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RESEARCH **Open Access**

A comparative study between the diagnostic performance of contrast-enhanced digital mammography and dynamic contrast-enhanced MRI in invasive lobular carcinoma of the breast

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Abstract

Background Invasive lobular carcinoma is the second most prevalent histological subtype of breast cancer after invasive duct carcinoma, with a reported increased incidence in the last two decades. It often presents with challenging imaging characteristics that lower the sensitivity of mammography in their detection and delineation of their extent. Moreover, an increased risk of having synchronous lesions in the same or opposite breast was reported in cases with invasive lobular carcinoma. This obviates the need for other imaging modalities, specifically contrast-enhanced imaging modalities, to improve early detection as well as allow precise determination of the extent of the disease. Our aim in this study was to compare the diagnostic performance of contrast-enhanced digital mammography and dynamic contrast-enhanced magnetic resonance imaging (MRI) in the local staging of invasive lobular carcinoma regarding the size, extensions, multiplicity and bilaterality.

Methods This study included 46 female patients with pathologically proven invasive lobular carcinoma. They underwent full-field digital mammography with a complementary ultrasound examination, contrast-enhanced digital mammography, and dynamic contrast-enhanced MRI. The findings encountered by the three imaging modalities were evaluated independently, and the results were compared with final histopathology.

Results In the current study, dynamic contrast-enhanced MRI study was the most sensitive modality in the detection of the index lesion, synchronous ipsilateral and contralateral lesions and achieved a sensitivity of 100% in each analysis as compared to contrast-enhanced digital mammography, which achieved a sensitivity of 97.8%, 85.7% and 80%, respectively. Regarding the assessment of the lesion extent to the surroundings, there was a tendency to overestimation by MRI examination.

Conclusions Although dynamic contrast-enhanced MRI is the most sensitive imaging modality for detecting the index lesion, multiplicity and bilaterality, contrast-enhanced digital mammography achieved comparable overall accuracy. Regarding the locoregional staging of invasive lobular carcinoma, there was a tendency for relative overestimation by MRI examination.

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Keywords Invasive lobular carcinoma, Contrast-enhanced digital mammography, Dynamic contrast-enhanced MRI

Background

Invasive lobular carcinoma (ILC) has a reported variable prevalence, accounting for 5–15% of all breast malignancies. There is a reported increased incidence in the last two decades, being the second most prevalent histological subtype after invasive duct carcinoma (IDC) [1, 2]. It originates from the lobular epithelium and is characterized by the lack of the adhesion protein E-cadherin. This results in a distinct diffuse growth pattern without inducing a significant desmoplastic reaction [3]. Most commonly it fails to form a palpable mass and manifests clinically with vague or absent clinical findings. Moreover, an increased risk of having synchronous lesions in the same or opposite breast is also present. This explains the difficulties encountered in diagnosing ILC, which is characterized by greater tumor size and advanced tumor stage at presentation as compared to IDC [4].

Invasive lobular carcinoma often presents with challenging imaging characteristics that may hinder its detection by screening imaging tools. The potential of conventional mammography and ultrasound is limited in the diagnosis of ILC, with a reported reduced diagnostic accuracy and sensitivity ranging from 57–81% to 5–70%, respectively [5]. The low sensitivity of mammography in the radiographic diagnosis of ILC has generated interest in other imaging modalities to improve early and more accurate detection as well as precise determination of the extent of the disease [6].

Other imaging techniques, such as breast MRI and contrast-enhanced digital mammography (CEDM), are more sensitive for detecting mammographically occult lesions. Compared with conventional mammography, magnetic resonance imaging (MRI) allows accurate estimation of the tumor size and more accurate detection of synchronous lesions in the same or contralateral breast. As a consequence, preoperative MRI significantly improved tumor staging accuracy and surgical planning and decreased re-excision rates through more appropriate oncologic resection [7, 8].

However, MRI has some limitations; in some studies, preoperative MRI was linked to an increase in mastectomies in ILC cases without affecting disease recurrence [9]. The reported reduced specificity of MRI can result in overtreatment (more extensive surgery procedures). Moreover, its limited availability and high cost warrant its use in selective cases [10].

Contrast-enhanced digital mammography is a promising imaging technique in the loco-regional preoperative staging and evaluation of disease extension for ILC, especially in the case of mass-enhancing lesions. Reported lower sensitivity was attributed to non-enhancing lesions or in cases presenting with non-mass enhancement. Also, the degree of enhancement of ILC on CEDM is reported to be weaker than IDC, and this means that weakly enhancing lesions may be malignant [11].

Our aim in this study was to compare the diagnostic performance of CEDM and dynamic contrast-enhanced MRI (DCE-MRI) in the local staging of ILC regarding the size, extensions, multiplicity, and bilaterality.

Methods

Patient demographics

This prospective study was conducted from February 2019 to August 2022 after obtaining approval from the ethics committee of our institute. One-hundred and seventy-five female patients with pathologically proven invasive lobular carcinoma were collected in this study. They were referred by the multidisciplinary team of our institute for diagnosis, local staging and premanagement evaluation. Patients who did not perform both contrast-enhanced modalities or had a contraindication to MRI were excluded from our study (*n*: 129). Finally, 46 patients who underwent both contrast-enhanced modalities (CEDM and DCE-MRI) were included in the study, and informed consent was obtained from them (Fig. 1). Among the included patients, 32 cases were presenting by unilateral palpable lumps, while 14 cases were referred for screening.

All the included patients underwent full-field digital mammography (FFDM) (Senographe Essential, GE Healthcare FFDM machine) with complementary ultrasound (LOGIQ ultrasound scanner, GE Healthcare) as a baseline examination. In 4/46 cases, negative mammographic and ultrasound results were found despite the worrisome clinical presentation of these cases; hence, the decision of contrast-enhanced study was taken for diagnosis. In the remaining 42 cases, and based on our institution protocol, contrast-enhanced studies were recommended after histopathological results of invasive lobular carcinoma in cases with breast density of category B, C, D, putting into consideration the reported likelihood of synchronous malignancy in the same or in the contralateral breasts. Accordingly, CEDM was initially requested for local staging and premanagement evaluation, considering its feasibility, preference and tolerance by the patients, and in selective equivocal cases,

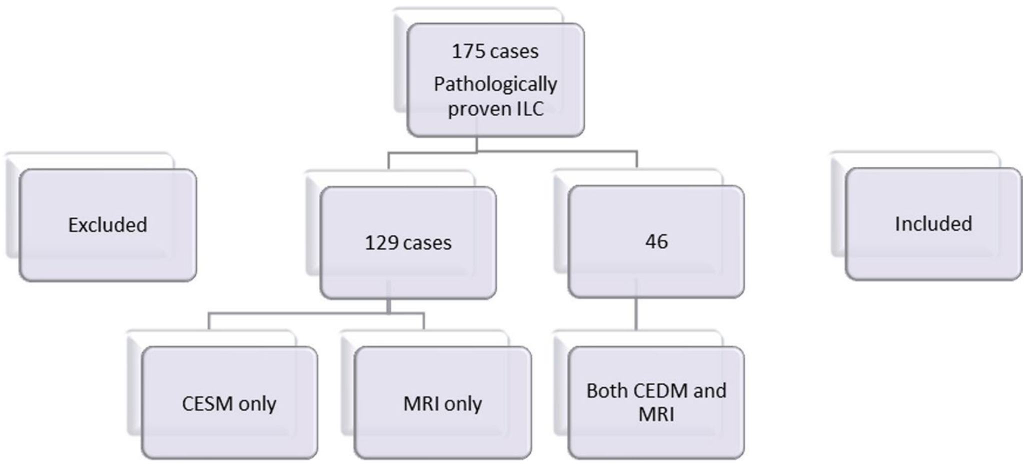

Fig. 1 A flowchart illustrating the selection of the study population, inclusion and exclusion criteria

DCE-MRI was then recommended according to the multidisciplinary team decision.

Contrast-enhanced digital mammography

During CEDM, a one-shot intravenous injection (of 1.5 mL/bodyweight of iodinated contrast agent) was performed with an injection rate of 3 mL/s followed by a 2-min delay before breast compression. Then, dual-energy CEDM image acquisition in the two standard positions (craniocaudal and mediolateral oblique views) was performed (GE Senographe DS Digital Mammography, USA). Low- and high-energy images were consecutively acquired in each view at intervals of no more than 20 s. Both low- and high-energy images were recombined and subtracted through appropriate image processing to obtain recombined enhanced images. This allowed reduced visibility of the parenchyma and highlighted the uptake of contrast agents.

Dynamic contrast-enhanced MRI

All the examinations were performed on a Siemens 1.5 T MRI system using a dedicated bilateral breast surface coil with the patient in the prone position. A precontrast series of axial T1-weighted turbo spin-echo (repetition time (TR)/time to echo (TE) = 307/4.6 ms), axial T2-weighted turbo spin-echo (TR/TE = 4.3 s/91 ms), axial short tau inversion recovery (STIR) (TR/TE = 5.2 s/71 ms; inversion time = 170 ms), diffusion sequences, and an apparent diffusion coefficient (ADC) map were established. Then a postcontrast dynamic series was done using six dynamic acquisitions after intravenous injection of 0.1 mmol/kg bodyweight of contrast material (gadolinium-diethylene tri amino pentaacetic acid; Gd-DTPA), using the dynamic THRIVE sequence (T1 high-resolution isotropic volumetric examination) (TR/TE = 5/2 ms).

Image analysis

Image analysis and interpretation of CEDM, and DCE-MRI examinations were done by two breast imaging radiologists with at least 10–15 years of experience in the field of breast imaging. They were blind to each other's analysis and other imaging findings. Re-evaluation was done in cases of disagreement, and agreement was achieved by consensus.

On both CEDM and DCE-MRI, the background parenchymal enhancement level was visually estimated. The extent of the lesion was assessed individually by each modality, including tumor size, extension to the skin, muscle or the nipple/areola complex. The presence of further lesions whether in the same or contralateral breast was also assessed.

Contrast-enhanced digital mammographic findings were evaluated using the recently published ACR BIRADS lexicon for CEDM (a supplement to American College of Radiology (ACR) BI-RADS® Mammography 2013). In low-energy images, findings were interpreted according to the mammography Breast-Imaging Reporting and Data System (BI-RADS) lexicon. In recombined images, the morphology of the enhancing abnormality was determined, whether mass, non-mass enhancement (NME) or enhancing asymmetry. The conspicuity of the lesion relative to the background enhancement was determined (low, moderate, high). Also, the extent of the enhancement was determined, whether partial enhancement, enhancement of the entire lesion, enhancement extent beyond the mammographic lesion or no enhancement.

Based on DCE-MRI BIRADS lexicon, the enhancing lesions were classified into mass, non-mass or foci. Lesions of mass enhancement were further evaluated for shape (round/oval or irregular), margin (circumscribed, not circumscribed or irregular), pattern (homogenous, heterogeneous, septations or ring enhancement) and intensity (faint, mild, moderate and intense). Lesions of NME were evaluated for distribution (focal, linear, segmental, regional, multiregional or diffuse), pattern (homogenous, heterogeneous, clustered and clumped) and intensity (faint, mild, moderate and intense).

The ability to detect and categorize the index lesion as suspicious based on its morphology and enhancement pattern, as well as the detection of multiplicity and bilaterality, was assessed in the 46 patients. The size of the enhancing lesions (whether mass or non-mass enhancement) and the relationship with the nipple, skin and pectoralis muscle were analyzed in 30/46 (65. 2%) cases, while 16/46 (34.8%) cases were excluded from such analysis as they were candidates for neoadjuvant chemotherapy (NACT) or palliative treatment. In dynamic MRI, a kinetic curve assessment was performed for each enhancing lesion. Also, all lesions were assessed for their signal intensity on different sequences, including T1, T2, STIR, diffusion-weighted imaging (DWI) and ADC maps.

The results were then compared to the pathology results obtained by core biopsy (in all cases) and following a surgical procedure (in 30 cases), which were used as the gold standard. The presence of multiple lesions was confirmed on the basis of final postoperative pathological results in 15/21 cases of which 6 cases performed core biopsy as well to exclude multicentricity which might cause alteration in the management plan. In cases who were eligible for initial NACT (6/21), multiple malignant lesions were confirmed based on their radiological response in follow-up examinations after clip insertion.

Statistical analysis

Statistical analysis was conducted using SPSS 22nd edition. Numeric variables were presented in mean standard deviation, and categorical variables were presented in frequency and percentages and were compared using the Chi-square test. A paired comparison of categorical data was conducted using Friedman's test. Sensitivity and specificity were calculated using 2×2 contingency tables. Any p value less than 0.05 was deemed significant. The interobserver agreement was tested using the Kappa measure of agreement (< 0.20; poor, 0.21–0.40; fair, 0.41–0.60, moderate, 0.61–0.80; good, 0.81–1.00; very good).

Table 1 Age distribution of the patients participating in the study

	Mean	Standard deviation	Median	Minimum	Maximum
Age	49.29	9.9	47.0	30.0	71.00

Table 2 Final histopathological diagnosis of the studied cases

Final diagnosis	Count	Percentage (%)
Pure ILC	22	47.8
ILC and LCIS	9	19.6
ILC and DCIS	3	6.5
ILC, LCIS, and DCIS	4	8.7
Mixed ILC and IDC	8	17.4

ILC Invasive lobular carcinoma, *LCIS* lobular carcinoma in situ, *DCIS* ductal carcinoma in situ, *IDC* invasive duct carcinoma

Results

This study included 46 patients; each had an index lesion that was pathologically proved as an invasive lobular carcinoma. Their ages ranged from 30 to 71 years (mean age: 49.4, standard deviation (SD) 9.9 years old) (Table 1). Thirty-two (32/46; 69.6%) patients complained of palpable breast lumps, while 14/46 (30.4%) were referred for screening. The final histopathological diagnosis was pure ILC in 22/46 (47.8%) cases, while 24/46 (52.2%) cases showed mixed pathology, as shown in Table 2. The most common ILC variant was the classic variant, noted in 39/46 cases (84.8%).

Considering the breast density among the studied population, 23/46 (50%) cases were assigned a category B, while 22/46 (47.8%) cases were assigned a category C or D. In contrast-enhanced studies, minimal background parenchymal enhancement was mostly noted in CEDM (in 22/46 cases, 47.8%), while moderate background parenchymal enhancement was mostly noted in DCE-MRI (in 18/46 cases, 39.1%). We found that the degree of parenchymal enhancement was significantly correlated with breast density category, with p values of 0.039 for MRI and 0.005 for CEDM.

In the current study, the estimated inter-observer agreement based on Kappa coefficient measurement was 0.96, 0.83 and 0.87 regarding the detection of the index lesion, detection of multiple lesions and detection of contralateral lesions, respectively, denoting very good agreement.

Detection of the index lesion

Invasive lobular carcinoma most frequently presented as masses on combined mammography/ultrasound examinations. That was shown in 14/46 cases (30.4%) on mammography and 32/46 (69.5%) cases on ultrasound. Suspicious calcification was only noted in 5/46 (10.9%) cases. Lesions were not identified in 9/46 (19.6%) cases on mammography and 4/46 (8.7%) cases on ultrasound.

Analysis of the morphological criteria of the index lesions was done by all imaging modalities. ILC lesions were described on CEDM most frequently as non-mass enhancement (*n*: 20/46; 43.5%), followed by enhancing mass (*n*: 14/46; 30.4%), combined mass and NME (*n*: 10/46; 21.7%). Enhancing asymmetry was noted in 1/46 case (2.2%). In 1/46 (2.2%) patients, there was no notable enhancement resulting in a false negative (FN) result (Fig. 2).

On the DCE-MRI examination, all the lesions were identified. They were most commonly seen as NME (*n*: 18/46; 39.1%) (Fig. 3), followed by combined mass and NME (*n*: 14/46; 30.4%), enhancing mass (*n*: 13/46; 28.3%), and enhancing mass with enhancing foci (*n*: 1/46, 2.2%). That was emphasized in Table 3. Regarding the kinematic features, 36/46 (78. 2%) cases showed type 3 (washout) curve, 5/46 (10.9%) cases showed type 2(plateau) curve, while 5/46 (10.9%) cases showed type 1 (continuous rising) curve.

The sensitivity of combined conventional mammography and ultrasound, CEDM and DCE-MRI examinations in the detection of index lesions was calculated individually and revealed that DCE-MRI had higher sensitivity (100%) when compared to combined conventional mammography and ultrasound, which had a sensitivity of 91.3%, and CEDM, which had a sensitivity of 97.8%, as shown in Table 4.

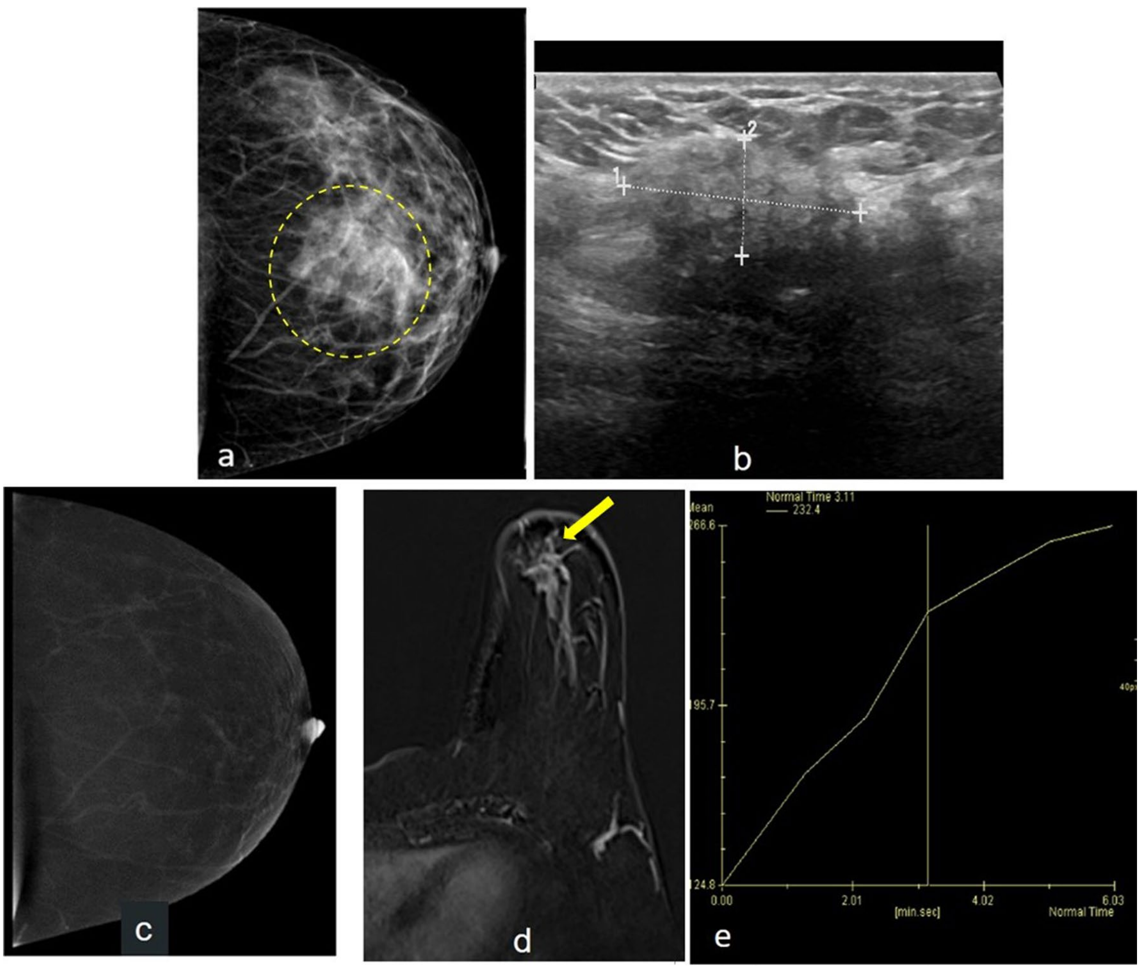

Fig. 2 A 53-year-old female coming for screening. Screening mammography CC view (**a**) showed a focal asymmetry in the UIQ of the left breast (circled) with corresponding altered parenchyma on complementary ultrasound examination (**b**). Pathology revealed ILC tubulo-lobular variant grade II. CEDM in CC view (**c**) showed no enhancing lesions. Axial postcontrast dynamic MRI series (**d**) showed corresponding focal clumped intense non-mass enhancement (arrowed) with time/intensity curve type1 (**e**). CC; craniocaudal, UIQ; upper inner quadrant, CEDM; contrast-enhanced digital mammography, DCE-MRI; dynamic contrast-enhanced MRI, ILC; invasive lobular carcinoma

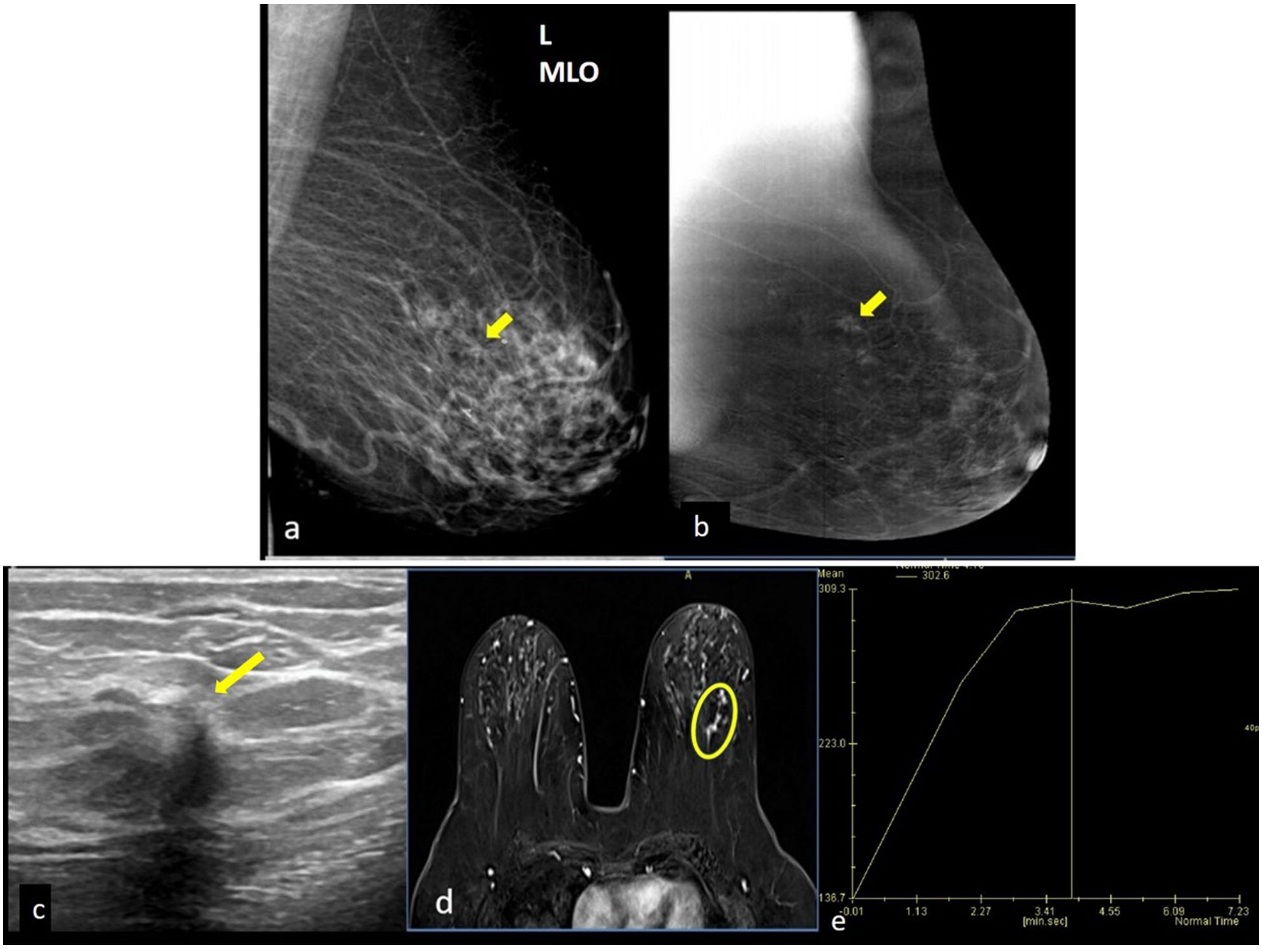

Fig. 3 A 65-year-old female coming for screening. Screening mammography MLO view of the left breast (**a**) showed subtle architectural distortion in the upper outer quadrant (arrowed). CEDM in MLO view (**b**) showed corresponding two small enhancing spiculated lesions of low conspicuity (arrowed). An ultrasound (**c**) was performed and showed a small area of parenchymal distortion with shadowing (arrowed). Pathology revealed ILC classic and pleomorphic variant grade II. Axial postcontrast dynamic MRI series (**d**) showed corresponding linear clumped intense non-mass enhancement with surrounding enhancing foci (circled) that displayed type 2 (plateau) curve (**e**). Postoperative pathology confirmed left multifocal malignant process

Table 3 Analysis of the morphology of the index lesions by CEDM and MRI

Morphology	CEDM		MRI	
	N	%	*N*	%
No enhancement	1	2.2	0	0
Non-mass enhancement	20	43.5	18	39.1
Mass enhancement	14	30.4	13	28.3
Combined mass and NME	10	21.7	14	30.4
Enhancing asymmetry	1	2.2		
ME and enhancing foci			1	2.2

CEDM Contrast-enhanced digital mammography, *MRI* magnetic resonance imaging, *NME* non-mass enhancement, *ME* mass enhancement

Locoregional staging

The lesion size and extent were analyzed in 30/46 cases, while 16 cases were excluded from such analysis for receiving neoadjuvant or palliative treatment. The agreement of tumor size measurement between different modalities and postoperative size was assessed and presented by Bland–Altman plots. There was high agreement between CEDM and pathology, MRI and pathology, and CEDM and MRI. Conversely, low agreement between pathology and combined conventional mammography and ultrasound sizes was found, as shown in Fig. 4. The correlation between size measured by the different modalities and postoperative pathology is shown in Table 5.

Concerning the lesion extent, postoperative pathology confirmed nipple invasion in 2/30 (6.5%) cases, with no

Table 4 Comparison of true positives and false negatives as well as the sensitivity of sono-mammography, CEDM, and DCE-MRI examination in the detection of the index lesion

Diagnostic indices	Combined conventional mammography and ultrasound		CEDM		MRI	
	N	%	*N*	%	*N*	%
True positive	42	91.3%	45	97.8%	46	100.0%
False negative	4	8.7%	1	2.2%	0	0.0%
Sensitivity	91.30%		97.83%		100.00%	

CEDM Contrast-enhanced digital mammography, *MRI* magnetic resonance imaging

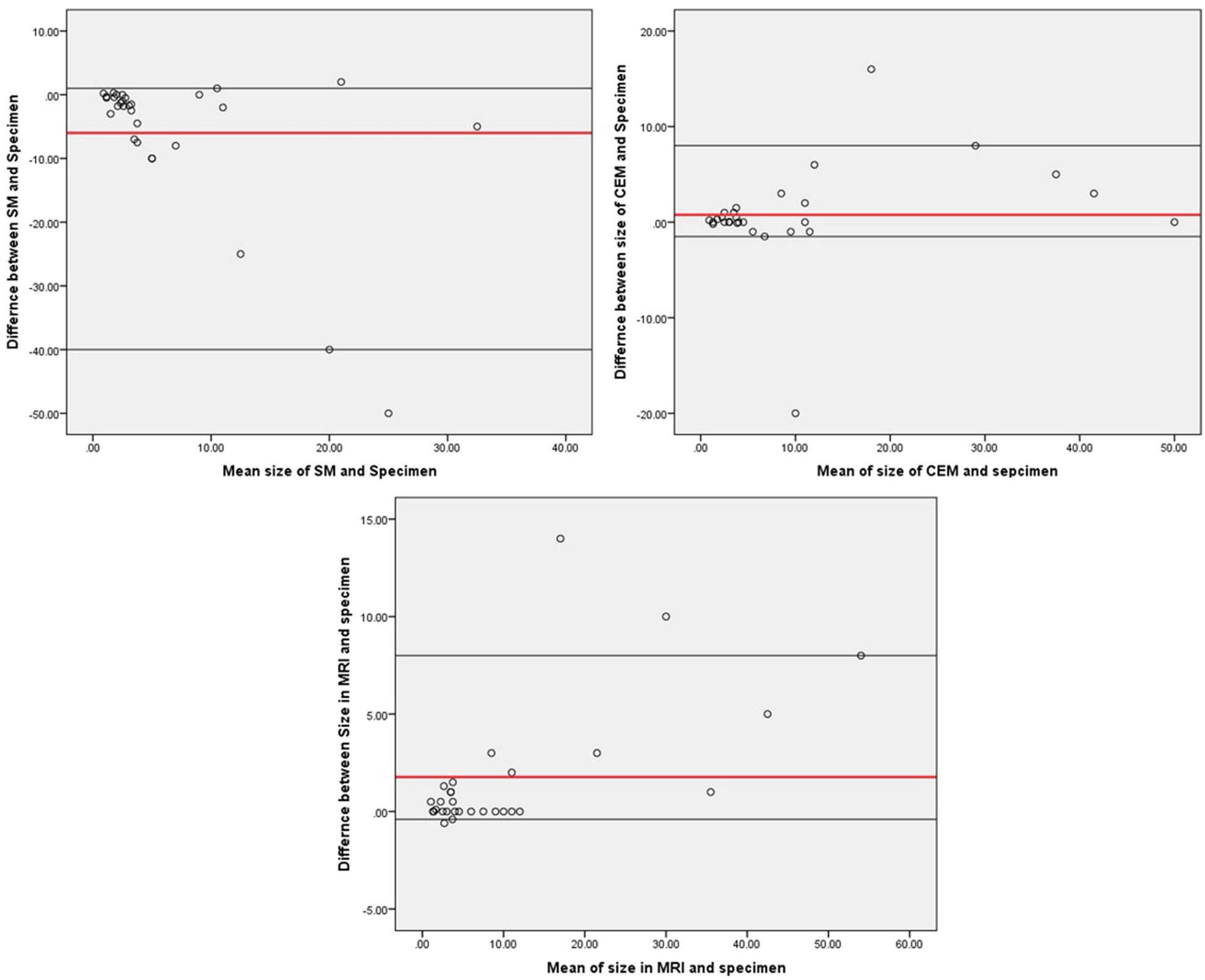

Fig.4 Bland–Altman plots for the comparison between different modalities and postoperative results

skin or pectoralis muscle invasion in any of the cases. Extension to the nipple was reported in 2/30 (6.5%) cases on CEDM and in 5/30 (16.67%) cases on DCE-MRI (no false positive (FP) cases by CEDM and 3 false positive cases by MRI). Muscle invasion was reported in 1/30 (3.3%) case by MRI but not by pathology. Also, skin invasion was reported by MRI in 1/30 (3.3%) case, although not proved by pathology, as shown in Table 6.

Detection of multiplicity

In our study, sono-mammography failed to detect multiplicity in 17/46 (37.0%) cases (false negative), while a

Table 5 Correlation between the size measured by different modalities and postoperative pathology

	Mean	Standard deviation	Median	Minimum	Maximum
Size by ultrasound	3.8	6.8	1.7	0.0	30.0
Size by CEDM	10.6	13.6	4.3	0.0	50.0
Size by DCE-MRI	11.5	14.3	4.5	1.3	58.0
Postoperative size	9.8	12.3	4.3	0.8	50.0

CEDM Contrast-enhanced digital mammography, *DCE-MRI* dynamic contrast-enhanced MRI

Table 6 Comparison between CEDM and MRI in the assessment of extension to the skin, muscle and nipple

	CEDM	MRI
True positive	2	2
True negative	28	23
False positive	0	5
False negative	0	0

CEDM Contrast-enhanced digital mammography, *MRI* magnetic resonance imaging

false interpretation of multiplicity was reported in 1/46 (2.2%) case (false positive). On the other hand, multiple lesions were truly identified in 21/21 (100%) cases on the DCE-MRI examination, yet they could not be identified in 3/46 (6.5%) cases on the CEDM. False interpretation of multiplicity was found in 1/46 (2.2%) cases on CEDM and 2/46 (4.3%) cases on DCE-MRI (Fig. 5). Dynamic contrast-enhanced MRI examination had a better sensitivity (100%) in the detection of multiple lesions with a negative predictive value (NPV) of 100% when compared to CEDM, which had a sensitivity of 85.7% and a NPV of 89.5%. As emphasized in Table 7, the overall accuracy of CEDM was 91.5%, while that of MRI was 95.5%. Combined mammography with US examination has achieved the least sensitivity (19%) and the least diagnostic accuracy (62.14%).

Detection of contralateral malignancy

Based on histopathological results, contralateral malignancy was found in 4/46 (8.7%) cases. Based on sono-mammography, contralateral suspicious lesions were considered in 5/46 (10.9%) cases (2 false positive lesions and 1 false negative lesion). True identification of contralateral malignancies was achieved by both CEDM and DCE-MRI examinations. On CEDM, contralateral lesions were falsely interpreted as malignant in 4/46 (8.7%) cases (false positive) (Fig. 6) and as benign in 1/46 (2.2%) patients (false negative) (Fig. 7). On MRI examination, false positive results of bilaterality were found in 3/46 (6.5%) cases. The accuracy measures and diagnostic indices of sono-mammography, CEDM and DCE-MRI were calculated individually as emphasized in Table 8.

Discussion

Owing to its pattern of growth, and its higher incidence of multiplicity and bilaterality if compared to other histological subtypes, ILC poses a specific challenge and may be missed clinically and radiologically in many cases, especially when depending on only mammography that shows relatively low sensitivity for ILC detection (56%–84%). This fact led to increased interest in other more sensitive imaging modalities such as DCE-MRI and CEDM that depend on direct visualization of tumor neovascularity [3].

This study aimed to compare the diagnostic performance of CEDM and DCE-MRI in the local staging of ILC regarding the size, extensions, multiplicity and bilaterality. It included 46 patients; each had an index lesion that was pathologically proved to be invasive lobular carcinoma. All patients underwent conventional mammography with complementary ultrasound, CEDM and DCE-MRI breast examination with the aim of diagnosis and premanagement evaluation by delineation of the lesion's extent, detection of multiplicity and contralateral malignancy.

In the current study, the relative shortcoming of combined conventional mammography and ultrasound in the detection of the lesion was evident with estimated sensitivity of 91.3%. This high false negative rate by mammography can be explained by a lack of mass formation in some cases and a lack of calcification in most cases, as reported by Wilson et al. [2].

Contrast-enhanced digital mammography achieved a sensitivity of 97.8% in detecting index lesions with one false negative case that showed no contrast uptake. On the other hand, DCE-MRI was the most sensitive imaging tool for the detection of the index lesion, achieving a sensitivity of 100% with enhancement detect in all cases. Our results were in agreement with Costantini et al. [12], they enrolled 38 patients in their study who performed both contrast-enhanced studies with an interval of one month, and based on their results, similar sensitivity of CEDM and MRI was achieved.

There was a significant difference between CEDM and MRI regarding the intensity of lesion enhancement (p value 0.0001), with more intense enhancement noted on DCE-MRI. That was in agreement with Li et al. [13], who reported that the mean score of enhancement intensity of malignant lesions on CEDM was significantly less than that for MRI.

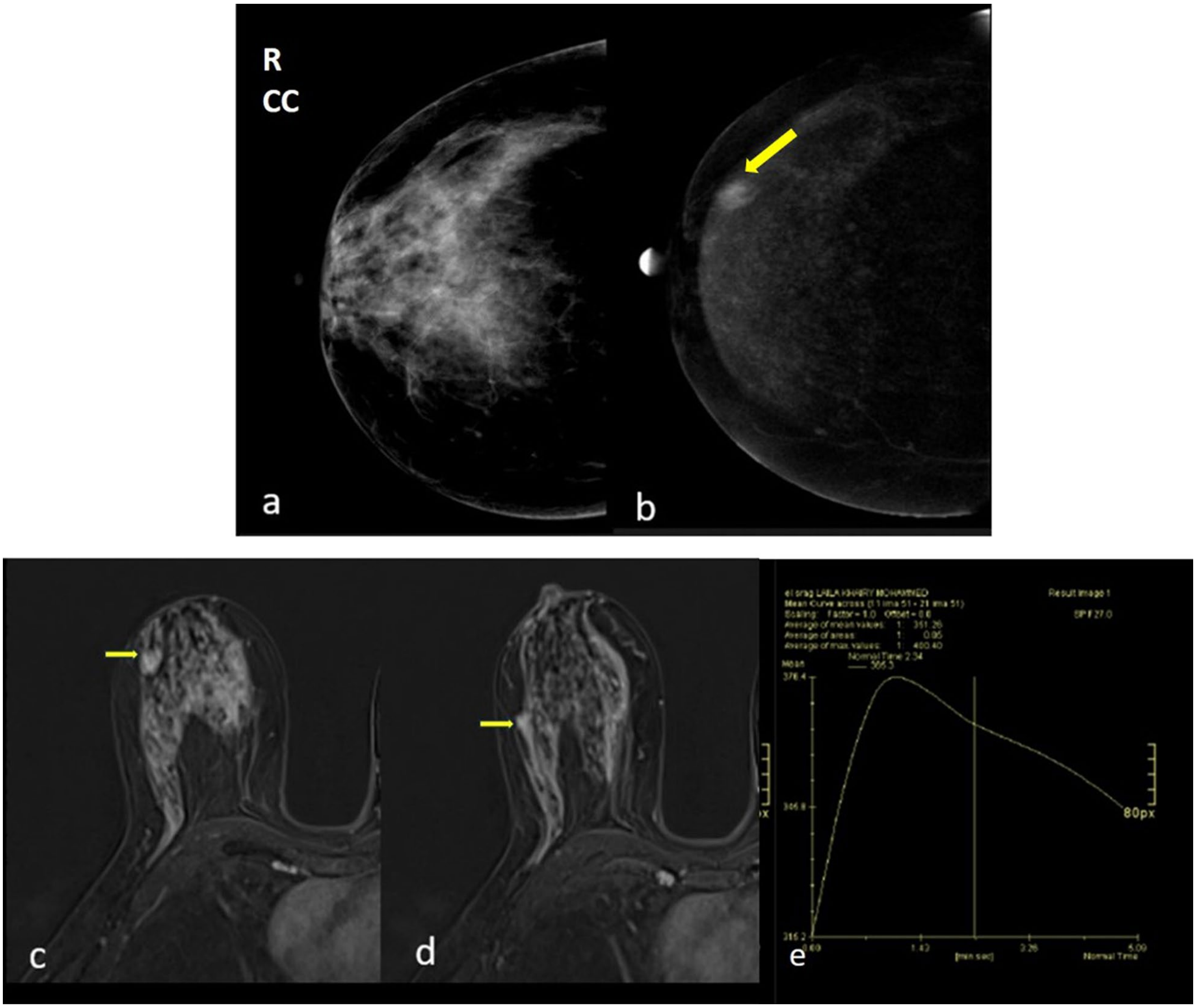

Fig. 5 A 44-year-old female coming for screening. Screening mammography CC view (**a**) view showed dense breast (ACR **c**) with no significant abnormality detected. CEDM in CC view (**b**) showed irregular homogenously enhancing mass of moderate conspicuity in the outer central region of the right breast (arrowed). Axial postcontrast dynamic MRI series (**d**) showed a corresponding irregular heterogeneously enhancing mass (arrowed) along with an enhancing nodule (arrowed) which is seen superior to the aforementioned mass, displaying a type 3 (washout) curve (**e**). Pathology revealed unifocal ILC grade I

Table 7 Comparison of the diagnostic indices of CEDM and DCE-MRI in the detection of ILC multiplicity

Statistics	Combined conventional mammography and ultrasound	CEDM	MRI
	Value (95% CI)	Value (95% CI)	Value (95% CI)
Sensitivity	19% (5.45–41.91%)	85.71% (63.66–96.95%)	100.00% (83.89% –100.00%)
Specificity	96.00% (79.65–99.90%)	96.00% (79.65–99.90%)	92.00% (73.97–99.02%)
Positive predictive value (*)	78.91% (31.14–96.87%)	94.39% (71.00–99.14%)	90.76% (72.22–97.38%)
Negative predictive value (*)	60.15% (54.72–65.34%)	89.53% (74.94–96.07%)	100.00% (83.89% –100.00%)
Accuracy (*)	62.14% (46.64–76.02%)	91.47% (79.43–97.67%)	95.52% (84.97–99.43%)

CEDM; Contrast-enhanced digital mammography, MRI; magnetic resonance imaging

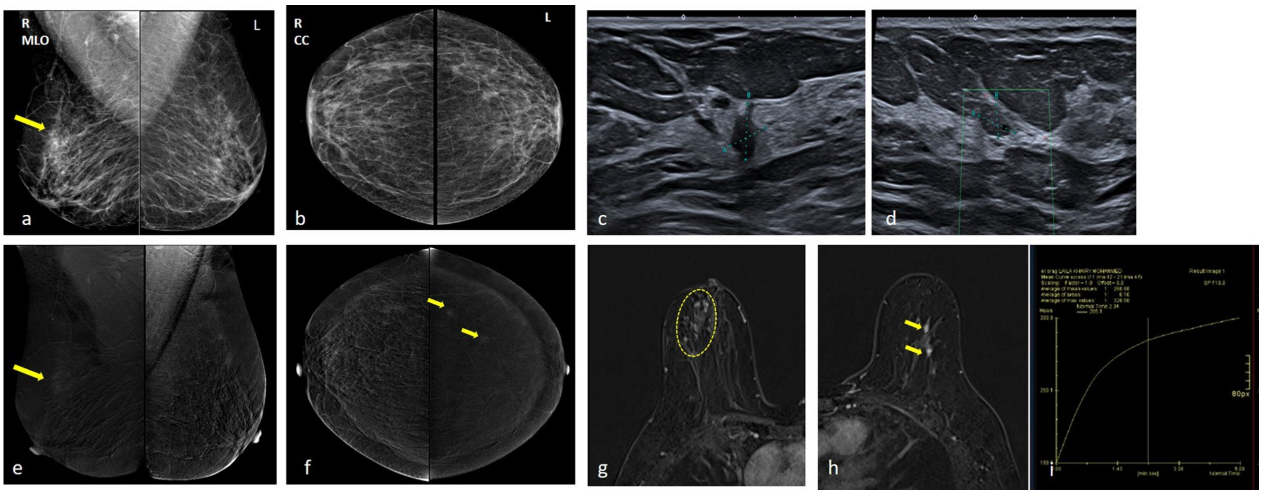

Fig. 6 A 56-year-old female coming for screening. Screening mammography MLO (**a**) and CC (**b**) views showed a focal asymmetry in the UOQ of the right breast with subtle parenchymal distortion (arrowed). Ultrasound examination showed a small hypoechoic lesion with angular margin in the right breast (**c**) and a small circumscribed lesion in the UOQ of the left breast (**d**). CEDM in MLO (**e**) and CC view (**f**) showed corresponding non-mass enhancement of mild conspicuity in the right breast (arrowed) and two indeterminate enhancing nodules in the left breast (arrowed). Axial postcontrast dynamic MRI series (**g**, **h**) showed clumped intense non-mass enhancement in the right breast of marked conspicuity displaying type 3 (washout) curve (circled), while the two enhancing nodules in the left breast (arrowed) displayed type 1 (continuous rising) curve (**i**) and was assigned as BIRADS 3. Pathology revealed multifocal ILC classic variant. The left breast lesions remained stable by ultrasound follow-up examination

Correct size estimation is mandatory for efficient breast cancer treatment and preoperative planning. The size was assessed in only 30 cases after the exclusion of cases that received NACT. In most cases, MRI showed a tendency to overestimate the size, and ultrasound showed a tendency for size underestimation, while in CEDM, there was both overestimation and underestimation, but to a lesser extent. Fallenberg et al. [14] attributed the accuracy of size assessment in CEDM over that in MRI, especially in ILC, to several factors. The most important is the strong background parenchymal enhancement level on DCE-MRI that may be added to the actual size of the tumor. Moreover, the associated motion artifacts have a tendency to occur more in MRI than in CEDM.

Accurate assessment of the tumor extension and its relation to the surroundings is fundamental as it greatly influences the surgical management [15]. We analyzed the disease extensions in only 30/46 cases. Accurate extent delineation was achieved by CEDM, yet there was a tendency to overestimate the disease extent by DCE-MRI as compared to the final histopathological results.

Invasive lobular carcinoma tends to be multifocal, multicentric and bilateral. The multifocality of ILC makes it more prone to incomplete surgical excision, with reported re-excision rates after breast-conserving surgery (BCS) ranging from 29 to 67% and conversion to mastectomy after the failure of BCS in 20–49% [15, 16]. In our study, CEDM was able to achieve a better sensitivity (85.7%), specificity (96%) and diagnostic accuracy (91.5%) than previously reported. The best sensitivity in detecting multiplicity was achieved by MRI (100%) with no FN cases, yet the specificity was lower compared to CEDM (92% versus 96%). Magnetic resonance imaging discovered the multiplicity in an additional 3/46 cases that were occult on CEDM, and this may be attributed to the significant difference in the intensity of the enhancing lesions between CEDM and MRI, allowing easier detection of tiny nodules and foci on MRI. Our results were in agreement with Chae et al. [17] who achieved a sensitivity of 100% in their study yet with much lower specificity (50%). Lobbes et al. [18] reported much higher specificity of CEDM than in MRI (91.5% versus 79.2%) in the detection of multifocal disease, and this may be attributed to the fact that they included all patients with ILC who performed any contrast-enhanced studies whether CEDM or MRI or both in contrary to our study design that included only patients who performed both contrast-enhanced studies resulting in smaller study population.

In this study, contralateral malignancy was identified in 4/46 cases (8.7%), and their pathologies were ILC, fibroadenoma with malignant transformation into IDC, IDC, and mixed ILC and IDC. Contralateral malignancy was considered in 5/46 cases on combined conventional mammography and ultrasound (2 FP lesions and 1 FN lesion), 9/46 cases on CEDM (4 FP lesions and 1 FN lesion) and 7/46 on DCE-MRI (3 FP lesions).

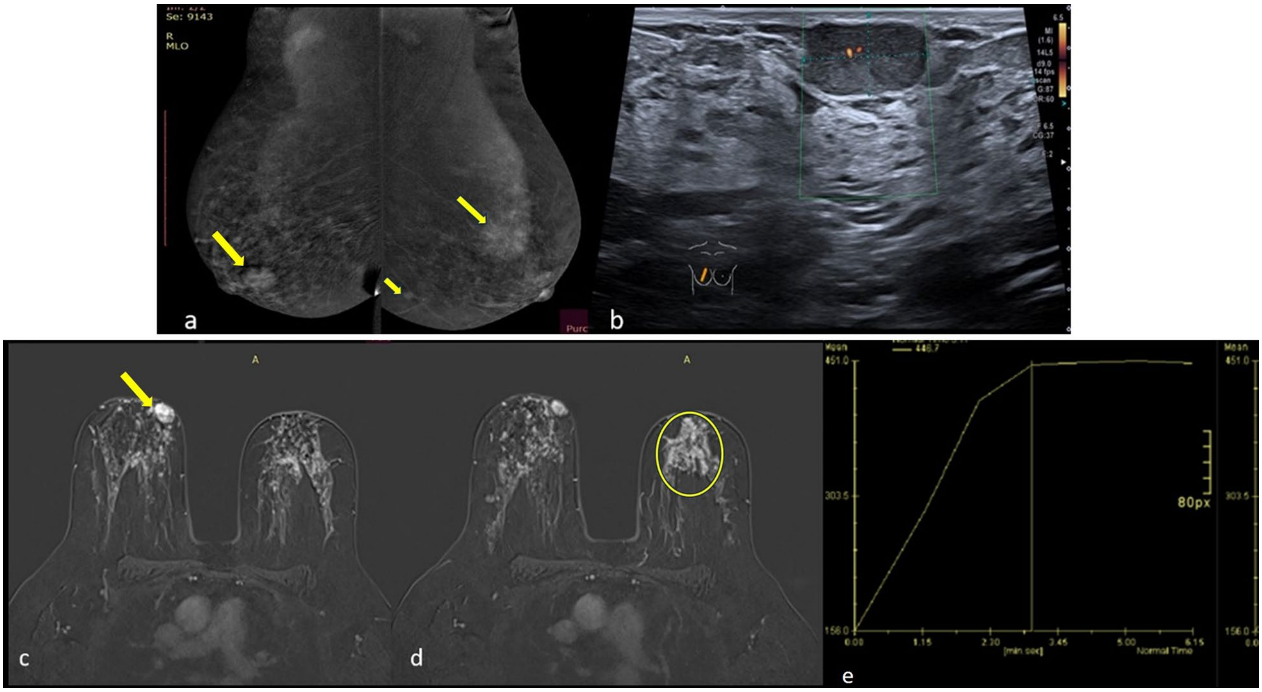

Fig. 7 A 56-year-old female with positive family history coming for screening. Screening mammography showed dense breasts (not shown). CEDM in MLO view (**a**) showed faint heterogeneous non-mass enhancement in the upper central region of the left breast along with another LIQ enhancing nodule (arrowed) which was assigned as BIRADS 4. An oval-shaped circumscribed enhancing mass is also noted in the inner para-areolar region of the right breast (arrowed) and was assigned as BIRADS 3. Second look ultrasound (**b**) was performed on the right breast lesion and showed an oval-shaped circumscribed isoechoic solid mass. Axial postcontrast dynamic MRI series (**c**, **d**) showed left retro-areolar heterogeneous intense non-mass enhancement (circled). The right breast lesion showed intense mass enhancement with dark internal septations (arrowed), yet with borderline kinematic features; plateau curve (**e**), so it was categorized as BIRADS 4. Pathology revealed left multicentric ILC grade II, while the right breast lesion was proved to be fibroadenoma with malignant transformation into invasive ductal carcinoma

Table 8 Comparison of the diagnostic indices of CEDM and DCE-MRI in the detection of bilaterality

Statistic	Combined conventional mammography and ultrasound	CEDM	MRI
	Value (95% CI)	Value (95% CI)	Value (95%CI)
Sensitivity	75.00% (19.41–99.37%)	80.00% (28.36–99.49%)	100% (39.76–100.00%)
Specificity	95.24% (83.84–99.42%)	90.24% (76.87–97.28%)	92.86% (80.52–98.50%)
Positive predictive value (*)	60.00% (25.72–86.66%)	50.00% (26.33–73.67%)	57.14% (30.94–79.87%)
Negative predictive value (*)	97.56% (87.98–99.54%)	97.37% (86.47–99.54%)	100%
Accuracy (*)	93.48% (82.10–98.63%)	89.13% (76.43–96.38%)	93.48% (82.10–98.63%)

CEDM Contrast-enhanced digital mammography, *MRI* magnetic resonance imaging

Magnetic resonance imaging was more sensitive (100%) than CEDM (80%) in the detection of bilaterality, yet the achieved specificity and diagnostic accuracy of DCE-MRI were slightly higher if compared with CEDM. Despite the small numbers of cases with bilateral malignancy included in our study, our results are still in accordance with what was reported by Fallenberg et al. [14], Lobbes et al. [18], Youn et al. [19] and about the comparable performance of CEDM and DCE-MRI regarding the detection of additional contralateral tumor foci.

Our study has some limitations. A small sample size was included in our study as we aimed to compare the diagnostic performance of both contrast-enhanced modalities, so we excluded those who missed any of these imaging modalities. On analyzing the extent of the lesion, we were obliged to exclude another set of patients who received NACT as our reference was the final histopathological results.

Conclusions

In conclusion, we found that contrast-enhanced studies are very beneficial for the premanagement evaluation of ILC. Based on our results, we found that DCE-MRI is the most sensitive imaging modality regarding the detection of the index lesion, detection of multiplicity and bilaterality owing to the conspicuity of the lesions' enhancement as compared to CEDM. However, if MRI examination could not be performed, then CEDM can be a good reliable alternative. Regarding the locoregional staging of ILC, there was a tendency for relative overestimation by the DCE-MRI examination, as compared to CEDM examination.

Abbreviations

MRI	Magnetic resonance imaging
ILC	Invasive lobular carcinoma
IDC	Invasive duct carcinoma
CEDM	Contrast-enhanced digital mammography
DCE-MRI	Dynamic contrast-enhanced MRI
FFDM	Full-field digital mammography
TR	Repetition time
TE	Time to echo
STIR	Short tau inversion recovery
ADC	Apparent diffusion coefficient
Gd-DTPA	Gadolinium-diethylene tri amino pentaacetic acid
THRIVE	T1 high-resolution isotropic volumetric examination
BI-RADS	Breast-Imaging Reporting and Data System
ACR	American College of Radiology
NME	Non-mass enhancement
NACT	Neoadjuvant chemotherapy
DWI	Diffusion-weighted imaging
SD	Standard deviation
FP	False positive
FN	False negative
NPV	Negative predictive value
ME	Mass enhancement
BCS	Breast-conserving surgery

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Author contributions

RMK designed the work. SF wrote the manuscript and was responsible for correspondence to journal. AEA helped in writing the manuscript and worked with MMH on data collection and interpretation. OMN and RMK contributed in reviewing the manuscript and interpretation. All authors have read and approved the final manuscript.

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Availability of data and materials

All are available with the authors upon request.

Declarations

Ethics approval and consent to participate

The protocol was reviewed and approved by the Ethics Committee of Cairo University.

Consent for publication

A written consent for publication was obtained for these cases.

Competing interests

The authors declare that they have no competing interests.

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