Fig. 3a, b.

A recent study by Sung et al. [24] concluded that CEM has the potential to be used as an alternative screening modality for women of high risk of developing breast

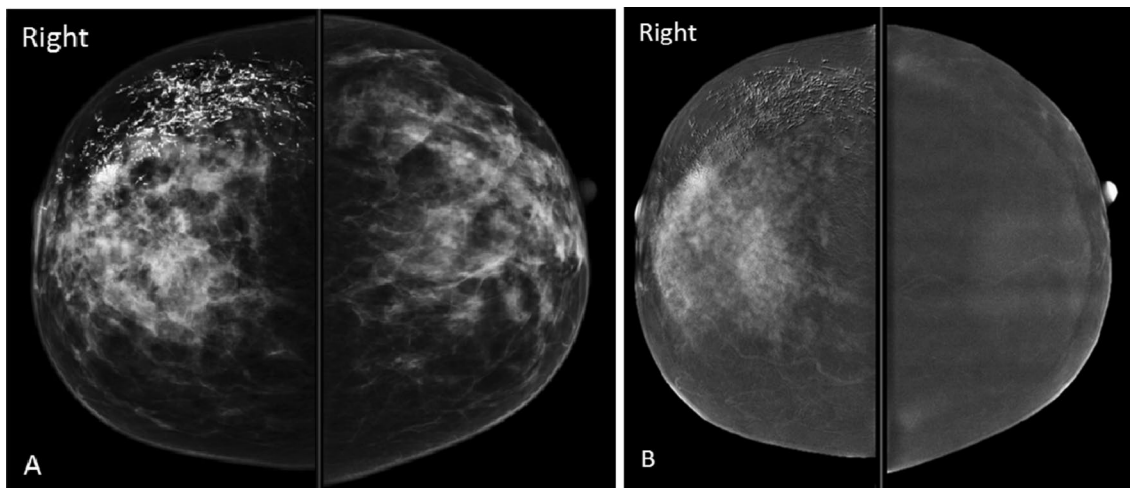


Fig. 2 A 35-year-old female that had a palpable left breast lump. **a** Bilateral digital mammogram craino-caudal views that showed right breast upper outer and central regional asymmetrical density and associate upper outer segmental clustered pleomorphic microcalcifications malignant looking masses that extent beyond the confine of the asymmetrical density. **b** CEM of both breasts craino-caudal view that showed heterogeneous enhancement of the right breast asymmetrical density, while the area involved with the clustered microcalcifications showed no contrast uptake. The case was proved to be invasive ductal carcinoma and ductal carcinoma in situ. CEM images provided information about the actual extent of the disease in the form of a vascular enhancing invasive component and the distribution of the non-enhancing component of calcifications. This can significantly change the management from breast-conservative surgery to mastectomy

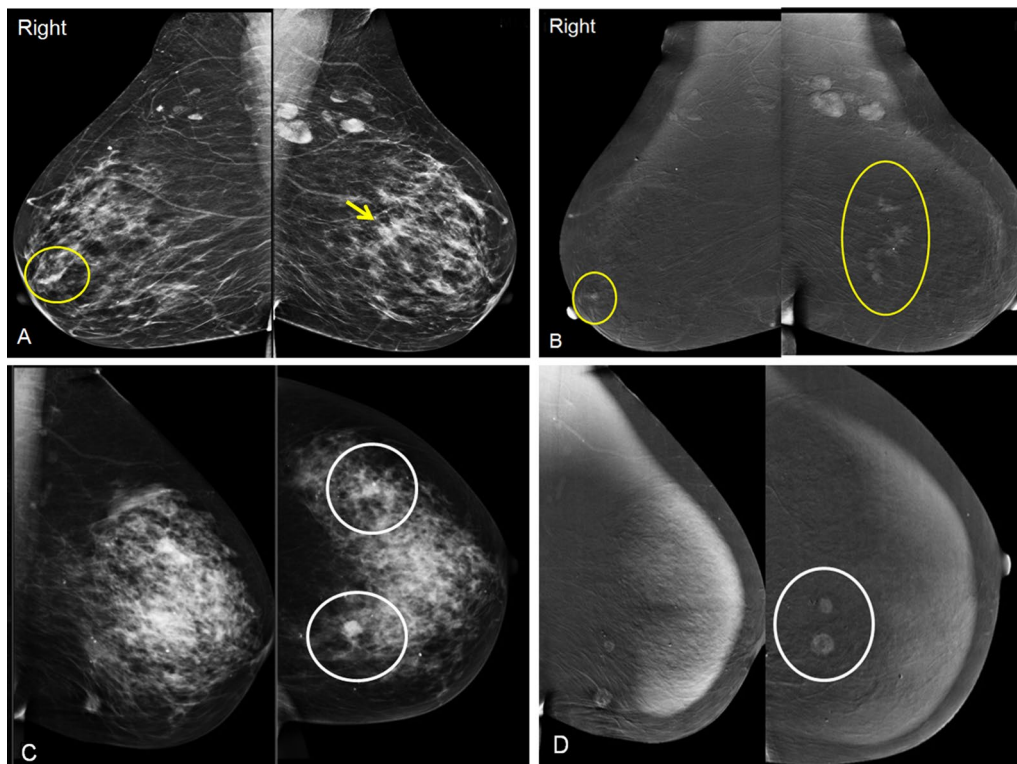


Fig. 3 Two cases: the first case was a 35-year-old female presented with left breast palpable lump. Biopsy revealed bilateral invasive ductal carcinoma. **a** Digital mammogram of both breasts MLO views that showed dense breasts with left breast deep central spiculated mass (BI-RADS 5) (arrow) and right breast retroareolar probably benign (BI-RADS 3) linear asymmetry (circle). **b** CEM of both breasts MLO views showed left breast mass that was seen on the mammogram and additional newly detected multiple adherent masses (BI-RADS 5- multifocal carcinoma) (circle). The right breast also presented retroareolar ill-defined focal nodule of contrast uptake corresponding to the linear opacity that was seen on the mammogram (BI-RADS 4 proved to be a contra-lateral carcinoma) (circle). The carcinomas were more obvious at the CEM. The second case was a 48-year-old high-risk female that needed a screening mammogram. Biopsy revealed left breast invasive ductal carcinoma. **c** Left-sided digital mammogram CC and MLO views that showed dense breast with upper outer and lower inner two ill-defined suspicious focal masses (circles). **d** CEM of the left breast confirmed the malignant suspicion of the left lower mass as it presented rim contrast uptake, moreover another similar focus was also noted nearby (i.e. multifocal not a unifocal carcinoma) (circle). The upper outer mass previously noted on the mammogram showed no contrast uptake (proved to be benign cyst by complementary ultrasound). CEM not only detected the breast masses, but also estimated the accurate extension of the cancer in spite of the high density of the breast parenchyma

cancer especially when MRI is unavailable or contra-indicated [24] (Fig. 3c, d). In another study performed by Xing et al. [25] on 263 breast lesions in 235 patients, they reported that the accuracy and the specificity of CEM were higher than those of MRI (81% and 89.5% for CEM versus 80.2% and 71.7% for MRI), and that the false-positive rate was lower (10.5% for CEM versus 19.8% for MRI) than MRI. The reported relatively low specificity and positive predictive value of DCE –MRI when used in screening have limited its wide-world use as a screening modality. In a study performed by Kuhl et al. [26] to investigate the prognostic significance of tissue changes that cause false-positive imaging diagnoses in MRI, they stated that not all false positive lesions are the same. They found that a significant fraction of lesions reported as false-positive diagnoses were

actually high-risk proliferative precancerous lesions. They thus proposed re-defining true positive lesions as those that impact further patient management and thus, proliferative lesions, especially those with atypia, can be considered true and not false positives, Fig. 4.

The use of CEM had been validated to recall screened cases in the RACER trial (Rapid access to contrast-enhanced spectral mammography in women recalled for the screening of the breast cancer) by Neeter et al. [27] that was published on 2019. The RACER trial is a prospective, multicenter, randomized controlled trial that aimed to assess whether we can replace the current standard of care (ultrasound and 3D digital breast tomosynthesis) of the re-called women that is suggested by CEM or not. They based their study on the results of the previously published literature which proved that CEM

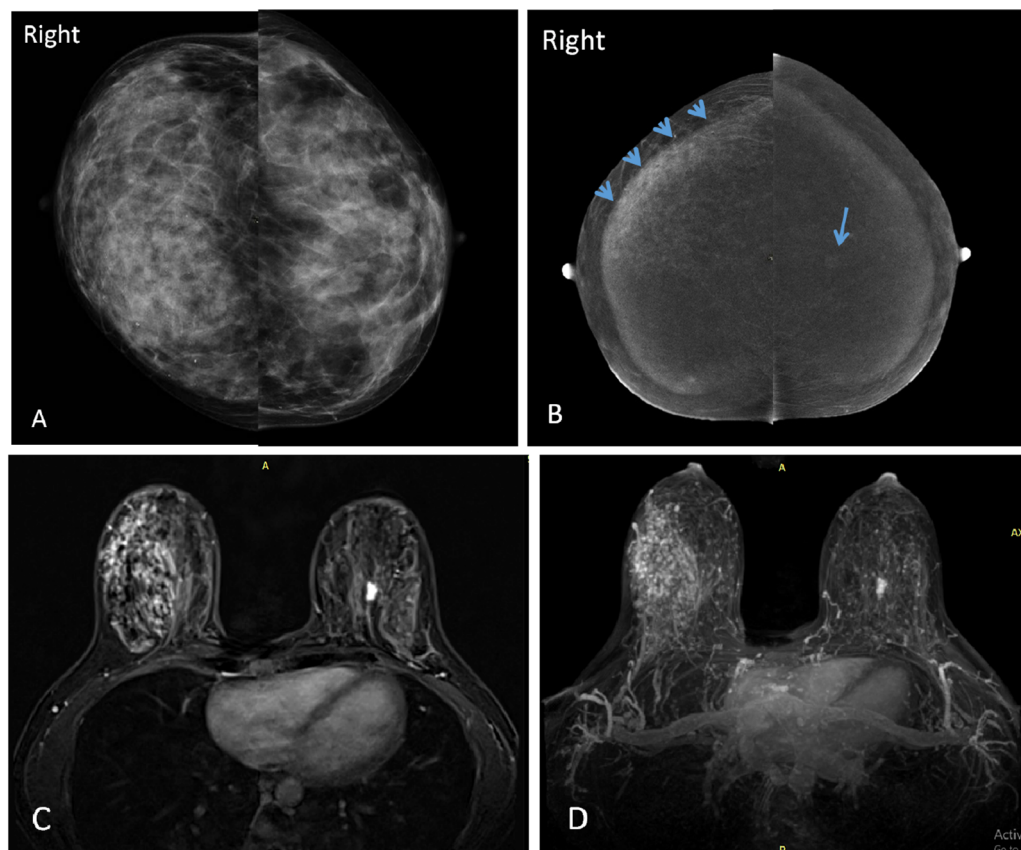


Fig. 4 A high-risk 35-year-old female with dense breasts. **a** Bilateral digital mammogram crano-caudal views that showed extremely dense breasts, BI-RADS zero. **b** Bilateral CEM, crano-caudal views that showed right breast lower outer faint asymmetrical regional non-mass contrast uptake of nodular pattern (arrow heads), BI-RADS 3 and left breast deep central faintly enhancing circumscribed focal tiny mass (long arrow), BI-RADS 2. **c** Early series of DCE-MRI and **d** Three-dimensional post-contrast maximum intensity projection images. According to MRI findings, there was right breast obvious non-mass clumped contrast uptake, suspicious of malignancy, BI-RADS 4c and left breast deep central benign looking tiny enhancing mass, BI-RADS 2. Based on MRI, biopsy was requested for the right breast non-mass enhancement, and the pathology result was benign proliferative disorder (fibrocystic changes and papillomatosis)

can reduce false-positive results while still maintaining high sensitivity [1, 6, 7, 12].

However, the role of CEM in screening is still debatable whether it should be used as a complementary tool in the diagnostic work-up of the re-called individuals or whether it can be used as a primary screening modality for individuals at high risk of developing breast cancer.

An important point to be considered is that the use of CEM in screening the high-risk individuals exposes them to multiple, repeated low-dose radiation which might lead to an increased risk of radiation-induced breast cancer [1, 28].

Screening with MRI alone without mammography in high-risk individuals is even recommended in some countries like Australia [29] and some European countries [30] to avoid radiation exposure of these individuals.

So, until further large-scale studies are performed and until there is a CEM-BIRADS lexicon that clearly

specifies the CEM indications and clinical applications, the use of CEM should be limited to the situations where MR imaging is unavailable or unfeasible.

*Lesion characterization and diagnosis

According to the 2013 MRI BIRADS lexicon, both the morphology descriptors and the kinematics have to be characterized for any identified breast lesion on MRI [31]. According to the morphology descriptors, lesions are classified into non-enhancing and enhancing. Non-enhancing lesions are almost always benign with few exceptions; the commonest of which is the low-grade ductal carcinoma in situ [32]. Enhancing lesions comprise malignant lesions as well as some benign breast lesions [12]. Enhancing lesions are then further classified into *foci* (<5 mm, non-space occupying), *mass* (space-occupying lesions), and *non-mass* (non-space occupying areas of enhancement). *Foci* are the most difficult to characterize.

Masses are further characterized by describing their shape (oval, rounded and irregular), margin (circumscribed and non-circumscribed), and internal enhancement pattern (homogeneous, heterogeneous, rim, dark septations). Oval or rounded masses with circumscribed margins that show homogeneous or dark septations are considered benign lesions, while irregular masses with non-circumscribed margins that show heterogeneous or rim enhancement are considered malignant. Non-mass lesions are further characterized by describing their distribution (focal, linear, segmental, regional, multiple regions and diffuse) and internal enhancement pattern (homogenous, heterogeneous, clumped and clustered ring). Using the dynamic sequences, a time/signal intensity curve is plotted and lesion kinematics can be described. According to lesion kinematics, three patterns are described: *type 1* continuously rising curve, *type 2*

borderline plateau curve and *type 3* early washout curves [33–35].

At present, there is no standardized approach for the interpretation of the breast lesions on CEM [35]. Basically, the evaluation of CEM examination requires the combined review of both the low-energy and the post-contrast subtraction images [6].

The low-energy images are identical to the standard mammography images and are thus interpreted according to the 2013, mammography BIRADS lexicon [36].

According to the mammography BIRADS lexicon [36], to characterize masses, the shape, margin and density are to be described. Rounded or oval masses with circumscribed margins and low density are considered benign, while irregular masses with indistinct or speculated margins and high density are considered malignant. Characterization of the breast calcification includes the morphology (benign as vascular, dermal, milk of calcium,

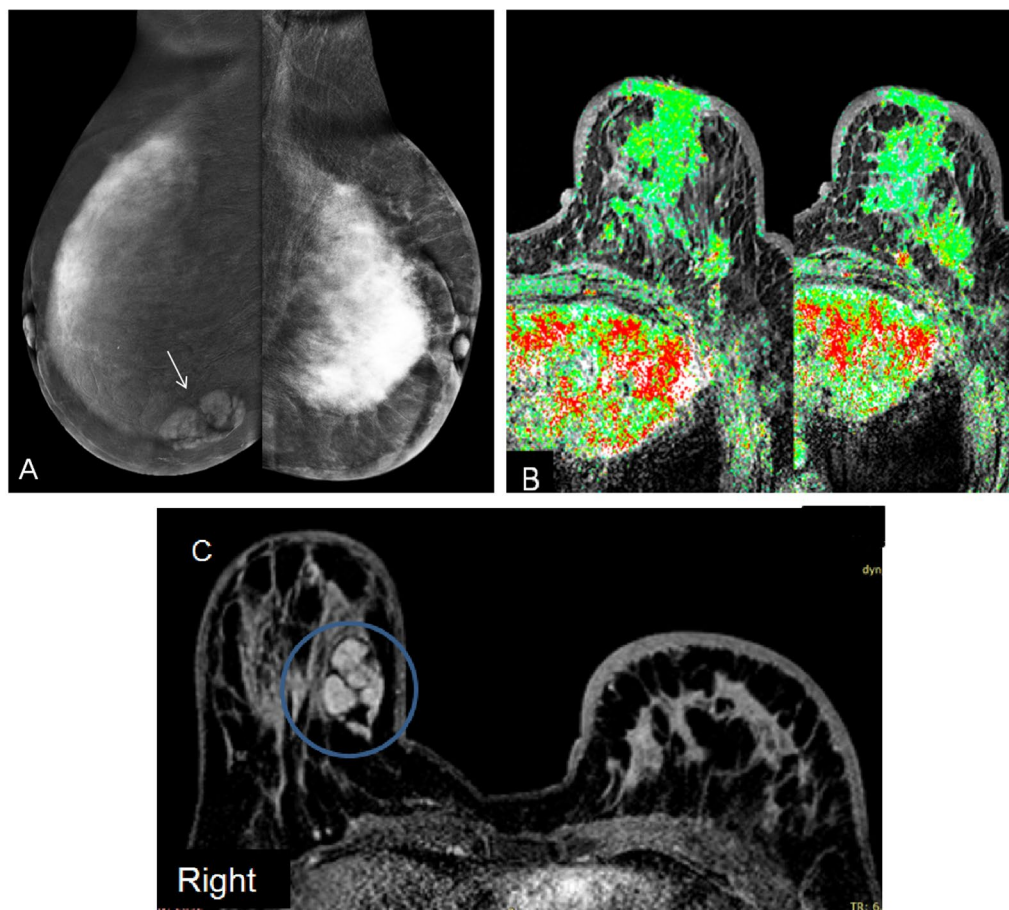


Fig. 5 Bilateral breast lesions; right fibroadenoma and left locally advanced carcinoma. **a** Bilateral CEM medio-lateral views that showed right breast lower inner mass of oval shape, circumscribed borders and dark internal septations (arrow) and left breast regional asymmetrical non-mass enhancement of clumped enhancement pattern. **b** Color mapping post-contrast MR image that showed malignant-looking soft tissue infiltration of the left breast. **c** Post-contrast MR image that displayed right breast mass with characteristics of fibroadenoma. CEM and post-contrast MR images showed comparable morphology descriptors for both benign and malignant breast pathologies

large linear, pop corn, dystrophic, punctate, ring and suture calcifications or suspicious/malignant as coarse heterogeneous, amorphous calcifications, fine pleomorphic and linear or branched linear calcifications) and the distribution (diffuse, regional, grouped, linear, or segmental).

The recombined images are evaluated to add-on the value of the low-energy images and correlate them with the characteristics of the contrast enhanced areas. Such action had the privilege of correlating focal distortion or the subtle enhancement that can be easily missed with areas of microcalcifications detected on the low-energy images [6].

A few small-scale publications have analyzed the correlation between the degree of enhancement on CEM and the tumor histological type [37, 38]. In a study by Kamal et al. [39], there were a confirmation on the feasibility to apply the MRI morphology descriptors for the characterization of breast lesions detected on CEM, Fig. 5 with the exception of the rim and the clustered ring patterns of contrast uptake; as these patterns were sometimes seen with breast abscesses, infected cysts and granulomatous mastitis and so eventually not specific for spotting the malignancy on CEM.

MRI had an advantage over CEM by its ability to characterize the fluid content within rim enhancing lesions on the T2- and T2-fat suppressed weighted images and thus could be used more often to suggest benign pathology rather than to exclude carcinoma [39].

On the other side, sometimes the performance of the CEM could be limited due to some technical and positioning errors. Non-mass contrast uptake sometimes is not that obvious and unless the breast is not dense, it could be misinterpreted as background contrast uptake (Fig. 4).

Missed cancers are more frequently located at the deep pre-pectoral region, the infra-mammary fold, the upper inner quadrant or deep at the axillary tail [40–42]. Breast implants can also impede the visualization of breast lesions on CEM. The breasts have to be carefully compressed, and the implant is to be displaced posterior to be able to see lesions within the breast parenchyma without rupturing the implant [43, 44].

So, for evaluation of the breast implants and confirm or exclude coexisting breast lesion, diagnosis of the breast lesions that are presented with inflammatory features and those that are located in the mammography hidden areas, it is recommended to use MRI breast instead of CEM to avoid missed and/ or misinterpreted breast lesions.

***Cancer staging before surgery**

Staging is a way of classifying breast cancer based on how large the cancer is and how far has it spread. In

other words, it describes the extent of the disease. Pre-operative staging is essential for treatment planning, and it helps in predicting the prognosis of the disease. The commonest used staging system is the tumor-node-metastasis (TNM) system proposed by the American Joint Committee for Cancer (AJCC). The latest update of the TNM staging system (8th edition) was declared in 2017 [45, 46]. In the new edition, the biomarkers are incorporated into the old anatomic TNM staging system if the immuno-histochemical examinations are available [47]. Such incorporation is needed to involve the impact of gene-expression profiling on the biology of the breast cancer [46].

Effective management depends on the accuracy of the pre-surgical assessment for the extent of the disease. The measurement of the tumor size and ascertaining multifocal or multicentric disease are essential items that have to be evaluated before deciding whether the patient will be prepared to mastectomy or breast conservation surgery.

It was proved that MRI is more accurate than conventional imaging examinations in the evaluation of the tumor extension and the detection of multifocal, multicentric and contralateral disease [47–50]. MRI is also highly sensitive in depicting chest wall infiltration which is identified on MRI as intrasubstance serratus anterior, intercostal muscles or rib infiltration.

However, from another point of view, some studies raised concerns about the low specificity of MRI and the consequent increase in the number of unnecessary extensive surgeries [34, 51].

Several studies have assessed the possibility of replacing MRI by CEM in the local staging of the cancer. These studies confirmed that both CEM and MRI were equivalently sensitive in detecting the index lesion size and in identifying additional lesions [52–54] (Fig. 3c, d). However, in a study performed by Helal et al. [55] that compared digital mammography, 3D digital breast tomosynthesis and CEM, the latter displayed the highest percentage regarding the underestimation of tumor sizes (10.2%) among these modalities. The underestimated lesions in their study were either spiculated masses or masses showing intra-ductal extension. Also, MRI is much superior to CEM in case of detection and characterization of the axillary lymph nodes, Fig. 6, and the assessment of the chest wall invasion; this is attributed to the physical limitation of mammography in imaging the axilla and chest wall [52–54, 56, 57].

So, CEM is cherished for the evaluation of the extent of the breast cancer and multiplicity and so it can replace MRI in the routine local staging of the breast cancer. Yet, MRI is still the examination of choice in the assessment of the immediate post-operative residual disease. Also, the use of CEM in estimating the size of markedly

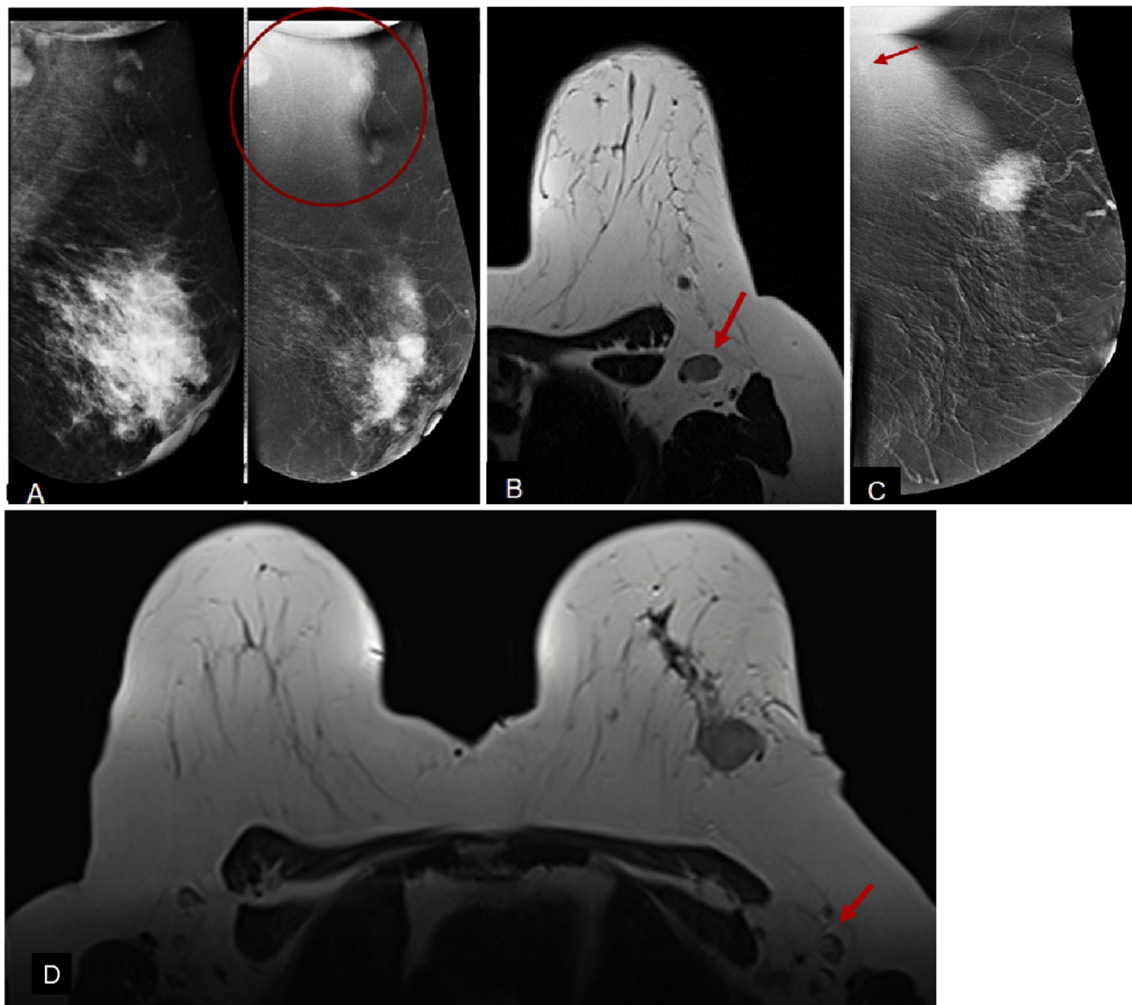


Fig. 6 Two different cases of primary breast carcinomas, (case 1 A and B, case 2 C and D). Digital mammograms and CEM medio-lateral views of breast carcinomas (a, c), the lymph nodes are noted at the mammograms (circles in (a) and arrow in (c)) but their differentiation are not clear on basis of the mammogram. On MR images (b, d), the malignant axillary node (arrow in B) could be easily discriminated from the benign one (arrow in d)

spiculated mass lesions, chest wall and skin infiltration and in the assessment of axillary lymph node status is still questionable.

*Follow up of the treated breast

With the development of breast cancer treatment regimens, the number of breast cancer survivors has increased. The follow-up of patients with treated breast cancer has posed an increasing workload on the breast imaging centers, and thus it has become essential to follow cost-effective regimens [58]. In the post-breast cancer surveillance, the patient follows one of four scenarios: (1) Patient presented with a *positive surgical margins* after breast cancer excision (2) *Asymptomatic* patient that require follow-up after surgical and medical

management (3) *Symptomatic* patient that showed up after surgical and medical management, and (4) Patients received *neo-adjuvant therapy*.

Immediate assessment of the treated breast after surgery for the presence of residual disease is often challenging because of the resultant inflammatory changes, operative bed seroma/hematoma, and scarring distortion, all of which may mimic residual malignancy [59, 60]. Although the role of CEM was assessed in some studies for the postoperative breast, its use in the immediate postoperative period has not yet been validated [61]. MRI has the ability to differentiate inflammatory collections and edema from residual malignancy [62].

Although there is no data to indicate that any imaging other than annual mammography and complementary



Fig. 7 Known case of left breast cancer post-mastectomy. **a** CEM of the right breast MLO and CC views that showed faint and vague contrast uptake at the lower portion of the breast (circle) that was not obvious at the CC view. **b** Further scanning by post-contrast MR imaging displayed evident focal area of non-mass enhancement easily depicted at the sagittal and axial reformatted 3D maximum intensity projection images (arrows). MRI was the modality that confirmed the possibility of contralateral carcinoma

(See figure on next page.)

Fig. 8 Two different cases: a case of right breast cancer post-conservative surgery and operative bed positive surgical margins. **a** Digital mammogram of both breasts MLO and CC views that demonstrated dense breasts and BI-RADS zero category of the mammogram. **b** CEM of the same views that showed operative bed numerous enhancing foci centered on the scar of the operative bed (circle) suggestive of recurrent carcinoma. The second case is a 53-year-old with pathologically proved triple negative invasive ductal carcinoma grade II. **c** Axial post-contrast MR imaging before chemotherapy that showed left breast enhancing mass (circle- proved carcinoma) and ipsilateral pathologically enlarged likely infiltrated axillary node (arrow). **d** Post-completion of the neo-adjuvant chemotherapy post-contrast MR image where there is almost complete resolution of the left breast carcinoma (arrow) and marked regression of the size of the ipsilateral lymph nodes (circle)

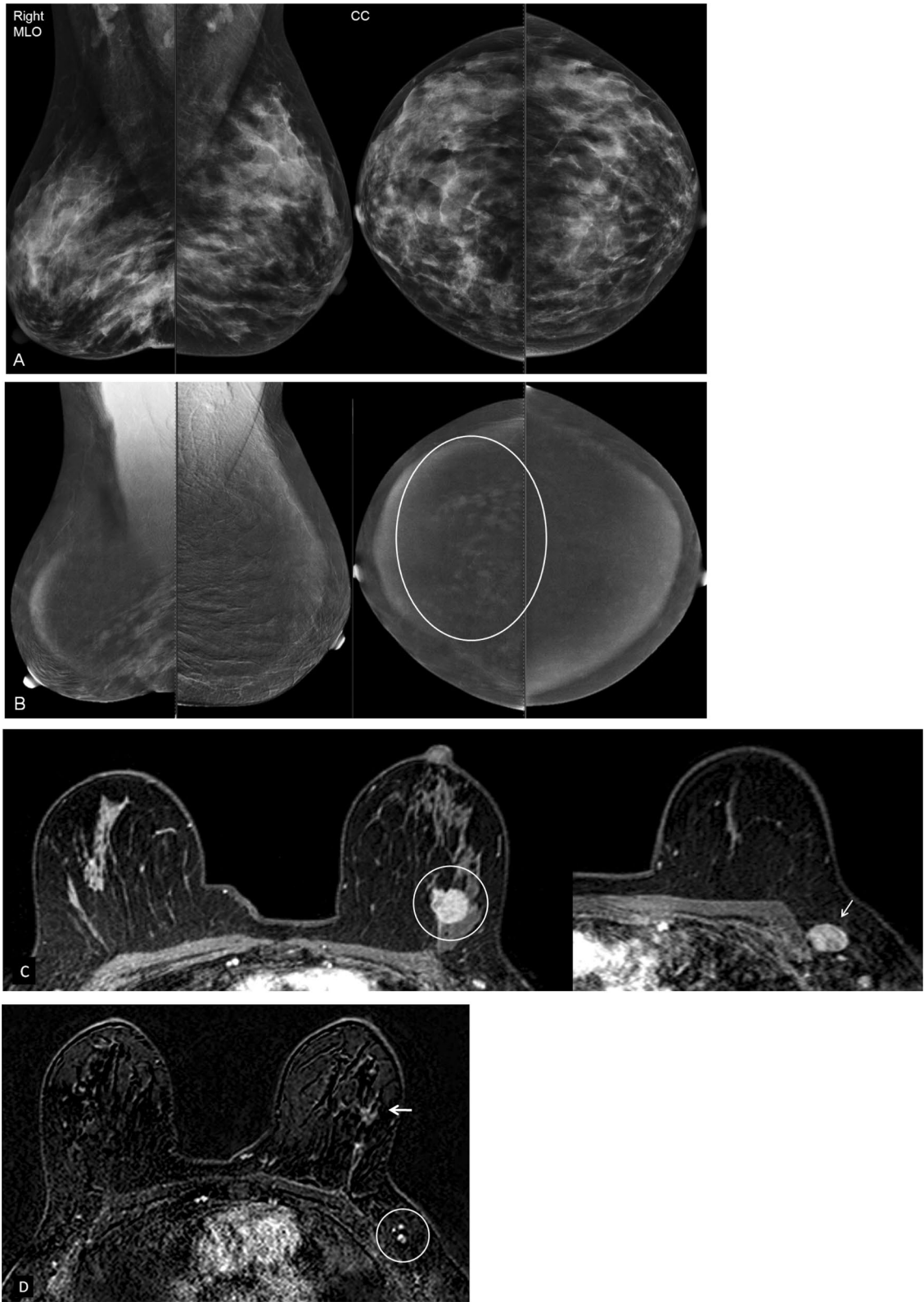


Fig. 8 (See legend on previous page.)

breast ultrasound points to a survival benefit in asymptomatic survivors, yet, the situation is different for symptomatic survivors or in those cases with positive clinical findings. In these cases, appropriate imaging should be immediately performed [63]. The aim of imaging in these patients is to detect ipsilateral recurrence or a new primary breast cancer in the treated or the contralateral breast so that conservative surgery or mastectomy ± reconstruction could be an option of management. In most of the cases, mammography and targeted ultrasound are enough to reach an accurate diagnosis. However, in patients with inconclusive findings and those with fixed implants, MRI is the modality of choice (Fig. 7). If no corresponding contrast enhancement is found on MRI, malignancy can be excluded with sufficient certainty, and the patient can be safely placed on a short-term follow-up study.

Few studies have been performed to test the validity to use CEM instead of MRI in the assessment of the symptomatic cases of breast cancer after surgery [61, 64] (Fig. 8a, b). Helal et al. [61] concluded that CEM is a credible technique that could be used in conjunction with the traditional mammogram to screen for cancer in the breast cancer patients which have been treated with surgery. However, sometimes the performance of the CEM is limited due to the inability to assess the mastectomy bed and the axillary node recurrence.

Neo-adjuvant chemotherapy (NAC) can induce tumor size reduction, improve the choice of the operation, and thus increase the probability of breast-conserving surgery [65]. During NAC, it is important to assess early tumor response so that treatment regimens can be appropriately tailored to obtain maximum tumor response. Imaging of the tumor response after completion of the course of the neo-adjuvant therapy can also provide valuable information about the extent of the residual tumor and enable better surgical plans to achieve a tumor-free margin. The absence of residual tumor cells in the primary tumor bed after NAC is strongly correlated with improved disease-free and consequently the overall patient survival [66, 67].

Dynamic contrast MRI has long been considered the best imaging modality for both monitoring tumor response to NAC and for the assessment of residual disease extent without competition (Fig. 8c, d). MRI expressed some disadvantages in the NAC context. MRI is highly sensitive to motion artifacts, and the examination is sometimes degraded by the metallic clips that are applied for the chemotherapy-responding tumors and eventually inadequate assessment of the residual tumor size may occur [65]. Moreover, the true extent of carcinomas presented with microcalcifications is not accurately defined using MRI (Fig. 2).

Iotti et al. [68] compared CEM and DCE-MRI in the evaluation of tumor response to NAC in a prospective study conducted on 54 women with breast cancer. Patients had undergone both CEM and MRI before, during and after NAC. They found that the size of the residual cancer measured by CEM and MRI were highly correlated, and they concluded that CEM was as reliable as MRI in assessing the response to NAC and identifying residual disease, and may be an alternative competent to MRI in case the latter modality was contraindicated or its availability was limited. In another study conducted by Barra et al. [69], they concluded that CEM was a feasible method to evaluate residual tumor size after NAC.

However, both modalities are not indicated for the routine annual follow-up of the asymptomatic breast cancer survivors.

Conclusions

CEM and MRI have many privileges but also there are flaws. CEM has shown comparable specificity to MRI so long the lesion is within the main confine of the breast. For the assessment of the extensive inflammatory/malignant breast lesions, deeply seated lesions and those located in the mammography hidden areas; MRI still takes the upper hand.

CEM is useful in the preoperative staging of breast cancer, post-treatment surveillance and the follow-up of patients who are receiving NAC.

The incorporation of CEM in screening high-risk individuals is still debatable.

There is no doubt about the quality of the MRI as a tool for breast imaging; it has a better safety profile (the contrast has less side effects and no risk of radiation induced cancer) and has a superior diagnostic performance compared to CEM. However, CEM is getting close; this lies in its accessibility, short-time procedure, requirement of less training and feasibility to standardize.

Abbreviations

DEC-MRI: Dynamic contrast-enhanced MR imaging; CEM: Contrast-enhanced mammogram; ACR: American College of Radiology; RACER: Rapid access to contrast-enhanced spectral mammography in women recalled for the screening of the breast cancer; BI-RADS: Breast imaging reading and data system; TNM: Tumor-node-metastasis; AJCC: American Joint Committee for Cancer; NAC: Neo-adjuvant chemotherapy.

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Authors' contributions

Guarantor of integrity of the entire study was done by KR. Study concepts and design were carried out by KR and MS. Literature research was done by MS, FA, EA and GM. None of them carried out clinical studies. Experimental studies / data analysis was carried out by MS, HM, FA and GM. None of them carried out statistical analysis. Manuscript preparation was done by KR, HM, EA and GM. Manuscript editing was done by KR, MS and HM. All authors read and approved the final manuscript.

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Availability of data and materials

The corresponding author is responsible on sending the used data and materials upon request.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of the Radiology Departments of an academic highly specialized multidisciplinary Hospital, and an informed written consent was taken from the patients that were included in the study. The committee's reference number is not applicable.

Consent for publication

All patients included in this research were legible; all of them were above 16 years of age. They gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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