

**MAMMOGRAPHY  
WITH CONTRAST IN  
THE EVALUATION OF  
MICROCALCIFICATIONS:  
A CASE REPORT**

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**Abstract:** **Introduction:** Contrast mammography (EMC) is an emerging breast imaging modality that portrays recombined images using iodinated contrast media. On this examination, the pattern of enhancement associated with microcalcifications of suspicious morphology may suggest underlying malignancy. **Objectives:** We present a case of a patient who presented enhancement associated with suspicious microcalcifications on contrast-enhanced mammography. In this study, we discussed the assessment of evidenced enhancement and its correlation with histopathological findings. **Methods:** The sample consists of a female patient aged between 50-70 years who underwent contrast-enhanced mammography during medical treatment at a health unit specializing in oncology in the city of Manaus/AM (Brazil). **Conclusion:** Although much research on contrast-enhanced mammography (EMC) has been developed, more studies are needed to assess and define the role of this imaging modality in the context of microcalcifications in order to establish correlations between other imaging methods and develop guidelines.

**Keywords:** Mammography with contrast, Mammography, Microcalcifications, Enhancement, Breast cancer, Ductal carcinoma in situ.

## INTRODUCTION

The interpretation of calcifications is very challenging and important for the breast radiologist in all imaging methods, as they commonly characterize the early manifestation of breast neoplasms. The lexicon of the Breast Imaging Data and Reporting System (BI-RADS), developed by the American College of Radiology (ACR), among many other things, is intended to standardize the terminology for describing calcifications and subdivides suspected types

into 2 categories: category 4B (amorphous, coarse heterogeneous and fine pleomorphic) and category 4C (linear fine branched/linear fine). Most biopsies performed for suspicious calcifications detected on mammography have a benign histological result.

New imaging techniques then become necessary in order to increase diagnostic accuracy in the presence of calcifications, given that radiological semiotics alone are unsatisfactory. Contrast mammography (EMC), which is an emerging breast imaging technique, may be useful, as studies have shown that enhancement of calcifications presented on examination suggests underlying breast cancer or ductal carcinoma in situ (DCIS).

Contrast-enhanced mammography (EMC), also called contrast-enhanced spectral mammography, contrast-enhanced digital mammography, and contrast-enhanced dual-energy mammography, has emerged as a viable alternative to contrast-enhanced breast MRI, allowing increased access to vascular imaging and reduced the cost. Two minutes before image acquisition, iodine-based contrast material is injected. Then, both breasts are radiographed in craniocaudal and mediolateral oblique views. At each step, compression is applied, followed by rapid acquisition of low- and high-energy images. These images are processed to generate recombined images. After each exposure, the compression is released. At the end, two images per breast and per view mode are acquired – one as a low-energy mammogram equivalent to digital mammography and the other recombined highlighting areas of contrast uptake.

Intravenous iodinated contrast materials are used in order to promote better visualization of tumor neovascularization through CEM. Vessels formed by the process of angiogenesis often leak the contrast

material, which spreads through the tumor tissue, generating an enhanced image. This allows a malignant tumor to be seen despite overlying dense breast tissue.

CEM has an advantage over full-field digital mammography (FFDM) and digital breast tomosynthesis (DBT), as they have limited accuracy in women with dense breasts with reduced sensitivity and do not perform a morphological and functional study of findings such as is observed in EMC. Furthermore, EMF is associated with a level of radiation exposure similar to that of digital mammography. It has also been shown to help improve accuracy compared to digital mammography and US in women with abnormal screening mammographic findings or symptoms of breast cancer. The method has been shown to provide similar sensitivity and specificity as demonstrated by breast magnetic resonance imaging (MRI) in the preoperative staging of patients with breast cancer and in monitoring the response after neoadjuvant chemotherapy.

Studies report that CEM has high sensitivity for the characterization of malignant findings, including microcalcifications, in patients undergoing screening. MSC demonstrates the morphology of microcalcifications on low-energy images and shows associated enhancement on recombined images. Several studies suggest that the presence of enhancement on the images suggests malignancy, but the absence of enhancement cannot exclude it. Therefore, it is concluded that there is no clear benefit in using CEM to evaluate suspicious breast calcifications, as well as in other methods. Therefore, as with MRI, suspicious calcifications on mammography must be biopsied, regardless of whether or not they show enhancement on EMC images. CEM has similar sensitivity to MRI in detecting invasive cancers, but few authors have evaluated the performance of

CEM for lesions that are represented only by calcifications without an associated mass.

## CASE REPORT

A 60-year-old mixed-race female patient sought medical attention after noticing a small ulcerated lesion in the left nipple region in January 2014. The lesion biopsy showed pagetoid melanoma. In June of the same year, the patient underwent left centralectomy with histopathological and immunohistochemical analysis of the surgical specimen, proving ductal carcinoma in situ associated with Paget's disease. In a control mammogram performed in November 2020, branched calcifications of the ductal path were evidenced, partially occupying the middle and posterior portion of the junction of the upper quadrants of the left breast (**Figure 01**). Spectral digital mammography with iodinated venous contrast was performed, which showed a small area of enhancement at the junction of the medial quadrants (**Figure 02**). Both the immunohistochemistry of the piece obtained by mammography-guided breast core biopsy (**Figure 03**) and the immunohistochemistry (**Figure 05**) of the surgical piece of the left radical mastectomy (**Figure 04**) to which the patient had to undergo later in July 2021, they maintained the result of high-grade ductal carcinoma in situ.

## DISCUSSION

Calcification has been shown to be a component in up to 50% of malignant breast lesions, and in 84% of ductal carcinomas in situ (DCIS), the presence of calcification was demonstrated by mammography. About 20-25% of microcalcifications without an associated mass that fall into category 4 (ACR BI-RADS) were later demonstrated to be malignant. Unfortunately, the suspicious morphological appearance on mammograms



Figure 01. Digital mammography - Left mediolateral-oblique view: heterogeneously dense breast with branched calcifications along the ductal path, partially occupying the middle and posterior portion of the junction of the upper quadrants.



Figure 02. Contrast mammography – Recombined image : a) Breast with an area of calcifications (thin arrows) with an area of enhancement (thick arrow) with irregular contours, measuring approximately 6.5 mm located at the junction of the medial quadrants. b) Enlarged image of the highlight area.



Figure 03. Image acquired by a slide mammography machine containing fragments with intermingled calcifications obtained by mammography-guided breast core biopsy.

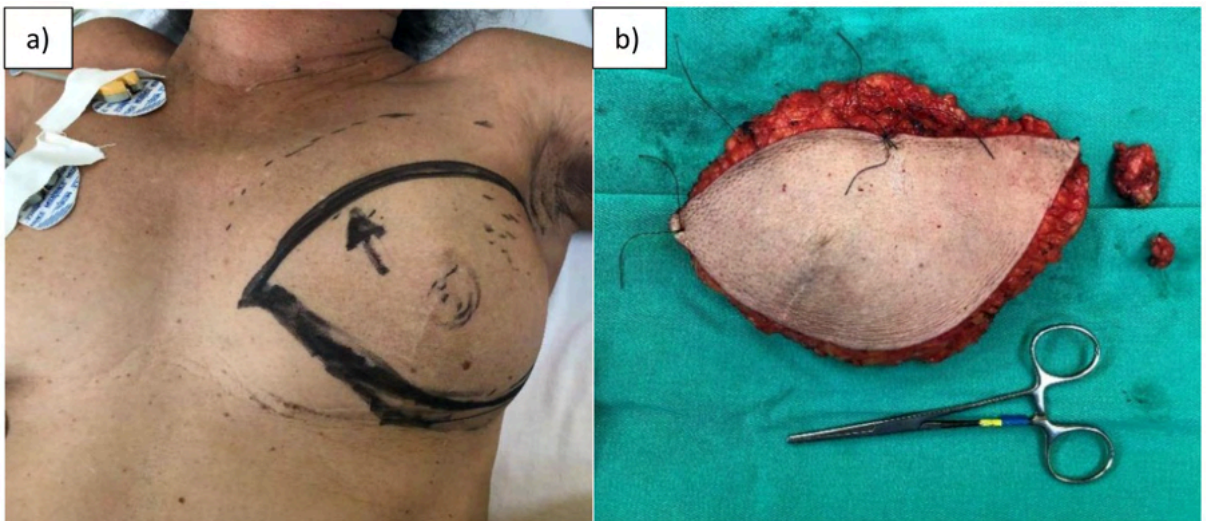


Figure 04. Left mastectomy with axillary lymph node excision: a) Pre -surgical marking. b) Surgical pieces obtained after the procedure.

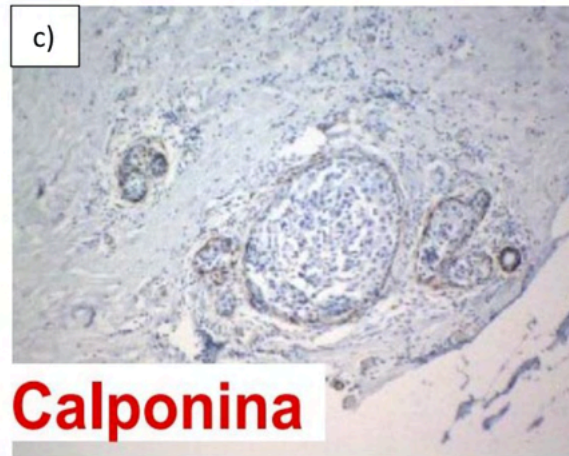
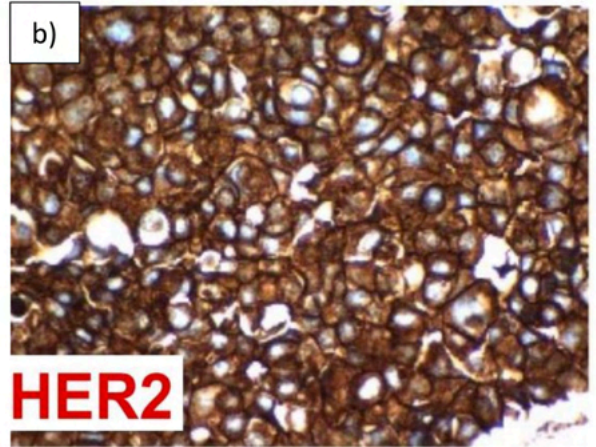
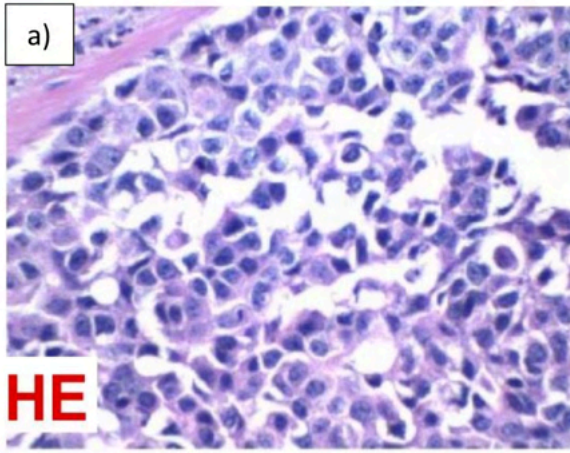


Figure 05. Immunohistochemistry of the surgical specimen from the mastectomy: a) Immunostaining of the sample by hematoxylin-eosin. b) There was immunostaining for full and intense membrane HER2 in > 10% of the tumor cells configuring a 3+ (positive) score for HER2. c) The positivity for the myoepithelial cell markers p63 and calponin confirmed the diagnosis of carcinoma in situ in the sample.

was variable with the probability of cancer ranging from 2 to 95%. Although morphological analysis can provide guidelines for the management of these patients, many calcifications are indeterminate, so the use of core breast biopsy is important in order to avoid unnecessary surgical biopsy for benign lesions or late diagnosis of malignant lesions. The conduct carried out in our case is in accordance with Cheung *et al.* (2016) because core breast biopsy was performed upon evidence of suspicious calcifications visualized on mammography.

According to the first version of the ACR BI-RADS lexicon for CEM, the images in our case would fall into the category of findings that appear in the low-energy images with associated enhancement in the recombined images. Regarding the evaluation of its morphology, we would classify the enhancement as a heterogeneous internal enhancement pattern, with moderate conspicuity and a partially enhanced mammographic lesion. Cheung *et al.* (2021) described the morphology of the enhancement differently and related it to the histopathological finding in their study. Morphology was classified as non-mass (cluster appearance without convex margin) or mass (appearance with more defined shape and convex margin). And for the purposes of describing the highlight texture, the terms used were 'frosted glass' and 'solid' to distinguish the 'weaker' and 'stronger' highlight respectively, in order to detail the transparency in relation to the underlying area. The study found that ground-glass and non-mass enhancements were closely related to DCIS, and the cases that showed both mass and solids enhancements were related to DCI. The present study showed disagreement when reporting a case of DCIS that showed a mass and solid enhancement on contrast-enhanced mammography. Our study also

showed disagreement with Depretto *et al.* (2020) who reported that MEC enhancement occurred more frequently in ICD lesions while absence of enhancement occurred predominantly in DCIS lesions and in microfocal ICDs.

The surgical procedure conducted in our case is in accordance with Cheung *et al.* (2021) who report that regardless of DCIS or invasive ductal carcinoma (ICD), management with subsequent surgical treatment is performed with conservative or total mastectomy.

## CONCLUSION

Based on the identification of microcalcifications of suspicious morphology, contrast-enhanced mammography (EMC) uses images recombined with iodinated contrast media to assess associated enhancement, which suggests underlying breast cancer or ductal carcinoma in situ (DCIS). This method has the potential to reconcile the relative ease, low cost, availability of mammography with the high sensitivity guaranteed by the contrast medium, in addition to presenting an exposure level similar to that of digital mammography. Although much research on EMF is under way, more studies are needed to assess and define the role of this imaging technique in the context of microcalcifications in order to establish correlations between other imaging methods and the development of informed conducts. Due to all these factors, the recommendation for calcifications with suspicious morphology remains biopsy, regardless of the enhancement shown on the images.

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