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Artificial intelligence as a negative predictive tool for breast cancer postoperative recurrence

Sahar Mansour^{1,2*} , Heba Azzam^{1,2} and Hany El-Assaly³

Abstract

Background Mammography alone is an ineffective method for breast cancer surveillance and diagnosing cancer recurrence. The aim was to evaluate the ability of artificial intelligence (AI) to read digital mammograms as an additive tool to exclude recurrence in the operative bed of known breast cancer patients following the different surgical procedures.

Methods We used a retrospective cohort study of post-surgery mammograms (n = 577). Imaging was performed within 6 months after the surgery or more. The AI solution used to read mammograms (AI-MMG) provided a targeted heat map of the operative bed, which was supported by a decision likelihood score percentage of cancer recurrence. The reference for suspicious or malignant-looking abnormalities (n = 62, 12.3%) was diagnosed by biopsy. A clear operative bed and benign-looking changes (n = 442) were confirmed by ultrasound characterization patterns and one year of intermittent follow-up.

Results The AI scoring percentage for a clear operative bed ranged between 0 and 26%, with a mean of $15\% \pm 5.4\%$. Operative bed benign changes ranged from 10 to 88%, with a mean of $48.2\% \pm 21.2\%$, while malignancy recurrence ranged from 65 to 99%, with an average of $87.7\% \pm 10.5\%$. The "ROC: Receiver Operating Characteristic" curve for AI to predict cancer in the surgical bed on mammograms was 0.906. The optimum cutoff value to distinguish between benign postoperative alterations and malignancy recurrence was 56.5% (95%, CI 0.824–1.060, p value < 0.001).

Excellent agreement between AI-MMG and pathology or ultrasound results was observed, and Kappa was 0.894, p value < 0.001.

Conclusions The use of artificial intelligence has enhanced the diagnostic performance of the postoperative mammograms to rule out recurrent malignancies in breast cancer surveillance.

Keywords Digital mammography, Artificial intelligence, Breast cancer, Suspicious breast lesions, Postoperative changes, Reconstructive breast surgeries

Background

Breast-conserving surgery is becoming more popular as a treatment option for breast cancer [1–4]. Architectural distortions and collections seen at the postoperative bed on mammography may be challenging to differentiate from recurrent malignancy [5, 6].

Breast density might also make it difficult to detect underlying issues on a mammogram. Furthermore, the identification of lesions could be impeded by inaccurate

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evaluation of complex patterns, substandard image quality, and the overload of high workflow [7].

The use of artificial intelligence (AI) in radiology has shown valid results in the detection of breast cancer, where the algorithms were able to distinguish different cancer patterns on mammography that were sometimes difficult to mark even by experts in the field of breast imaging [8].

AI offers a supplementary tool to enhance interpretation during the postoperative period [6].

We aimed to evaluate the additive role of artificial intelligence in reading the first mammogram after surgery as a one-stop procedure to exclude recurrence in the operative bed of known breast cancer patients.

Methods

The study is a retrospective cohort analysis approved by the ethical committee of the Faculty of Medicine, and a waiver of informed consent was applied to all the included patients. The study assessed post-surgery mammograms ($n=577$). Imaging was performed 6 months after the surgery or more, either for routine post-treatment surveillance or to assess clinically detected abnormalities at the operative bed.

The age of the patients ranged from 40 to 65 years (mean age 43.89 ± 5.99).

The types of surgeries were breast conservation ($n=436$, 75.6%) in the form of lumpectomy ($n=49$, 8.5%), quadrantectomy (the commonest type of surgery, $n=315$, 54.6%) (Figs. 1, 2, 3, and 4), oncoplastic surgery ($n=72$, 12.5%), and reconstructive surgeries ($n=141$, 24.4%) post-mastectomy presented by autologous tissue flaps ($n=68$, 11.8%) (Fig. 5) or prosthetic implants (73, 12.6%) (Fig. 6).

Inclusion criteria: Screened and symptomatic known breast cancer patients of all ages who underwent breast mammograms as a part of cancer surveillance, for a duration of 6 months or more after surgery.

Exclusion criteria: (i) Breast cancer patients who did not perform conservative or reconstructive breast surgeries. (ii) The patient was diagnosed by an initial mammogram and ultrasound of benign postoperative changes and performed no follow-up or biopsy for confirmation.

Equipment

Full-field regular digital mammography; Amulet Innovality (Fujifilm Global Company, Japan); and Senographe Pristina 3D (GE Healthcare, UK).

Breast was imaged in two views: mediolateral oblique and cranio-caudal and viewed on a monochrome 5-megapixel medical workstation with extended view (2048×2560 pixels; 21.3 inches; Barco).

Ultrasound examination was done for all cases using hand-held ultrasound (LOGIQ S8-GE device) provided by a superficial linear probe (7–12 MHz).

An artificial intelligence 2D solution was applied to mammograms archived on the PACS system (Lunit INSIGHT MMG ver. 1.10.2, Seoul, South Korea, version 2021) and was used for scanning and reading digital mammograms (AI-MMG).

Image analysis and interpretation

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

Benign postoperative abnormalities: seroma, hematoma, fat necrosis, scarring.

Mammographic abnormalities following the standard “Breast Imaging Reporting and Data System” in the BI-RADS ACR Atlas 5th Edition 2013 [9] were: (1) masses described by their shape, margin, and density; (2) calcifications described by their morphology and distribution; and (3) asymmetry or distortion described by their distribution.

The used AI algorithm provided pixel-level abnormalities in the form of a heat map and a maximum scoring percentage for the probability of malignancy within the range of <10% to 100% (100% represents the highest level of suspicion).

The probability of malignancy is: 100% definite cancers, 99–76% probably cancer, 75–51% possibly cancer, 50–26% possibly non-cancer, 25–10% probably non-cancer, and 9–0% most likely non-cancer.

Suspicious or malignant-looking abnormalities ($n=62$, 12.3%) were biopsied by a 14-G needle for tissue diagnosis. A clear operative bed and benign-looking changes ($n=442$) were confirmed by ultrasound characterization patterns and one year of intermittent follow-up.

Cases with autologous silicone implants: AI solution was applied to mammograms, and the percentage range for intact ($n=67$) or intracapsularly ruptured ($n=6$) implants was calculated. The status of implants was confirmed by complementary MR imaging (Achieva, Philips Medical System, Best, the Netherlands, Release 2.6, and Level 3) with a 1.5 Tesla magnet.

Included sequences: i) axial T2-weighted sequences; ii) axial T2-weighted inversion recovery; iii) axial silicone suppression sequence; and iv) dynamic post-contrast acquisition were performed using six series of 3D THRIVE acquisition—1 before and 5 after power injection of 0.1 mmol/kg BW of contrast.

Statistical analysis

Data were analyzed in the form of the diagnostic indices: sensitivity, specificity, positive predictive value (PPV),

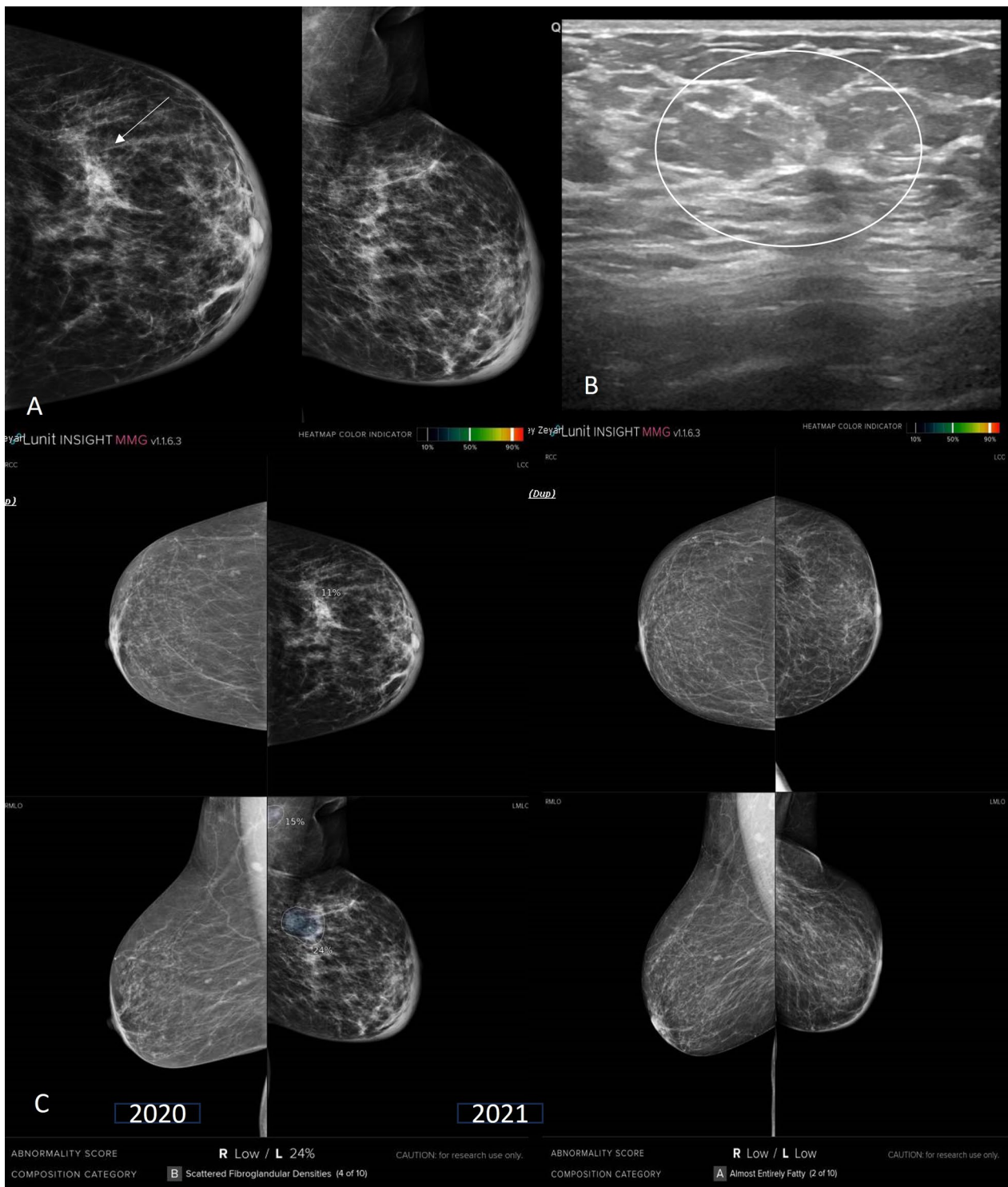


Fig. 1 A 69-year-old female patient performed conservative breast surgery. **A:** Left breast mammography (cranio-caudal and mediolateral views). There is an upper outer distortion and increased density on the surgical bed (arrow). **B:** Ultrasound shows a subtle deformation at the operation site (circle). **C:** In 2020, the AI-MMG four-view image showed a marked surgical bed and abnormality scoring percentage of 24% (probably non-cancerous). In the following year (2021), the operating bed's density and distortion (scarring) decreased significantly, as did the AI scoring, which fell below 10% (definite non-cancer)

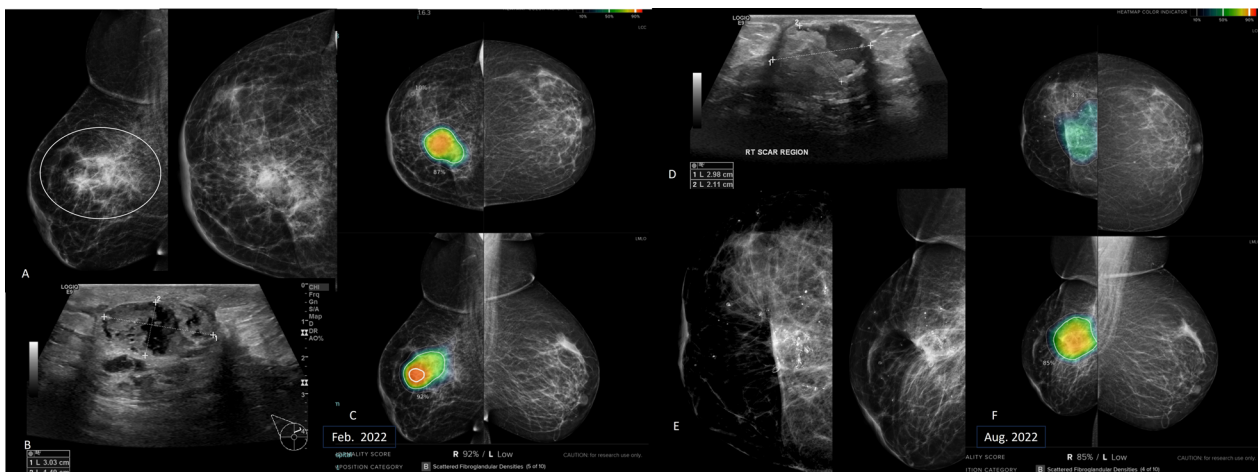


Fig. 2 A 55-year-old female patient underwent conservative breast surgery. **A:** Right breast mammography (cranio-caudal and mediolateral views). Operative bed distortion, increased density at the upper inner quadrant (surgical site-circle), in addition to thickened breast trabeculae, inward traction of the nipple, and diffuse dermal thickening. **B:** Ultrasound of the operative bed revealed a complex mass with an echogenic vascular solid component. **C:** The AI-MMG four-view image showed an intense color hue of the operative bed and a remarkably high abnormality scoring percentage of 92% (probably cancer). The operative bed mass was diagnosed as “operative bed benign changes,” presumed to be fat necrosis, and was given ultrasound close follow-up for a 6-month duration. **D:** A follow-up ultrasound image showed a suspicious increase in size in the form of a more solid component and a vertical orientation of growth. **E:** The mammogram revealed replacement of the operative bed density and distortion by grouped calcifications. **F:** The AI-MMG image displayed a high abnormality scoring value of 85% (probably cancer). A biopsy revealed ductal carcinoma in situ (i.e., cancer recurrence)

negative predictive value (NPV), and accuracy. For comparing categorical data, the Chi-square (χ^2) test was done. An exact test was used instead when the expected frequency was less than 5.

Results

The study included 577 postoperative mammograms following conservative or reconstructive breast surgeries. The left breast was the most common side of surgery in 277 cases (55%).

Conservative breast surgeries and reconstructive surgeries with an autologous flap were subjected to statistical analysis ($n=504$).

Reconstructive breast surgeries with silicone implants were excluded from the statistical evaluation since the AI solution used was trained for cancer and non-cancer abnormalities seen in mammograms, not silicone integration.

Simple analysis was done in the form of range and mean values for AI scoring percentage.

The AI solution was applied to mammograms for cases with reconstructive surgeries with autologous implants ($n=73$). A range of AI scoring percentages from 10 to 67%, a mean of 19.6% to 14.7%, was observed. Six implants showed intracapsular rupture that was confirmed by MR imaging and displayed a score range of 45% to 67%, a mean of $58.7\% \pm 11.9\%$ (Fig. 6).

None of the implant-applied cases displayed a recurrence of malignancy.

Operative bed was clear in 412 (81.7%), showed benign changes in 74 (14.7%), and recurred malignancy in 18 (3.6%). The histologic types of the recurrent malignancy were invasive ductal carcinoma (72%, $n=13/18$) and ductal carcinoma in situ (28%, $n=5/18$).

All cases showed operative bed distortion in the mammogram.

Asymmetry was the morphology descriptor seen at the operative bed in 126 mammograms. A clear operative bed was noted in 116 cases of them on ultrasound. The remaining 10 cases showed benign findings as confirmed by ultrasound in eight cases (five seromas, one fat necrosis, and two operative bed scarring), and malignancy was displayed in two cases as confirmed by biopsy.

Calcifications were noted in 81 mammograms; benign calcifications were presented in 75 mammograms, which on ultrasound correlated with a clear operative bed ($n=54$) or benign changes ($n=18$). Suspicious calcifications were noted in six mammograms.

Mass was the descriptor noted at the operative bed in 21 cases, and ten of them proved to be recurrences by ultrasound and biopsy.

The operative bed features in the mammogram are presented in Table 1.

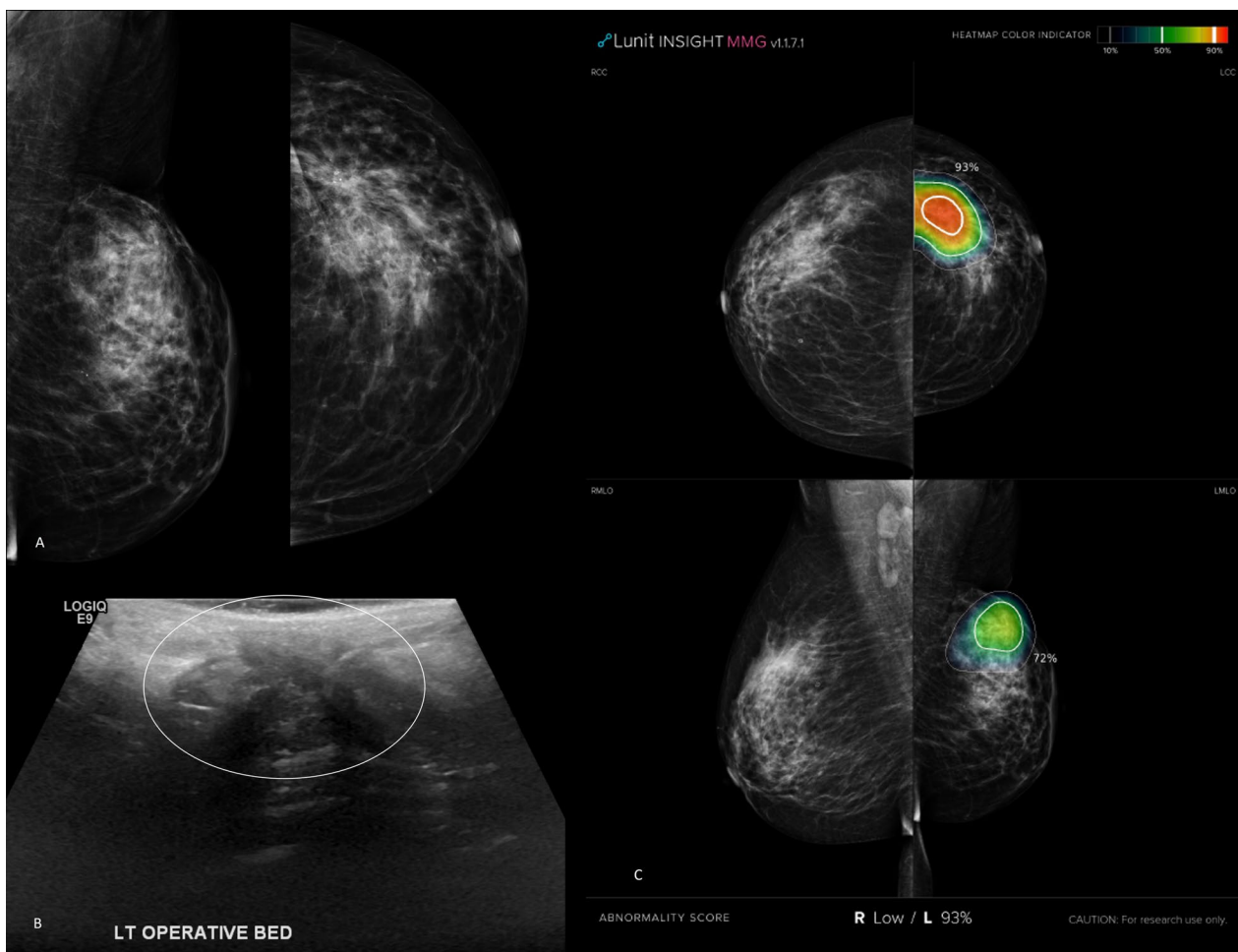


Fig. 3 Oncoplastic breast surgery in a 57-year-old female patient. **A:** Left breast mammography (cranio-caudal and mediolateral views). Upper outer dermal dimpling, marked scarring, increased density, and amorphous calcifications. **B:** Ultrasound of the operative bed revealed an indistinct, non-mass area of distortion (circle). **C:** The AI-MMG four-view image showed marking of the operative bed and presented a remarkably high abnormality scoring percentage of 93% (probably cancer). The surgical excision showed no features of malignancy. The AI solution overestimated operational changes such as breast cancer

Mammograms were categorized as BI-RADS 3 in 261 (51.8%), BI-RADS 4 in 221 (43.8%), and BI-RADS 5 in 22 (4.4%) cases.

Quantitative evaluation of the operative bed by AI-MMG suggested: i) probability of cancer recurrence (scoring 99%–76%) in 34 cases (6.7%) (Figs. 2 and 3); ii) possibility of cancer (scoring 75%–51%) in 37 cases (7.3%); iii) possibility of non-cancer (scoring 50%–26%) in 25 (4.9%); iv) probability of non-cancer (scoring 25%–10%) in 377 (75%), (Fig. 1); v) most likely non-cancer (scoring 9%–0%) in 31 cases (6.1%), (Fig. 4).

For statistical indices, at a mammogram, BI-RADS 3 is considered benign, and BI-RADS 4 and 5 are considered malignant. Regarding AI-MMG operative bed

scoring, probably cancer and possibly cancer (99%–51%) were considered malignant, and the probability of non-cancer (50%–0%) was considered benign.

The percentage of probability of malignancy showed a higher average value than benign changes and clear postoperative cases (p value < 0.001).

The AI scoring percentage for a clear operative bed ranged from 0 to 26%, with a mean of $15\% \pm 5.4\%$. Operative bed benign changes displayed a score range from 10 to 88%, mean $48.2\% \pm 21.2\%$, and malignancy recurrence range from 65 to 99%, mean $87.7\% \pm 10.5\%$.

Receiver operator characteristic (ROC) curve for AI to predict cancer in the operative bed on mammograms was 0.906; the correlating best cutoff point to discriminate between abnormalities into benign postoperative

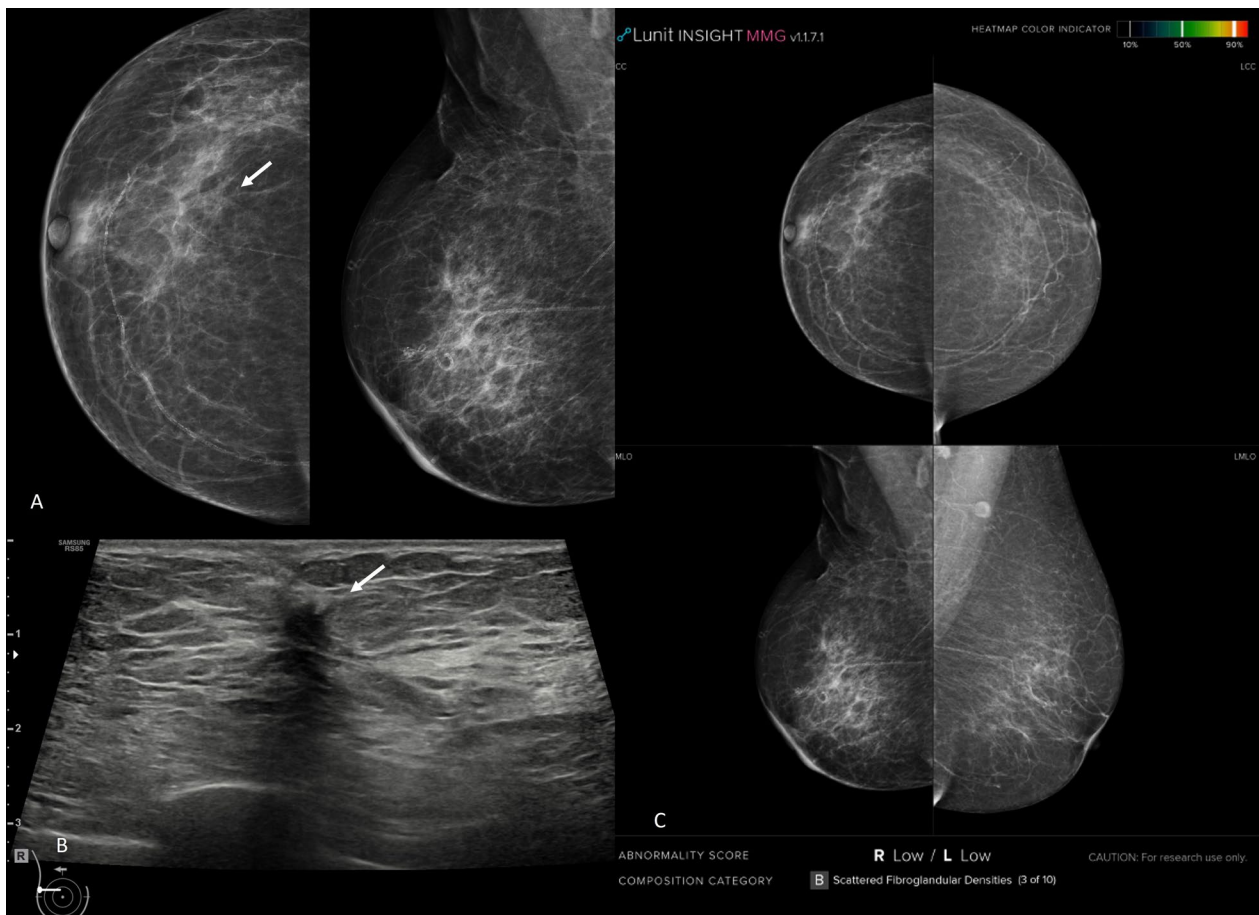


Fig. 4 Conservative breast surgery performed for a 78-year-old female patient. **A:** Right breast mammography (cranio-caudal and mediolateral views). A focal area of distortion is seen in the upper outer quadrant (arrow). **B:** Ultrasound of the operative bed revealed a suspicious, indistinct, tiny mass lesion (arrow). **C:** No marking was noted at the AI-MMG four-view (definitely no cancer). Wire localization and an excision biopsy revealed no malignancy

changes and malignancy recurrence was 56.5% (95% CI 0.824–1.060, p value < 0.001) (Fig. 1).

The correlation between the mammogram, AI-MMG, and standard of reference (pathology or ultrasound findings) is shown in Table 2.

Excellent agreement between AI-MMG and pathology/ultrasound results was observed; Kappa was 0.894, p value < 0.001.

Discussion

Mammographic imaging in patients after breast-conserving surgery is difficult because the surgical procedure affects the natural breast anatomy. Even radiologists find it difficult to distinguish between typical postoperative changes and true recurrence results, so it is critical to understand the expected postsurgical imaging findings and keep our expertise up to date for ensuring an accurate interpretation [10, 11]. Benign postoperative features are generally implied as “leave-alone” features [5].

The current work was a retrospective study that aimed to analyze the impact of using AI-MMG as a supportive tool to read mammograms after surgery. The standard reference was either ultrasound for the benign changes supported by a one-year intermittent follow-up or biopsy results for the suspicious-looking findings.

It is a pioneer study in the field of breast imaging that has interfered with discussing other studies that illustrated the same issue, mentioned studies with similar results, or contradictory studies, with an explanation for the causes of differences between studies of the same concern.

The first mammogram after lumpectomy and radiation will become the new standard against which future mammograms of the remaining breast tissue are compared.

The used AI solution applied abnormality scoring percentages to the included mammograms, and the best cutoff point to discriminate abnormalities into benign postoperative changes and malignancy recurrence was

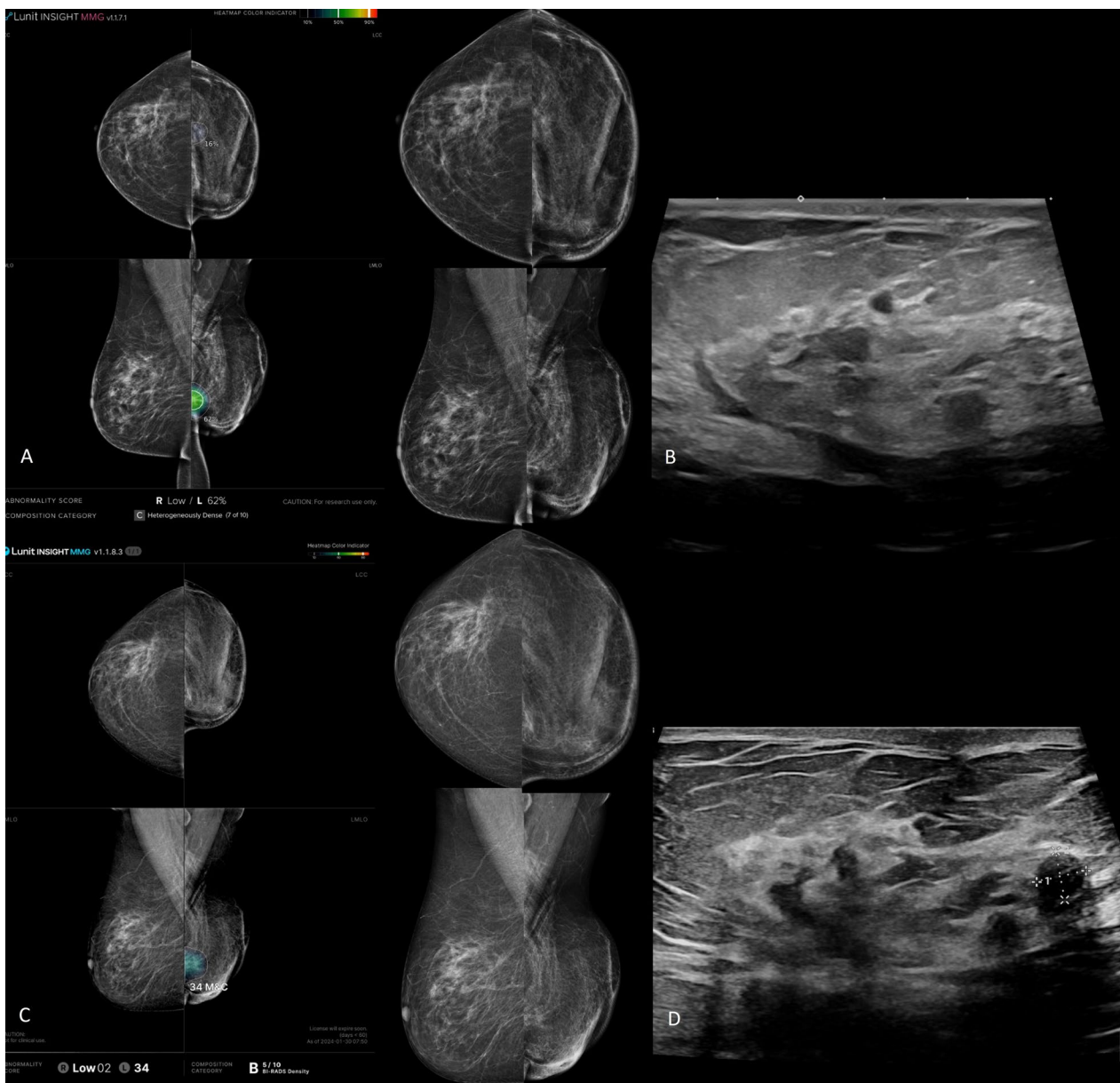


Fig. 5 Reconstructive surgery with an autologous flap breast surgery performed for a 57-year-old female patient. **A:** AI-MMG four-view image and mammography of a reconstructed left breast (cranio-caudal and mediolateral views). A lower outer focal area of distortion was marked and given a high score of 62% (possibly cancer). **B:** The targeted ultrasound image showed multiple oil cysts and minimal distortion (operative scarring). **C:** A year later, a follow-up AI-MMG four-view showed a decreased scoring percentage of 34% (possibly non-cancer). **D:** Ultrasound of the operative bed showed a reduced size and number of cysts and normally appearing glandular tissue

56.5%. It yielded a sensitivity and negative predictive value of 100%, and the specificity of mammography was enhanced from 51 to 89.1%.

Technologies based upon AI can improve postoperative care by detecting problems early on imaging. AI solutions detect infection, hematoma, or other changes by performing clinical monitoring and evaluating mammograms on their own. This would allow for more

timely intervention and a lower risk of complications [12].

Follow-up images of the included mammograms in the study after surgery showed subtle changes or stationary features. A precise assessment of the operative bed abnormalities was achieved through abnormality scoring percentage: a decrease in the scoring percentage in follow-up images is suggestive of benign changes (including

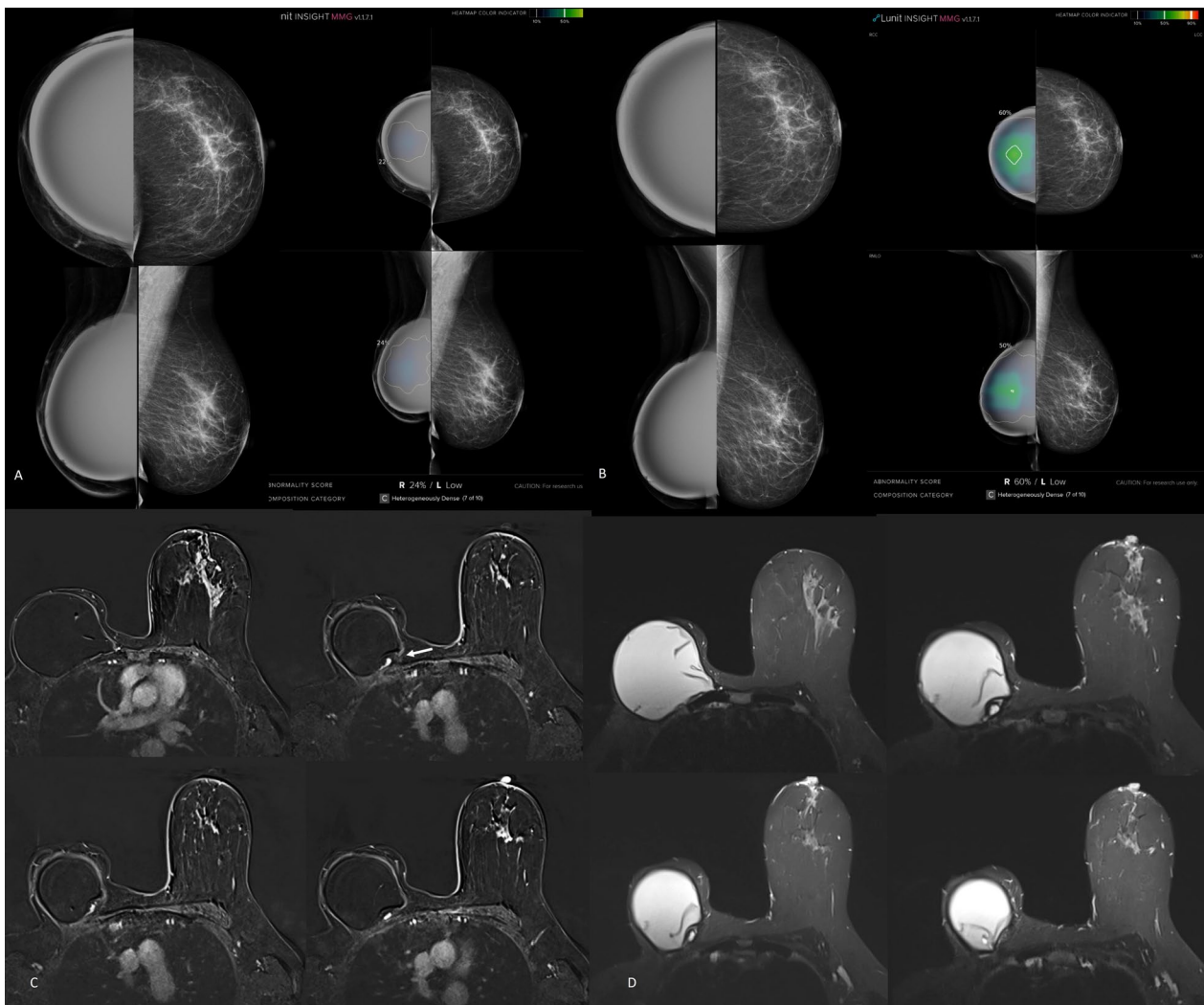


Fig. 6 Reconstructive breast surgery with implant application in a 42-year-old female patient. **A:** Mammography and AI-MMG four-view image showed a reconstructed right breast. The AI scoring of the implant was low percentage (24%). **B:** One year later there was an increase of the AI scoring percentage of the implant reached 60%. **C:** Post-contrast and **D:** T2-weighted. MR images showed the implant's inner wall appeared collapsed, indicating an intracapsular rupture of a single-lumen silicone gel breast implant that had a "lumen within a lumen" appearance. Note the posterior capsular wall granuloma (arrow in C)

those with high scoring at the initial mammogram), while a progressive increase in the scoring percentage was indicative of cancer recurrence (Figs. 1, 2, 5 and 6).

The presence of architectural deformities and neo-density does not always indicate a cause for concern, as tissue scarring after surgery can simulate recurrence [13]. Also, microcalcifications that are casting, fine linear, as well as linear branching, and do not correspond to fat necrosis are suspicious. They frequently have a similar morphology to the underlying cancer. Fat necrosis is identified when fat-like lucency is observed around or inside the

calcific densities, and recurrence is suspected when the calcifications relate to mass density in the region [11].

The current study found 239 false-positive mammograms, which decreased to 53 when the AI approach was implemented. However, AI overestimated scarring (distortion) and neo-densities (asymmetries) near the surgical bed, resulting in a low number of accurately detected positive cases (25.3%). These findings were consistent with the results reported by Ng et al. [14], which suggested that using AI to detect recurrent breast cancer in the postoperative period would be difficult because distortion at the surgical bed would

Table 1 The operative bed features in mammogram presented the current work

Descriptors		Number (total = 504)	Percentage
Mass	Yes	21	4.2
	No	483	95.8
Distortion	Yes	504	100
	No	0	0
Asymmetry	Yes	126	25
	No	378	75
Calcifications (n=81, 16.1%)	Yes		
	Benign	75	14.8
	Malignant	6	1.2
	No	423	84

Table 2 Diagnostic performance of DM and AI-MMG in the assessment of postoperative breast

	DM	AI-MMG
<i>Diagnostic performance</i>		
FN	5	0
TP	13	18
TN	247	433
FP	239	53
<i>Statistical indices</i>		
Sensitivity	72.2%	100%
Specificity	51%	89.1%
PPV	5.2%	25.3%
NPV	98%	100%
Accuracy	51.6%	89.5%
+ve LHR	1.47	9.17

DM = digital mammogram; AI-MMG: artificial intelligence on mammogram; FN = false negative; TP = true positive; TN = true negative; FP = false positive; PPV = positive predictive value; NPV = negative predictive value; LHR = likelihood ratio

mimic cancer spiculations, leading to misperception by the AI solution in the form of high scoring values.

To minimize scarring, surgeons should make incisions along skin tension lines, such as in skin folds or creases. Such a pattern of surgery showed no marking by the used AI solution at the operative bed, and consequently, less expected false-positive results from operative-related scarring and distortion were reached.

Striae radiate from the areola outward in the breast; therefore, ideal incisions are circumferential. Following reduction mammoplasty, the frequently inconspicuous vertical scar may be caused by the proper angle of the incision line on the Wise pattern relative to the real or virtual direction of the radial striae on the breast. The commonly seen enlargement of the horizontal scar

in the inframammary fold happens when two wound edges with cross-cut collagen fibers are adapted [15].

A Sweden study [16] assessed microcalcification clusters in mammograms and risk of breast cancer and showed an association between grouped calcifications and a 20% increased risk of breast cancer (hazard ratio (HR) = 1.20; 95% CI = 1.13–1.28). The risk was more pronounced in premenopausal women (HR = 2.93; 95% CI = 1.67–5.16) than in postmenopausal ones. The presence of microcalcification was significantly associated with ductal carcinoma in situ breast cancer (odds ratio (OR) = 2.03; 95% CI = 1.13–3.36).

In coincidence, we detected malignancy in association with calcifications in 50% (n = 9/18), and 56% of them (n = 5/9) were ductal carcinoma in situ. Other descriptors of cancer recurrence were masses in 39% (n = 7/18) and asymmetries (neo-densities) in only 11% (n = 2/18).

The used AI solution detected all the recurrent malignancies irrespective of their morphology descriptor in the mammogram (true positive n = 18/18), and thus the positive predictive value of the mammogram had increased five times its initial value (from 5.2 to 25.3%). In addition to a 100% probability value, the patient does not have a recurrence.

While collecting cases for the current work, we found cases of reconstructive breast surgery by applying silicone implants (n = 73). The AI solution used provided a scoring percentage of 10%–67%, and six of them showed intracapsular rupture. The reference for rupture was MR imaging, and the correlated mean AI abnormality scoring percentage in the mammogram was 58.7% ± 11.9%. There is still no statistical mention of an AI solution for reading mammograms or silicone integration.

A study performed in 2023 [17] involved over 80,000 women to explore the use of artificial intelligence in breast cancer screening. Women with breast implants (n = 2763) were excluded, as the AI software had not been validated for that subgroup.

In 2021, Myung et al. [18] evaluated the predictive ability of different machine learning packages to discover challenges in 568 breast reconstruction patients who underwent abdominal flaps. They concluded that AI technologies might be efficiently used to assess the likelihood of adverse patient outcomes in reconstructive breast surgery.

Another work in 2024 [19] proposed a novel, generalizable use of an unsupervised learning algorithm to categorize a total of 14,274 female patients' subgroups based on comorbidities, modality of breast reconstruction, and postoperative results.

However, both studies were retrospective and focused mainly on the factors contributing to the rejection of

the autologous flaps rather than the detection of cancer recurrence.

Further studies are required to focus on the role of AI in detecting the probability of maintenance for reconstructive surgeries post-mastectomy, whether autologous flaps or applied silicone implants, in addition to the detection of cancer recurrence.

There were limitations to the current work: (1) its retrospective work nature limited the ability to follow the documentation of the risk factors of the studied subjects for developing cancer. (2) Clinical, detailed demographic data of the cases and previous investigations were not analyzed. This work was based on and mainly concerned with the current imaging findings. Follow-up ultrasound/MR imaging was used as the standard reference for benign-looking postoperative findings not as one of the studied variables.

From our experience, it is recommended to research the validity of the use of AI abnormality scoring percentage as a follow-up tool for breast cancer cases with a documented clear operative bed.

Conclusions

The use of artificial intelligence has enhanced the diagnostic performance of the postoperative mammograms to rule out recurrent malignancies in breast cancer surveillance.

Abbreviations

AI	Artificial intelligence
AI-MMG	Artificial intelligence for reading mammograms
ACR	American college of radiology
BI-RADS	Breast imaging-reporting and data system
BW	Body weight
CI	Confidence interval
FP	False positive
FN	False negative
HR	Hazard ratio
MR imaging	Magnetic resonance imaging
OR	Odds ratio
PACS	Picture archiving and communication system
ROC	Receiver operating characteristic
SPSS	Statistical package for the social sciences
3D THRIVE	Three dimensional T1-weighted high-resolution isotropic volume examination

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Not Applicable.

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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