

A new technique waiting to improve in the diagnosis of breast cancer: Contrast-enhanced mammography

The diagnosis of breast cancer: Contrast-enhanced mammography

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Abstract

The contrast-enhanced mammography technique, which was developed to reduce the false negativity and false positivity rates of full-field mammography, especially in dense breasts, and received FDA approval in 2011, has not been fully recognized even in the area of radiology. Based on this deficiency, this article aimed to give brief information about the advantages and disadvantages of contrast-enhanced mammography compared to digital mammography and breast magnetic resonance imaging, imaging technique, indications, and patient selection.

Keywords

Breast Cancer, Contrast-Enhanced Mammography, Dense Breast

DOI: 10.4328/ACAM.20720 Received: 2021-05-31 Accepted: 2021-08-19 Published Online: 2021-09-24 Printed: 2022-03-15 Ann Clin Anal Med 2022;13(Suppl 1): S63-66

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Introduction

The most common cancer in women is breast cancer. With screening mammograms since the 1960s, there have been a significant decrease in breast cancer-related mortality rates [1]. With the widespread use of digital mammography in the 2000s, mammography has made great progress in diagnostic performance. It provides an opportunity for 2 or 3-dimensional tomosynthesis and computer-aided detection (CAD) scans [2]. Now, it is possible to achieve higher predictive diagnostic results by making contrast-enhanced mammography (CESM) images, especially in dense breasts. In this context, contrast-enhanced mammography is an important radiological development that awaits widespread use.

Why Contrast-Enhanced Mammography?

Advantages compared to digital mammography

Patients with dense breast parenchyma, as Type C-D according to the American College of Radiology Breast Imaging Reporting and Data system (ACR-BIRADS), may be screened with contrast-enhanced mammography instead of classical mammography, since the sensitivity of conventional mammography decreases significantly. In such breasts, when mammography and ultrasonography are performing together, the diagnostic accuracy is 71%, while it can be reached 78-80% when performed with CESM [3]. Studies show that the diagnostic accuracy of full-field digital mammography (FFDM) in breast cancer screening is 90% and ultrasonography is 92%, while the CESM sensitivity is close to 100% [4]. In a study evaluating the advantages of CESM over FFDM, it has been shown that CESM increased sensitivity to 100% (+ 3%), specificity to 88% (+ 46%), positive predictive value (PPV) to 76% (+ 37%) and negative predictive value (NPV) to 100% (+ 3%) [5]. In other words, CESM significantly reduces the false positivity rates of digital mammography; therefore, it reduces the rate of unnecessary follow-ups, examinations and procedures. If no pathological findings are detected in CESM, there is no need for additional examination for one year. This is especially important in reducing anxiety in patients with high risk or positive family history or in patients who will be followed up at short intervals upon suspicious findings. The most important advantage for radiologists; the learning curve is small compared to mammography, ultrasonography and magnetic resonance imaging (MRI). In other words, it is not a procedure that requires extensive experience as in mammography or MRI to evaluate [6].

Advantages compared to breast MRI

Neovascularization occurs with vascular endothelial growth factor (VEGF) released from rapidly growing tumoral lesions that usually go into partial necrosis secondary to malnutrition. Because of the high permeability of these vascular structures that develop rapidly and disorganized and are immature, the contrast material escapes to the tumor interstitium and enhances more than the ground breast tissue. This phenomenon is the basis for breast MRI and CESM [7].

Although magnetic resonance imaging is currently the gold standard in breast cancer diagnosis, lesion specificity is low, false positivity rates are high, the cost is very high, examination time is long, and it is not available in every center [8]. MRI shows enhancement and increases unnecessary invasive

procedures and biopsy rates with difficult procedures in lesions such as atypical ductal hyperplasia, benign fibrocystic disease, fibroadenoma, infection, papilloma, radial scar and complex sclerosing lesions [9]. In addition, low grade-new-onset ductal carcinoma in situ (DCIS) or other malignant lesions may be negative for MRI since adequate enhancement is not observed. CESM provides anatomical and functional information in breast lesions with a lower cost and examination time, similar to MRI. The advantage of CESM is that it can detect suspicious findings such as microcalcification, distortion, and spiculation accompanying pathologies such as DCIS on low-energy images. Therefore, CESM is superior to MRI in detecting low-grade tumors and DCIS. Lesion specificity is also superior to MRI [10]. In addition, dense ground parenchymal enhancement in dense and fibrocystic breasts significantly reduces MRI sensitivity. In cases with high-risk dense breast structure with dense breast parenchyma, MRI sensitivity decreases up to 77% [11]. Therefore, CESM is superior to MRI to evaluate only tumor neovascularity by ruling out benign parenchymal enhancements, providing a non-complex, simpler and clearer image.

CESM is a growing technique for breast cancer detection and diagnosis, with the same levels of sensitivity and specificity as contrast-enhanced breast MRI. Because of its similar performance and ease of application, CESM is being adopted in multiple indications previously reserved for MRI, such as problem-solving, the extent of the disease in newly diagnosed patients, and evaluation of treatment response to neoadjuvant chemotherapy [2]. In addition, the fact that the examination time is significantly shorter than MRI and eliminates false positivity rates of MRI is an important advantage in terms of practical use [11].

How is CESM performed?

Low osmolarity iodinated contrast agents similar to the contrast used for computed tomography (CT) are used to obtain contrast images. Contrast agent concentration should be 330-370 mg/ml. (e.g., Omnipaque, GE Healthcare). Contrast agents should be used at 1.5 mL/kg per kilo as in standard abdominal tomography scans. The injection rate of contrast material should be 2-3 mL/s. The breast is taken into compression approximately for 2 minutes after the injection, and dual-energy (low-energy (23–32 kVp) and high-energy (45–49 kVp)) images are taken in standard craniocaudal (CC) and mediolateral oblique (MLO) positions. Recombined images are created by subtracting low-energy images from high-energy images. That eliminates densities from the background breast tissue and highlights only areas of iodine uptake. It takes less than 6 seconds to acquire an image pair. Room time is slightly longer than standard mammography, nearly 10 minutes. Low and high energy beams are related to peak kilovoltage (kVp) and filtration. It is possible to say low-energy when the kVp value is 28-32; high-energy when the kVp value is 45-49 (Figure

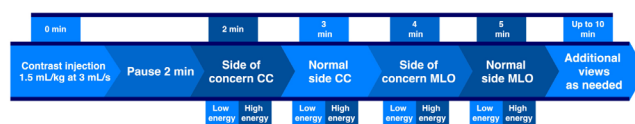


Figure 1. Briefly schematic demonstration of contrast-enhanced mammography technique

1). Copper filters can be used to further harden the high-energy beam [12-14]. Recent estimates show that based on breast tissue thickness and density, the radiation dose delivered to the patient may be 81% higher for CESM than standard 2D digital mammography and 48% higher than 3D tomosynthesis with considering 2 separate radiation exposures per position for imaging [14].

CESM Indications

FFDM sensitivity in ACR BIRADS Type C-D cases with dense breast structure does not exceed 30-60% [11-14]. It is the main indication to perform annual CESM instead of conventional digital mammography to screen patients with this dense breast parenchyma (Figure 2). Generally, all indications for breast MRI are also valid for CESM. It can be used to evaluate the distribution of a suspicious lesion detected in mammography, with its similar sensitivity to MRI. Again, it can be used instead of MRI in the local staging of the diagnosed cancer and in evaluating the other breast. It has been shown that CESM is as

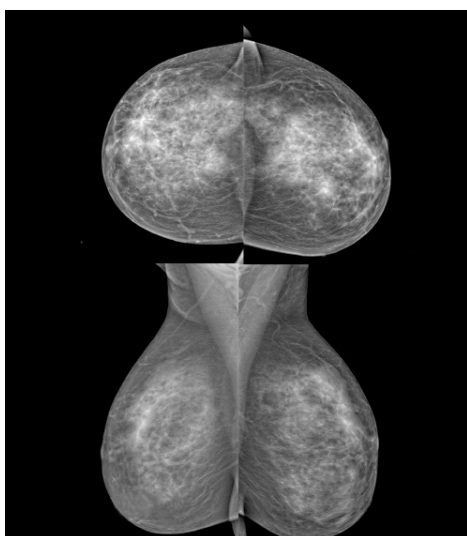


Figure 2. a) Full-field digital mammography (FFDM) image of a patient with Type D breast density.

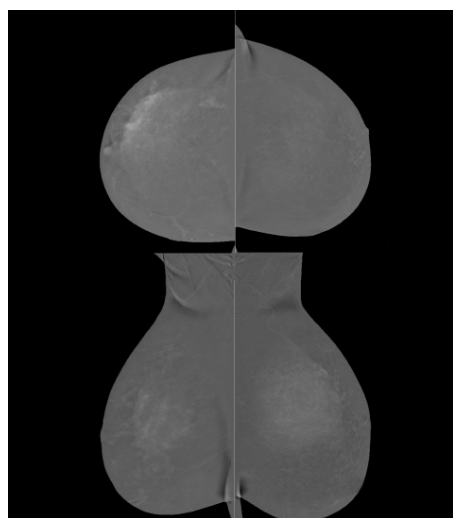


Figure 2. b) In contrast-enhanced mammography images of the same patient, contrast enhancement showing asymmetric regional distribution in the upper outer quadrant of the right breast with respect to the left is observed (consistent with malignancy).

effective as MRI in evaluating the neoadjuvant treatment response. It can be used as an alternative to MRI, especially in cases where there is a contraindication for MRI such as pacemaker, claustrophobia, metallic foreign body.

Disadvantages of CESM

When CESM applies, even though the pulsed radiation exposure is shot twice (low-dose and high-dose) is considered the most important limitation of the examination, it is within safe limits. According to the American College of Radiology standards, the radiation dose to be exposed to a breast in a mammographic examination should not exceed 3 mGy. Despite twice exposures with CESM, high-quality images can generally be obtained with a dose of 1.7-2 mGy, under the limit of ACR. Therefore, the high radiation exposure dose can be ignored. However, using iodinated contrast material in such a screening examination is the most important disadvantage of the application. Adverse scenarios such as hypersensitivity reactions (<0.6% in last generation non-ionic iodinated contrast media and mild allergic reactions) and acute renal failure in patients with renal insufficiency (which can be minimized with abundant hydration) prevent the widespread use of the CESM. However, chest wall invasion and internal mammary lymph node involvement, which can mainly be detected by MRI and affect the stage in posterior-located tumors, cannot be clearly evaluated with CESM. That is one of the important weaknesses of the procedure. In these cases, it may be necessary to perform a complementary MRI after CESM [11-14].

Patient selection

Performing annual screening mammograms with CESM in high-risk patients will provide an advantage in terms of diagnosis. In patients with a lifetime risk of breast cancer is 20%, in BRCA or other hereditary germline mutation carriers, patients with a history of radiation to the chest wall, patients diagnosed with LCIS in any breast, patients with a family history of breast cancer under the age of 40, in cases with breast cancer in their first and second-degree relatives, CESM can be used instead of FFDM for screening purposes [14].

Conclusion

CESM is a reliable and practical imaging method that increases diagnostic sensitivity and specificity of mammography, reduces unnecessary interventional procedures and recall rates in the diagnosis of breast cancer, especially in high-risk patients with dense breast structure. Although the use of CESM in the world is low for now, it is an important radiological development that may increase rapidly when many potential indications and advantages for clinical use are considered.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:

Deniz Esin Tekcan Şanlı, Duzgun Yildirim. A new technique waiting to improve in the diagnosis of breast cancer: Contrast-enhanced mammography. *Ann Clin Anal Med* 2022;13(Suppl 1): S63-66