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A Radiologist's Perspective in Breast Cancer

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Abstract: Breast cancer is the most common malignancy in females with a steadily increasing incidence and the second leading cause of cancer death. One out of seven women either has or will develop breast cancer in her lifetimes. A gamut of investigations is available for its detection. The advantage and disadvantage of each of them is discussed below. Screening mammography is very useful in the early detection of non-palpable breast masses. It is recommended every 1 to 2 years in women of 40-49 years and every year in 50 years age group. Diagnostic mammography is done in clinically palpable lesions. BIRADS system of reporting provides a useful framework for categorizing the recommendation for management of a breast mass. Sonography is used not as a screening modality but primarily to differentiate between solid and cystic masses and to provide ultrasound guided biopsies and aspiration. Other methods of biopsy include fenestrated grid (X-ray Mammography) guided and Stereotactic guided biopsy. Ductogram is procedure of choice for evaluating the cause of nipple discharge. Role of MRI in the present scenario is restricted to specific conditions where a mammography is less sensitive (as in dense breast) with the high risk of malignancy.

Keywords: *Breast carcinoma, mammography, ultrasound.*

Introduction

Hope for altering the course of breast cancer and improving the mortality rates and five-year survival rates entirely depends on its early detection. Detection and evaluation of breast masses can be one of the most challenging and rewarding areas of Radiology. The following article attempts to give a Radiologist's perspective of imaging of the breast for cancer, with primary emphasis on Mammography and ultrasound.

Initial Imaging protocol for a patient presenting with a clinically palpable mass should vary with patient's age and family history of breast cancer, as shown in Table 1.[1]

Table 1 : Imaging Protocol vis-a-vis patients age

Patients age (years)	Imaging protocol
Younger than 20	Sonography only
20-30 years	Sonography first. Mammography (usually unilateral single view) if U/S does not show a simple cyst.
30-35years	If no close family history of breast cancer, same as for age 20-30.If mother or sister with breast cancer, same as for age 35 and older.
35 and older	Bilateral two view per breast mammogram first. Sonography if mammography negative or nonspecific.

Mammography is the preferred examination for breast especially in females more than 40years.It detects 75% of cancer at least a year before they can be felt. It has a false negativity rate of 8-10%. Also 1-3% of women with a clinically suspicious abnormality are known to have a normal mammography as well as sonography[2].

There are two types of mammography - screening and diagnostic mammography. Screening mammography is done in asymptomatic patients. It is recommended every 1-2 year in women of 40-49 years age group and once every year after 50 years age group. It can be done in <40years age group in case of very strong family history of breast cancer. [2] Diagnostic mammography is performed in symptomatic patients, for e.g.: palpable breast lump or nipple discharge. Several additional views are done when required in diagnostic mammography.

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For screening mammography each breast is imaged separately in both cranio-caudal (CC) and medio-lateral oblique (MLO) views. Supplemental views include lateromedial (LM), Mediolateral (ML), exaggerated CC views, Magnification views, spot compression views and others. Special skin markers can be used.

Breast compression is necessary to flatten the breast so that:

a. Maximum amount of tissue can be imaged and examined.
b. It allows lower dose of radiation.
c. Immobilization of breast allows reduction of motion blur .
d. Reduces X-ray scatter and improves quality.

Breast Imaging Reporting & Data System (BIRADS)

The American College of Radiology (ACR) has developed a Breast Imaging Reporting and Data System (BI-RADS), intended to standardize terminologies used in the mammography report as well as to outline the organization of the report[3]. It contains a lexicon of standard terminology and a coding system with a specific course of action.

It consists of an overall description of breast parenchymal pattern as : (1) extremely dense; (2) heterogeneously dense; (3) scattered fibroglandular density; (4) entire fat.

Lexicon/Terminology

A. Mass : This term is a space occupying lesion seen in two different projections.

B. Density: This term is used if a potential mass is seen in only one single projection.

   a) Circumscribed (well-defined or sharply-defined) margins: The margins are sharply demarcated with an abrupt transition between the lesion and the surrounding tissue.

   b) Indistinct (ill defined) margins: The poor definition of the margins may be due to infiltration by the lesion and this is not likely due to superimposed normal breast tissue.

   c) Spiculated Margins: The lesion is characterized by lines radiating from the margins of a mass.

C. Architectural Distortion: The normal architecture is distorted with no definite mass visible. This includes spiculations radiating from a point, and focal retraction or distortion of the edge of the parenchyma. Architectural distortion can also be an associated finding.

D. Asymmetric Density: It is visible as asymmetry of tissue density with similar shape on two views, but completely lacking borders and the conspicuity of a true mass. It could represent an island of normal breast, but its lack of specific benign characteristics may warrant further evaluation. Additional imaging may reveal a true mass or significant architectural distortion.

E. Calcification:

Amorphous or Indistinct Calcifications: These are often round or "flake" shaped calcifications that are sufficiently small or hazy in appearance that a more specific morphologic classification cannot be determined.

Pleomorphic or Heterogeneous Calcifications: These are usually more conspicuous than the amorphic forms and are neither typically benign nor typically malignant irregular calcifications with varying sizes and shapes that are usually less than 0.5 mm in diameter.

Fine, Linear or Fine, Linear, Branching (Casting) Calcifications: These are thin, irregular calcifications that appear linear, but are discontinuous and under 0.5 mm in width. Their appearance suggests filling of the lumen of a duct involved irregularly by breast cancer.

Benign Calcifications: Benign calcifications are usually larger than calcifications associated with malignancy. They are usually coarser, often round with smooth margins and are much more easily seen.

Table 2 : Assessment Categories in Breast Cancer

Assessment Categories	
Category 0 / Need Additional Imaging Evaluation	Finding for which additional imaging evaluation is needed. Almost always used in a screening situation and should rarely be used after a full imaging work up.
Category 1 / Negative	The breasts are symmetrical and no masses, architectural disturbances or suspicious calcifications are present
Category 2 / Benign Finding.	This is also a negative mammogram with no mammographic evidence of malignancy Involuting, calcified fibro- adenomas, multiple secretory calcifications, fat containing lesions such as oil cysts, lipomas, galactoceles, and mixed density hamartomas all have characteristic appearances, and may be labeled with confidence.
Category 3 / Probably Benign Finding - Short Interval Follow-Up Suggested.	Findings having very high probability of being benign. It is not expected to change over the follow-up interval, but the radiologist would prefer to establish its stability.
Category 4 / Suspicious Abnormality - Biopsy Should Be Considered	These are lesions that do not have the characteristic morphologies of breast cancer but have a definite probability of being malignant. The radiologist has sufficient concern to urge a biopsy.
Category 5 / Highly Suggestive of Malignancy - Appropriate Action Should Be Taken	These lesions have a high probability of being cancerous. Referring clinician should be alerted immediately.

Table 3 : Management of Breast mass based on BIRADS classfication

Category	Description	Risk of Malignancy	Care Plan and Comments
1.	Negative	5 in 10,000	Continue annual screening mammography for women 40 years or older.
2.	Benign finding, non-cancerous	5 in 10,000	Same as above. This category is for cases with a characteristically benign finding (e.g., cyst, fibroadenoma).
3.	Probably benign finding	<2%	Usually, 6-month follow-up mammography is performed. Most category 3 abnormalities are not evaluated with biopsy.
4.	Suspicious abnormality	25-50%	Most category 4 abnormalities are benign but may require biopsy.
5.	Highly suggestive of malignancy	75-99%.	Classic signs of cancer are seen on the mammogram. All category 5 abnormalities are typically evaluated with biopsy; if the results are benign, repeat biopsy is done to ensure correct sampling.

Interpretation of abnormal mammogram :

Mass lesion: Whenever one comes across a mass lesion, one has to describe them under the following headings-

A. Shape of the lesion :

1. Round-commonly seen in benign masses exceptionally sarcoma, lymphoma and mucinous carcinoma)
2. Oval-typically fibro-adenomas fall under this category
3. Lobular mass with undulations is seen in both benign and malignant condition.
4. Irregular shape - by and large seen in malignant cases.

However benign conditions like inflammatory masses can also have irregular shape. Hence, U/S correlation is required.

B. Margins:

It constitutes an important criteria in evaluation of any mammographic lesion. They can be sub-classified under the following headings:

1. Circumscribed: largely seen in benign masses. However, medullary/mucinous malignancies can also appear circumscribed.
2. Lobulated margin: seen in both benign and malignant lesions.
3. Obscure: due to overlying fibro-glandular tissue.
4. Ill defined/poorly marginated: both benign and malignant lesion.
5. Spiculated margin: largely seen in malignant condition. (>95% probability) with the exception of radial scar/changes due to previous surgery.
6. Irregular margin or micro lobulate margins are also strong suspect of malignancy.

C. Density:

Malignant lesions especially schirrous cancers have greater density than normal breast tissue. Fatty lesions such as oil cyst, lipomas, galactocoele, and hamartomas have very low density.

D. Calcification:

As described under BIRADS.

Associated findings like skin/trabacular thickening, nipple retraction, architectural distortion, asymmetric density, axillary adenopathy should be noted.

Malignant lesion: Mammographic criteria for a malignant lesion are broadly considered under the following heads.

- Direct signs
  Mass lesion
  Microcalcification
- Indirect signs
  Asymmetric density
  Architectural distortion
  Breast edema

Direct signs - Malignant mass lesions typically appear as central dense lesions with spiculated border. The most diagnostic appearance of an invasive breast cancer either ductal or lobular is an irregularly shaped mass with spiculated margins and high density with or without calcification. The spiculation results from

a desmoplastic response as the tumor extends into the surrounding tissue .Other causes for spiculation include radial scar, fat necrosis, and previous surgery. In malignant lesion, density is more than the adjacent glandular tissue as compared to benign masses. In the absence of previous surgery, a lesion with dense center with spiculated margin is virtually diagnostic of breast cancer. As compared to ductal carcinoma, invasive lobular carcinoma has a tendency to diffusely infiltrate the breast tissue and may masquerade as an asymmetric density and be visible only in one view[4].

Micro-calcification: It is another direct sign of presence of malignancy. It may or may not be associated with mass lesion. It is found in clusters and is pleomorphic /granular type having different shape, size, density, with > 5 calcific foci in 1 cm diameter and must always be investigated further with FNAC/ excision biopsy. The indeterminate calcification also labeled as indistinct or amorphous type are also associated with malignancy. Fine branching /casting type are highly suspicious of malignancy and usually seen in ductal carcinoma in situ.

Indirect signs of malignancy:

Asymmetric density-Many times, we do not find the presence of direct signs i.e. spiculated mass or micro-calcification but we may only pickup early malignancy as focal asymmetrical density or architectural distortion-especially lobular invasive variety. Summation artifact is also seen as asymmetrical density but is seen only in one view. Hormone replacement therapy HRT is another cause leading to asymmetric density

Architectural distortion: It is commonly seen in infiltrating duct carcinoma, lobular invasive and also in post operative scarring and radial scar.

Other associated findings seen in mammography in carcinoma of breast:

Edema of breast due to angio-lymphatic spread, seen as diffuse increase in density involving a large part of breast. Other causes for edema include post irradiation changes, inflammatory pathologies, post axillary surgery, enlarged axillary lymph nodes causing lymphatic obstruction and consequent to general body edema. Skin thickening, nipple retraction, are other features associated with malignancy, can be clinically correlated.

Some carcinoma may have relatively well circumscribed margin which include medullary, mucinous (colloid) and papillary carcinoma. Primary breast lymphoma, tumors of mesenchymal origin (osteosarcoma, fibrosarcoma, liposarcoma) present with minimal marginal irregularity and no calcification. Metastases to breast from extra mammary neoplasms are most common from melanoma with other possibility like lymphoma, leukemia, ovarian and soft tissue sarcoma. These lesions generally tend to be well circumscribed, single or multiple, U/L or B/L and have similar appearance to multiple cysts or fibroadenoma.

Phyllodes tumor is an uncommon mass, mostly benign but 5% have malignant potential. It grows rapidly 5-10cm size, appearing round, oval or slightly lobulated lesion with high density with relative well defined margins, with no calcification.

Current role of ultra sound in breast imaging:

Although U/S has not proved useful in breast cancer screening, it has become a valuable problem solving tool, particularly in differentiation of cysts from solid masses.

Indications for breast U/S:

1. *Differentiation of cysts from solid masses:* Ultrasound is 96 to 100% accurate in diagnosis of cysts[5]. in circumscribed or obscured non calcified masses seen on mammography or found on palpation. It also avoids unwanted biopsies performed for benign cysts.
2. *Evaluation of a palpable mass that is not visible in a radio-graphically dense breast in mammography*. U/S is of great value here, to localize and characterize such masses into solid or cystic types, and further helps in U/S[6] guided biopsies. If a palpable mass is not visible by either mammography or U/S, the lesion should be assumed to be solid and biopsy should be considered if clinical findings are suspicious for malignancy.
3. *Assessment of a mass that cannot be completely evaluated by mammography because of location*. In rare cases, a palpable mass cannot be placed on the mammographic plate due to extreme peripheral location in a very thin patient.
4. *Evaluation of a young patient <30 years with a palpable mass*. The breast of such patients tends to be radio-graphically denser and also more sensitive to radiation and also with a lesser incidence of cancer. For this reason, we usually perform a U/S as the initial study. If it is cystic, no further evaluation is required. If solid or not visible on U/S, one can go in for a single view mammogram, primarily to look for micro-calcification.
5. *Evaluation for an abscess*: Mammography is very difficult because of pain and edema and often does not demonstrate discrete abscess, just showing an area of increased density due to inflammation. U/S is an excellent method for detecting abscess cavity and for guidance for surgical or percutaneous drainage.
6. Guidance for Interventional procedure.

Inappropriate use of U/S:

1. As a screening modality.
2. As a routine evaluation of post operative breast cancer.
3. Evaluation of asymmetric breast density:
4. It does not detect micro-calcification and many small solid masses are sonographically invisible.

It has an unacceptably high false negative rate (20-47%).It also fails to detect a number of non palpable mammographically occult carcinomas. It also has a substantial false positive rate. Use of U/S as an adjuvant to mammography may add up to 7.4% of its accuracy[7].

Sonographic appearance of solid masses: The benign ones like fibroadenoma are oval, smooth, isoechoic or hypoechoic. Also, most benign lesions are broader than taller. The sonographically visible malignant lesions, such as infiltrating carcinomas are irregular, hypoechoic with speculated margins with posterior acoustic shadowing and are generally taller than broader (AP dm>Transverse dm)[9]. Malignant lesions on colour Doppler show an increased resistivity index (RI > .07) and shows increased peripheral vascularity. However, these are not very reliable criteria.

Needle biopsy techniques:

The ability to obtain a definitive diagnosis of a breast lesion without surgery has changed the face of breast radiology. Based upon the lesion's location and surgeon's choice, the following guided procedures are available which provide satisfactory results.

I. U/S guided: (a) FNAC, (b) Hookwire localization, (c) Core biopsy,
II. Fenestrated grid (x-ray mammography) guided : (a) FNAC, (b) hook wire,
III. Steriotactic guided : (a) core biopsy, (b) hook wire, (c) FNAC,
IV. MR directed biopsy with MR compatible wires and needles. (not widely available).

V. CT guided I/V bolus pre-operative needle localization

U/S guided technique: It is extremely useful in both palpable and non palpable masses; should be the first investigation of choice, being simple, quick, safe, cheap, accurate, non-ionizing. It has a sensitivity of 77-97% with a specificity of 91-100%.

U/S guided hookwire localization is performed in non-palpable lesion where in FNAC has been non conclusive or in highly suspicious lesions (both BIRADS III &IV). U/S guided core biopsy should be reserved for FNAC failure cases only.

Fenestrated grid guidance: Perforator grid compression plate is a standard attachment with most of International manufacturers of dedicated mammographic equipment. It is much cheaper and more easily available as compared to steriotactic guided biopsy which is much more costly (equipment cost is more than the cost of mammography unit). Hence it is not so widely available. But it is the most accurate of all procedures, ideally suited for core biopsies and or in evaluation of suspicious clusters of micro-calcification, mammographically detected non-palpable lesion not appreciated on high-resolution sonography and for deeper lesions in large fatty replaced breast.

Ductogram

A ductogram, or galactogram, is the diagnostic procedure of choice for determining the cause of U/L single pore spontaneous nipple discharge and helps in guiding accurate surgical intervention[8]. In this x-ray procedure, a fine plastic tube is placed into the opening of the duct in the nipple. A small amount of contrast medium is injected, which outlines the shape of the duct on an x-ray image and shows whether a mass is present inside the duct. Features of ductal carcinoma include irregular filing defects, wall irregularity with ductal distortion all seen in the dilated ductal system.

Magnetic Resonance Imaging (MRI)

Role of MRI in breast cancer detection is limited to specific clinical situations and currently only used as a diagnostic adjunct, for further characterizing the extent of invasive breast cancer in select population of younger women in the high risk group (strong family history) with dense breast, where mammography is less sensitive and in other situations like presence of implants and surgical scarring and multiple areas of distortion secondary to surgery[10].

Main Advantages include tomographical capability, chemical information, function of tissue vascularity, high sensitivity for invasive carcinoma in breast, with dense parenchyma and chest wall visualization and of course non ionizing nature.

Disadvantages of MRI: High cost of scan and contrast, availability, time consuming, expertise required in interpretation, volumes of data, enhancement varies with menstrual cycle, unable to image micro-calcification, low specificity (many benign lesions and normal tissue enhance).

Normal breast: MR appearance:

Pre contrast T1WI-fat is seen as high signal intensity (bright), glandular and ductal structures are intermediate signal intensity, fibrous tissue and ligament of Cooper having low signal intensity (dark). Pectoralis muscles have intermediate signal intensity and lung has low signal intensity on all sequences.

Women with glandular breast should be imaged in the mid cycle to minimize enhancement of background breast parenchyma that might limit lesion detectability[11]. Simple cysts do no enhance on post contrast T1WI and show high signal on T2WI.Fibroadenomas often produce a high and rapid signal intensity change that mimics the enhancement pattern of invasive carcinoma. Invasive breast carcinoma are low signal intensity on T1 precontrast MR sequence, that increase to 90% or greater in signal intensity within the first 60-90sec on 2-D dynamic scan with a cut off point of 70%enhancement at 1minute[12]. On a 3-D volumetric scan, cancers show >300units of enhancement at 5-10minute post infusion[13]. Axillary, internal mammary adenopathy, muscle, bony involvement, cross metastasis can also be identified.

Future potential of MRI includes MR directed biopsy especially in MR detected lesions that are not seen even on retrospect on mammography or U/S.MR compatible needles and wires are available.

Digital mammography, computer aided diagnosis and tele-mammography: A mammographic system that acquires images directly in digital form and thus overcoming the limitations of conventional mammography such as contrast, noise, resolution. It has post processing, storage, retrieval, reproduction and transport of images.

Computer aided detection and diagnosis are two potential revolutionary technology in which the radiologist can attain a second opinion from the image analysis, from a computer by using artificial intelligence to estimate the likelihood of malignancy.

Tele-mammography is the transmission of mammographic image from one location to another, anywhere on earth, in a digital format. It allows online interpretation, discussion, second opinion, interactive teaching conferences, all from a distant location.

Summary: With the ability to perform a good diagnostic mammography, breast U/S, ductography, MRI, Scinti-mammography, cyst aspiration, abscess drainage, steriotactic or U/S guided percutaneous biopsy, the modern breast radiologist should play the central role in breast cancer diagnosis. The future holds even more exciting challenges for the radiologist, as percutaneous lumpectomy is becoming a reality. Thus the breast radiologist, armed with the techniques and the technologies of the twenty-first century, truly stands on the threshold of a new era.

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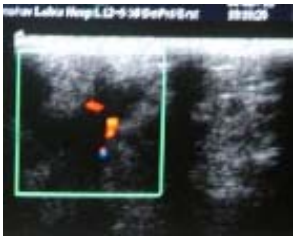
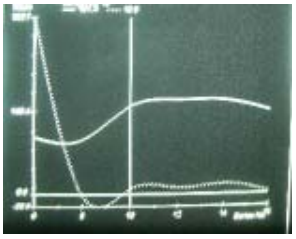
Case 1. *(a)*

Case 1. *(b)*



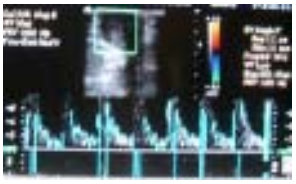
Case 1. *(c)*

Case 1. *(d)*



Case 1. *(e)*

Case 2. *(a)*



Case 2. *(b)*

Case 2. *(c)*

Case1 ***Infiltrating duct Carcinoma :***

(a) Mammography right breast showing irregular mass lesion with increase density with ill-defined spiculated margin.

(b) Ultrasound showing irregular hypo echoic mass lesion whose depth is > AP diameter. There is posterior acoustic shadowing.

(c) Doppler shows increase peripheral vascularity.

(d) MRI Post Contrast T1 weighted images showing hyperintense mass lesion right breast with intense enhancement within 60 seconds,

(e) with complete washout of contrast.

Case 2. Infiltrating ductal Carcinoma:

(a) Mammography shows ill-defined mass lesion with asymmetric density.

(b) Ultrasound showing hypo-echoic solid mass with high RI.

(c) MRI showing intensely enhancing infiltrating lesion.