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Contrast-Enhanced Mammography: An Innovative and Accessible Technique in Breast Imaging

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Abstract **Review Article**

Contrast-enhanced mammography (CEM), also known as angiomammography, is a novel breast imaging technique combining full-field digital mammography with dual-energy acquisition following intravenous iodinated contrast injection. It enables both morphological and functional assessment of breast tissue by highlighting tumor-related angiogenesis. In the context of breast cancer, the most common malignancy in women and a leading cause of cancer-related mortality, improving diagnostic accuracy remains a major clinical challenge. This paper aims to describe the principles, technique, clinical indications, advantages, limitations, and future perspectives of CEM. This fast and widely accessible modality allows visualization of contrast enhancement patterns associated with tumor vascularity, improving lesion detection, particularly in dense breast tissue. Main indications include loco-regional staging, assessment of response to neoadjuvant chemotherapy, evaluation of equivocal findings, and suspicion of recurrence. CEM offers several advantages over MRI, including wider availability, lower cost, shorter examination time, and good patient tolerance. Its diagnostic performance, particularly sensitivity and specificity, is comparable to MRI in selected indications. It is also a valuable alternative in patients with contraindications to MRI.However, limitations include radiation exposure, iodinated contrast use, technical constraints, and potential false-negative findings in certain histological subtypes. In conclusion, contrast-enhanced mammography is an emerging and promising tool in breast cancer imaging. Its future integration into clinical practice will depend on protocol standardization, technological optimization, and the development of interventional and artificial intelligence applications.

Keywords: Contrast-enhanced mammography, Breast cancer, Angiogenesis, Dual-energy imaging, Diagnostic accuracy, Iodinated contrast media.

I. INTRODUCTION

Breast cancer arises from the epithelial cells of the mammary glandular system, which includes the lobules and the lactiferous ducts. [1]

It is the most common cancer among women in France, with approximately 61,000 new cases diagnosed annually, accounting for nearly one-third of all female cancers.

Despite significant therapeutic advances, breast cancer remains the leading cause of cancer-related mortality in women, with around 12,000 deaths each year. However, improvements in screening and treatment strategies have substantially increased survival rates, currently reaching approximately 88% at five years. [2]

Organized screening programs are offered every two years to women aged 50 to 69 years, based on a standard mammographic examination performed in two projections for each breast, independently read by two certified breast radiologists.

Contrast-enhanced mammography (CEM), also referred to as angiomammography, is a dual-energy digital mammography technique combined with intravenous iodinated contrast injection. Similarly to magnetic resonance imaging (MRI), it allows visualization of tumor-related angiogenesis through the detection of contrast enhancement patterns.

This technique was approved by the U.S. Food and Drug Administration (FDA) in 2011 for clinical use in breast cancer detection. [3]

II. Objectives

The aim of this work is to present contrast-enhanced mammography as a recent and promising technique in breast imaging.

First, it seeks to describe in a clear and structured manner the examination workflow, including patient preparation, image acquisition, and interpretation.

It also aims to define the main clinical indications and contraindications of the technique in order to establish its optimal use in routine clinical practice. Particular attention is given to its diagnostic performance, accessibility, and complementary role alongside other breast imaging modalities.

Furthermore, this work discusses the current limitations of contrast-enhanced mammography, including technical constraints, organizational challenges, radiation exposure, and the use of iodinated contrast media.

Finally, it explores future perspectives, particularly its potential integration into breast cancer diagnostic and follow-up strategies, as well as expected improvements in protocols, standardization, and clinical practice.

III. Contrast-Enhanced Mammography (CEM / Angiomammography)

Contrast-enhanced mammography (CEM), also known as angiomammography, is a relatively recent breast imaging technique, first reported in 2003 [4]. It combines full-field digital mammography with intravenous injection of iodinated contrast media.

This technique improves breast cancer detection by up to 20% compared with standard mammography, particularly in dense breast tissue, where the sensitivity of conventional mammography is significantly reduced [5]. It therefore plays a major role in improving lesion conspicuity in this subgroup of patients.

1. Examination Protocol

CEM is performed following intravenous administration of iodinated contrast material, similar to contrast-enhanced computed tomography (CT). The main contraindications include severe renal impairment (estimated glomerular filtration rate < 30 mL/min/1.73 m²) and known hypersensitivity to iodinated contrast agents.

For each mammographic projection, two images are acquired simultaneously:

- a low-energy (LE) image (26–32 keV),
- a high-energy (HE) image (45–49 keV), designed to detect iodine-specific attenuation.

A recombined image is subsequently generated by subtracting the low- and high-energy acquisitions, enabling visualization of contrast enhancement.

Technical Procedure

- The patient is positioned in a seated or standing position depending on equipment.
- Intravenous contrast injection is performed using an automatic injector through a peripheral venous line.
- The first image acquisition is typically performed approximately 2 minutes after the start of injection, beginning with the non-suspected breast.
- The total examination time ranges from 5 to 7 minutes, from injection to final image acquisition.

2. Image Interpretation

Low-Energy Images (LE)

Low-energy images are equivalent to standard digital mammography. The iodinated contrast is not visible at this stage. These images allow conventional morphological analysis, including assessment of :

- Masses
- Architectural distortions
- Microcalcifications

They remain essential for structural evaluation of breast lesions.

High-Energy Images (HE)

High-energy images are acquired above the iodine K-edge and are not directly interpretable. Their primary role is to detect iodine uptake, which reflects tissue vascularization.

Recombined Images

Recombined images are generated by subtracting low- and high-energy data, allowing visualization of contrast enhancement associated with tumor angiogenesis.

Their interpretation follows MRI-like enhancement patterns, distinguishing:

- **Mass enhancement:** well-circumscribed or spiculated nodular lesions
- **Non-mass enhancement:** diffuse, linear, or segmental enhancement patterns

These enhancement characteristics are highly suggestive of tumor vascularity and improve lesion characterization.

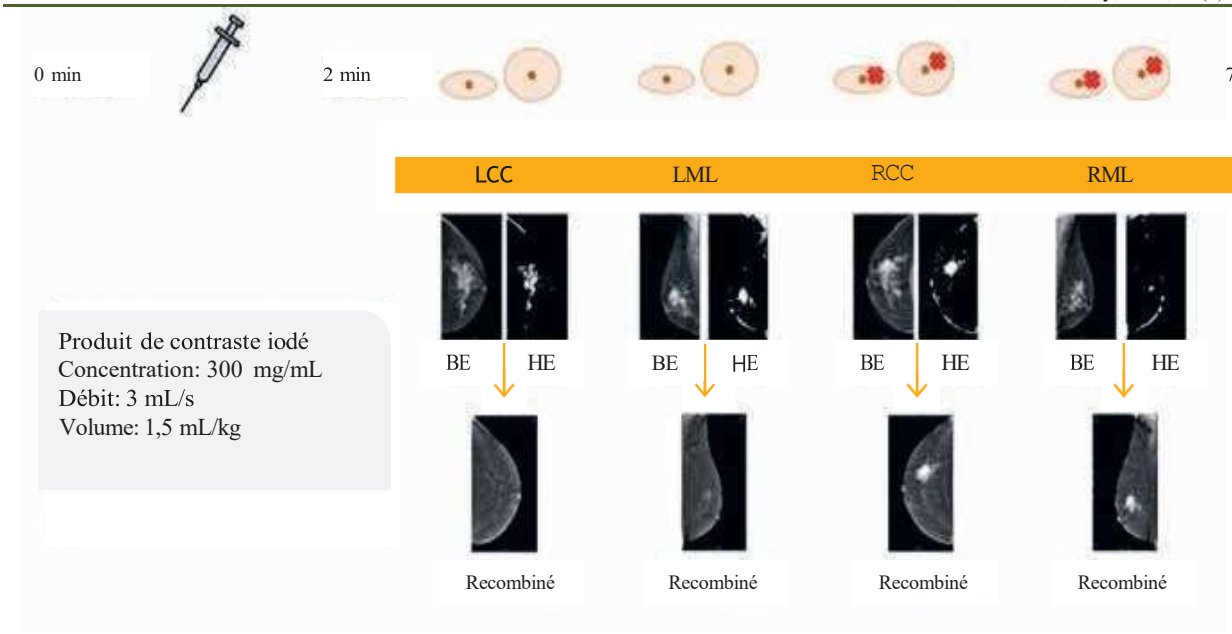


Figure 1: Schematic representation of the contrast-enhanced mammography examination protocol

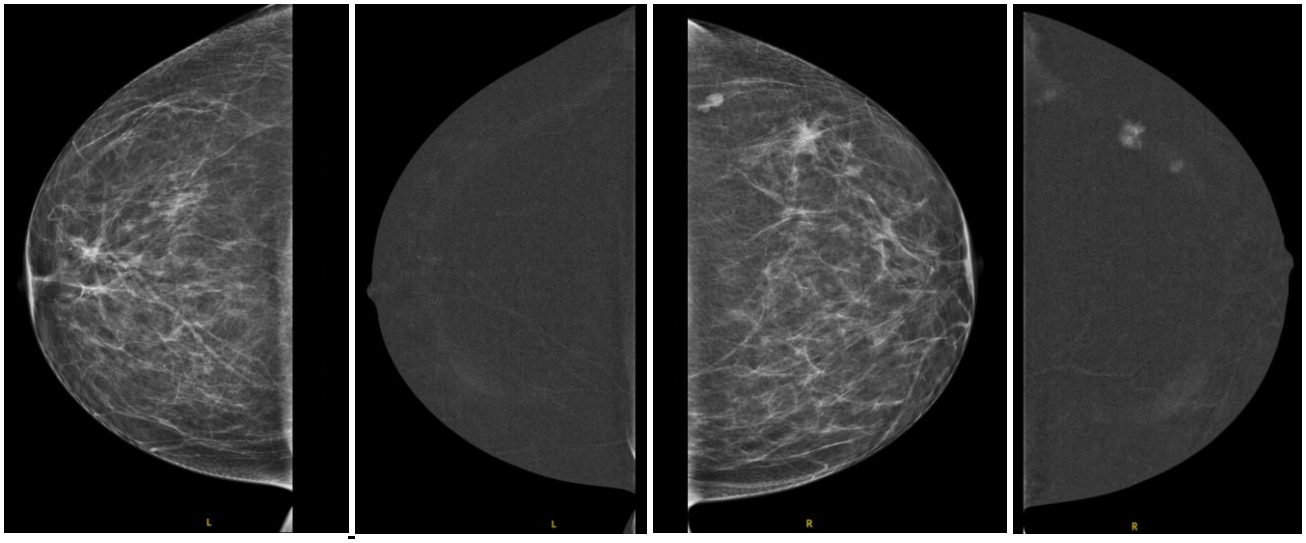
2. Indications

The current indications for contrast-enhanced mammography are largely comparable to those of breast MRI, with the exception of screening in women at very high risk of breast cancer.

a. Locoregional staging and detection of additional lesions

Contrast-enhanced mammography allows accurate assessment of tumor size and demonstrates high positive predictive value in the detection of additional ipsilateral or contralateral lesions.

However, certain breast cancer subtypes, particularly invasive lobular carcinoma and mucinous carcinoma, may exhibit minimal or absent enhancement on contrast-enhanced mammography, similarly to what is observed on breast MRI [6,7].



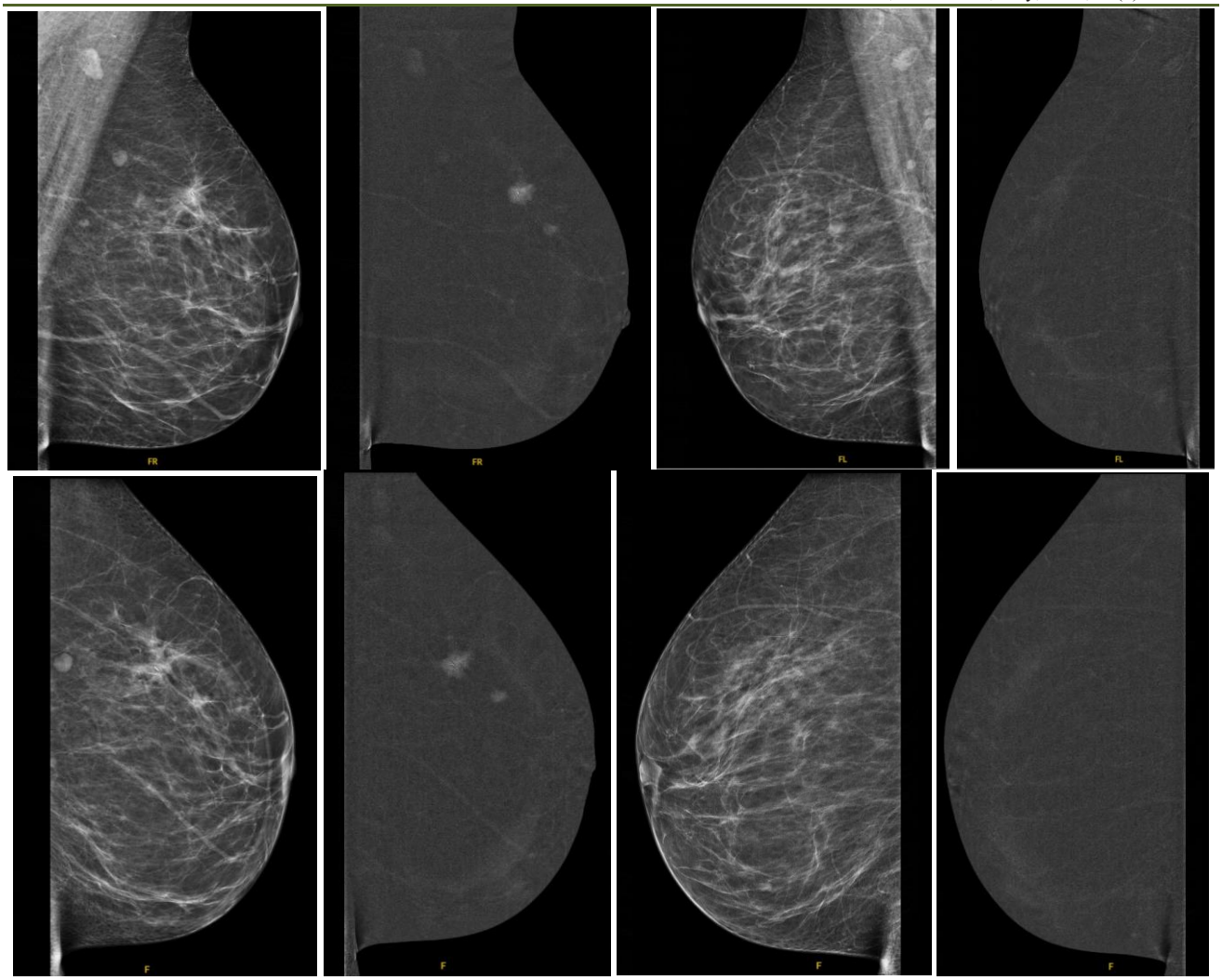


Figure 2: Contrast-enhanced mammography demonstrating a secondary lesion in the left breast as part of preoperative staging

b. Assessment before and after neoadjuvant chemotherapy

Breast MRI is commonly used for the evaluation of tumor response before and after neoadjuvant chemotherapy, allowing early assessment of treatment efficacy. Contrast-enhanced mammography represents a valuable alternative to MRI in this setting.

Several studies have demonstrated comparable diagnostic performance between the two modalities in terms of sensitivity, specificity, positive predictive value, and negative predictive value [7,8].

c. Suspicion of local recurrence

Post-treatment changes in patients undergoing breast-conserving therapy may significantly complicate the radiological assessment of local recurrence. Any new or evolving finding on mammography or ultrasound during follow-up should therefore be considered suspicious.

In this context, contrast-enhanced mammography may be useful prior to biopsy in cases of equivocal imaging findings. However, evidence regarding its diagnostic performance in this specific indication remains limited, with a lack of dedicated published studies.

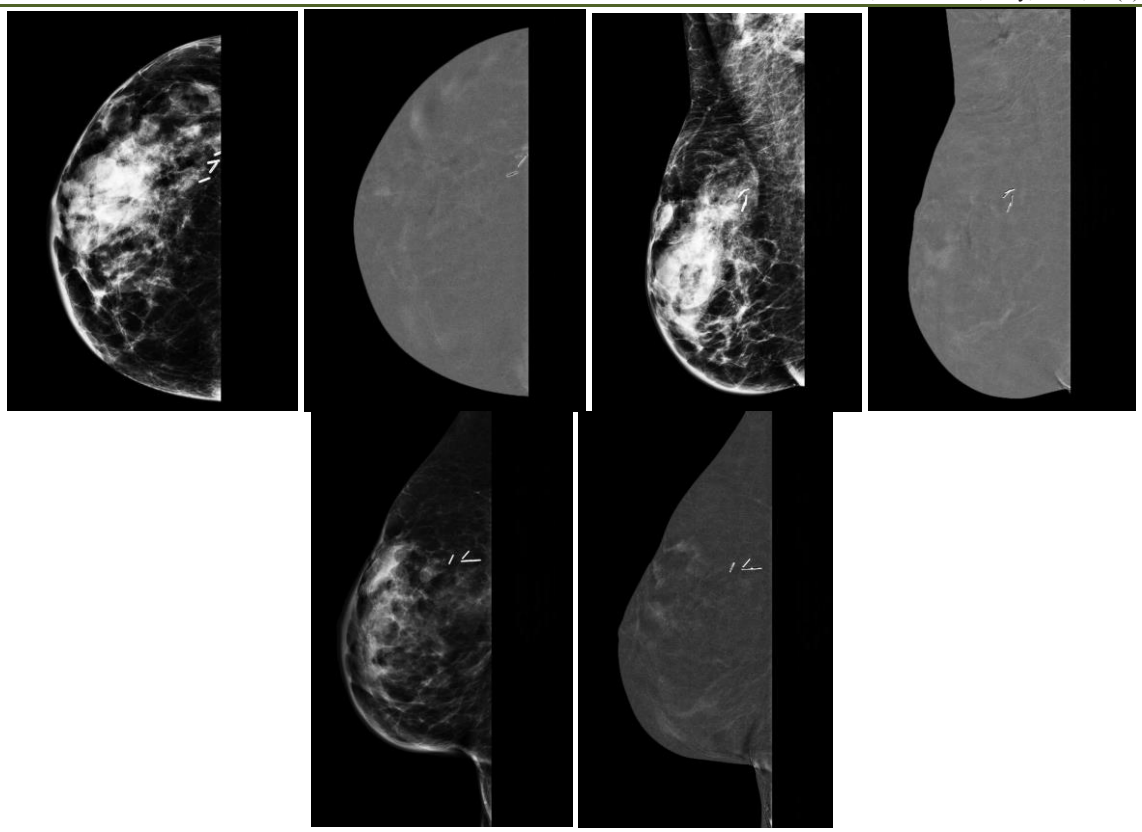


Figure 3: Patient evaluated for positive surgical margins after partial mastectomy of the right breast, in preparation for re-excision. Contrast-enhanced mammography shows no suspicious enhancement. Benign microcalcifications are present (BI-RADS 2)

d. Diagnostic challenges

Contrast-enhanced mammography demonstrates higher sensitivity and specificity compared with standard mammography [9,10]. In cases of clinical or radiological uncertainty, the detection of breast cancer using this modality shows a sensitivity of approximately 85% and a specificity of 77% [11].

However, as with MRI, certain benign lesions may also exhibit contrast enhancement. The most commonly reported enhancing benign lesions include fibroadenomas, papillomas, and epithelial hyperplasia [12].

To date, no studies have directly compared the diagnostic performance of contrast-enhanced mammography and MRI in cases of diagnostic uncertainty following conventional mammography and ultrasound evaluation.

e. Screening in high-risk patients

Currently, breast MRI remains the reference imaging modality for screening women at very high risk of breast cancer [10]. Contrast-enhanced mammography is not yet recommended as a primary screening tool in this population.

3. Advantages of Contrast-Enhanced Mammography

a. Accessibility, workflow efficiency, and examination time

Contrast-enhanced mammography is more widely accessible than MRI and can be performed immediately after conventional breast imaging when clinically indicated. The examination time is short, with image acquisition lasting less than ten minutes.

In addition, it is generally better tolerated by patients compared with breast MRI. Patients report lower anxiety levels, improved comfort, faster procedure time, and reduced noise exposure.

b. Alternative in case of MRI contraindications

CEM represents a reliable alternative to breast MRI in patients with contraindications such as pacemakers, metallic implants, breast expanders, gadolinium allergy, or severe claustrophobia [14].

c. Diagnostic performance

Both MRI and CEM are characterized by high sensitivity. However, CEM appears to offer improved specificity in several studies [6].

Furthermore, CEM allows visualization of microcalcifications on low-energy images while simultaneously assessing associated contrast

enhancement on recombined images, improving lesion characterization through spatial correlation.

d. Learning curve and workflow optimization

Interpretation of CEM images has a relatively short learning curve for breast radiologists. Moreover, performing ultrasound immediately after CEM by the same operator improves workflow efficiency and reduces the number of involved practitioners, thereby optimizing patient management.

e. Cost-effectiveness

The cost of CEM is significantly lower than that of MRI, representing an important advantage in terms of healthcare system resource utilization and cost-effectiveness.

f. CEM-guided biopsy: technique overview

The most commonly used approach is the lateral (horizontal) access, which provides optimal lesion visualization due to more uniform breast compression using a non-perforated compression paddle and reduces needle-related artifacts. This approach also allows a pre-fire check image with the needle positioned at the target site.

At the beginning of the procedure, skin marking is performed over the lesion location. A preliminary three-dimensional acquisition is obtained to assess lesion surroundings and identify anatomical landmarks such as calcifications, vessels, or fatty lobules.

The breast is then decompressed prior to intravenous injection of iodinated contrast (350 mg I/mL concentration, 1.5 mL/kg dose, injected at 3 mL/s). Approximately two minutes after injection, the breast is recompressed and repositioned. Dual-energy acquisitions (low and high energy) are performed to generate recombined images highlighting lesion enhancement within the biopsy window.

Spatial coordinates are then calculated using stereotactic acquisitions at +15° and −15° angles. After local anesthesia of the skin entry point and needle tract, biopsy samples are obtained. A marker clip is deployed at the end of the procedure to localize the biopsy site.

This technique is rapid, well-structured, and familiar to breast radiologists already experienced in interventional procedures under ultrasound, stereotactic guidance, tomosynthesis, or MRI.

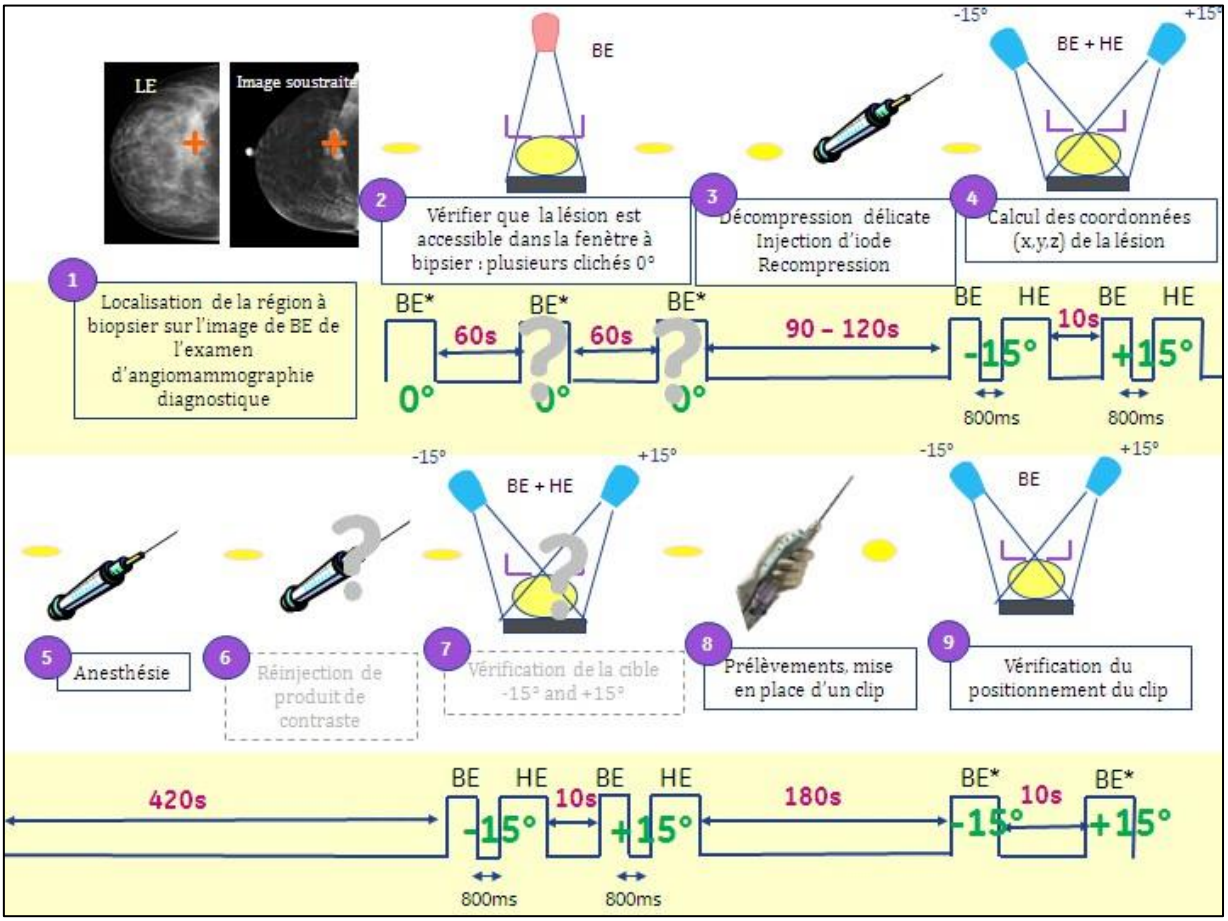


Figure 4: Schematic representation of a contrast-enhanced stereotactic biopsy procedure, including the time interval (in seconds) between each image acquisition [21]

4. Limitations and Drawbacks of Contrast-Enhanced Mammography

a. Radiation exposure

Contrast-enhanced mammography is an X-ray–based imaging modality. Reported data indicate that the mean glandular dose is slightly higher than that of standard digital mammography, for which the mean glandular dose ranges between 0.9 and 2.3 mGy [15]. Therefore, its use as a primary screening tool is currently not recommended.

b. Adverse effects of iodinated contrast media

As with computed tomography, it is essential to assess patients for a history of allergic reactions to iodinated contrast media and to evaluate renal function prior to examination.

The risk of hypersensitivity reactions to iodinated contrast is higher than that associated with gadolinium-based contrast agents used in MRI [16].

c. Technical limitations for deep lesions

As in conventional mammography, certain breast lesions may not be adequately visualized on CEM, particularly those that are very deep, medial, subclavicular, or located at the periphery of the breast.

d. False-negative findings

Certain histological subtypes, including invasive lobular carcinoma, mucinous carcinoma, and ductal carcinoma in situ, may demonstrate minimal or delayed enhancement, similar to MRI, potentially leading to false-negative results.

e. Artifacts

Artifacts commonly observed in standard mammography, such as those related to deodorant, creams, or hair interposition, may also be seen in CEM.

In addition, CEM-specific artifacts may occur due to residual iodinated contrast material on the skin or compression paddle, resulting in contamination artifacts on recombined images.

f. Future perspectives

Contrast-enhanced mammography is an expanding imaging modality, with a continuously increasing number of installed systems worldwide. Since 2023, a dedicated BI-RADS lexicon for CEM interpretation has been introduced, standardizing reporting and improving diagnostic consistency [17].

Lesions detected on CEM typically require complementary ultrasound evaluation. In cases of imaging concordance, integrated diagnostic assessment is performed, with possible immediate biopsy. However, in some cases, no ultrasound correlate is identified, and biopsy under CEM guidance may be required.

Artificial intelligence and radiomics are emerging fields of interest in breast imaging research, with growing applications in contrast-enhanced mammography [18].

IV. CONCLUSION

Contrast-enhanced mammography represents a major advancement in breast imaging. By combining morphological and functional assessment, it significantly improves diagnostic accuracy, particularly in cases where conventional imaging modalities are inconclusive.

This technique is accessible, rapid, cost-effective, and well tolerated, making it a valuable alternative to breast MRI, especially in patients with contraindications or limited access to MRI. Its integration into routine clinical practice is further facilitated by workflow efficiency and the possibility of comprehensive patient management within a single imaging session.

In addition, its utility in specific clinical contexts, such as dense breast evaluation and treatment monitoring, reinforces its growing role in breast imaging. Future development will depend on protocol optim ;njnization, standardization of interpretation, and the expansion of interventional applications, including CEM-guided biopsy.

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