Imaging in Breast Cancer

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9.1 Introduction

Breast cancer is the most common cancer in female population worldwide and consensus shows increasing trend in future which is concerning [1]. Diagnosis of breast cancer encompasses clinical palpation, imaging evaluation and histopathological confirmation. Imaging plays significant role in work up of breast cancer patients. It envisages diagnostic evaluation of patient, image guided biopsy of the lesions, surveillance follow up after treatment and tumor localization at the time of biopsy or surgery. The basic imaging modalities include Mammography, ultrasound (USG) and Magnetic Resonance Imaging (MRI). Mammography is the one of the important diagnostic tools which is proven to reduce mortality due to breast cancer by early detection with sensitivity ranging from 83 to 95% [2]. However, its sensitivity and accuracy decreases to 30–48% in dense breasts [3]. Ultrasound and MRI are the modalities used to evaluate such breasts with dense glandular parenchyma and also as screening modalities in younger patients. Many studies have shown increased cancer detection rate with USG as the screening modality especially in younger patients with dense breasts and also when it is used in adjunct to mammography [4, 5]. In a Japanese randomized trial, addition of ultrasound had better sensitivity of cancer detection, that is, 91.1% as compared to 77% with mammography alone; however with reduced specificity (87.7% vs 91.4%) [6]. MRI is superior in detection of additional occult cancer foci and larger index cancers (18% vs 7.2%) as compared to mammogram [7, 8]. However, MRI is expensive technique, needs

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contrast injection and is time consuming. Since each modality has its own advantages and disadvantages; there has to comprehensive evaluation using multiple modalities with case base approach.

The last few decades have witnessed immense progress and development in the field of breast imaging which includes evolution of full field digital mammography from screen-film mammograms, advent of computer aided detection, digital breast tomosynthesis and contrast enhanced mammography; addition of elastography to B-mode USG and Diffusion weighted & dynamic contrast enhanced sequences using dedicated breast coils in MRI.

9.2 Imaging Techniques

9.2.1 Mammography

Mammography is considered as the optimal imaging modality in screening for breast cancer. However, its role is limited in cases of dense and glandular breasts [3, 9, 10]. An effective mammogram requires high quality images with optimal contrast resolution at low radiation dose. Hence, the mammography equipment and techniques are different from standard radiographs of other anatomical parts. Conventional screen-film mammogram (SFM) was considered as the standard for breast imaging during screening, diagnosing and follow up. However, it had limitations like inability to perform any post processing, variations while developing the films in dark room and limited dynamic range [11]. Full-field digital mammography (FFDM), though expensive than SFM, has overcome these limitations and has largely replaced the latter. It does not require any dark room film development and images can be viewed directly on the high-resolution consoles which improves efficiency and accuracy also as it enables post processing of the images.

The basic evaluation is performed by obtaining standard two views of breast-craniocaudal (CC) and a mediolateral-oblique (MLO) view. The former view is obtained with vertical X-ray beam while the latter is taken with a 45° tube angulation with horizontal. The breast is pulled and compressed with compression paddle so as to include maximum possible parenchyma in the view. Table 9.1 describes the

Table 9.1 Criteria for well-positioned mediolateral oblique and craniocaudal views

For MLO view
• Nipple should be seen in profile
• Pectoralis muscle should extend inferior to the posterior nipple line, which is an imaginary line drawn from the nipple to pectoralis muscle or film edge and perpendicular to the pectoralis muscle
• An open inframammary fold should be visible
• There should be no skin folds superimposed on the breast
For CC view
• Nipple should be in profile
• The posterior nipple line is drawn from the nipple to the pectorlalis muscle or film edge and the length of this line should be within 1cms of the line on MLO projection

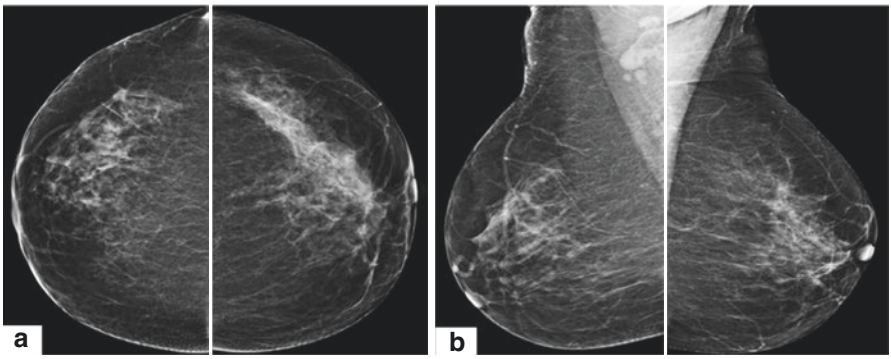

Fig. 9.1 Interpretation of mammogram: The mammograms should be read in optimally lighted room with Craniocaudal (**a**) and Mediolateral oblique (**b**) views of both breasts placed side to side for comparability of tissues

criteria defining well positioned MLO and CC views. Supplementary views are taken in special cases as problem solving tools.

Interpretation of mammogram is done with MLO and CC views of both breasts placed side by side so that symmetry of the breast tissue can be studied. For example, right and left MLO projections should be viewed together and similarly CC projections should be viewed together (Fig. 9.1). The mammograms should be systemically approached with description of the breast density followed by the normal or abnormal findings and then, secondary changes in skin, subcutaneous tissue and nipple-areola complex followed by axillary nodal status.

The abnormal findings on mammogram are categorized into mass, calcification, architectural distortion or asymmetry. A breast mass is defined as three-dimensional space occupying lesion seen on both views which is assessed for its size, shape, margin and density. Benign lesion like intramammary lymph node is seen as round to oval, circumscribed, iso to hyperdense lesion with fatty hilum or lucent center-and is categorized as BI-RADS category 2 while classic malignant mass (BI-RADS 4c or 5) will be denser, irregular, spiculated with or without pleomorphic calcification, architectural distortion, skin and nipple retraction (Fig. 9.2).

Calcifications are evaluated for number, distribution and morphology. Benign calcifications typically are coarse, larger than 0.5 mm and/or have lucent center. These include involuted or involuting fibroadenomas, dermal, dystrophic and vascular calcifications. Calcifications with high probability of malignancy, on the other hand, are irregular, smaller than 0.5 mm and are pleomorphic-variable in size, shape and density.

Architectural distortion refers to focal trabecular distortion and focal speculation & retraction of the parenchyma whereas asymmetry is a soft tissue finding identified on one view with no matching tissue at similar location in contralateral breast parenchyma.

At the end, depending on the descriptors, BI-RADS (Breast Imaging Reporting and Data System) category should be assigned [12] (Table 9.2).

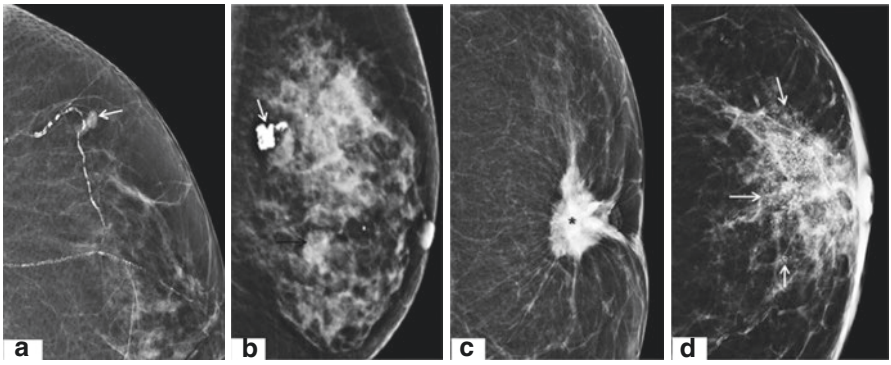

Fig. 9.2 Imaging features on mammograms: Benign lesions are seen as oval to round (arrows in **a** & **b**), circumscribed, low to equal density (white arrow in a, black arrow in **b**) lesions with lucent center (**a**) or with coarse popcorn calcification (white arrow in **b**) within. (**c**) Spiculated high density mass with overlying skin thickening and retraction of nipple is categorized as highly suspicious for malignancy. Tram track vascular calcification (**a**) and popcorn calcification (white arrow in **b**) are classic benign calcifications whereas (**d**) scattered pleomorphic calcifications with architectural distortion, skin thickening suggest underlying malignancy

Table 9.2 ACR BI-RADS mammographic assessment categories

Category	Description	Likelihood of malignancy	Next step in evaluation
0	Incomplete; need additional imaging evaluation or comparison with previous imaging	Unknown	Additional mammographic views; evaluation with USG or MRI; comparison with previous imaging
1	Negative	Essentially 0% likelihood of malignancy	Routine screening
2	Benign finding	Essentially 0% likelihood of malignancy	Routine screening
3	Probably benign finding	>0% but ≤2%	Short interval (6 month) follow up
4	Suspicious abnormality 4a: Low suspicion for malignancy 4b: Moderate suspicion for malignancy 4c: High suspicion for malignancy	>2% but ≤95% >2% but ≤10% >10% but ≤50% >50% but <95%	Biopsy
5	Highly suggestive of malignancy	≥ 95%	Biopsy
6	Known malignancy	N/a	Definitive treatment

9.2.1.1 Computer Aided Detection

Computer-aided detection (CAD) is a software system that is designed to highlight areas of concern like masses and calcification and thus serve as a second reader. It thus reduces the chances of overlooking these abnormalities because the radiologist then evaluates the sites more carefully. It has been shown that it increases the cancer detection rate but is associated with high false positive rates [13, 14].

9.2.1.2 Digital Breast Tomosynthesis and Synthesized View

Dense glandular parenchyma is a known limitation of mammography. It may hide the mass or may simulate a mass on mammogram giving both false negative or false positive information respectively. The technique of Digital breast tomosynthesis (DBT) has gained wide acceptance as it provides consecutive sectional images, of breast which helps to distinguish between the normal glandular breast tissue from a true lesion. (Fig. 9.3) Hence, DBT has become an integral part of FFDM for interpreting mammograms [15–20]. However, addition of DBT to FFDM increases radiation to breast. With this view, recently, there have been further advent of obtaining a 2D image or synthesized view from these tomo images which has been claimed to be as good as the standard FFDM image [21–25]. Multiple studies are going on in this respect as this will have major implications in term of reduction of radiation dose.

9.2.1.3 Contrast Enhanced Mammography

Combining high resolution mammography with functional information obtained with contrast enhancement will offer another potential application for mammography especially to study and assess neovascularity in the breast masses or malignancies.

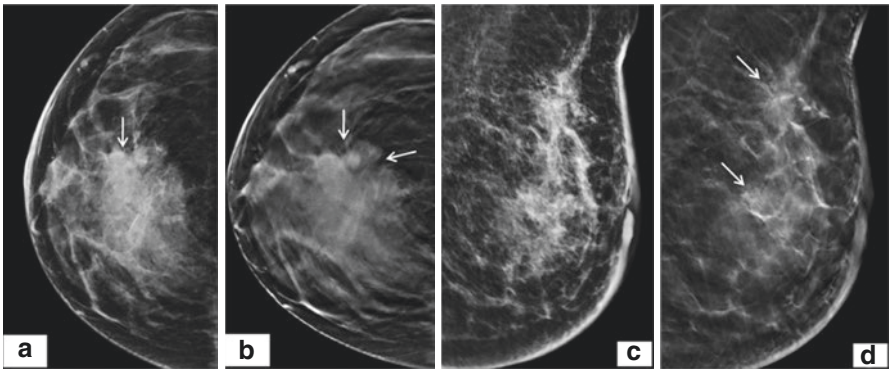

Fig. 9.3 Digital Breast tomosynthesis: (**a**) Craniocaudal view of right breast show presence of an irregular mass of equal density (arrow) with indistinct margins; (**b**) Tomosythesis slice of same could highlight spiculated margins of the mass (arrows). (**c**) MLO view of left breast in a different patient shows diffuse architectural distortion with skin and trabecular thickening; however, tomosynthesis (**d**) revealed two equal density masses in upper and central quadrant with spiculated margins (arrows) suggesting multifocal/ multicentric disease

Many authors have highlighted its potential role as an adjunct modality with high cancer detection rate as compared to conventional mammography, tomosynthesis and ultrasound [26] with comparable accuracy when compared to MRI [27].

9.2.2 Ultrasound

Ultrasound (USG) is the most commonly used modality in assessment of breast diseases- either as an adjunct or independently. It is cost effective, readily available, less time consuming (when compared to MRI) and has no risk of radiation exposure to patient or operator. Breast USG is performed using high frequency (5–15 MHz) linear array transducer with patient lying supine in radial and anti-radial planes followed by axillary evaluation.

The abnormality is detected and morphology is carefully assessed. The mass is evaluated in terms of its size, location, shape, orientation, margins, echogenicity and posterior acoustic features. Oil cysts and simple cysts are categorized into BI-RADS 2-seen as circumscribed hypo to anechoic lesions with posterior acoustic enhancement. A hypoechoic mass which is round to oval, wider than taller, circumscribed with no echogenic halo or posterior acoustic shadowing- is classified under probably benign BI-RADS category. Most commonly fibroadenomas, cluster of microcysts and complicated cysts fall into this category. Stability over one to two years reassigns the lesion into category 2; however during follow up, any change in the lesion upgrades the BI-RADS to 4 and mandates biopsy. On the other hand, malignant mass of category 4c or 5 will be seen as a hypoechoic mass with antiparallel orientation, irregular shape, not circumscribed margins (angular, microlobulated or spiculated) showing posterior acoustic shadowing and thick echogenic halo (Fig. 9.4).

Role of USG is not only limited to differentiate solid and cystic lesions but also to characterize solid lesions. It is the imaging modality of choice in young females, below 30 years of age, who have predominantly glandular parenchyma which limits evaluation with mammography. USG assessment also enables evaluation of patient for image guided biopsy in same setting.

9.2.2.1 Elastography

Ultrasound elastography evaluates tissue stiffness based on explanation that the malignancies tend to be harder due to schirrhous nature while the normal breast and benign lesions tend to be softer [28]. The technique has evolved from assessing the tissue elasticity by applying manual pressure which faced significant interobserver variability to shear wave elastography (SWE) where an acoustic radiation force impulse (ARFI) is induced in the tissues and the wave propagation is captured by the USG probe [29, 30]. It provides qualitative as well as quantitative elasticity parameters of the abnormality with respect to normal breast tissue and these can be compared. (Fig. 9.5) Studies have shown that malignant lesions have significantly higher elasticity values than the benign lesions [31–33]. Hence, SWE is considered as an adjunct technique in evaluation of breast masses especially in BI-RADS 3 & 4 category masses.

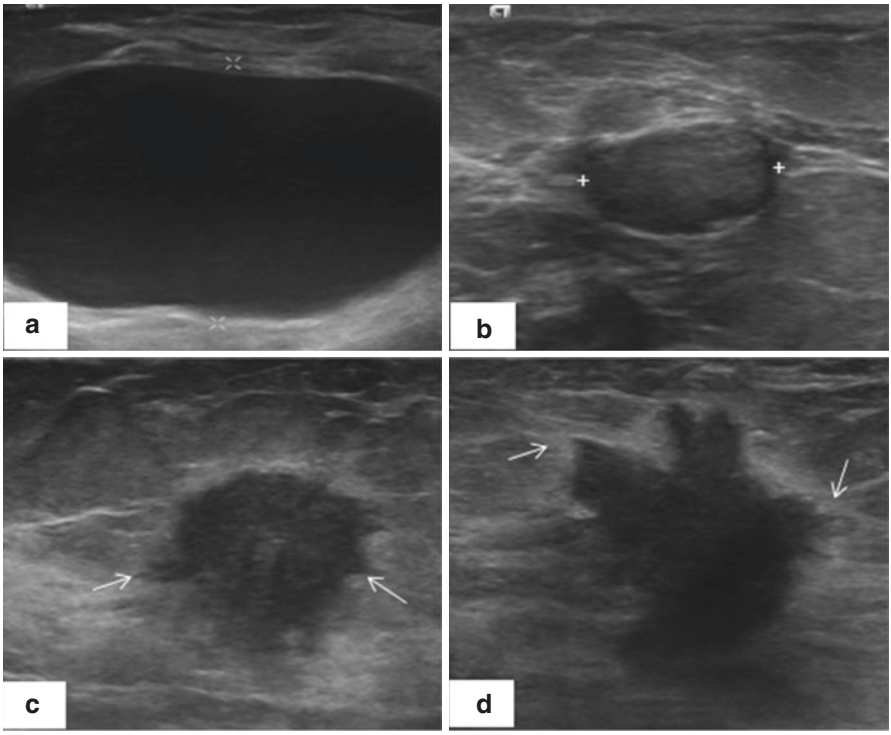

Fig. 9.4 Imaging features on ultrasound: Benign BI-RADS 2 lesions seen as simple anechoic cyst (**a**) and (**b**) circumscribed, oval, wider than taller lesion, stable over 2 years (sequential imaging not shown) with posterior enhancement. (**c**, **d**) Hypoechoic lesions which are taller than wider, have angular or spiculated margins (arrows in **c**), thick echogenic rim (arrows in **d**) and posterior shadowing are highly suspicious for malignancy and are assigned BI-RADS 4c/5

9.2.2.2 Contrast Enhanced Ultrasound

During last few years, contrast enhanced ultrasound (CEUS) has gained popularity especially in liver diseases to characterize various hepatic lesions [34]. Its role has also been evaluated in demonstrating the patterns of vascularity in benign and malignant breast lesions. Several studies have proven the potential of CEUS in differentiating malignant from benign lesions in breast with varying sensitivity (67–95%) and specifity (58–62%) but its role needs to be validated further for clinical application and utility [35].

9.2.3 MRI

MRI has sensitivity of more than 90% in detection of breast carcinomas [36]. Owing to its better soft tissue resolution and demonstration of enhancement kinetics post contrast administration, it offers promising role in evaluation of patients with breast implants and post lumpectomy recurrences. Contrast enhanced MRI is based on

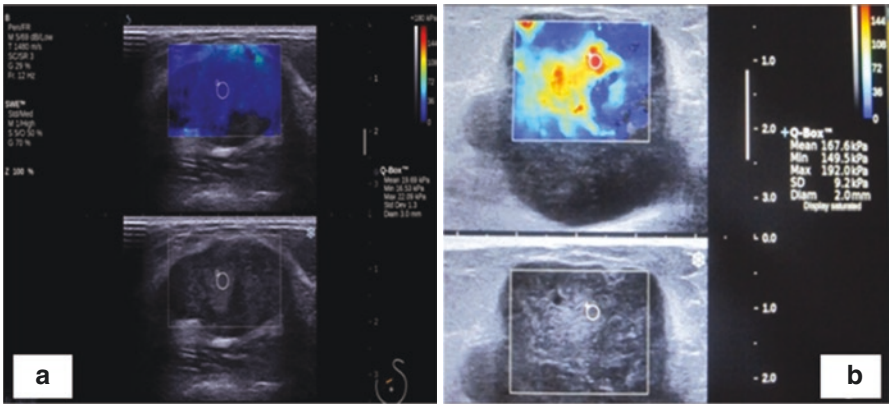

Fig. 9.5 Ultrasound Elastography: (**a**) B-mode ultrasound showing round hypoechoic lesion with circumscribed lobulated margins. The lesion shows low elasticity values (homogeneous blue color with Emean 21.6 kPa) on shear wave elastography suggesting benignity; in contrast to (**b**) high elasticity values (heterogeneous color coding with red color on qualitative assessment and quantitative value of Emean 167.6 kPa) in another mass raising index of suspicion for malignancy

depiction of neoangiogenesis within the malignant lesions: these new vessels have increase capillary permeability causing leakage of contrast which is seen as enhancement on the post contrast sequences. (Fig. 9.6).

Breast MRI is performed using dedicated breast coils at 1.5T or higher strength MR field. Patient lies down prone with breasts placed in the cups provided within the coil. Adequate cushioning is applied to avoid motion artifact as the examination might take more than 30 min. Precontrast T1, T2 and diffusion weighted sequences are obtained in axial planes followed by dynamic contrast enhanced fat suppressed T1 weighted sequences which are acquired sequentially at every 1 min for 5–7 min.

Like mammography, bilateral breasts are studied together while interpretation for proper comparison, in MRI. Description includes background enhancement of glandular tissue, morphological features and enhancement pattern of any mass or focus and characteristics of nonmass like enhancement (NME), if any. Like mammogram, on MRI, mass is seen on all the pre and post contrast sequences. It has to be evaluated morphologically (shape, margin and enhancement) and functionally in terms of kinetics of contrast enhancement. Benign cysts are seen as well-defined lesions with hyper intense signal on T2 WI with no abnormal enhancement. Rim enhancement can be seen in complicated cysts. Fibroadenomas may show homogeneous or heterogeneous enhancement with well-defined margins. Spiculated margins are frequently seen in malignancies and radial scars. Ductal carcinomas show varied imaging features- may show rim or central enhancing areas or present as NME lesions.

MRI is radiation free and is highly sensitive in detecting recurrences post radiation therapy and post-surgery. It is performed to detect implant rupture and pick up lesions in breast parenchyma in these patients. MRI has served as useful tool in

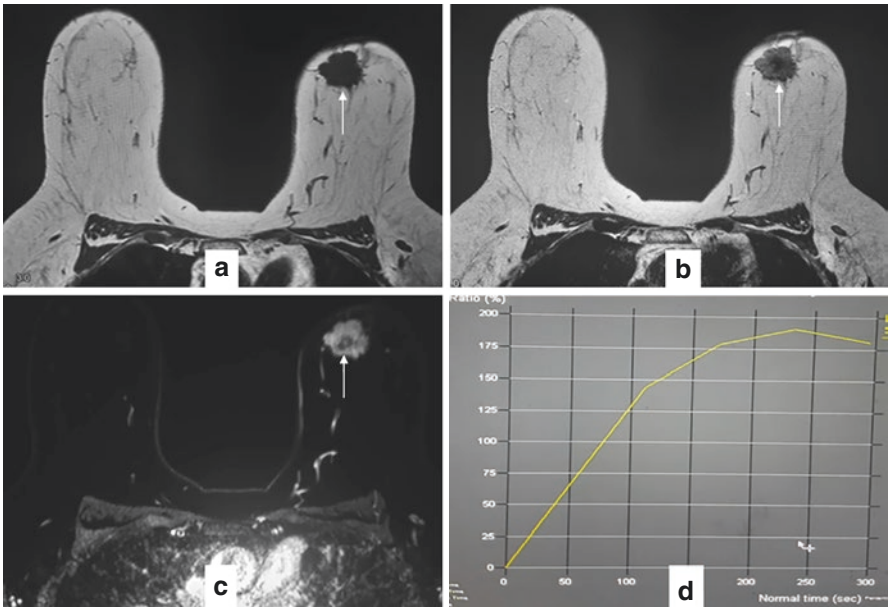

Fig. 9.6 Imaging features of carcinoma on MRI: Spiculated hypointense mass on T1 and T2 weighted images (arrows in **a**, **b**) showing intense enhancement (arrow in **c**) and type III kinetic curve (**d**) raise high suspicion for malignancy

screening high risk patients and patients with dense breasts. However, it is limited by its low specificity as it relies on tissue enhancement which can be seen in many other non-malignant lesions like lymph nodes, papilloma, radial scars resulting in false positive examinations leading to unnecessary biopsies. In addition, MR is costly, time consuming and is unable to image calcifications. Hence, it is used in selected situations (Table 9.3).

9.2.4 Positron Emission Tomography

^{18}FDG PET has emerged as another imaging modality in evaluation of breast cancer patients especially in locally advanced breast cancers. PET incorporated with CT at the same setting has increased sensitivity in detecting distant unsuspected metastases. Garg et al. showed that when compared to conventional imaging for tumor staging, PET/CT upgraded the staging and influenced management in approx. 18% of patients [37]. They emphasized the role of PET/CT in evaluation in patients with locally advanced breast cancer as it helps in accurate staging, appropriate decision making and prognosticating the patients [37]. The modality has been studied and found suitable for staging, monitoring response after neoadjuvant chemotherapy and for loco-regional recurrence [38, 39].

Table 9.3 Indications for dynamic contrast enhanced MRI

Screening • Women at high risk of breast cancer (e.g., BRCA mutation) • Post breast implants
Diagnosis • Indeterminate palpable finding with negative mammogram and ultrasound • Suspicious lesion on mammography which could not be seen on USG • Bloody nipple discharge • Occult primary in metastatic axillary lymph nodes
Staging • Preoperative evaluation before conservative surgery • To detect multifocal or multicentric cancer • To detect recurrence/ residual disease post lumpectomy • To evaluate chest wall invasion • In patients with limited mammographic evaluation like dense breasts, DCIS without microcalcification, invasive lobular cancer
Post treatment study • Early response assessment to neoadjuvant chemotherapy • Residual disease after completion of chemotherapy • To differentiate recurrence from post operative scar

9.3 Image Guided Interventions

Breast interventions majorly encompasses biopsy from suspicious site under USG, stereotactic or MRI guidance as it enables accurate tissue sampling and reduces need of multiple repeat biopsies as compared to blind biopsies. Increase in incidence of breast cancer and its association with genetic mutation predisposing younger age group to higher risk of cancer mandates stringent follow up by screening and surveillance programs. This has led to early pick up of non-palpable suspicious lesions which need guided biopsy or excision after hook wire localization. Institution of neo-adjuvant chemotherapy (NACT) in the treatment regime of breast cancer has improvised the surgical outcome as it reduces the overall tumor burden making breast conservative surgery possible (BCS) [40]. However, many times there is complete clinical and radiological response to NACT and surgery is warranted to establish pathological complete response. In such settings, tumor marker placed pre-chemotherapy serves as the target for site for surgical removal. Thus, these localization techniques have therapeutic as well as diagnostic applications. Various image guided breast interventions have been discussed in detail in the dedicated intervention chapter.

9.4 Future Vision

Mammography has witnessed drastic changes and reformation in last few decades. Screen-film mammograms have largely been replaced by Full Field Digital Mammograms with or without tomosynthesis. Moreover, synthesized two-dimensional view (2D view) from tomosynthesis is being evaluated to replace

standard 2D views in population based screening programmes since it reduces the radiation dose to breasts. Contrast enhanced mammography is in early stage at present and its role though looks promising but still needs validation for incorporation in routine clinical practice. Similarly, USG has its established role in breast evaluation with incorporation of elastography for assessment of BI-RADS 3 and 4 lesions. Contrast enhanced ultrasound can be used in assessment of breast lesions but has not been a part of any guidelines so far. Both elastography and CEUS are being studied for their potential role in predicting responders and non-responders amongst patients on NACT. MRI, on other hand, has been the problem-solving tool in majority of situations owing to its cost and availability. Abbreviated MRI for intermediate risk population consists of shorter MRI breast protocol reducing the image acquisition and interpretation time, has shown comparative results and may become the standard screening modality for such patients in future [41].

To conclude, full field digital 2D mammography remains the standard screening and diagnostic modality for breast diseases with CAD, tomosynthesis and ultrasound as supplement modalities. In young patients, USG and MRI are preferred imaging tools than mammography as the latter has lower sensitivity in this population. MRI is used for screening of high risk patients like BRCA mutation positive patients. Not only in diagnostic setting but also in the setting of interventions, all imaging modalities have become an indispensable part of patient management.

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