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The integration of artificial intelligence with contrast-enhanced mammogram in the work up of suspicious breast lesions: what do you expect?

Sahar Mansour[1,2*], Heba Azzam[1,2] and Hany El-Assaly[1]

Abstract

Background The enhancement overlaps at contrast-enhanced mammogram (CEM) between benign and malignant breast abnormalities presents a high probability of false-positive lesions and subjects females' candidate for screening and diagnostic mammograms to unnecessary biopsy and anxiety. The current work aimed to evaluate the ability of mammograms scanned by artificial intelligence (AI) to enhance the specificity of CEM and support the probability of malignancy in suspicious and malignant looking breast lesions.

Methods The study included 1524 breast lesions. The AI algorithm applied to the initial mammograms and generated location information for lesions. AI scoring suggested the probability of malignancy ranged from 100% (definite cancers) and < 10% (definite non-cancer) and correlated with recombinant contrast enhanced images.

Results The malignant proved abnormalities were 1165 (76.5%), and the benign ones were 359 (26.5%). BI-RADS 4 category was assigned in 704 lesions (46.2%) divided into 400 malignant (400/704, 56.8%) and 304 benign (304/704, 43.2%). BI-RADS 5 category presented by 820 lesions (53.8%), 765 of them were malignant (765/820, 93.3%) and 55 were benign (55/820, 6.7%). The sensitivity of digital mammogram whether supported by AI (93.9%) or contrast media (94.4%) was significantly increased to 97.2% ($p < 0.001$) when supported by both methods. Improvement of the negative predictive value (from 80.6% and 79.6% to 89.8%, $p < 0.05$) and the accuracy (from 91.1 and 88.8 to 94.0%, $p < 0.01$) was detected.

Conclusions Contrast-enhanced mammogram helps in specification of different breast lesions in view of patterns of contrast uptake and morphology descriptors, yet with some overlap. The use of artificial intelligence applied on digital mammogram reduced the interpretational variability and limited attempts of re-biopsies of suspicious looking breast lesions assessed by contrast-enhanced mammograms.

Keywords Contrast-enhanced mammogram, Digital mammography, Artificial intelligence, Breast cancer, Suspicious breast lesions

Background

Contrast-enhanced mammogram (CEM) is one of the techniques that developed to be a problem-solving application in case breast lesions showed suspicious features on routine conventional imaging. Such modality is sensitive to detection of tumor multiplicity, delineation of the local extent of disease and consequently would be

*Correspondence:
Sahar Mansour
sahar_mnsr@yahoo.com
[1] Women's Imaging Unit, Radiology Department, Kasr El Ainy Hospital, Cairo University, Manial, Cairo, Egypt
[2] Radiology Department, Baheya center for early breast cancer and treatment, Cairo, Egypt

beneficial in the preoperative staging and monitoring of the response of breast cancer to neoadjuvant chemotherapy [1].

Although CEM is considered the best imaging tool to estimate accurately breast diseases especially when MR imaging is contraindicated, and ongoing studies were directed to consider its usage in the screening of breast cancer [2], yet, categorization on contrast images may exhibit a problem because some of the benign abnormalities as fibroadenomas, intraductal papillomas, inflammatory disorders, and pseudoangiomatous stromal hyperplasia (PASH) can display atypical contrast uptake [3]. Regarding the same concept, some carcinomas could go with "no enhancement" pattern [4].

The use of AI in radiology had shown valid results in detection of breast cancer, where the algorithm was able to distinguish different cancer patterns on mammography that sometimes was difficult to mark even by experts in the field of breast imaging [5].

The current work assessed the impact of reading digital mammogram by artificial intelligence on the diagnostic performance of breast abnormalities suggestive malignant (BI-RADS 4 and 5 categories) in correlation with contrast-enhanced mammogram.

Methods

The study is a retrospective analysis that was approved by the ethical committee of the research center, and a waiver of the informed consent was applied for all the included patients. The current work analyzed a total of 1596 mammograms. The inclusion criteria were fulfilled by 1524 mammograms of 1488 females (18 cases showed bilateral diseases).

Inclusion criteria

Mammograms with suspicious imaging criteria (BI-RADS 4 or 5 categories' abnormalities) as mass lesions (with indistinct/spiculated margin), areas of parenchyma distortion, focal asymmetries, or suspicious clustered microcalcifications and required contrast-enhanced mammograms to clarify.

Suspicion of malignancy on mammogram was supported by detection of indistinct mass/non-mass lesions on ultrasound examination.

Exclusion criteria

- Mammograms showed typical features of benign and probably benign lesions (BI-RADS 2 and 3).
- Follow-up mammograms of the treated breasts (post-operative, chemo- or radiotherapy).
- Mammograms with suspicious lesions yet CEM were not available.
- Cases with missing pathology report.

The age of the patients ranged from 40 to 73 years (mean age 43.89 ± 5.99).

Artificial intelligence was applied to the initial mammograms and correlated to the recombinant contrast images for areas of contrast uptake at CEM.

Results of histopathology were obtained by surgery (mastectomy, breast conservation surgery, oncoplastic surgery, or wire localization and excision biopsy) and true tissue core biopsy (used needle was 14 G).

Equipment

- Full-field regular digital mammography provided with dual-energy contrast-enhanced mammography unit; Amulet Innovality (Fujifilm Global Company, Japan) and Senographe Pristina 3D machine (GE Healthcare, United Kingdom).

  Two standard views, medio-lateral oblique and cranio-caudal, were acquired for each breast. A two monochrome 5-megapixel liquid crystal display (2048×2560 pixels; 21.3 inches; MFGD5621HD, Barco) was used to evaluate the mammograms.
- Hand-held superficial ultrasound (LOGIQ S8-GE device) provided by a high-frequency linear probe (7–12 MHz) was used for the ultrasound examination.
- CEM images were obtained 2 min following the injection of a non-ionic iodinated contrast agent. Injection was performed as one-shot injection of 1.5-ml/kg body weight at the rate of 2–3 ml/s.

For each view, a pair of low- and high-energy images were acquired. Low-energy images were acquired at kilovoltage values of 26 up to 31 kVp to simulate the regular mammographic images. High-energy images were acquired at 45–49 kVp to obtain iodine-sensitive images.

Recombinant (contrast-based) images were obtained by subtraction of the low- from the high-energy images. Reduction of the background parenchymal contrast uptake is required to increase conspicuity of the enhancing breast abnormalities.

The mammography machine was provided with artificial intelligence software (Lunit INSIGHT MMG ver. 1.10.2, Seoul, South Korea, version 2021) for scanning and reading non-contrast-based digital mammograms.

Image analysis and interpretation

Mammograms were reviewed retrospectively in consensus by two radiologists (with 25 years and 20 years of experience in breast imaging).

Reading of the breast lesions was based on the standard "Breast Imaging Reporting and Data system" in the BI-RADS ACR atlas 5th edition 2013 [6] and the BI-RADS ACR atlas for contrast-enhanced mammography (A supplement to ACR BI-RADS® Mammography 2013) 2022 [7].

The sequence of reading was as follows: first, the preliminary digital mammograms and complementary ultrasound for BI-RADS 4 and 5 abnormalities. Second, the regular mammogram was scanned by AI, and the abnormality scoring percentage was recorded. Third CEM images were interpreted for areas of contrast uptake.

Breast abnormalities that showed contrast enhancement were interpreted with regard morphology descriptors (masses, calcifications, and asymmetry/distortion) and enhancement characteristics (internal enhancement, lesion enhancement relative to background, and extent of enhancement).

Enhancing lesions seen only at the recombinant images were interpreted by enhancement characteristics only, while non-enhancing abnormalities were analyzed by morphology descriptors and no enhancement criteria to be involved.

Morphology descriptors

- *Masses* described by shape, margin, and density.
- *Calcifications* described by morphology and distribution.
- *Asymmetry and/or focal distortion* analyzed by distribution.

Enhancement characteristics

- *Internal enhancement* as homogeneous, heterogeneous, or rim.
- *Lesion conspicuity* as low, moderate, or high (subjective).
- *Extent of enhancement* in the form of 1. partial enhancement, 2. complete enhancement, 3. presence of enhancement beyond the mammographic lesion, and 4. enhancement of the surrounding tissue adjacent to the lesion.

The used AI was the commercial setting (LUNIT INSIGHT AI-MMG, FDA approved for reading mammogram in 2019). The algorithm trained in two stages: Stage 1 included learning low-level features followed by stage 2 for learning high-level features based on finetuning of stage 1 data input. AI provided location information for the included lesions through, (i) heat map that targeted the abnormality in the craino-caudal and medio-lateral oblique views, (ii) tracing outlines to cover the disease extent, and (iii) scoring percentage of the probability of malignancy for these lesions that ranged from < 10% till 100%. The AI scanned image is a collective four views image (two cranio-caudal and two medio-lateral obliques), and the maximum scoring percentage was displayed at the bottom of the resultant image. "Low" assign means low risk of < 10% to be a cancer, and 100% represents the highest level of suspicion.

The categorization of the probability of malignancy was based on He et al. [8]: 100% for definite cancers, 76–99% for probably cancer, 51%–75% for possibly cancer, 26–50% for possibly non-cancer, 10–25% for probably non-cancer, and 0–9% for definite non-cancer.

Statistical analysis

Data were analyzed in the form of the diagnostic indices: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. For comparing categorical data, the Chi-square (c2) test was performed. Exact test was used instead when the expected frequency is < 5.

The best cutoff value of AI for the detection of malignancy presented by ROC curve (area under curve analysis). Testing agreement between categorical variables was done via kappa measure of agreement. *P* value less than 0.05 was statistically significant.

Confidence interval percentage (CI %) was done for the range of the abnormality scoring values elicited by the AI software: the narrower the interval (upper and lower values), the more precise is the AI estimate.

Results

The study analyzed 1596 mammograms of 1540 females who had performed CEM either to (i) re-grade problematic mammograms or (ii) do further evaluation of high-density breast parenchyma (ACR c and d).

The number of the selected mammograms was downgraded to 1524 as 59 mammograms were BI-RADS 2 and 3 (showed benign and probably benign lesions), nine mammograms showed suspicious lesions, yet CEM images were not available and pathology results were missed in four cases.

The variety of pathologies included in the current work ($n = 1524$) and their assigned BI-RADS categories (i.e., category 4 or 5) is presented in Table 1, based on the combined mammogram and ultrasound examination.

The size of the included abnormalities was estimated on the recombinant contrast-enhanced images; ranged from: (i) less than or equals to 10 mm in 239 (15.7%), (ii) 10 to 20 mm in 861 (56.5%), (iii) 20 to 50 mm in 342 (22.4%), and (iv) more than 50 mm in 82 (5.4%) lesions.

Table 1 Histopathologic varieties of BI-RADS category 4 and 5 abnormalities

Histologic diagnosis	BI-RADS 4 (*n* = 704, 46.2%)	BI-RADS 5 (*n* = 820, 53.8%)	Total (*n* = 1524)
Malignant (n = 1165, 76.5%)			
Ductal carcinoma in situ	25	51	76
Invasive ductal carcinoma	223	619	842
Mucinous carcinoma	30	10	40
Invasive lobular carcinoma	39	59	98
Papillary carcinoma	37	3	40
Micropapillary carcinoma	29	4	33
Tubular carcinoma	6	15	21
Mixed invasive lobular and tubular carcinoma	1	4	5
Malignant phyllodes tumor	10	–	10
Benign (n = 359, 23.5%)			
Atypical ductal hyperplasia	62	32	94
Intraductal papillomatosis	47	–	47
Fibrocystic changes	21	14	35
Fibroadenoma	40	–	40
Pseudoangiomatous stromal hyperplasia	30	1	31
Benign phyllodes tumor	13	–	13
Epithelosis	37	–	37
Nodular sclerosis/sclerosis adenosis	39	7	46
Infectious mastitis	3	–	3
Granulomatous mastitis	9	–	9
Fat necrosis	3	1	4

The malignant proved abnormalities were 1165 in number (76.5%), and the benign ones were 359 (26.5%) lesions.

BI-RADS 4 category was assigned in 704 lesions (46.2%), 400 of them were malignant (400/704, 56.8%) and 304 were benign (304/704, 43.2%), while BI-RADS 5 category was assigned for 820 lesions (53.8%), 765 of them were malignant (765/820, 93.3%) and 55 were benign (55/820, 6.7%).

The most common benign disease with suspicious or malignant looking features was atypical ductal hyperplasia (ADH). Thirty-four percent of ADH was assigned BI-RADS 5 category (i.e., features of highly suspicion of malignancy).

The descriptors of the included lesions at the contrast-based mammogram are demonstrated in Table 2.

Improvement of the parameters was greatly achieved when the AI abnormality scoring elicited was considered in interpreting the contrast-enhanced images.

The diagnostic performance of the contrast mammogram after consideration of the AI scoring was superior to that of the mammogram aided by AI alone and contrast-enhanced mammogram alone, Figs. 1 and 2.

The BI-RADS category of contrast mammography with consideration of the AI scoring was correlated with the pathology, Fig. 2.

The sensitivity of digital mammogram was significantly increased when the findings were supported by the scoring of the AI algorithm or the functional information elicited by the contrast enhancement each at a time (from 93.9 and 94.4% to 97.2%, $p < 0.001$). Comparable results were presented by the negative predictive value (from 80.6 and 79.6% to 89.8%, $p < 0.05$) and the accuracy (from 91.1 and 88.8% to 94.0%, $p < 0.01$).

The statistical indices were done to evaluate the diagnostic performance of AI-aided mammogram in correlation to the contrast-enhanced mammogram, Table 3.

The AI performance to suggest probability of malignancy in suspicious and malignant looking breast lesions was plotted by the highest area of the ROC curve, and it was 0.936 (95% CI 0.887–0.967) which correlated with the cutoff value of 0.41 for the AI abnormality scoring.

Discussion

Researchers have started to investigate AI with CEM, and the preliminary results are promising [9].

Although most of the depicted lesions at CEM have a correlation with the mammogram images and/or the ultrasound scans, sometimes there are enhancing lesions on the recombined images with no mammographic or sonographic correlate to confirm the need for biopsy [10].

Table 2 The contrast-enhanced mammogram morphology descriptors and contrast uptake features in the study

Descriptors	Malignant ($n=1165$)	Benign ($n=359$)	Total ($n=1524$)
Mass (n = 777, 51%)			
Shape			
Rounded/oval	223	162	385
Irregular	353	39	392
Margin			
Circumscribed	172	194	366
Indistinct/spiculated	404	7	411
Internal enhancement			
Homogeneous	289	187	476
Heterogeneous/rim	287	14	301
Extend of enhancement			
Partial enhancement	57	34	91
Complete enhancement	406	159	565
Enhancement beyond the lesion	66	–	66
Enhancement of the surrounding tissue	47	8	55
Asymmetry/distortion (non-mass) (n = 430, 28%)			
Distribution			
Focal	48	12	60
Segmental	203	73	276
Regional	83	11	94
Enhancement			
Yes	297	67	364
No	37	29	66
Calcifications (n = 317, 21%)			
Shape			
Amorphous	41	41	82
Coarse heterogenous	124	21	145
Clustered pleomorphic	90	–	90
Enhancement			
Yes	157	4	161
No	98	58	156

Deep learning can automatically detect lesions and so help the radiologists to get a precise diagnosis [11]. The ability of artificial intelligence to discriminate malignancy is less likely to be affected by the high breast density and so significantly improves the radiologists' performance [12, 13].

Few studies have dealt with the application of AI algorithm on CEM images to be used for the diagnosis of breast cancer. The idea is still under invention.

In the current work, we correlated suspicious or malignant looking descriptors detected at contrast-enhanced mammography with the scanning outcomes of the artificial intelligence applied on mammograms.

(See figure on next page.)

Fig. 1 A 43-year-old female presented by focal mastalgia at the upper outer quadrant of the left breast proved to be intraductal papilloma and atypical ductal hyperplasia. **A** Bilateral digital mammogram (cranio-caudal views). There was suspicious asymmetry and distortion (circle) at the upper outer quadrant of the left breast. A magnified view of the left breast abnormality seen at "**B**." **C** Ultrasound image of the abnormality presented an irregular partly indistinct solid mass (BI-RADS 4). **D** AI scanned four view mammograms displayed low probability of cancer (38% possibly not cancer) of the left breast abnormality. **E** Recombinant images of contrast mammogram (medio-lateral oblique and cranio-caudal views) presented an indistinct non-mass heterogeneous enhancement (arrow) at the left breast. A magnified view of the left breast abnormality seen at "**F**" justified the probability of cancer and BI-RADS 4 category. The case was considered true negative by AI and false positive by contrast-enhanced mammography

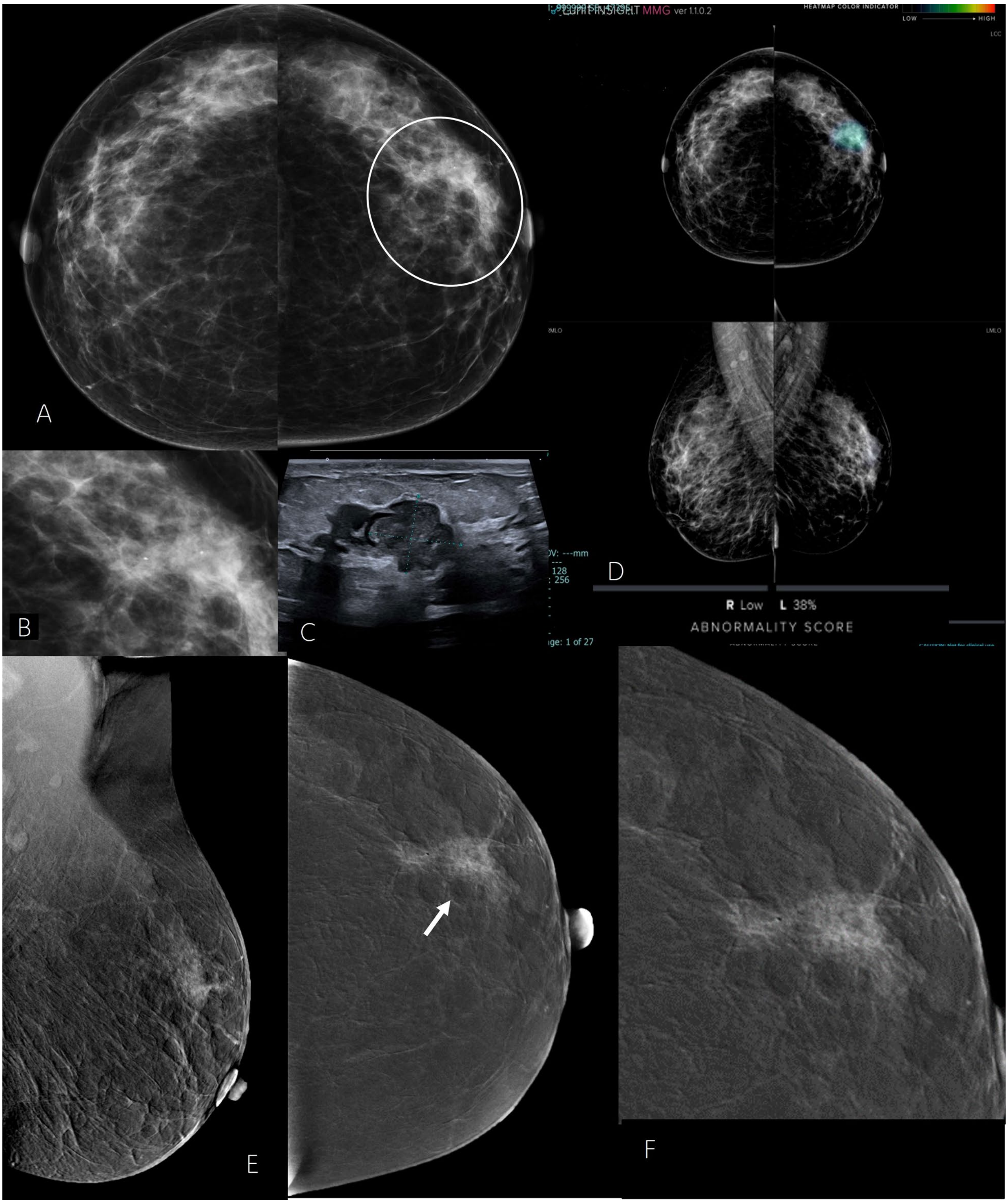

Fig. 1 (See legend on previous page.)

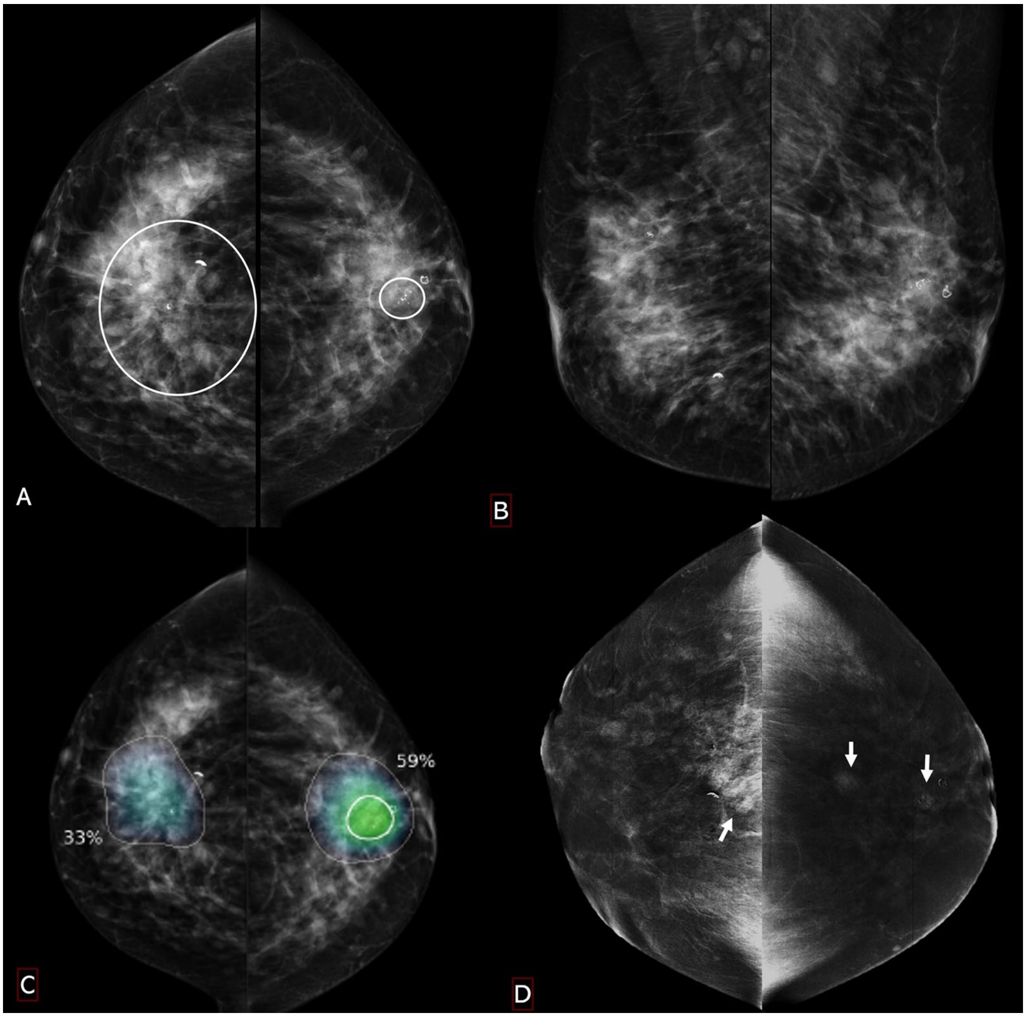

Fig. 2 Bilateral suspicious breast lesions in a 50-year-old female complaining of bilateral brownish nipple discharge. The right side lesion proved to be sclerosing adenosis, and left one was ductal carcinoma in situ with invasion capsulating sclerosing adenosis. **A** Cranio-caudal views and **B** medio-lateral oblique views of digital mammogram, showing a rounded lobulated mass at the upper outer quadrant of the right breast and a cluster of amorphous calcifications at the left breast, both abnormalities categorized BI-RADS 4 (circles). **C** AI scanned mammogram showed low scoring of the right breast abnormality (33%, possibly non-cancer) and relatively high scoring of the left side cluster (59%, possibly cancer). **D** Contrast-enhanced mammogram (cranio-caudal views) showed enhancing lesions (arrows); deep central mass (BI-RADS 4) at the right breast and two focal lesions at the left breast, one anterior that represented the suspicious cluster of calcifications (BI-RADS 4) and another one posterior that was found to be benign looking mass likely an adenoma on ultrasound (image not supplied). AI scoring of suspicion was the more compatible with the pathology results

This study included 1488 females who presented 1524 suspicious and malignant looking (BI-RADS 4 or 5) breast lesions. Eighteen cases displayed bilateral diseases.

Jochelson et al. [14] had reported a sensitivity that reached 96% for CEM compared to the regular digital mammogram. Another multi-observer study stated that CEM even more improved the diagnostic performance of the breast imaging radiologist (sensitivity was 96.9%, and specificity was 69.7%) [15].

Earlier work that focused mainly on CEM suggested a very high sensitivity that reached 100% and specificity of 87.7% [16].

But unlike the current work, they included studying screening mammograms with indulgent of all benign and malignant looking breast lesions not just the suspicious looking ones. Our work presented sensitivity of 94.4% and specificity of 70.7% for BI-RADS categories 4 and 5 breast lesions.

Table 3 Diagnostic performance of AI-aided mammogram, contrast-enhanced mammogram, and AI aided to mammogram supported with contrast-enhanced mammogram

	AI-MMG	CEM	AI-MMG + CEM
Diagnostic performance			
FN	71	65	33
TP	1094	1100	1132
TN	295	254	291
FP	64	105	68
Statistical indices			
Sensitivity	93.9%	94.4%	97.2%
Specificity	82.2%	70.7%	81.1%
PPV	94.5%	91.3%	94.4%
NPV	80.6%	79.6%	89.8%
Accuracy	91.1%	88.84%	94.0%
+ve LHR	1.1564	1.35347	1.36708
−ve LHR	1.1301	1.19377	0.93002

FN false negative, *TP* true positive, *TN* true negative, *FP* false positive, *PPV* positive predictive value, *NPV* negative predictive value, and *LHR* likelihood ratio

False-positive ($n=105$) breast lesions diagnosed by CEM included: intraductal papillomatosis ($n=23$), atypical ductal hyperplasia ($n=17$), PASH ($n=11$), nodular sclerosis ($n=9$), granulomatous mastitis ($n=9$), epitheliosis ($n=9$), proliferative fibrocystic mastopathy ($n=8$), benign phyllodes ($n=8$), adenomas ($n=7$), and fat necrosis ($n=4$).

Suspicious abnormalities found on the regular mammogram or contrast-based images were re-analyzed regarding the abnormality scoring percentage elicited by the AI algorithm through scanning of the non-contrast mammogram images (i.e., the primary regular mammograms).

Significant increase in the diagnosis was achieved when AI scanned digital mammogram and correlated with the evaluation of the CEM, the sensitivity was enhanced from 93.9% for mammography and 94.4% for contrast study to 97.2% ($p<0.001$). Accuracy was uplifted to reach 94.0%.

Such outcome was achieved when a cutoff value for the AI abnormality scoring percentage of 0.41 was applied.

The number of false positive was lowered from 105 to 68 lesions when AI-aided mammogram was used in addition to the CEM for re-categorization of the suspicious and malignant looking breast lesions detected previously on the digital mammograms.

The previous work supported the idea that the radiologists were more likely to reach a rapid and precise decision for categorization of the breast lesions in case AI was applied to their work [15].

With the use of AI scanning for digital mammograms, the sorting of the different breast lesions and the need for biopsy was more achievable [17–19].

Several trails have done to apply the AI algorithm directly on the CEM images, to our knowledge, the current work is a pioneer study that suggested the use of AI to scan the traditional mammogram images so that the diagnostic performance of the contrast-based images would be upgraded, and the abuse of such valuable tool of breast cancer diagnosis would be limited, Fig. 3.

CEM images were evaluated by a previous study [20] which proposed an algorithm on 50 breast lesions by the aid of a support vector machine classification and radiomics analysis. Comparable to the current work, they achieved an accuracy of 90% in distinguishing malignancy. Their work presented a decrease in the number of false-positive results while our study showed a significant upgrade in the true-negative outcome: The AI scanned mammograms presented a negative predictive value of 80.6%, the CEM presented 79.6%, and the value was enhanced to 89.8% when the scoring of the AI algorithm impacted the diagnostic findings of the CEM, $p<0.05$.

Our results also agreed with Massafra et al. [21], who studied 53 patients through applying a computer-aided detection (CAD) and random forest classifiers on contrast-based mammograms with resultant sensitivity and specificity of 88.37% and 100%, respectively**.**

Like the current work, in 2018, Danala et al. [22] discriminated breast lesions ($n=111$ lesions) into benign or malignant categories with the aid of a perceptron-based multilayer machine learning. They stated that the recombined images add valuable information to achieve the best diagnostic performance. The consideration of the low energy and the recombined images significantly improves the classification of breast lesions (AUC of 0.848 ± 0.038). In the same year, another study was done by Gao et al. [23], who used deep learning on 49 contrast-based mammographic studies and reached an accuracy of 89% in evaluation of the included cases**.**

Studies have shown high anxiety levels in patients who had never undergone a breast biopsy and anxiety levels remain elevated above baseline till pathology results declared [24]. It is so traumatic if this experience is to be repeated in case the biopsy result was benign while the abnormality looked malignant or suspicious on the mammogram and, moreover, if such morphology suspicion was supported by abnormal enhancement at the contrast-based study.

During the current experience, there were malignancies only detected on contrast-based mammography that were hideous to conventional imaging and were not scored by the AI as well ($n=7$). These lesions were

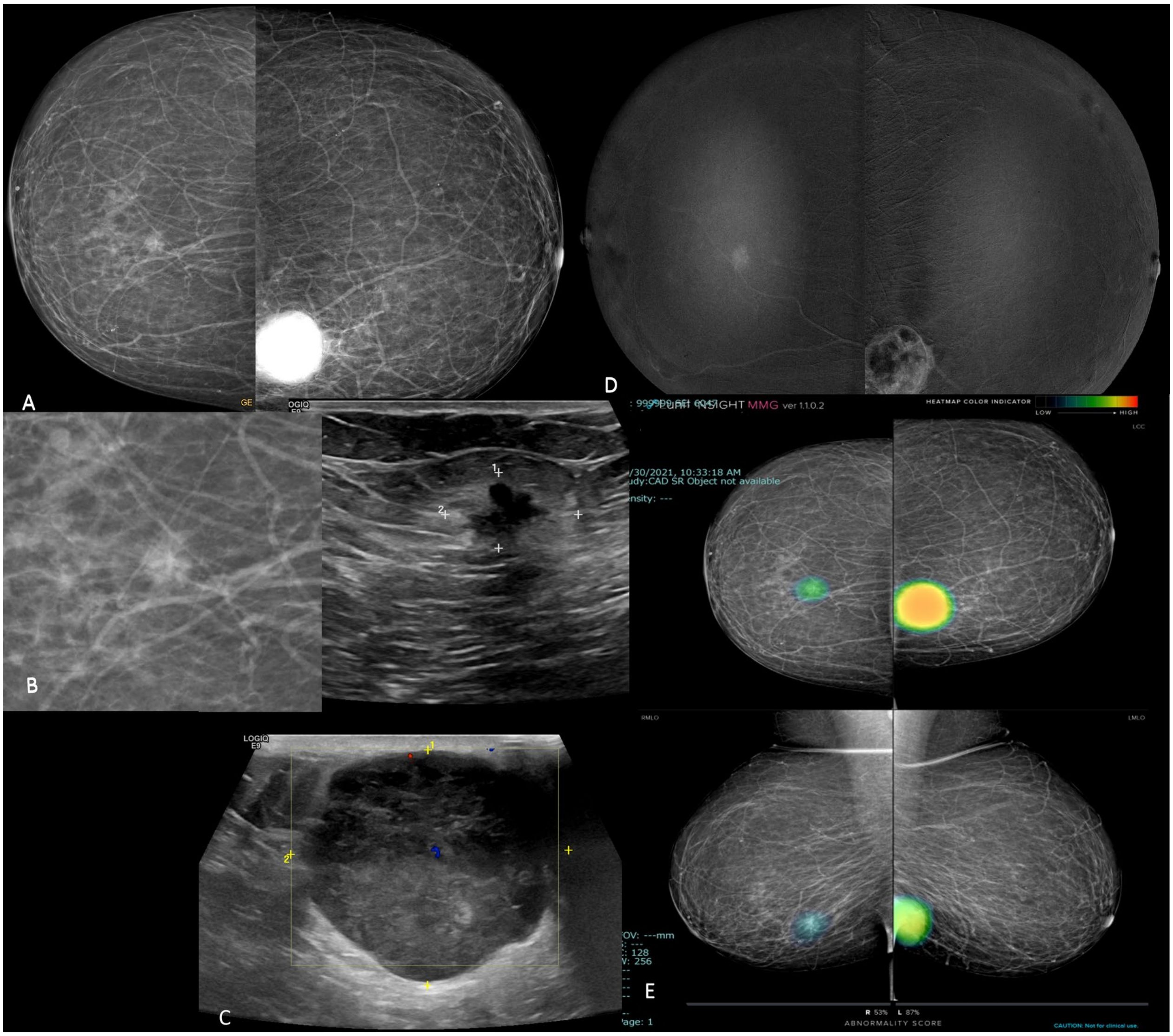

Fig. 3 Bilateral breast masses in a 57-year-old female presented for diagnostic mammogram proved to be bilateral invasive ductal carcinoma; right grade II and left grade III. **A** Bilateral mammogram cranio-caudal view that showed an indistinct faintly dense irregular mass (BI-RADS 4) at the deep central portion of the right breast and a circumscribed dense rounded mass (BI-RADS 3) at the lower inner quadrant of the left breast. **B** Magnification view and ultrasound image of the right breast mass, features at ultrasound confirm the suspicion of malignancy in the form of margin spiculation and perifocal desmoplastic reaction that upgraded the BI-RADS category from 4 to 5. **C** Ultrasound image of the left breast mass presented purely solid texture. The point of suspicion was the large size of the mass. **D** Bilateral contrast-enhanced mammogram cranio-caudal view that displayed malignant looking features of the left breast mass (BI-RADS 5). **E** AI scanned mammogram presented 53% (possibly cancer) scoring for the right breast mass and 87% (probably cancer) scoring for the left breast mass. Although the left breast mass showed features of a probably benign lesion (i.e., BI-RADS 3) on digital mammogram, yet contrast-enhanced mammogram and AI features suggested likely malignant probability that matched with the pathology results

discovered incidentally during the scanning of the concurrent suspicious lesions, Fig. 4.

For statistical purposes, incidental abnormal contrast uptake found only at CEM was not included in the study results. The current work focused on the ability to use AI for enhancing the specification of contrast-enhanced mammogram and was not involved with the comparison between AI and contrast-enhanced mammogram to detect breast lesions/carcinomas.

It is recommended to use CEM in dense breasts (ACR c and d) that show nodular parenchymal pattern, especially if cancer was concomitant with marked inflammatory changes to get the proper staging of the existing cancer and exclude contralateral carcinoma. Such privilege of

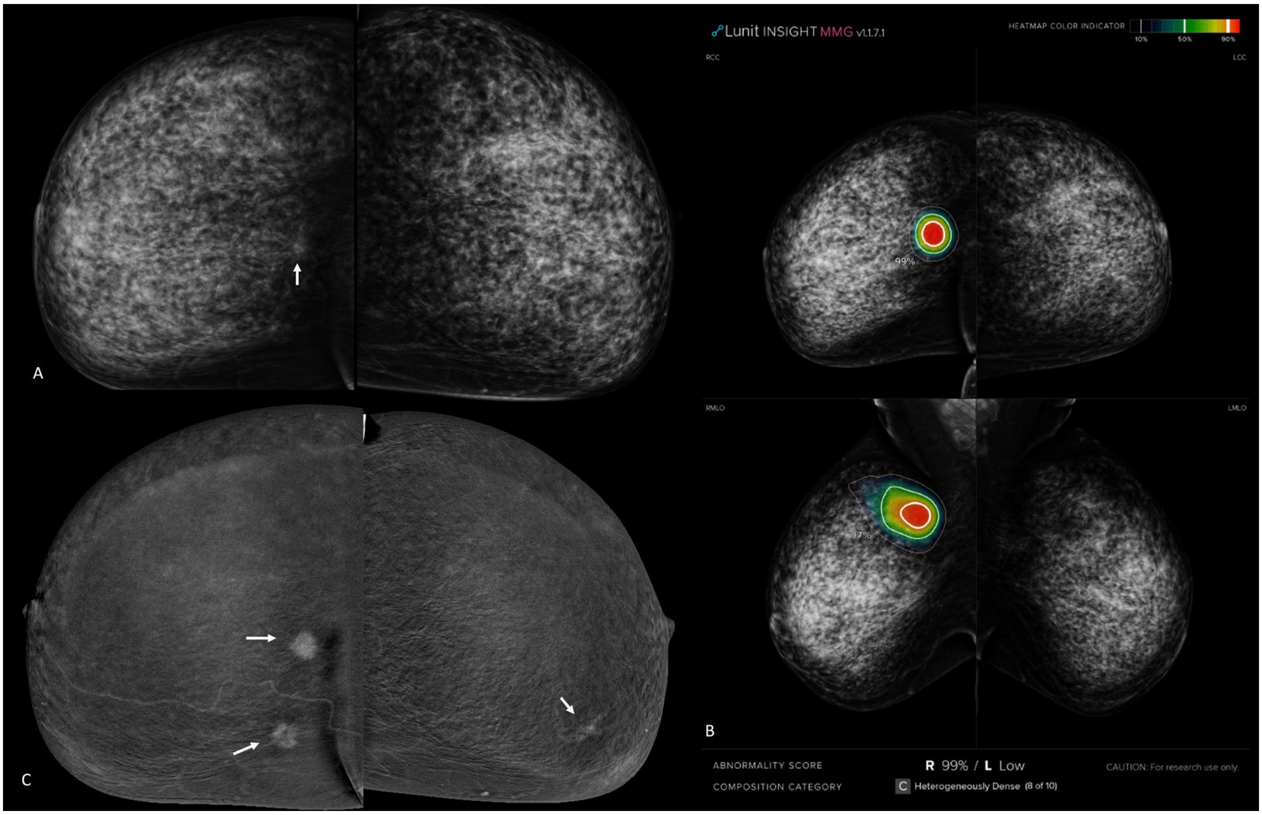

Fig. 4 Bilateral invasive ductal carcinoma (right grade II and left grade III) in a 52-year-old female presented for screening mammogram and showed dense breast (ACR d). **A** Mammographic cranio-caudal view displayed a suspected small mass with indistinct borders (arrow), BI-RADS 4 at the deep central portion of the right breast (obviously appreciated at digital mammogram). **B** AI scanned mammogram (cranio-caudal and medio-lateral oblique views) detected and scored the mass for being malignant (suspicion confidence scoring was 99%). No other areas were marked by the AI. **C** CEM detected multiple distribution of the right breast carcinoma (arrows) and contralateral proved malignancy in the form of faintly enhancing non-mass (only appreciated at the contrast images, arrow). AI supported the specification of the right breast mass on mammogram, yet the high density of the breast affected the performance of the algorithm to do proper staging of the right breast and categorization of the left breast carcinoma

CEM could affect the patient's management and follow-up rather than decide the need for interventional procedure thus minimize the patient's anxiety and expenses of health care.

This study has some limitations. First, patients undergoing CESM had a suspicious abnormality on mammogram, the selection of cases was focusing on lesions with malignant potential, so the conclusions may not practically applicable to patients presented in general for breast examination with contrast-based mammography. Second, the study was retrospective, so this implies that there was a selection bias, mainly oriented to diagnostic mammogram, with an overrepresented percentage of cancer patients. Another limitation is that multifocality and multicentricity carcinomas have not been addressed since we decided to focus upon detection and diagnosis rather than tumor staging. Finally, the study included both pre- and postmenopausal patients, who were evaluated in different phases of the menstrual cycle, so there was no standardization for the background contrast uptake in correlation of lesion conspicuity; however, there are still no data to indicate if there is an effect of the phase of the menstrual cycle on the background contrast uptake in CEM.

Conclusions

Contrast-enhanced mammogram helps in specification of different breast lesions in view of patterns of contrast uptake and morphology descriptors, yet with some overlap.

The use of artificial intelligence applied on digital mammogram reduced the interpretational variability and limited attempts of re-biopsies of suspicious looking breast lesions assessed by contrast-enhanced mammograms.

Abbreviations

ADH	Atypical ductal hyperplasia
ACR	American College of Radiology
AI	Artificial intelligence
AUC	Area under the curve
BI-RADS	Breast Imaging-Reporting and Data System
CI	Confidence interval
CAD	Computer-aided detection
CEM	Contrast-enhanced mammogram
CNNs	Convolutional neural networks
DCIS	Ductal carcinoma in situ
FP	False positive
IDC	Invasive ductal carcinoma
ILC	Invasive lobular carcinoma
kVp	Kilovoltage peak
NPV	Negative predictive value
PASH	Pseudoangiomatous stromal hyperplasia
PPV	Positive predictive value
SPSS	Statistical Package for the Social Sciences

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Author contributions
MS is the guarantor of integrity of the entire study. AH and MS contributed to the study concepts and design. MS and EH contributed to the literature research. MS, AH, and EH contributed to the clinical studies. MS, AH, and EH contributed to the experimental studies/data analysis. MS and AH contributed to the statistical analysis. MS, AH, and EH contributed to the manuscript preparation. MS, AH, and EH contributed to the manuscript editing. All authors have read and approved the final manuscript.

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Availability of data and materials
The corresponding author is responsible for 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 Department of El Kasr ElAiny Hospital, Cairo University, which is an academic governmental supported highly specialized multidisciplinary hospital. A waiver of informed consent was obtained.

Consent for publication
All patients included in this research were legible, above 16 years of age. The study was waived to get written informed consent from the included patients.

Competing interests
The authors declare that they have no competing interests.

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