

The Role of Imaging Techniques in Diagnosis of Breast Cancer

GHEONEA IOANA ANDREEA⁽¹⁾, RALUCA PEGZA⁽²⁾, LUANA LASCU⁽³⁾,
SIMONA BONDARI⁽¹⁾, ZOIA STOICA⁽¹⁾, A. BONDARI⁽¹⁾

⁽¹⁾ Department of Radiology and Imaging, University of Medicine and Pharmacy Craiova; ⁽²⁾ Service de Radiologie de l'Hopital Notre-Dame de Bon Secours, Centre Hospitalier Regionale, Metz-Thionville; ⁽³⁾ Radiology and Imaging Department, County Emergency Hospital, Craiova

ABSTRACT Breast cancer is the most common type of cancer in women worldwide. Advances and ongoing improvements in imaging technologies have improved the sensitivity of breast cancer detection and diagnosis, but each modality is most beneficial when utilized according to individual traits such as age, risk, and breast density. Mammography is considered the “gold standard” in the evaluation of the breast lesions from an imaging perspective. Ultrasound examination and magnetic resonance imaging are being offered as diagnostic techniques and as adjuncts to the pre and postoperative workup. Despite all of these advances, it is still the case that no single imaging modality is capable of identifying and characterising all breast abnormalities and a combined modality approach will continue to be necessary. In this overview we evaluate the role of various imaging techniques in the diagnosis of breast cancer based on an assessment of current trends.

KEY WORDS Breast, Mammography, Ultrasound, Magnetic resonance Imaging

Introduction

Text Breast cancer is the second leading cause of cancer deaths in women today and the most common cancer in women. Breast cancer commonly affects women older than 40 years of age; however, younger women can also be affected, especially those with a genetic predisposition [1].

The increasingly early detection of breast cancer has resulted in significant improvements in the rate of cure in this disease. Numerous imaging modalities are now available to the breast radiologist and recently there have been exciting new developments which show great promise for the future.

This article will review the most interesting of these new modalities as well as improvements and developments in established techniques. Some of the techniques facilitate lesion detection, such as full field digital mammography (FFDM), computer aided detection (CAD), sonoelastography (SE), others are aimed more at lesion characterisation and increasing the specificity of the examination, for example ultrasound, magnetic resonance imaging (MRI) and nuclear medicine. In addition, a number have an increasingly important role to play in directing and evaluating patient management. Despite all of these advances, it is still the case that no single imaging modality is capable of identifying and characterising all breast abnormalities and a combined modality approach will continue to be necessary.

IMAGING TECHNIQUES

Mammography

Mammography is essentially the only widely used imaging modality for breast cancer screening. It is effective in reducing breast cancer mortality rates in numerous studies. However, the success of any screening program of asymptomatic women depends on the detection of subtle and small lesions. Improvements over the last decade in the quality of performance and the reporting of mammography studies are the most important advances in breast imaging [2].

Screen-film mammography (FSM) has long been considered as a “gold standard” for breast cancer screening [3] (Fig. 1 a,b). In addition to its ability to provide adequate visualization of soft tissue abnormalities, its particular strength is the ability to depict subtle calcifications (Fig. 2 a,b).

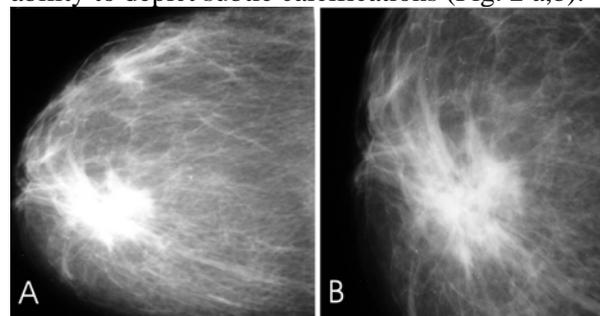


Figure 1a,b: Mammography before surgery, cranio-caudal view and magnification – left breast tumor with malignant characteristic.

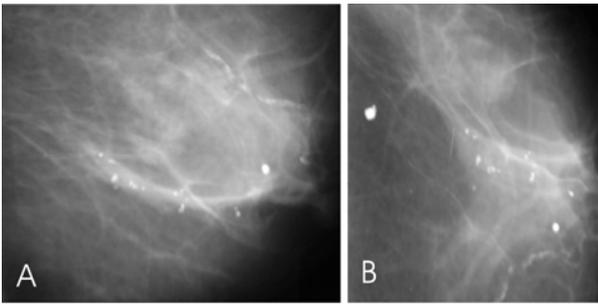


Figure 2a,b: Mammography, magnification and orthogonal view showing cicatriceal type calcifications after intervention for an invasive ductal carcinoma.

While screen-film mammography is a powerful tool for initial detection and subsequent follow-up of suspicious lesions, it has certain inherent limitations which are difficult to overcome. The most important and widely acknowledged weaknesses of screen-film mammography are associated with its limited dynamic range, contrast characteristics, susceptibility to suboptimal film processing conditions, and granularity. It also presents significant limitations in detecting very subtle lesions, especially in the presence of dense glandular tissue [4]. Standard film-screen mammography (FSM) has advantages in terms of cost and availability over the newer technology, full-field digital mammography (FFDM). Digital mammography is more expensive, at least at the onset [5].

With full-field digital mammograms (FFDM), each component of the imaging chain (image acquisition, display and storage) can be optimised. Contrast can be manipulated to increase lesion conspicuity [6]. A recent study found more consistent image quality with better contrast, fewer artefacts, fewer technically inadequate films and slightly better lesion characterisation when conventional and digital mammograms of the same breasts were compared [7]. The technologist can take images and almost instantaneously review them to assure proper positioning and technique. Once the quality of the exposures is assessed, the technologist can repeat any images deemed necessary. The processing time is reduced overall by at least 80%, which dramatically improves efficiency [8]. Postprocessing of the images can reduce the number of recalls for technical reasons or for magnification. Digital imaging is useful in performing and streamlining needle localization and stereotactic procedures. The time necessary for a patient to remain still and in compression for these procedures is greatly reduced when using digital imaging. An important advantage of digital imaging over the traditional approach involves image storage and transfer. The

digital techniques can improve visualization in dense breasts, cosmetically implanted breasts, processes involving the skin, and microcalcifications.

The National Cancer Institute evaluated nearly 50,000 women in a trial comparing these modalities [9]. The results showed that although FFDM and FSM are equivalent for the entire population, FFDM is significantly better for breast cancer detection in women younger than 50 years (regardless of breast tissue density), women with heterogeneously dense or extremely dense breasts (regardless of age), and in pre- or peri-menopausal women. No benefit was seen in women over 50 years of age, in those with fatty breasts, or in those who were postmenopausal.

Special computer algorithms have been developed to assist in the detection of suspicious findings such as speculations and calcifications. Also, soft-copy or computer displays allow for the ready incorporation of computer-aided detection (CAD) and diagnosis programs that can further improve the sensitivity of cancer detection.

CAD programs are commercially available systems that use computer software to assist the mammographer in detecting or identifying potentially suspicious abnormalities on a mammogram. The CAD program identifies potential abnormalities on the images and marks areas on the study that the computer considers to be suspicious [10]. Numerous studies have demonstrated the positive effects of CAD on breast cancer detection rates in screening mammography. CAD does not seem to significantly increase recall rates, although the algorithms allow for many false-positive prompts. CAD has the greatest potential impact on finding microcalcifications, particularly in dense breasts that might otherwise be overlooked by radiologists.

Ultrasonography

Ultrasonography is now a major mode of imaging for the clinical diagnosis of breast cancer. In the last years, it has undergone significant improvements that have extended its utility for breast imaging. Important clinical advances in breast US have been the improved benign/malignant differentiation of solid breast lesions and the use of US to guide interventional procedures such as needle aspirations, core-needle biopsies, and pre-biopsy needle localizations of breast masses or calcifications [11, 12]. Extended field of view imaging provides panoramic high-resolution images of the entire breast. Tissue harmonic imaging has the potential to improve

lesion–background contrast and proximal resolution both for breast lesions and in particular the axilla, resulting in an improvement in overall image quality despite some problems with posterior acoustic shadowing [13]. Another level of improvement to ultrasound analysis of breast masses is the development of more sensitive color Doppler and power Doppler ultrasound machines, which has the ability to detect flow in solid masses and even to differentiate that flow.

Tissue elasticity imaging technology is expected to be a new modality for breast diagnosis, based on hardness as a tissue characteristic that is affected by tissue disease such as cancer. Different approaches of elasticity imaging have been investigated, and at present some are at the stage of developing a practical system. In recent years, Krouskop et al. [14] measured the elasticity of some diseased tissue of breast and prostate in vitro and showed that the elasticity (Young's modulus) of most malignant tissues was larger than that of normal tissues. Therefore, by measuring tissue elasticity quantitatively, it can be performed tissue diagnosis based on the mechanical properties of tissues. Sonoelastography (SE) display the relative stiffness of lesions compared with the stiffness of surrounding tissue. According to the equipment type, various colors (256 hues) or gray shades are super imposed on 2D images. Stiff areas are coded in blue or dark gray tints, while softer, elastic tissues appear in red, green or bright shades of gray [15,16]. Stiffer areas deform less easily than do their surroundings and are depicted as dark on strain images, whereas softer areas deform more easily than do their surroundings and are depicted as light. Malignant masses typically appear dark and have high contrast with background breast tissue during deformation. Benign masses typically appear lighter and have lower contrast with background breast tissue during deformation [15] (Fig. 3).

Strain ratio is obtained by comparing lesion deformability with the compression response of normal surrounding tissue, and generally a ratio above 5 is considered suspicious.

To classify elastographic images, the 5-score system proposed by Ueno and co-workers [17] was considered, because it can be easily correlated to the 5-score BI-RADS classification, thus allowing a practical management of the lesions. However, a slight adjustment of Ueno scoring descriptors was undertaken according to the panel assessment of an Italian Multi-Centric Team of Study for Sonoelastography Evaluation [20].

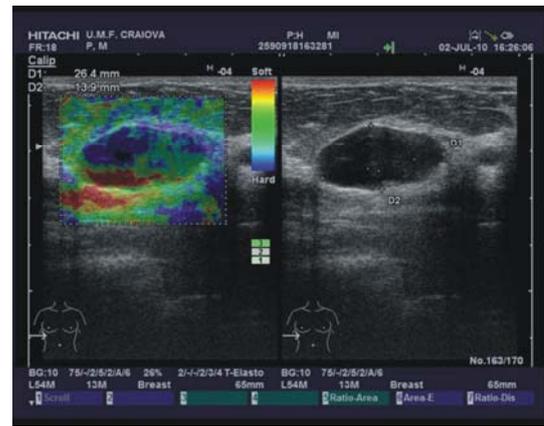


Figure 3: A typical elastographic appearance (blue, green, red) of a right breast cyst.

In addition, malignant lesions tend to be larger on US strain images than on corresponding B-mode US images, perhaps because of the desmoplastic reaction commonly associated with malignancy (17, 18, 19, 21, 22) (Fig. 4).

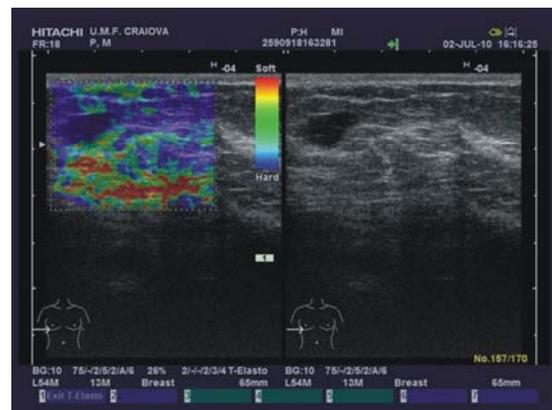


Figure 4: Ultrasound elastography of ductal invasive carcinoma in a 51 year old patient with blue elastic appearance and desmoplastic reaction - an elasticity score 5.

Some breast cancers may display benign features (score 1-3) on elasticity imaging [21] such as: non-differentiated or papillary ductal carcinoma (DCI), mucinous or medullary DCI, inflammatory carcinoma, hypercellular, necrotic or pseudo-cystic malignant tumors, post-biopsy hemorrhagic lesions or deep small neoplastic nodules [22]. Large cancers, over 2.5 cm in diameter, occasionally have benign elastic features (score 2) [23].

False positive results from elastography include lesions with firmer components causing the higher scores: sclerosing adenosis, fibrous mastopathy, hyalinized and calcified fibroadenomas (Fig. 5).



Figure 5: A lesion in the right breast predominantly blue on elastography with an elasticity score of 3 in a 56 year old patient which was diagnosed as a calcified fibroadenoma.

False negative results on elastography corresponded to ductal carcinoma in-situ and invasive non-scirrhus carcinomas; however, there is no significant difference for mean elastography scores between scirrhus and non-scirrhus invasive carcinomas [16].

In the literature the sensitivity and specificity for sonoelastography ranged between 77.6% and 86.5% values, respectively between 84.7% and 89.8%, when it was considered benign lesions with elasticity scores 1-3 and malignant lesions with elasticity scores 4-5 [24].

Magnetic Resonance Imaging

MRI has exceptional sensitivity for the detection of breast cancer and can depict cancers that are entirely occult on conventional imaging. Reported sensitivities for invasive cancers using dynamic intravenous gadolinium-based contrast agents are consistently greater than 90% [25,26]. Dynamic contrast enhanced breast MRI is clinically used to provide volumetric three-dimensional anatomical information and physiologic information that are indicative of increased vascular density and vascular permeability changes associated with angiogenesis. Three different patterns of dynamic contrast enhancement were described. The type I shows slow, progressive contrast uptake over time and is suggestive of benignity. The type II contrast pattern (plateau) shows a rapid uptake in contrast and then a plateau or leveling off of uptake, suggesting malignancy. The type III curve shows rapid uptake of contrast and then a sudden complete wash-out of contrast. The type III pattern (wash-out) is indicative of malignancy [27,28]. One of the most widely used indications for imaging is to preoperatively evaluate known

tumors for size of tumor, extent of disease, multicentricity, and multifocality (Fig. 6 a,b,c,d).



Figure 6 a,b,c,d: Magnetic resonance imaging in a 55 years old patient showing multifocal invasive lobular carcinoma.

Perfusion and diffusion imaging techniques may help differentiate between benign and malignant masses. The apparent diffusion coefficient (ADC), a marker of cellularity, is lower in invasive malignancies [29]. Malignant tumours appear to have higher relative blood volumes than normal breast tissue and benign tumours, so perfusion imaging may provide another non-invasive means of tissue characterisation.

Some advantages of MRI of the breast are that it can be used in women with denser breasts, it is non-ionising, it can determine multi-focal cancers and it is useful in determining if the cancer has spread to the chest wall. It can also be used to

check for recurrence of cancer in women who have undergone lumpectomy (Fig. 7 a,b,c,d).

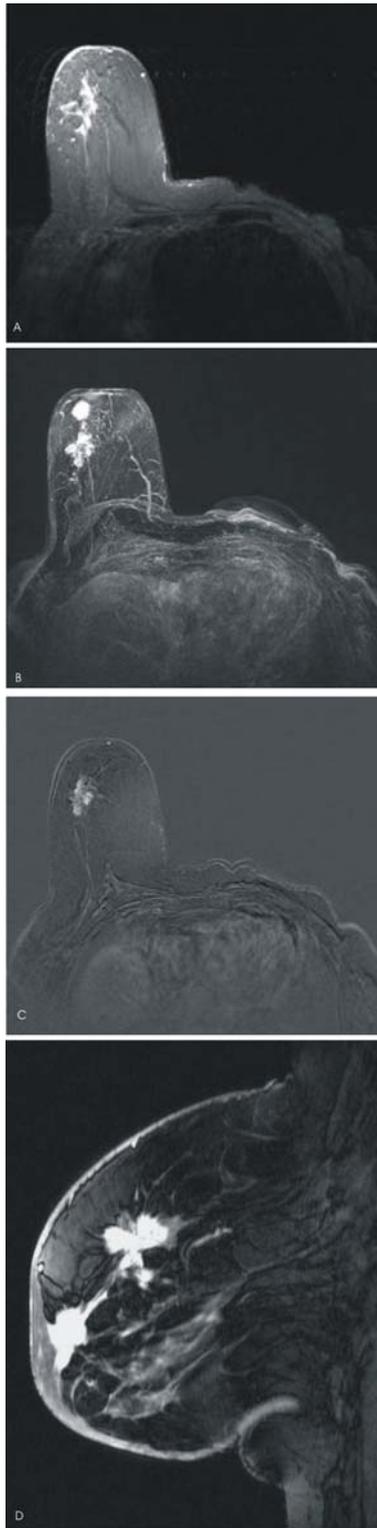


Figure 7 a,b,c,d: Magnetic resonance imaging sequences with and without contrast showing relapse in right breast after left mastectomy.

MRI can see breast implants and look for ruptures. MRI can distinguish mature scar at the site of lumpectomy from recurrence with sensitivities of 93% to 100% and specificities of

88% to 100%. Breast MRI is being used increasingly as a problem solving tool in patients at high risk for developing breast cancer such as those with BRCA mutations or for indeterminate findings on a mammogram [30].

The disadvantages are that it is expensive, requires injection of a contrast agent for functional imaging. Specificity can be limited; it is highly sensitive to small abnormalities, cannot image calcifications, can induce claustrophobia and requires long scan times in comparison to x-ray mammography [31].

Another promising technique in breast cancer diagnose is proton magnetic resonance spectroscopy (MRS). This technique allows for quantitative characterization of total or composite choline concentration that has been shown to be elevated in malignant tumors compared to normal breast tissue [32]. MRS is a nonvasive technique that does not require contrast injection and demonstrates improved sensitivity and specificity when used as an adjunct to breast MRI [33,34]. MRS is being actively investigated and show promise for early determination of the effectiveness of neoadjuvant chemotherapy for locally advanced breast cancer [35]. Several studies on MR spectroscopic imaging showed improved specificity for this new imaging modality [36].

Positron-Emission Tomography or Positron-Emission Mammography

Positron emission tomography (PET) is one of the newest imaging techniques. A radioactive substance is injected into an arm vein and goes to places in the body where the cells are most active, especially in the cancerous tissue. This substance gives off small amount of radiation that is detected by a special PET scanner to form an image. A PET scan may be combined with computed tomography (CT) to provide both an anatomical and functional view of the suspect cells. Breast density, previous surgery or radiotherapy do not affect the results of PET and unlike MRI, benign breast disease will be negative on PET.

Many groups have studied the role of PET in the evaluation of suspicious breast lesions, with sensitivity values ranging between 80 and 90%, and specificity values between 71 and 95% [37]. In a series of 117 patients with primary breast cancer, Schirrmeister and colleagues showed that PET was twice as sensitive as the combination of mammography and ultrasound in detecting multifocal tumor involvement of the breasts and could upstage the disease in some cases [38]. PET is limited by a lower sensitivity in detecting some breast tumors because of their small size,

metabolic activity, histological subtype, microscopic tumor growth pattern and proliferation [39].

PET may be useful in identifying involved axillary nodes and distant metastases knowing that axillary nodal status is an important prognostic indicator in breast cancer patients [40]

PET has shown to be more accurate than clinical examination and allows evaluation of more distant nodal groups [41]. PET provides additional information regarding unsuspected distant metastases, and it is more sensitive in the detection of bone metastases than technetium bone scans, particularly when they are osteolytic. It is more accurate than conventional imaging when clinical suspicion of recurrence is high and is able to assess tumour response to primary hormonal and chemotherapy early on after commencement of treatment [42,43].

Although PET can be a useful adjunct to mammography in characterizing breast tumors, this technique is limited by a low sensitivity to detect small tumors and lobular carcinomas [39]. The lack of evidence to demonstrate clear advantages over other complementary techniques and the high cost of PET imaging has limited the use of this tool in the routine diagnosis of primary breast cancer.

Conclusions

The past two decades have seen major improvements in our ability to diagnose patients with breast cancer. These advances have been achieved largely through the use of screening mammography to detect lesions at earlier points in their evolution. Recent studies show that breast ultrasound and breast magnetic resonance imaging (MRI) are frequently used adjuncts to mammography and these techniques enhance the radiologist's ability to detect cancer and assess disease extent, which is crucial in treatment planning and staging. Positron emission tomography (PET) also plays an important role in staging breast cancer and monitoring treatment response.

As imaging techniques improve, the role of imaging will continue to evolve with the goal remaining a decrease in breast cancer morbidity and mortality.

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Correspondence Adress: Ioana Gheonea, MD, MSc ; Department of Radiology and Imaging, University of Medicine and Pharmacy Craiova; Petru Rares Street, No 2, Craiova – 200349, România; E-mail: iagheonea@gmail.com