Contrast-Enhanced Mammography: diagnostic potential and complementary role in screening

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KeyWords:

Mammography with contrast medium; Breast cancer; Screening; BI-RADS; Diagnostic accuracy; Cohen's Kappa.

Abstract

Contrast-enhanced mammography (CEM) represents one of the most prominent innovations in breast diagnostics. This is a hybrid technique, combining digital mammography images with iodinated contrast injection, allowing for better visualization of areas with increased vascularity, which are typically associated with malignant lesions. In this study we report our experience, held at the Diagnostic Imaging Unit of the Sant'Ottone Frangipane Hospital in Ariano Irpino, analyzing the data collected in the period from 1 January 2025 to 1 July 2025. During this interval, 642 screening mammograms were performed. 22 patients (2.3%) were recalled for EMF, following a finding of BI-RADS 3 or greater on screening mammography. The analysis focuses on the distribution of EMFs according to the BIRADS classification, the type of contrast agent used, as well as the evaluation of the correlation between positive EMF results and the histological outcome obtained by vacuum-assisted breast biopsy (VABB).

Introduction

Breast cancer is the most diagnosed neoplasm in the female population and, at the same time, is one of the main causes of cancer mortality. The mammography screening program is aimed at the early diagnosis of breast cancer [1], in order to reduce mortality related to these diseases. Conventional mammography is a first-level examination in the screening program, but it has known limitations, particularly in the evaluation of dense breasts or in the characterization of non-calcified lesions or lesions with blurred margins, which may be difficult to see or difficult to interpret diagnostically. In these cases, in-depth diagnosis with second-level examinations is essential to improve diagnostic accuracy and more precisely define the patient's clinical management [2-4]. The use of CEM allows to obtain a functional evaluation of the lesions, since, through the infusion into the vein of an iodinated contrast medium, the uptake of the drug is studied to highlight any areas of tumor neoangiogenesis. This approach makes it possible to detect alterations that are not always visible on traditional mammography or ultrasound, especially in equivocal radiological pictures or characterized by limited diagnostic specificity. Therefore, this translates into a more precise risk stratification and a more effective clinical orientation, with a reduction in both false positives and false negatives, thus optimizing the selection of patients who are candidates for biopsy and reserving invasive and minimally invasive diagnostic investigations only for cases with a strong suspicion of malignancy. Numerous studies have shown a higher sensitivity of EMF compared to traditional mammography and diagnostic accuracy comparable to MRI, with the advantage of having wide accessibility, lower costs and reduced execution times [5-8]. The present publication aims to evaluate the diagnostic role of EMF and its integration into the screening program, as well as the differences in contrast medium used and the analysis of BI-RADS, through the analysis of data collected at the Diagnostic Imaging Unit of the Ariano Irpino hospital, with particular attention to cases called for diagnostic in-depth analysis after screening mammography with BI-RADS greater than or equal to 3.

Materials and methods

The study was conducted on a sample of 642 patients undergoing mammography screening at the Diagnostic Imaging Unit of the Sant'Ottone-Frangipane Hospital in Ariano Irpino, in the time interval between 1 January 2025 and 1 July 2025. Among the 642 patients screened, 22 (2.3%) were called back for further investigation
diagnostic test, specifically for the execution of the CEM examination, as a BI-RADS greater than or equal to 3 emerged on traditional mammography. There were 620 patients not recalled (67.7%). Clinical and personal data were collected from medical records and radiological reports.
We evaluated:

- Average age of the sample,
- BI-RADS at the CEM,
- Type of contrast medium used,
- BI-RADS on histological.

In this retrospective study, a total of 22 contrast-enhanced mammograms performed at our hospital were analyzed. Patients presented clinical indication for contrast examination for diagnostic completion following suspicious findings on traditional mammography, ultrasound or clinical symptomatology. All examinations were performed with a dedicated mammography machine with dual energy. The acquisition of mammographic images took pla-

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ce in the first instance 2 minutes after intravenous injection of the contrast medium, first in the caudal skull and, subsequently, in oblique mid-lateral projection, starting from the suspect breast. After 8 minutes from the injection, the acquisition of the same projections continues, thus obtaining a "later" contrastographic phase, through which we evaluate the possible impregnation of the lesion by contrast medium.

The contrast agents used in the CEM study at our operating unit are basically two:

- Omnipaque 350
- Ultravist 370

The images were analyzed by assigning a BI-RADS category according to the updated ACR criteria. In this study, the comparison between BI-RADS at EMF and histopathological diagnosis is also included, in order to evaluate the accuracy, sensitivity and specificity of the method.

Results

22 contrast-enhanced mammograms (EMFs) were analyzed. The mean age of the patients was 58.6 years (range: 44-72 years).

The table shows the BI-RADS values obtained after the EMF exam and the relative percentages.

BI-RADS 5: Highly suspicious for malignancy. Urgent biopsy.

BI-RADS 4: suspicion of malignancy. Indication for biopsy. Intermediate risk.

BI-RADS 3: Probably benign. Follow-up recommended.

BI-RADS 2: benign. No action required, beyond normal follow-up.

A sample of 22 patients who underwent contrast-enhanced mammography (CEM) were included in the study. The patients were divided into two groups, each consisting of 11 subjects. The subdivision took place according to the type of iodinated contrast medium used:

- GROUP A (n=11): Ultravist 370 (iopromide);
- GROUP B (n=11): Omnipaque 350 (iohexol).

Both contrast agents were administered intravenously according to standardized protocols. All patients were administered a volume of 1.2 ml/kg of contrast medium via automatic injector, followed by 30 ml of saline. The acquisitions took place in compliance with the standard protocol and respecting the times of the contrastographic phases.

The analysis of the sample of patients who underwent EMF showed the following:

N. 22 patients who underwent EMF, of which 6 EMF NEGATIVE. The remaining 16 patients underwent further investigations, specifically biopsy (VABB), as the BI-RADS value on contrast-enhanced mammography was greater than or equal to 3. Now the BI-RADS obtained at the histological will be analyzed and compared with the BI-RADS obtained from the CEM.

We constructed a biopsy-EMC contingency table and calculated the concordance between the two methods by means of Cohen's Kappa coefficient [9], considering the ascending order of suspicion of BI-RADS (B1 to B5).

Distribution of cases:

- B5 at biopsy and B5 at EMF: 9 patients (complete agreement)
- B5 biopsy and B4 CEM: 2 patients (downgrade to CEM)
- B3 biopsy and B3 CEM: 1 patient (agreement)
- B3 biopsy and B4 CEM: 1 patient (upgrade to CEM) • B2 biopsy and B3 CEM: 1 patient (upgrade to CEM)
- B2 biopsy and B4 CEM: 1 patient (upgrade to CEM)
- B1 biopsy and B4 CEM: 1 patient (labeled upgrade to CEM)

Agreement:

Cohen's Kappa value is 0.37 and shows a moderate agreement between EMF and histology, underlining how EMF should be considered a complementary tool to biopsy, particularly in cases with borderline or ambiguous radiological features, in which the risk of diagnostic over- or underestimation is greater (Figure 1).

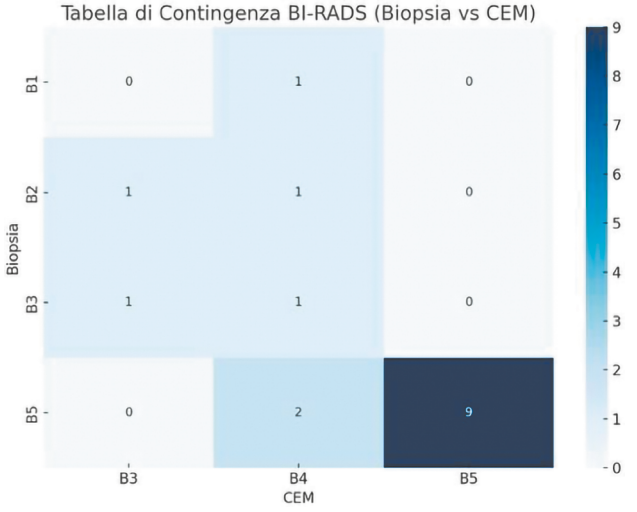

Figure 1.

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Discussion

In this retrospective study, we included a sample of 22 patients who underwent contrast-enhanced mammography (EMF) and, subsequently, where necessary, we assessed the proportion of patients for whom there was a need to supplement with a next-level examination, such as biopsy. In this way, we were able to evaluate the concordance between the BI-RADS assigned to the EMF and the definitive histological outcome. Patients had an average age of 58.6 years, representative of a relatively young breast disease population and in line with the age group involved in screening and prevention programs. This figure is particularly relevant, as it suggests a growing adherence to advanced diagnostic tools even at a potentially early age for tumor onset, opening up encouraging prospects for timely diagnosis. In this context, the use of EMF takes on a strategic role: in younger women, often with dense breast parenchyma, the use of contrast medium can significantly increase the sensitivity in the detection of vascularized lesions, improving the effectiveness of screening and reducing the risk of underdiagnosis. An iodinated contrast agent, specifically iohexol and iopromide, administered according to CEM protocols, was used in all patients. Iopromide offers a slightly higher contrast, especially useful in small or poorly vascularized lesions, while iohexole, despite having a slightly higher osmolarity, is used without clinical evidence of less tolerability than other contrast agents. Therefore, both contrast agents are iodinated, but not ionic: iopromide manifests less of the sensation of heat. Both drugs have a similar safety profile: no patient reported severe shock, but only common effects, such as a feeling of heat, urge to urinate, mild redness. However, being iodinated contrast agents, they are classified as hyperosmolar, although Ultravist 370 has a slightly lower osmolarity, so it creates less stress on the kidneys. The choice to use one rather than the other took into account several factors, including the age of the patient, clinical history, and the size of the lesion to be analyzed. At CEM, the distribution of BI-RADS showed a predominance for the high categories: 9 patients were classified as BI-RADS 5, 5 patients with BI-RADS 4, 2 patients with BI-RADS 3. This data reflects the high sensitivity of EMF in detecting signs of suspected malignancy, but also raises the question of a possible tendency to diagnostic overestimation, particularly in borderline or low-risk cases.

The comparison with the histological examination highlighted:

Complete concordance in the 9 cases of BIRADS 5, confirming the high positive predictive power of EMF for frankly malignant lesions. However, in borderline or benign cases, EMF has shown a tendency towards diagnostic upstaging, classifying as BI-RADS 4 some lesions that have been found to be benign (B1–B2) or intermediate risk (B3) on histology. The Cohen Kappa coefficient used in our study measures the level of agreement between two observatories or methods, correcting the expected agreement by pure chance [11].

According to the Landis and Koch classification, values between 0.21-0.40 indicate moderate agreement, 0.41-0.60 fair, 0.61-0.80 good, and over 0.80 excellent [11]. However, the formula to calculate it is:

$$\kappa = \frac{\Pr(a) - \Pr(e)}{1 - \Pr(e)}$$

Where:

Pa (proportion of agreement observed) = number of times EMF and histology agreed ÷ total number of cases.

Pe (proportion of agreement expected per case) = calculated on the basis of the marginal distributions of the categories (BI-RADS at EMF and histology).

In our studio:

The 22 cases analyzed were considered.

Example: 9 patients with B5–B5 agreement, 1 with B3–B3 agreement, plus others with differences (upgrade/downgrade).

A contingency table was constructed between EMC and Histology.

The PA (effective agreement ≈ 10/22 ≈ 0.45) was calculated. The Pe (random expected agreement based on the distributions of B1-B5) was calculated.

Applying the formula, □ = 0.37 was obtained, which according to Landis and Koch indicates a moderate agreement [11].

This suggests that EMF has an excellent sensitivity for frankly malignant lesions, but in borderline cases the concordance with histology is not complete, highlighting the need to integrate the method with biopsy for diagnostic confirmation [9,10,12].

Conclusions

These results indicate that EMF, while demonstrating excellent diagnostic sensitivity, especially in malignant cases, has limited specificity, with the risk of false positives in less defined pictures. Therefore, EMF is confirmed as a highly useful tool as a decision support, but not a substitute for biopsy, particularly in cases with doubtful conventional imaging.

Conflict of interest

The authors declare that they have no conflicts of interest.

Contributions by the authors

M. Volpe: concept and supervision. L. Guarino: concept, data acquisition and technical analysis. A. Massaro: data acquisition; A. Fico: bibliographic review and drafting support. All authors have read and approved the final version.

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Ethical Statements

Patients provided written informed consent for the publication of the clinical case and related diagnostic images

Clinical case

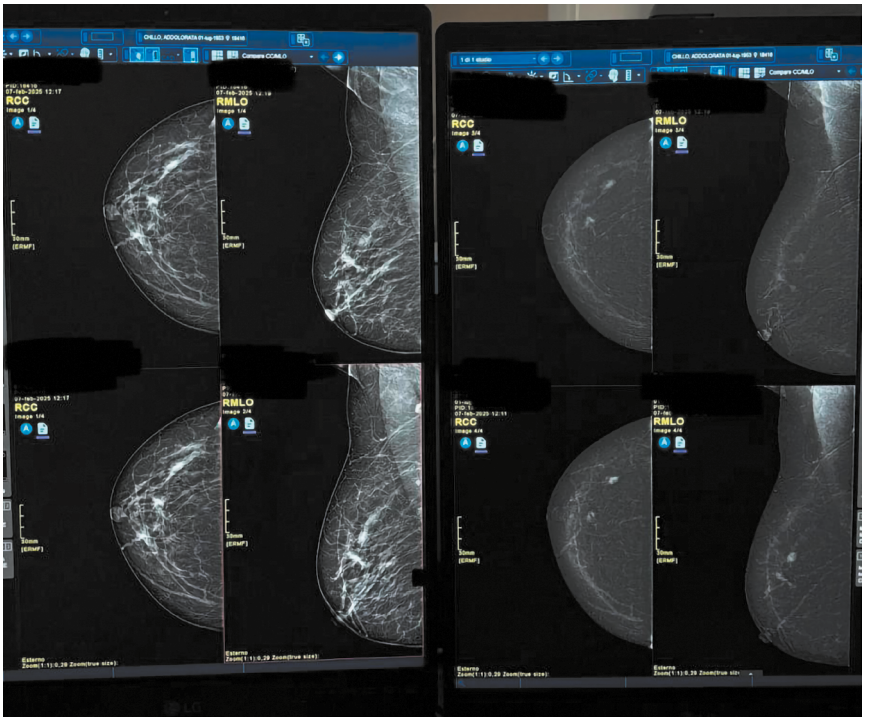

Figure 1:
Mammary lesions on the right breast highlighted in CEM. Two capturing masses are observed: one in the retroareolar area (11 mm, spiculate margins, BI-RADS 5 classification) and another in the QSE (10 mm, oval appearance, BIRADS 4). Arrows indicate injuries. Following biopsy with VABB (Vacuum-Assisted Breast Biopsy), histological examination showed the presence of infiltrating lobular carcinoma, lobular carcinoma in situ, and ductal carcinoma in situ (both high and low grade).

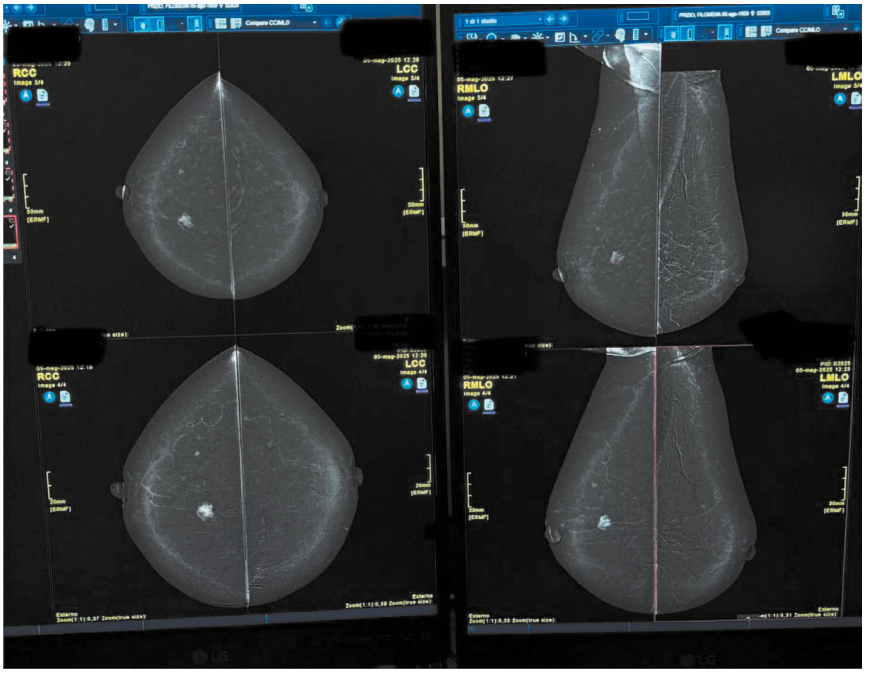

Figure 2.
Contrast-enhanced mammography (EMF)- Carcinoma case multifocal infiltrator
The examination shows a mass of 15 mm at the upper inner quadrant/union with the central quadrant (QSI/UQC), with coarse calcification and intense, early contrastographic impregnation; characters compatible with a BIRADS classification 5.At a distance of about 38 mm, at the upper-outer quadrant (QSE), a second nodulation of 4 mm is highlighted, with similar detection characteristics. On the left, no areas of contrast medium impregnation are observed.
On biopsy by VABB, infiltrating carcinoma was confirmed.

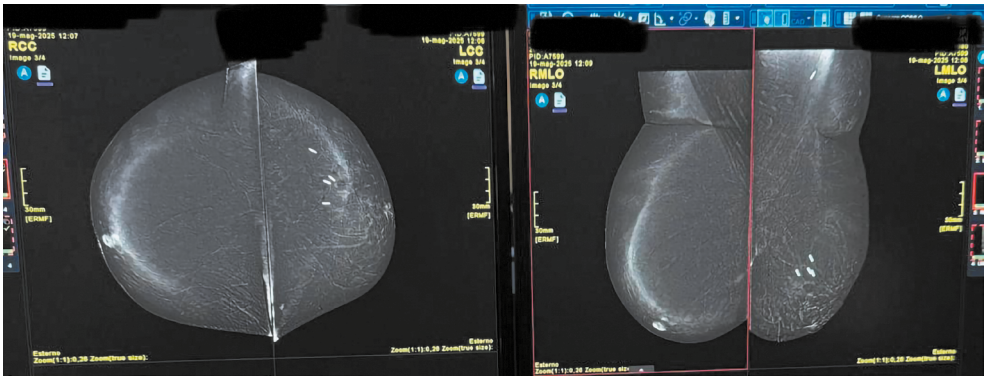

Figure 3.
Contrast-enhanced
EMF performed on both breasts. On the left, quadrantectomy (QUART) results are highlighted, with visibility of surgical clips in place. No areas of contrastographic impregnation are observed either on the right or on the left. Supplementation with targeted ultrasound showed no clinically significant axillary lymphadenopathies. In light of the findings, the painting has been classified as BIRADS 2. Considering the low probability of malignancy, the examination ended with the EMF study alone, without indication for biopsy.

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