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RESEARCH

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Resistant inflammatory breast lesions: can AI exclude malignancy?

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Abstract

Background Numerous underlying causes can lead to inflammatory breast disorders. A wide range of non-specific symptoms may be presenting symptoms, which could cause a delay in diagnosis and thus improper therapy. Studies on artificial intelligence (AI) are rapidly developing and offer a wide range of possible uses in breast imaging. Artificial intelligence-based computer-assisted diagnosis (AI-CAD) holds promise in the field of mammography. It demonstrated diagnostic performances that are equivalent to or even better than those achieved by stand-alone methods. The current work aimed to identify whether AI can improve the performance of mammography in diagnosing inflammatory breast diseases and excluding the underlying malignancy in cases resistant to treatment that may reduce the need for interventional procedures such as biopsy.

Methods Our study was a retrograde one done on 34 patients with pathologically proven inflammatory breast lesions.

Results Suppurative breast lesions gave high false positive results. This was also the case with granulomatous mastitis; while simple inflammatory lesions gave true negative results on AI interrogation.

Conclusions Artificial intelligence can be of great value in diagnosing simple inflammatory breast lesions thus following up on such lesions can usually be sufficient without asking for unneeded biopsies. On the other hand, our study showed that AI had high false positive results in suppurative lesions and granulomatous mastitis. Consequently, ultrasonography can be more reliable in their diagnosis.

Keywords Artificial intelligence, Mammography, Granulomatous mastitis

Background

There are several diverse underlying causes of inflammatory breast illnesses, such as common benign infections, non-infectious inflammation, and inflammation that are brought on by underlying breast cancer [1].

Inflammation of the breast parenchyma is referred to as mastitis, and it frequently manifests as discomfort, edema, warmth, erythema, and fever which could be a long-lasting, debilitating condition [2].

Mammography and ultrasonography (US) can be performed as the initial diagnostic action for any breast mastitis. The presenting changes are frequently non-specific (focal asymmetric density, poorly defined hypoechoic mass, etc.) [3].

Computer-aided detection (CADe) techniques have been under development for many decades to identify potentially malignant changes within medical images [4].

Studies on (AI) and radiomics can offer a wide range of uses in breast imaging, such as a prediction of breast cancer risk, lesion identification, and categorization.

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Artificial Intelligence (AI) has been applied to several imaging modalities, as mammographic examination, US, and magnetic resonance imaging (MRI) [5].

The utilization of artificial intelligence-based computer-assisted diagnosis (AI-CAD) in mammographic examination has demonstrated diagnostic performances that are equivalent to or even better than those achieved by stand-alone methods [6].

The aim of the work was to identify whether AI can improve the performance of mammography in diagnosing inflammatory breast diseases and excluding underlying malignancy in cases resistant to treatment that may reduce the need for additional interventional procedures such as biopsy.

Methods

Patients

The current study was a retrospective one. Thirty-four female patients with 34 pathologically confirmed inflammatory breast lesions participated in this retrospective analysis.. Their age ranged between 44 and 68 years. The mean age was 44.8 ± 8.6. This study was performed in the radiology department, at our institute between November 2022 and November 2023. The ethical committee at our institute approved our research.

Proper history taking was done for the patients enrolled in the current study. They were asked for history of previous breast cancer or previous known primary (which was not found in our study population). Patients complaining of clinical signs of breast inflammation were referred to our department to perform bilateral sono-mammographic examination. Afterward, they were referred to the physician for proper medical treatment and were asked to repeat the US examination after completing their medical treatment, usually after 10 to 14 days. Nonresolution or poor response to medical treatment was an indication for histopathological confirmation. We excluded young female patients (less than 40 years) who underwent ultrasonography with no mammography done for their diagnosis. Also, we excluded patients where AI images were not available at the time of data collection. The data of the patients were collected using Paxera fuji PACS system.

Mammography

Bilateral mammography was performed using Senograph 2000 Full Field Digital Mammography GE Healthcare. For every breast, two standard views were obtained: mediolateral (MLO) and craniocaudal (CC) positions. A standard mammography involving two images acquired for each breast typically requires a total dose of approximately 0.4 millisieverts (mSv). Image interpretation was done by two experienced radiologists in mammography, (6 and 4 years of experience) giving a subjective assessment of mammography abnormalities guided by the ACR / BIRADS "Breast Imaging Reporting and Data System" Atlas 2013. Images were evaluated by the two radiologist separately. In case of inconcensus, a third party was consulted.

Ultrasonography

An ultrasonography device (GE machine) with a 9–13 MHz linear probe was used. The radiologists performed all the real-time scanning. Finally, a definitive interpretation was reached. During the examination, patients lay flat with both arms lifted, and a liquid-based gel was applied to the area of interest. The breast quadrants were examined radially, and the skin-to-pectoral fascia depth was thoroughly examined. The axillary lymph nodes were then examined.

Ultrasound-guided biopsy was arranged for patients with poor response to medical treatment. The area of interest was sterilized, and injection of local anesthesia was performed followed by the introduction of a 16G Tru-cut needle. The needle (guided by ultrasound) was used to obtain at least four to six cores from the area of concern. The tissue core biopsied was fixed in 10% neutral buffered formalin and was sent for histopathological verification. Inflammation was diagnosed in the presence of inflammatory cells and absence of malignant cells in the tissue cores.

AI

The AI software processed and scanned each breast's four standard CC and MLO views. Any abnormalities that were identified and classified by the system algorithm were localized by the AI software. AI analysis was carried out via both quantitative as well as qualitative standards. Regarding the qualitative criteria, a data visualization uses a color-hued "heat map" to depict the extent of abnormality. The hue of the color is not a pure pigment, but rather a combination of many colored patches (i.e., not separate hues). In the mammography pictures, this combination of colors identifies the breast lesion. The hues varied from a soft turquoise blue to a vibrant red. A spectrum of colors was layered upon one another, with the degree of color hotness increasing in parallel with a rise in the abnormalities scoring percentage number, which indicates the degree of suspicion regarding malignancy.

On the other hand, quantitative criteria: "Abnormality scoring" is a numerical assessment of the degree of confidence for the suspicion of malignancy that varies from 1 to 100. The highest level of suspicion is expressed by the value 100, which reflects the probability of malignancy (PoM) score identified for each lesion, which goes from

1 to 100%. (100% denotes the greatest degree of suspicion, while 1% denotes the lowest degree) that is appreciated at the bottom of the mammographic image. In our study, we considered the cutoff value for malignancy 50%, according to *Mansour* et al., [7] above 50 up to 99% to be considered probably malignant.

We classified the AI group into three categories (non-cancer when the AI Score gave 10% or less, probably non-cancer when the AI score gave from 10 to 50%, and probably cancer when the AI score was given from 51 to 99%. The probability of malignancy with AI and the BIRADS score by the radiologist for each breast was correlated with the histopathological results.

Statistics

An Excel spreadsheet was established for data entry. The analyses were performed with SPSS software (Statistical Package for the Social Sciences, version 24, SSPS Inc, Chicago, IL, USA). Frequency tables with percentages will be used for categorical variables, and descriptive statistics (mean and standard deviation) was used for numerical variables. Either paired Student's t or Mann–Whitney tests were used to compare quantitative variables, while McNemar or McNemar–Bowker tests were used to analyze categorical variables. A p-value < 0.05 is considered statistically significant. Correlation with tumor size was studied by calculating Pearson's correlation index.

Results

Our study included 34 patients; those patients were referred to the radiodiagnosis department from November 2022 to November 2023. Regarding the demographic distribution of the patients, they were between 44 and 68 years old, with a mean age of 44.8 ± 8.6 years (Table 1). They were all married. Regarding the symptoms among the studied population, pain was found in all studied patients (100%), fever in 14 patients (41.2%), and lump in 18 patients (52.9%) of the studied patients.

All patients underwent mammographic examination which revealed unilateral breast lesions. Mammography showed partly obscured lesions in 10 patients (29.4%) (Figs. 1, 2), focal asymmetry in 17 patients (50%) (Figs. 3, 4), coarsened trabeculations in 6 patients (17.6%), and well-circumscribed lesions in 1 patient (2.9%).

Table 1 Description of age in all studied patients

	Studied patients (N = 34)
Age (years)	
Mean ± SD	44.8 ± 8.6
Min – Max	44–68

Regarding the description of BIRADS in all studied patients, there were 16 patients (47%) of BIRADS III (Fig. 2), 12 patients (35.3%) of BIRADS Iva, 5 patients (14.7%) of BIRADS IVc (Fig. 5), and 1 patient (2.9%) of BIRADS V in the studied patients (Fig. 6).

Histopathology was done for all 34 cases. It revealed suppurative smears in 13 patients (38.3%), granulomatous smears in 15 patients (44.1%), and 6 patients (17.6%) with inflammatory smears as shown in Fig. 7.

Patients with granulomatous mastitis showed non-specific features on their mammography like focal asymmetries, distortion, and coarsened trabeculations. Their US imaging features also showed ill-defined masses or hypoechoic areas with some showing sinus formation and thickening of the overlying skin.

For the AI qualitative value, each breast was assigned a category and an AI abnormality score. At a cut-ff value of 51% abnormality score, the AI software showed that 47.1% ($n = 16$) of the cases were considered malignant "high" breast lesions (AI risk of malignancy score ≥ 51%) and 52.9% ($n = 18$) breast lesions were considered benign "low" (AI percentage risk of malignancy score < 51%). As for the AI quantitative value, it was definite non-cancer in 9 patients (26.5%), probably non-cancer in 9 patients (26.5%), and probably cancer in 16 patients (47%) of the studied patients (Table 2).

As regards density, it was ACR A in 1 patient (2.9%), ACR B in 13 patients (38.2%), ACR C in 16 patients (47.1%), and ACR D in 4 patients (11.8%) of the studied patients (Table 2).

After correlating the AI results to the histopathological types (Table 3), we found that:

- In patients with *definite non-cancer* by AI, there were 3 patients (33.3%) with suppurative smear, 2 patients (22.2%) with inflammatory smear, and 4 patients (44.4%) with granulomatous smear.
- In patients with *probably non-cancer* by AI, there was 1 patient (11.1%) with a suppurative smear, 4 patients (44.4%) with an inflammatory smear, and 4 patients (44.4%) with a granulomatous smear.
- In patients with *probably cancer* by AI, there were 9 patients (56.3%) of suppurative smear and 7 patients (43.7%) of granulomatous smear.

Our study revealed that there was no statistically significant difference (p-value = 0.528) between AI qualitative value results and histopathology results.

The final diagnosis of the lesions was determined by the histopathology results, and after comparing the AI

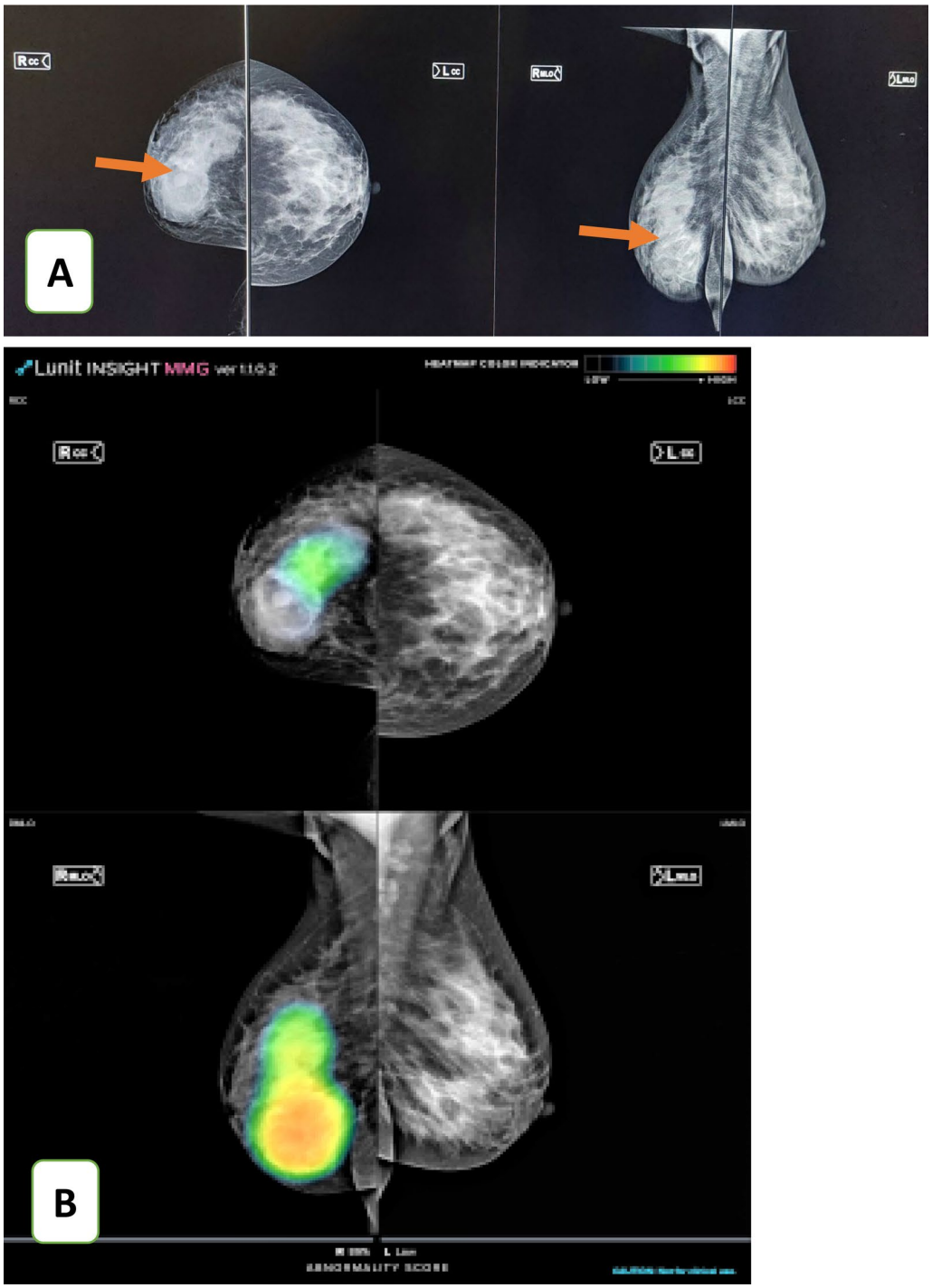

Fig. 1 A 49-year-old female came with a right breast lump and pain. **A** Mammography images revealed the right LIQ obscured mass lesion. (BIRADS 3). **B** AI highlighted an area of the right breast lesion with an 89% risk of malignancy and the color hue map gave a mix of colors with predominant yellow and orange colors. Pathology revealed a complicated galactocele. AI showed the area of concern in the right breast as a malignant lesion; however, it was proved to be benign by pathology. (FP results)

abnormality score to the pathology results (Table 4), the AI showed 47.1% ($n=16$) as false positive (FP) results and 52.9% ($n=18$) as true negative cases.

The mammography matches the pathology results in 16 of the cases (the pathologically benign) and mismatches the results in 18 cases giving FP results (pathologically benign) (Table 5).

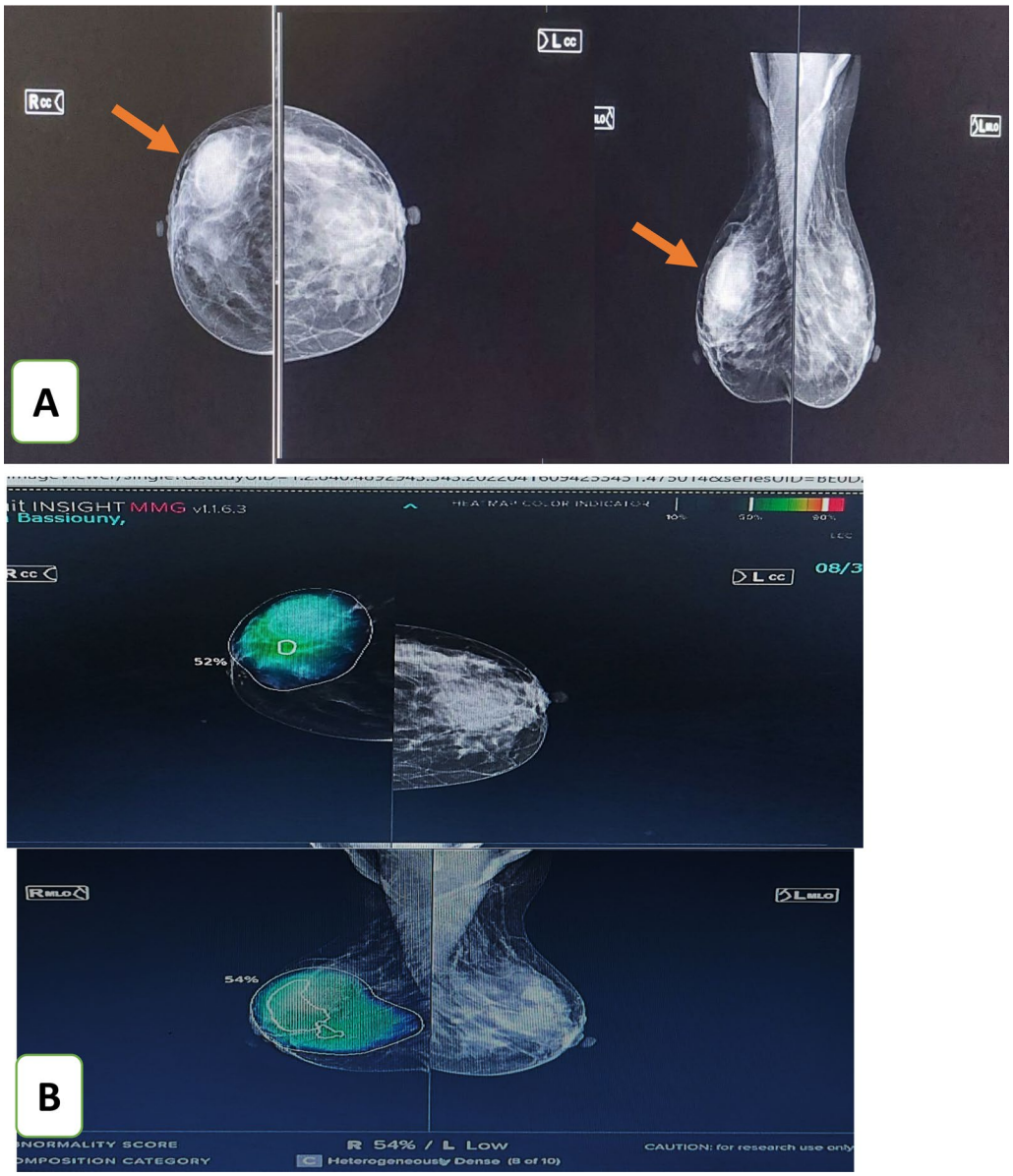

Fig. 2 A 53-year-old female came with a right breast painful lump. **A** Mammography images revealed the right UOQ partly obscured mass lesion. (BIRADS 3). **B** AI highlighted an area of the right breast lesion with a 54% risk of malignancy and the color hue map gave a turquoise and faint green color. Pathology revealed a complicated cyst (suppurative smear). AI showed the area of concern in the right breast as a malignant lesion; however, it was proved to be benign by pathology. (FP results)

Discussion

Numerous underlying factors can lead to inflammatory breast diseases. Understanding specific imaging features may be beneficial for improved treatment of inflammatory breast illnesses, as it can occasionally be challenging to differentiate between mastitis and breast cancer based solely on a clinical basis [8]. A pathologic diagnosis is required for some conditions not only to rule out underlying malignancy but also to reach a specific diagnosis especially if a treatment strategy is unsuccessful [9].

The aim of the current study was to identify whether the AI was able to differentiate between different subtypes of breast inflammations or not. We performed a retrograde study on 34 female patients who presented with clinical signs of breast inflammation. All patients underwent mammography, ultrasonography, and finally histopathology. We reviewed the AI images for those patients and compared them to the mammography, while the pathology was the gold standard for the diagnosis.

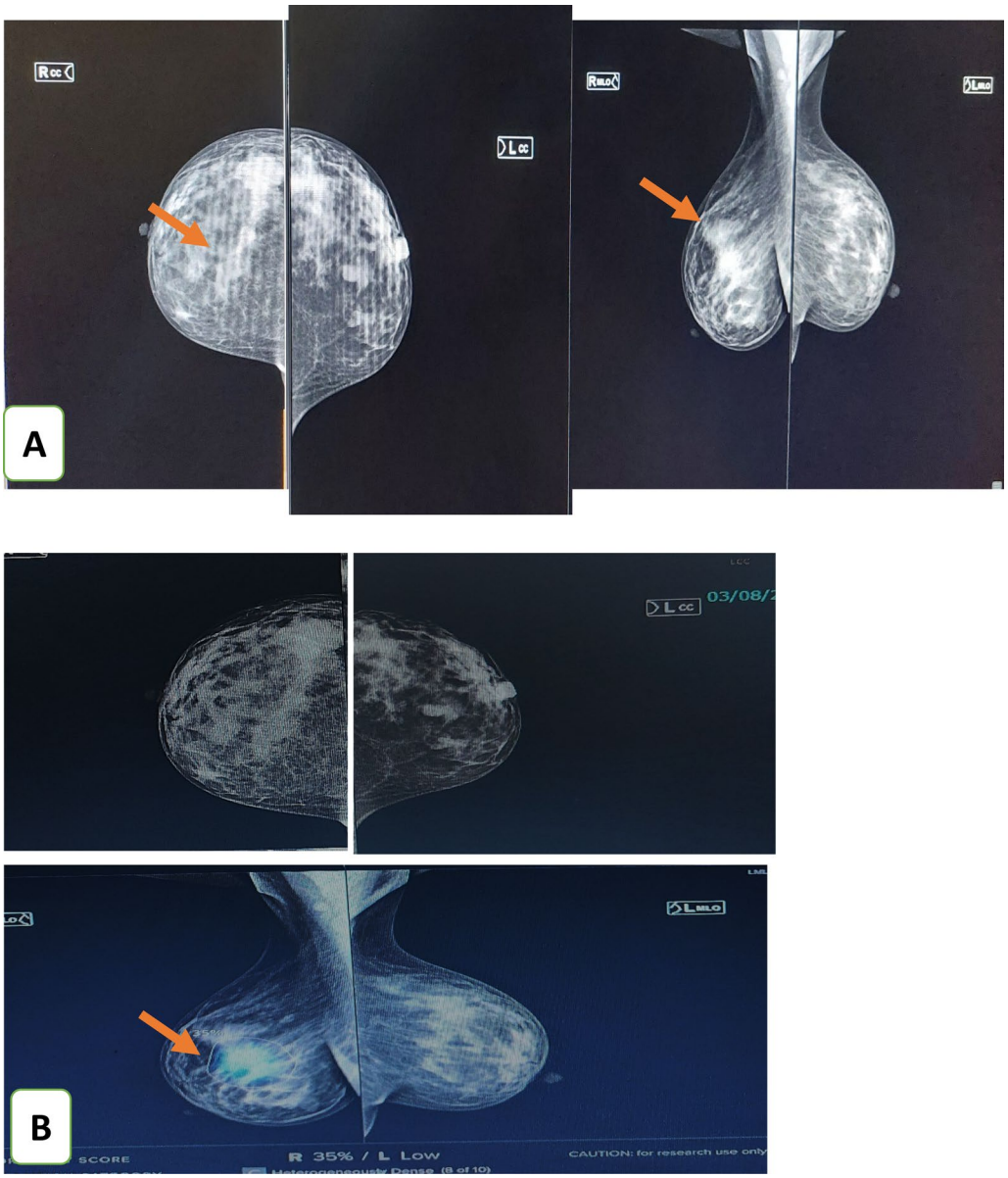

Fig. 3 A 47-year-old female came with a right breast tenderness. **A** Mammography revealed heterogeneously dense breast with multiple bilateral obscured opacities (confirmed to be cysts by US) and right upper inner focal asymmetry (BIRADS 4). **B** AI showed it as a non-malignant lesion. Histopathological assessment proved to be benign (inflammatory parenchyma (inflammatory smear)) by pathology. (True negative results)

We divided our cases into three groups based on their final pathology reports. Thirteen patients were classified as the suppurative group, six as the inflammatory group, and 15 as the granulomatous group.

The breast lesions identified during the current work were assigned a category and an AI abnormality score. The AI revealed that 47.1% ($n=16$) of the breast lesions were malignant. (AI risk of malignancy score was > 51%) abnormality score while 52.9% ($n=18$) breast lesions were assigned benign by AI.

After correlating the AI results with histological subtypes, we found that:

- In patients categorized as "definite non-cancer" by AI, there were 3 patients (33.3%) with suppurative smear, 2 patients (22.2%) with inflammatory smear, and 4 patients (44.4%) with granulomatous smear.
- In patients categorized as "probably non-cancer" by AI, there was 1 patient (11.1%) with a suppurative smear, 4 patients (44.4%) with an inflammatory

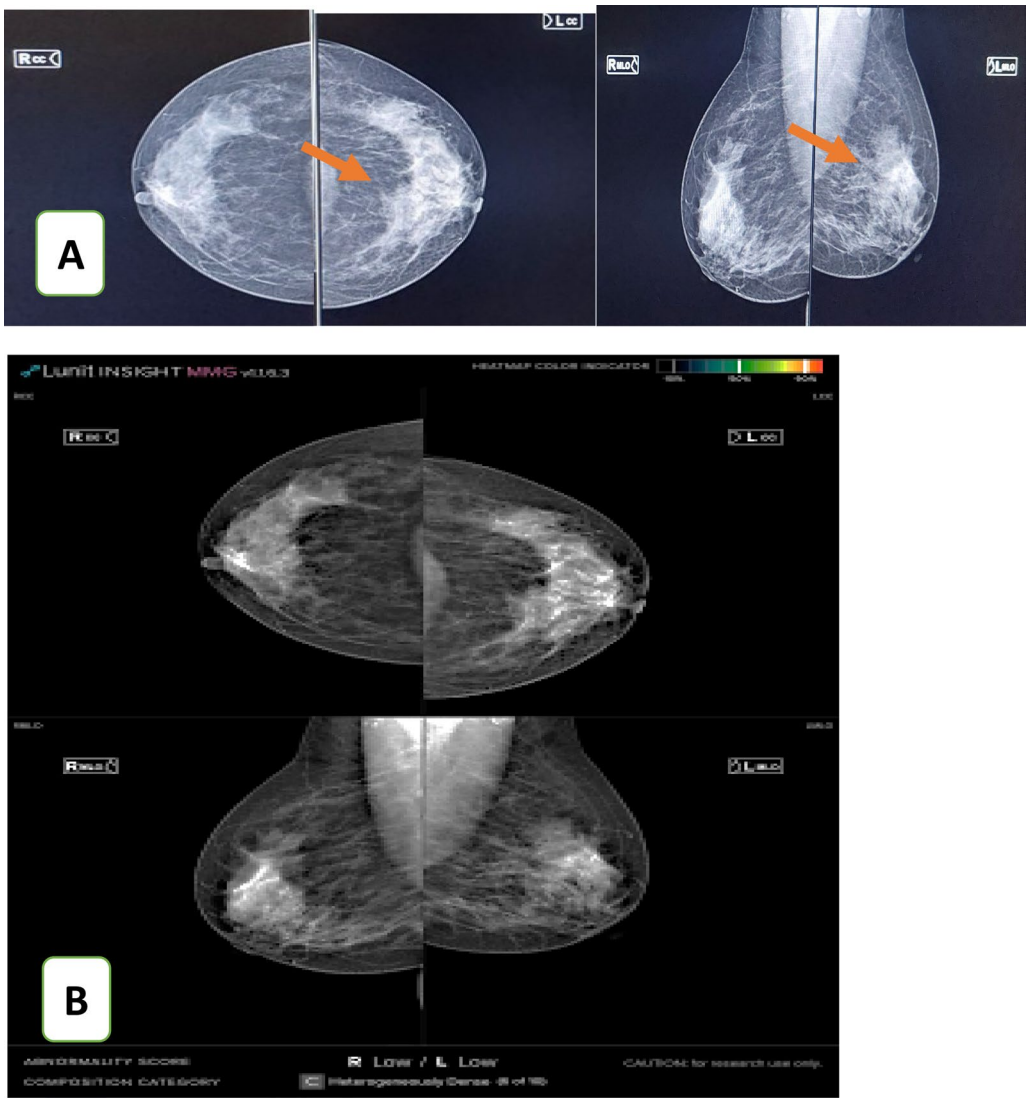

Fig. 4 A 42-year-old female came with a left breast pain. **A** Mammography revealed left upper central focal asymmetry (BIRADS 3). **B** AI did not detect any lesion in the area of concern in the left breast, so it is considered a low risk of malignancy. Pathology revealed; inflammatory parenchyma (inflammatory smear); (True negative results)

smear, and 4 patients (44.4%) with a granulomatous smear.

- In patients categorized as "probably cancer" by AI, there were 9 patients (56.3%) of suppurative smear and 7 patients (43.7%) of granulomatous smear.

High AI risk of malignancy was seen in 47.1% ($n=16$) cases. Those were considered FP lesions on AI. These were suppurative lesions ($n=9$) and granulomatous lesions ($n=7$). Low AI risk of malignancy was seen in 52.9% ($n=18$) cases, those were considered true negative lesions on AI. These ($n=18$) were suppurative lesions ($n=4$), inflammatory lesions ($n=6$), and granulomatous lesions ($n=8$) (Table 2).

Our study included six cases with proven inflammatory disease. All the six cases were diagnosed by AI as "probably/definitely non-cancer" cases. This gave the AI a true negative rate of 100% in suspected inflammatory disease (high specificity).

As for the pathologically proven suppurative group, 13/34 cases (38.2%). The AI diagnosed nine of the 13 cases 9/13 = 69.2% as "probably cancer". Those are considered FP cases. Thus, the specificity of AI to exclude cancer in cases of suppurative disease was 4/13 = 30.7% (Low specificity).

Granulomatous mastitis cases in our study showed non-specific findings on mammography as well as on ultrasonography. This also matched Guirguis et al. [10]

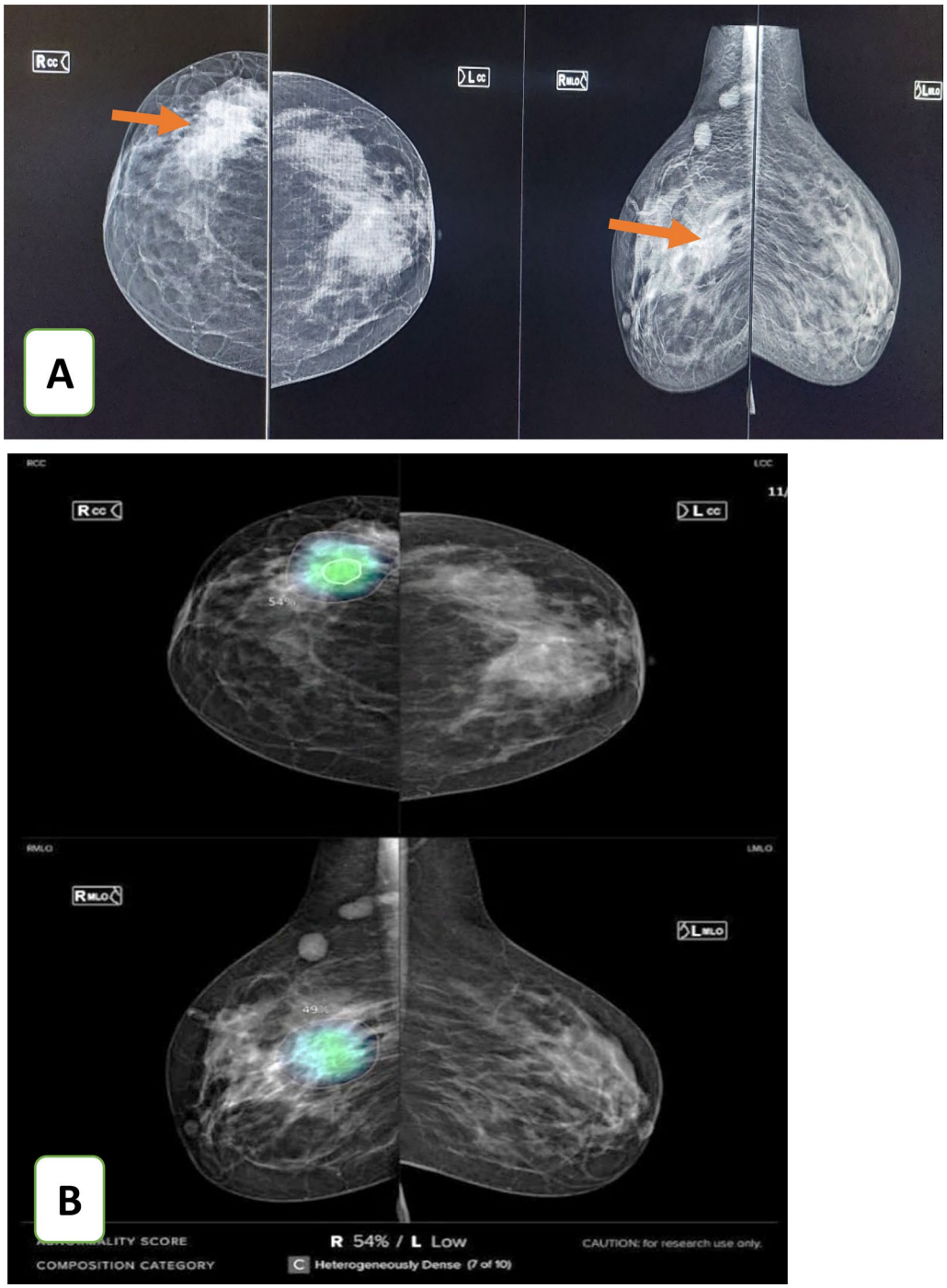

Fig. 5 A 41-year-old female patient came complaining of a right breast lump. **A** Mammography revealed a right UOQ focal asymmetry with distortion that was given a BIRADS 4C. **B** AI highlights an area of the right breast lesion with a 54% risk of malignancy. The color hue map was predominantly pale blue and light green. Pathology revealed granulomatous mastitis. (FP by both mammography and AI)

who also stated that granulomatous mastitis can show occult findings in some cases, and sometimes can be even indistinguishable from malignant breast lesions.

We noticed in our study that AI showed better results only in the inflammatory group unlike the granulomatous and the suppurative groups. This might be because

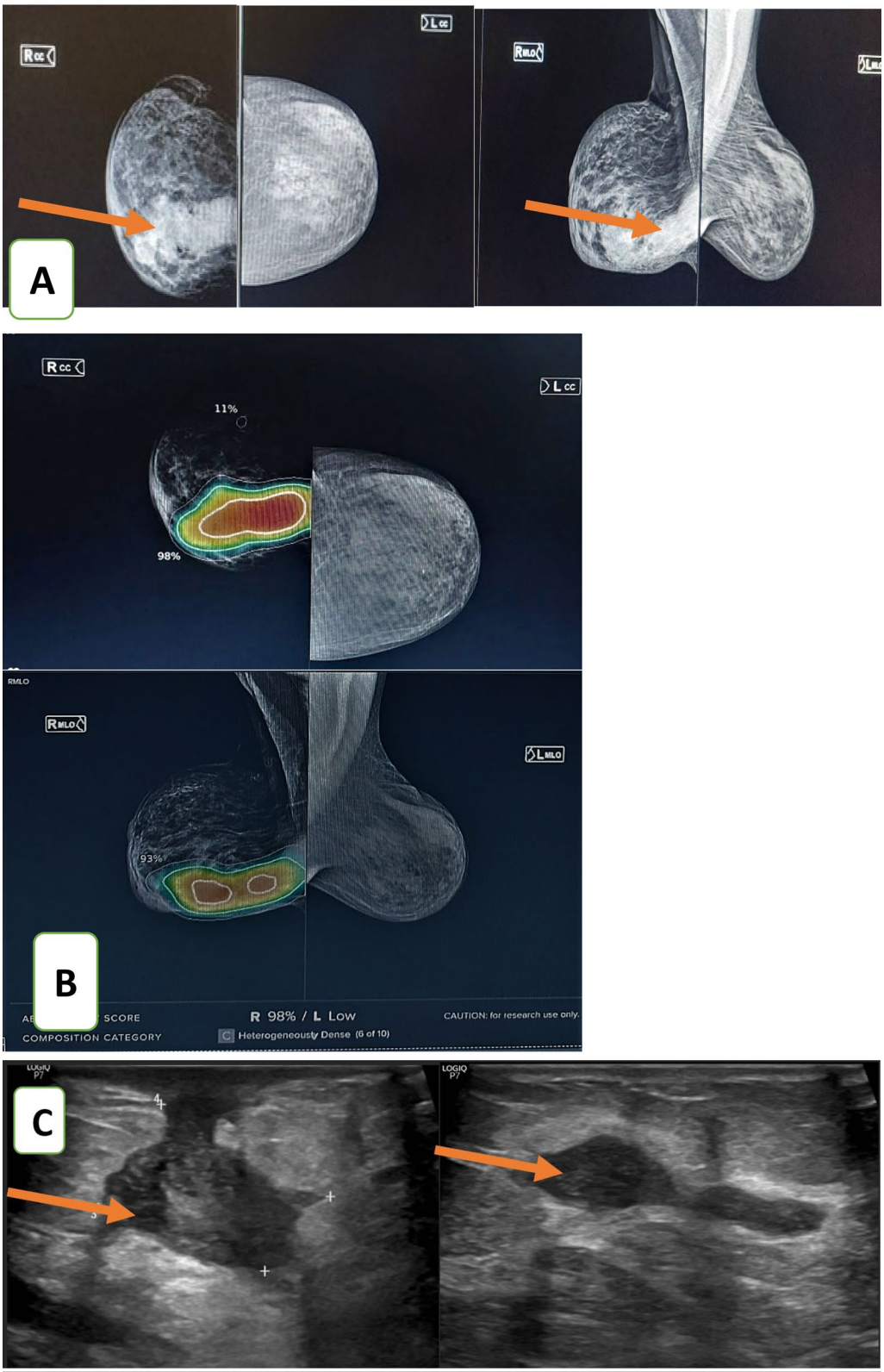

Fig. 6 A 62-year-old female came with a tender right breast lump. **A** Mammography revealed a right large dense lesion with an ill-defined outline, with coarsened trabeculations and skin thickenings (BIRADS 5) **B** The AI highlighted an area of the right breast lesion with a 98% risk of malignancy. The color hue map showed predominantly red and yellow colors. **C** Ultrasound images showed irregular hypoechoic masses with tubular extensions. Pathology proved to be granulomatous mastitis. (FP by both mammography and AI)

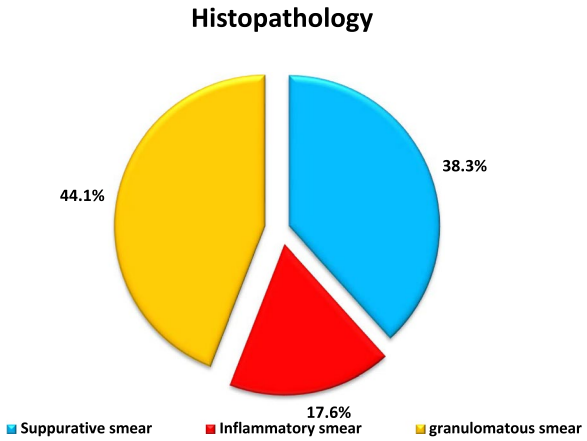

Fig. 7 Description of Histopathology in the studied patients

Table 2 AI qualitative and quantitative AI values among the studied patients

	Studied patients (N = 34)	
Artificial intelligence qualitative value		
Low	18	52.9%
High	16	47%
Artificial intelligence quantitative value		
Definite non-cancer	9	26.5%
Probably non-cancer	9	26.5%
Probably cancer	16	47%
Density		
ACR A	1	2.9%
ACR E	13	38.2%
ACR C	16	47.1%
ACR D	4	11.8%

tissue breakdown and abscess formation in the latter two groups might mimic malignancy as per AI analysis. However, this needs further studies with larger study groups to prove this possibility.

By mammography, true negative results were 16/34 (47.1%) while FP results were 18/34 (52.9%).

In our study, in inflammatory breast lesions, the mammography specificity (without using AI) was 47.1%, while the AI specificity was 52.9%. AI was found to be more specific in cases proven pathologically to be inflammatory.

It is noted that most granulomatous cases with non-cancer ($n = 8$) results by AI 5/8 (62.5%) were ACR class B breast density. Also, most inflammatory cases with non-cancer results by AI 4/6 (66.6%) were ACR class C which correlates with Kim et al. [11] who found that radiologists' performance was more influenced by breast density than AI's diagnostic ability, leading to a notable increase in radiologists' AI-assisted performance in dense breasts.

To our knowledge, there are no studies performed to evaluate the diagnostic capabilities of AI in cases of breast inflammatory lesions alone. Yet, we would like to open the scope for studying the potential benefits of AI in the exclusion of breast cancer among inflammatory breast lesions.

Limitations

Our study showed some limitations. Since we have not included pathologically proven malignant cases (inflammatory breast cancer) in our study, we could not detect false negative cases or true positive cases. Thus, we could not calculate the sensitivity of the AI. Also, the relatively small sample size was included in our study. The AI

Table 3 Comparisons between histopathological types and AI qualitative value

	AI qualitative value						Stat.test	P-value
	Definite non-cancer (n = 9)		Probably non-cancer fn = 9)		Probably cancer (n = 16)			
Histo pathology								
Suppurative	3	33.4%	1	11.1%	9	56.3%	$X^2 = 3.1$	0.528 NS
Inflammatory	2	22.2%	4	44.4%	0	0%		
Granulomatous	4	44.4%	4	44.4%	7	43.7%		

NS: p-value > 0.05 is considered non-significant

Table 4 AI false positive and false negative results

AI results in correlation to pathology	Count (n)	Percentage (%)
False positive	16	47.1%
True negative	18	52.9%

Table 5 Mammography results in correlation to the pathology results

Sensitivity of mammography in correlation to pathology	Count (n)	Percentage (%)
False positive	18	52.9%
True negative	16	47.1%

algorithm does not consider complimentary US findings in the diagnosis which might be of great help to reach the final interpretation.

Conclusions

We found that AI can be useful in diagnosing simple inflammatory breast lesions thus following up can be sufficient with no need for biopsies. Our study showed that AI has high FP results in suppurative lesions and granulomatous mastitis. Consequently, ultrasonography can be more reliable in their diagnosis.

Abbreviations

AI	Artificial intelligence
BIRADS	Breast imaging reporting and data system
CADe	Computer-aided detection
CC	Craniocaudal
FP	False positive
LIQ	Lower inner quadrant
MRI	Magnetic resonance imaging
MLO	Mediolateral oblique
US	Ultrasonography
UOQ	Upper outer quadrant

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Author contributions
SI had designed this study. NM, EA, SN, and RH contributed to the data collection, data analysis, and processing. All authors shared together in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The data supporting the conclusions of this article are available upon reasonable request from the authors.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethical Research Committee of the Faculty of Medicine at Cairo University in Egypt. The ethical approval code is MS-516-2022. Verbal consent was taken from the legal guardians of all patients accepting to participate in our research work.

Consent for publication
The legal guardians of all patients included in this research 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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