A Review of Various Modalities in Breast Imaging

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Abstract

Background: The spread of breast cancer has become one of the health challenges in human societies. Breast cancer is the most common type of malignancy in women, and one of the three most common cancers worldwide, along with lung and colon cancer. Nowadays, breast cancer is the second cause of death after cardiovascular diseases. In general, about one out of eight women (about 12%) suffer from this disease during their life in the USA and European countries. If breast cancer is detected at an early stage, its survival rate will be very high. Several methods have been introduced to diagnose breast cancer with their clinical advantages and disadvantagesRecently, other new modalities like positron emission tomography, 99mTc-sestamibi scintimammography, and electrical impedance tomography (EIT) are also being offered. However, there is still controversy over the most appropriate use of these new modalities. Based on the literature, this review evaluates the role of various modalities used in the screening and diagnosis of breast cancer.

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Introduction

The spread of breast cancer has become one of the health challenges in human societies. Breast cancer is the most common type of malignancy in women, and one of the three most common cancers worldwide, along with lung and colon cancer. In 2012, there were ~ 1.7 million new cases of cancer worldwide, and about 31% of them led to death. Breast cancer is the second leading cause of death after cardiovascular diseases. About one out of eight women (about 12%) suffer from this disease during their life in the USA and European countries **(1).**

Mammography

Mammography is specialized medical imaging that uses a low dose x-ray system to see inside the breasts. A mammography exam, called a mammogram, aids in the early detection and diagnosis of breast diseases in women **(1).**

Mammography has common clinical applications including:

-Screening mammography to detect early cancer in asymptomatic women.

- Diagnostic mammography to image the breast for diagnosis of a previously identified suspicious breast lesion.

-Surveillance mammography to assess recurrence of malignancy in women with known breast cancer.

- Needle localization and tumor marking to obtain tissue samples from breast masses that appear suspicious on screening or diagnostic

mammography and tumor marking for surgery**. (2)**

 Screening mammography: Screening mammography is the primary imaging modality for early detection of breast cancer. Mammography may detect cancer one and a half to four years before a cancer becomes clinically evident **(3).**

For early detection by screening, linear growth pattern of tumors and that breast cancer has not spread at the time when tumors are detectable at mammography. Thus, if the assumptions of tumor growth are not correct or if growth of tumors is heterogenic, screening mammography might not be an adequate tool to reduce the burden of breast cancer **(4).**

The same machines are used for screening and diagnostic mammograms. However, diagnostic mammography takes longer to perform than screening mammography and the total dose of radiation is higher because more x-ray images are needed to obtain views of the breast from several angles **(2).**

Although a screening examination should ordinarily be limited to craniocaudal (CC) and mediolateral oblique (MLO) views of each breast, on occasion, supplemental views may be required to visualize breast tissue completely or optimally, but such views are not ordinarily part of the routine screening examination except for women with implants. When pathology is suspected, a recommendation for additional imaging studies, diagnostic mammography or biopsy may be warranted **(1).**

Additional views, such as anterior compression, cleavage view or an exaggerated CC view may be obtained to maximize imaging of all breast tissue **(5).**

The U.S. Preventive Services Task Force, (7) recommends biennial screening mammography for women aged 50 to 74 years. The **Yasin et al., (6)** recommend yearly screening mammography starting at age 40. The over whelming majority of screening mammograms will end up classified as Breast Imaging Reporting and Data System (BI-RADS) 1

And 2. A small percentage of mammograms (approximately 5 to 9%) will need additional imaging for further evaluation, short interval follow-up or possibly a biopsy **(8).**

Diagnostic mammography: Diagnostic mammography is performed in women or men who present with breast complaints or have an abnormal clinical examination, and in women who have abnormal screening mammography. Patients with specific breast symptoms, such as a palpable lump, nipple discharge, or focal pain should undergo diagnostic mammography **(5).** Diagnostic mammography uses specialized views to determine exact size and location of breast abnormalities and to image the surrounding tissue and lymph nodes. Typically, several additional views of the breast are acquired and interpreted during diagnostic mammography **(9).**

- Spot compression (also called cone compression) may be used to get a closer view of one area of the breast during diagnostic mammography. To get a clearer image, a small compression plate separates the breast tissue in an area and pushes normal breast tissue out of the way. The images may be magnified to make it easier to see small suspicious areas. These close-up views can show tiny deposits of calcium that look like small white spots on a mammogram. The size, distribution, and morphology of calcifications are seen best on magnification views. In addition, magnification views can provide details regarding margins of masses **(10)**

-A 90-degree lateral view is a true lateral view of the breast. This view may help in confirming the presence of a benign pattern of calcifications, called milk of calcium deposition, associated with benign breast microcysts. Other views that may be obtained in a diagnostic work-up are

tangential views, to further evaluate a palpable area or to confirm calcifications are dermal in etiology and rolled views **(5).**

Approximately 7% of diagnostic mammograms will achieve a BI-RADS 3 assessment. Only 2% of diagnostic mammograms will receive a BI-RADS 4 or 5 assessment and will require biopsy **(8).**

 Mammographic examination: A mammogram involves exposing the breast to x-rays. These x-rays are both transmitted through the breast tissue as well as scattered to the surrounding tissue. The x-rays are attenuated based upon the characteristics of the breast tissue and are then absorbed as latent images on the recording device. The latent image is processed and displayed for diagnostic purposes **(5).**

Routine evaluation includes obtaining two views CC and MLO of each breast. In the CC view, the breast is lifted and positioned on the plate and compression is applied from above. In the MLO view, the breast is compressed and imaged from the side. Breast positioning is critical. Improper positioning may lead to exclusion of parts of the breast from the field of view, risking non-visualization of a cancer **(11).**

Adequate breast compression is necessary to obtain good quality mammograms. Compression increases the image contrast and decreases the radiation dose. Since compression causes homogeneous breast thickness, x-ray penetration is uniform through the tissues. Compression also reduces motion and minimizes superimposition of tissues, improving the diagnostic quality of the study. In mammographic compression of the breast no quantitative standards or guidelines are available. Compression can be personalized by applying the same pressure to all breasts, so pain scores are reduced without affecting absorbed glandular dose or image quality **(12).**

Compression ideally should be applied until the breast is held firm and immobile. However, the degree of pain and discomfort experienced during the examination affects the utilization of regular mammography. Patient-controlled compression, oral or topical analgesics, and cushioned paddles may minimize discomfort **(5).**

The radiation dose absorbed by the breast depends upon the breast tissue thickness, with the dose absorbed increasing with the thickness of the breast. The mean glandular dose exposure for a breast that is 4.2 cm thick should not exceed 0.3 rads per image **(1).**

Types of mammography:

Mammogram x-rays pass through the breast tissue and are converted to light by fluorescent screens. This light causes a chemical reaction in the film emulsion that is processed and displayed as a grayscale image. In a film screen (analog) mammogram, the image is captured, displayed, and archived for storage in a film**.** Film mammogram has multiple attributes that make it an appropriate medium for mammography**:**

 High spatial resolution (up to 20-line pairs per millimeter) allows demonstration of micro calcifications, lesion margins, and speculations.

 High contrast resolution permits differentiation of subtle differences in soft tissue densities.

 The film is easily displayed.

 Normal areas of the breast image can be masked to improve visualization of abnormalities.

 Multiple examinations can be viewed on serial view panels.

However, film screen mammography has a number of disadvantages, compared to full field digital mammography **(5).**

A limited dynamic range makes it difficult to image all components of the breast (fat and dense tissue) optimally, and to differentiate

between small cancers and surrounding breast tissue of similar density.

The inability to manipulate the image following exposure may lead to retakes and increased radiation dose to the patient.

Film is subject to artifacts from processing and storage.

Films may be misfiled, lost, or otherwise not readily retrievable

when comparisons are needed.

Recent advances in mammography include digital mammography, computer-aided detection (CAD) and breast tomosynthesis **(1).**

Digital mammography, also called full-field digital mammography (FFDM) converts the X-ray photons to an electronic signal, which is further processed and displayed as a gray scale image. There are two main types of digital imaging systems used to acquire digital images: direct radiography, where the image is transmitted directly to the radiologist's workstation, and computed radiography, where a cassette based removable detector is inserted into an external reading device to generate an image. The patient's experience during a digital mammogram is similar to having a conventional film mammogram **(1).**

Breast tomosynthesis:

Also called three-dimensional mammography and digital breast tomosynthesis (DBT), is an advanced form of breast imaging where multiple images of the breast from different angles are captured and reconstructed into a three-dimensional image set **(13).**

Although the radiation dose for some breast tomosynthesis systems is slightly higher than the dosage used in standard mammography, it approved by the US Food and Drug Administration (FDA) for routine clinical use as an adjunct to standard mammography **(14)**.

Sensitivity and specificity of screening mammography is significantly improved with the addition of tomosynthesis to digital mammography. In the diagnostic setting, tomosynthesis improves lesion characterization, increasing rates of cancer detection, and according to most studies, decreasing the false negative rate **(15).**

CAD may improve the sensitivity of mammographic screening to a limited extent. This may be offset by a higher recall rate, and the potential for overdiagnosis. CAD has not been proven to improve mortality rates from breast cancer screening, and the costs associated with the equipment and increased recall rate with CAD may outweigh possible marginal benefits **(5).**

Breast ultrasound

Ultrasound (US) is a valid supplemental screening tool in women with dense breast tissue because it is widely available and low cost. The sensitivity of DM for the detection of breast cancer is reduced to 47.8–64.4% in patients with dense breasts, and bilateral screening US, using a high-frequency transducer, allows the detection of early stage mammographically occult breast cancers **(16).**

Available commercial systems use linear arrays operating at around 10–14 MHz with close to 100% bandwidth ranging from 5 to 18 MHz. Several studies showed the primary role of the US as a screening tool in women with dense breasts. **Berg et al., (17)** have published the most significant multi-institutional trial, showing an increase in the diagnostic yield of breast cancer of 4.2 per 1000 women screened.

Other previous studies found that most cancers detected were invasive (91.7%), with a mean size of 10 mm, and the only limitation was an increase in biopsies compared to mammography alone. However, the performance of bilateral handheld ultrasound makes it a challenge for screening, in terms of physician time for exam

execution and interpretation (workflow of nearly 20 min). Due to these limitations, automated breast ultrasound (ABUS) was introduced, a new ultrasonography technique with the purpose of overcoming the operator-dependence of handheld US, increasing the reproducibility of the examination. Nowadays, two main categories of automated breast ultrasound systems are available: prone and supine scanners. Moreover, ABUS allows multiplanar reconstructions, especially the coronal view, also known as the "surgical view" (in which the breast is positioned in the same way that it is oriented on the surgical table), and it provides important information, such as the retraction phenomenon **(18).**

The coronal view allows significantly lower reading times and represents a valuable feature in the screening setting; diagnostic performance makes the complete multiplanar assessment mandatory. The main limitations of ABUS systems are the exclusion of axillary regions from the field of view and the absence of tools to assess vascularity and tissue elasticity. The first screening work using ABUS was performed by Kelly et al. This multicenter study compared mammography alone versus automated whole breast ultrasound (AWBU) plus mammography in 4419 women with dense breasts and/or at elevated risk of breast cancer. They found an improvement in cancer detection of 3.6 per 1000 women screened with the addition of AWBU, and sensitivity increased from 40% for mammography alone to 81% for the combined modalities. Of note, recalls increased from 4.2% for mammography alone to 9.6% adding AWBU **(19).**

An Italian review of **Zanotel at al., (20)** has evaluated the potential and limitations of ABUS as a method of choice and adjunctive tool to screening mammography in women with dense breast tissue. Multiple studies have demonstrated similar sensitivities, cancer detection rates, diagnostic accuracy rates, and image quality for ABUS and US; however, ABUS had significantly longer execution times than US. The role of ABUS is still debated. A further evolution is in the attempt to merge the ABUS and the DBT into a single device. The advantage of this new device is the ability to perform ABUS directly without decompressing the breast, in the same position in which the DBT is acquired. In this way the alterations identified with DBT could thus be better investigated without having to return the patient at a later time and without even having her move. These still initial experiences must be validated on a large scale, but from the first results the technique seems to be of sufficient quality to identify malignant lesions and could lead to important logistical and economic advantages, especially in the screening setting **(20)**

MRI breast imaging:

The aim of breast MRI is to obtain a reliable evaluation of any lesion within the breast. It is currently always used as an adjunct to the standard diagnostic procedures of the breast, i.e., clinical examination, mammography and ultrasound. Whereas the sensitivity of breast MRI is usually very high, specificity—as in all breast imaging modalities—depends on many factors such as reader expertise, use of adequate techniques and composition of the patient cohorts. Since breast MRI will always yield MR-only visible questionable lesions that require an MR-guided intervention for clarification, MRI should only be offered by institutions that can also offer a MRI-guided breast biopsy or that are in close contact with a site that can perform this type of biopsy for them. Radiologists involved in breast imaging should ensure that they have a thorough knowledge of the MRI techniques that are necessary for breast imaging, that they know how to evaluate a breast MRI using the ACR BI-RADS MRI lexicon, and most important, when to perform breast MRI. This manuscript provides guidelines on the current best practice for the use of breast MRI, and the methods to be used, from the European Society of Breast Imaging (EUSOBI) **(21).**

Breast ce-MRI was introduced into clinical practice in the 1980s and is now widely used around the world. It is best practice to use a field strength of at least 1.5 T to acquire images at a sufficiently high spatial resolution and a dedicated breast coil with at least four channels (modern designs have 16 channels or more) to obtain diagnostic-quality images. The patient lies prone during the acquisition, which can have a variable duration depending on the study protocol used, from the few minutes of the new ultrafast sequences to the long time required by spectroscopic imaging **(1).**

The basic multiparametric ce-MRI protocol most used includes: the non-contrast enhanced acquisitions (T2-weighted and diffusion-weighted imaging (DWI)); the native T1-weighted acquisition; and subsequently, the contrast-enhanced series. Reporting of breast MRI is standardized in the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS). In good clinical practice it is important that radiologists who report a breast ce-MRI are also skilled in conventional images—mammography, ultrasound and tomosynthesis—and that since MRI often highlights lesions that are occult with conventional imaging, there is the possibility of performing MRI guided interventional maneuvers such as localization and biopsies **(24).**

Trying to improve lesion classification, new sequences such as DWI techniques, spectroscopic imaging and quantitative assessment of contrast material enhancement have been introduced in recent years in breast MRI. A multiparametric approach has been shown to increase the specificity of breast ce-MRI up to values equal to 90%. In particular, the use of DWI is useful to discriminate when it is necessary to perform a biopsy (ADCs greater than 1.4–3 _ 10□3 mm2/sec are exceptionally rare in cancers) but also in predicting the ki67 Index in invasive ductal carcinomas. Particular fast-field echo axial T1-weighted imaging with coronal reconstruction sequences were also evaluated for the study of axillar lymph nodes **(22).**

The main uses of breast MRI are preoperative staging of breast cancer, screening of high-risk patients, evaluation during neoadjuvant chemotherapy, carcinoma of unknown primary origin (CUP syndrome) and problem solving. In the preoperative staging of breast cancer, MRI has been shown to have a greater sensitivity than conventional imaging with values close to 100%; MRI allows a better

assessment of the extent of the index lesion, with 75% of lesions differing less than one centimeter from the post-operative histology; a better assessment of the extension of the ductal component in situ associated with invasive lesions; and above all, MRI is able to identify 20% of the additional malignant lesions in the ipsilateral breast and 4–5% of additional malignant lesions in the contralateral breast. Five percent of additional malignant lesions identified by MRI are biologically more relevant than the index lesions **(23).**

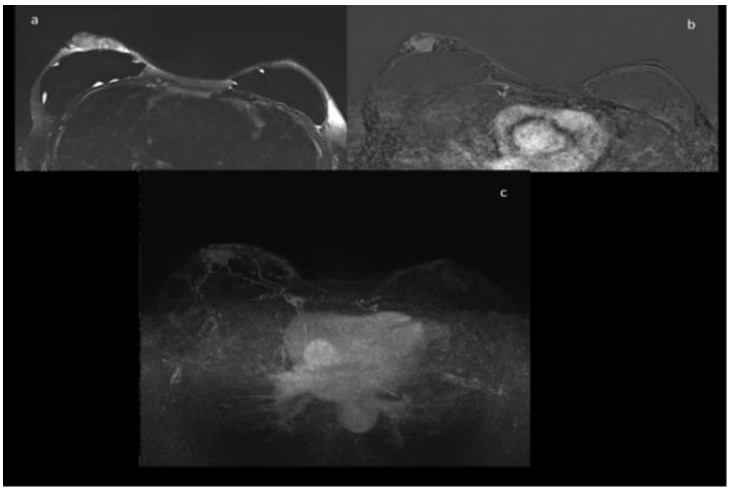

Figure 1: A 43-year-old patient with BRCA2 gene mutation; the patient underwent prophylactic mastectomy. At the annual ce-MRI screening a mass with irregular margins was identified in the retroareolar area of the right breast, corresponding at the US second look to a suspicious hypoechoic nodule that undergoes core needle biopsy with the diagnosis of invasive

lobular carcinoma. (**a**) T2-weighted imagine; (**b**) contrast-enhanced image; (**c**) MIP image.

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