Volume-5, Issue-6, June - 2016 • ISSN No 2277 - 8160

Research Paper | Medical Science

Imaging Modalities for The Diagnosis of Breast Carcinoma: A Review

Tarun Narang	Post Graduate student, Dept. of Radiodiagnosis, Rohillkhand Medical College Near Pilibhit byepass road Bareilly (U.P.) Pin-243001
Shweta Arora Narang	Assistant professor, Dept of physiology.House No-556-R, Model Town Panipat (HRY) Pin-132103
Pradeep Parakh	Professor & Head, Dept. of Radiodiagnosis, RMCH, Bareilly.
Lalit Kumar	Professor, Dept. of Radiodiagnosis, Rohillkhand Medical College Near Pilibhit byepass road Bareilly (U.P.) Pin-243001

ABSTRACT

Breast cancer is the most common type of cancer in women and the second leading cause of cancer related deaths in the worldwide. Several improvements in diagnostic protocols have enhanced our ability for earlier detection of breast cancer, resulting in improvement of therapeutic outcome and an increased survival rate for breast cancer victims but each modality is most useful when utilized according to individual traits such as age, risk and breast density. Various imaging modalities used these days are Mammography, Ultrasonography, Magnetic resonance imaging, Positron emission tomography, Thallium-201 scintimammography

KEYWORDS : Breast cancer, Imaging, Mammography.

Introduction :-

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].

This article reviews the imaging techniques currently in use for the diagnosis of breast cancer, including mammography, positron emission tomography (PET), magnetic resonance imaging (MRI), and thallium-201.

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 characterization and increasing the specificity of the examination, for example ultrasound, magnetic resonance imaging (MRI) and nuclear medicine.

IMAGING TECHNIQUES

Mammography

Mammography is the most effective method of detecting early breast cancer which is not clinically palpable. It can identify small foci of cancer within the breast which otherwise cannot be diagnosed. This has resulted in a 30% reduction in the mortality of breast cancer in women over 50 years of age[2].

Mammography has been shown to be quite sensitive in detecting breast cancer, but frequently it cannot be used to accurately differentiate benign from malignant lesions[3]. The only definitive means of confirmation of a suspicious lesion seen on mammography is excisional biopsy. In recent years, the clinical use of fine-needle aspiration cytology and stereotactic core biopsy of the breast has become more common[4].

Screen-film mammography(FSM) has long been considered as a "gold standard" for breast cancer screening[5] (Fig. 1). 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).

Figure 1: Mammography-speculated lesion on the craniocaudal view of the left breast.

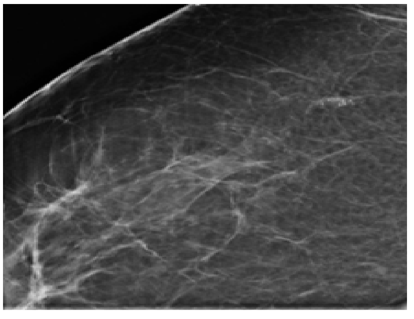


Figure 2: Mammography, magnification view showing fine pleomorphic calcifications with a linear distribution in the right breast at 10 o'clock posterior depth after intervention for an invasive ductal carcinoma.

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 [6]. 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[7].In a study, when conventional and digital mammograms of the same breasts were compared[8], they found more consistent image quality with better contrast, fewer artifacts, fewer technically inadequate films and slightly better lesion characterization.

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 reported sensitivity and specificity of mammography vary from 55% to 94% and 88% to 99%, respectively, the results being influenced by the variability in technology and prevalence of disease in a screening population. The positive predictive value also has been reported to vary from 10% to 35%[9].

Factors that affect the positive predictive value of mammography

Kopans has described the factors influencing the positive predictive value of mammography[10]. These include:

1. Prior probability of cancer in patients been screened (prevalence of the disease).
2. Percentage of women being screened for the first time, which inversely affects the positive predictive value.
3. Size and stage of the disease. This is probably the most important factor in assessing the positive predictive value. In the population of women with more advanced disease and larger tumors, the positive predictive value of mammography is more favorable but of course these women have a worse prognosis.
4. Interval cancer rate.

Computer-aided detection(CAD) program identifies potential abnormalities on the images and marks areas on the study that the computer considers to be suspicious[11].

Ultrasonography

Ultrasonography is now a major mode of imaging for the clinical diagnosis of breast cancer. 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[12,13]. 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[14]. 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.

Different approaches of elasticity imaging have been investigated, and at present some are at the stage of developing a practical system. Krouskop et al[15] 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.

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 [16,17]. 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[16].

To classify elastographic images, the 5-score system proposed by Ueno and co-workers[18] was considered, because it can be easily correlated to the 5-score BI-RADS classification, thus allowing a practical management of the lesions.

Some breast cancers may display benign features (score 1-3) on elasticity imaging[19] such as: non-differentiated or papillary ductal carcinoma (DCI), mucinous or medullary DCI, infammatory carcinoma, hypercellular, necrotic or pseudo-cystic malignant tumors, post-biopsy hemorrhagic lesions or deep small neoplastic nodules[20]. Large cancers, over 2.5 cm in diameter, occasionally have benign elastic features (score 2)[21].

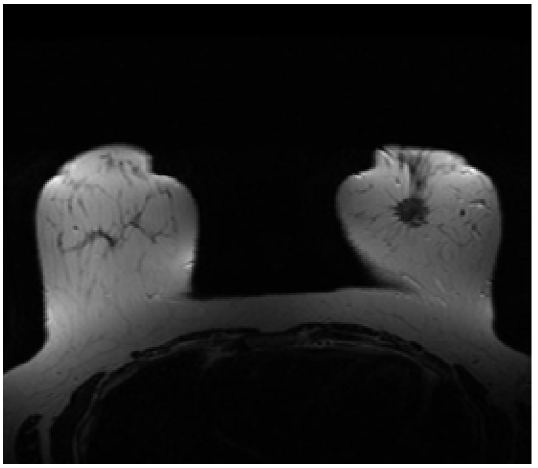
In addition, malignant lesions tend to be larger on US strain images than on corresponding Bmode US images, perhaps because of the desmoplastic reaction commonly associated with malignancy[18,19,20].

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[22].

Magnetic Resonance Imaging (MRI)

MRI has exceptional sensitivity for the detection of breast cancer and can depict cancers that are entirely occult on conventional imaging. In a study, Harms et al[23] performed MRI of the breast with rotating delivery of excitation of resonance. In 30 breasts with 47 malignant lesions and 27 benign lesions, MRI had a sensitivity of 94% and a specificity of only 37. The authors concluded that MRI of the breast can be used in patients with mammographically dense breasts or in patients with silicone implants/injection, and to stage disease in patients who are candidates for lumpectomy.

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[24,25].



Magnetic resonance imaging showing spiculated mass lower quadrants of the left breast.

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[26]. Malignant tumors appear to have higher relative blood volumes than normal breast tissue and benign tumors, so perfusion imaging may provide another non-invasive means of tissue characterization.

In a different paper, Harms et al[27] reported that fat-suppressed three-dimensional MR breast imaging demonstrated all cancers in 47 patients with known breast carcinomas; however, the positive predictive value of MRI as determined by this group is no better than that of conventional mammography. This group showed that breast cysts are hyperintense, whereas masses are hypointense on precontrast images.

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[28]. 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[29].

Positron-Emission Tomography (PET)

Positron emission tomography 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.

For the diagnosis of primary and malignant breast carcinoma, Lilien[30] reviewed the world PET literature through early 1993 which pertained to breast cancer detection. There were 97 cases of breast cancer patients reported using PET; overall sensitivity and specificity were 100% and 85%, respectively. Tse et al[31] applied a whole-body imaging technique to patients with breast masses or mammographic abnormalities using FDG. This was part of a clinical trial to evaluate the feasibility of PET imaging to identify primary breast cancer. In this study, PET correctly predicted the diagnosis of 12 of the 14 breast cancers. Lymph node status of 11 of the 14 patients was also diagnosed correctly. This was the first study to prospectively evaluate the feasibility of using whole-body PET imaging with FDG to detect breast cancer; nevertheless, two false-negatives were seen, and there were three patients with false-negative axillary lymph nodes.

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[32].

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[33]. PET has shown to be more accurate than clinical examination and allows evaluation of more distant nodal groups[34]. 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[35,36]. 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[37].

Scintimammography using ^{201}Tl

The first use of this agent for breast imaging was reported in 1978 by Hisada et al in two patients with known breast cancer[38]. This group evaluated 173 patients with malignant tumors and 76 benign lesions; there were two patients with known breast cancers in the series. The authors concluded that ^{201}Tl tumor imaging had a sensitivity and specificity of 64% and 61%, respectively, in this pilot study. Subsequently, Sluyser and Hoefnagel[39] reported on the use of ^{201}Tl imaging in a series of 15 patients. Since all 15 patients had known carcinomas of the breast, no conclusion can be drawn about the sensitivity and specificity in the use of the radiopharmaceutical.

Recently, Waxman et al[40] evaluated 81 female patients with ^{201}Tl scintigraphy of the breast because of palpable breast masses. In addition, 30 females with no palpable breast abnormalities were studied. Of 44 patients with palpable breast carcinomas, 42 (96%) abnormalities were detected using ^{201}Tl. In 19 patients with palpable breast abnormalities shown on biopsy to be benign fibrocystic disease, no abnormallities were detected on ^{201}T1 studies. This group concluded that ^{201}T1 scintigraphy of palpable breast lesions is an effective test for evaluation of these masses. Sensitivity for detection of malignant masses greater than 1.5 cm was high. However, highly cellular adenomas may demonstrate significant ^{201}T1 uptake, resulting in false-positive 201scintimammography. Also, the technique of supine imaging is not optimal for imaging the posterior aspect of the breast and separating it from the chest wall. Therefore, it is questionable whether the sensitivity and specificity reported by Waxman et al[40] can be reproduced at other centers.

In conclusion, mammography remains the procedure of choice in screening asymptomatic women for breast cancer. However, in patients with symptoms, other types of imaging play an important role in the detection of malignancies. The high cost and lack of availability of PET and MRI largely preclude their use . ^{201}Tl is not the imaging agent of choice because of its washout and redistribution mechanism in tumor cells; low photon energy also makes this agent less optimal for imaging.

References :-

1. National Cancer Institute. SEER 1973-2001 public use data. Accessed online at: http://seer.cancer.gov/publicedata/.
2. Anderson 1, Aspergen K, Janzow L et al. Mammographic screening and mortality from cancer: the Malmo Mammographic Screening Trail. *Br Med J* 1988;297:943-948.
3. Sickle WA. Mammographic feature of 300 consecutive non-palpable breast cancers. *AJR* 1986;146:661-663.
4. Parker SH, Lovin JD, Jobe WF, Luethke JM, Hopper KD, Yakes WF, Burke BJ. Stereotactic breast biopsy with a biopsy gun. *Radiology* 1990;176:741-747.
5. Karellas A, Vedantham S. Breast cancer imaging: a perspective for the next decade Med Phys. 2008;35:4878-4897.
6. R. M. Nishikawa, G. E. Mawdsely, A. Fenster and M. J. Yaffe. Scanned- projection digital mammography, Med. Phys. 1987;14:717-727.
7. Berman CG. Recent advances in breast-specific imaging. Cancer Control. 2007;14:338-349.
8. Obenauer S, Luftner- Nagel S, von Heyden D. Screen film versus full field digital mammography: image quality, detectability and characterisation of lesions. Eur Radiol 2002;12:1697-1702.
9. Humphry LL, Ballard DJ. Early detection of breast cancer in women. *Prev Pract* 1989;16:115-132.
10. Kopans DB. Positive predictive value of mammography. *AJR* 1992;158:521-526.
11. Baum F, Fischer U, Obenauer S, et al. Computer aided detection in direct digital full-field mammography; initial results. Eur Radiol. 2002;12:3015-3017.
12. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination and breast US and evaluation of factor that influence them: an analysis of 27,825 patient evaluations. Radiology 2002;225:165-175.
13. Moss HA, Britton PD, Flower CD, Freeman AH, Lomas DJ; Warren RM. How reliable is modern breast imaging in differentiating benign from malignant breast lesions in the symptomatic population? Clin Radiol 1999;54:676-682.
14. Kubota K, Hisa N , Ogawa Y. Evaluation of tissue harmonic imaging for breast tumours and axillary lymph nodes. Oncol Rep 2002; 9:1335-1338.
15. Krouskop TA, Wheeler TM, Kalle F, et al. Elastic moduli of breast and prostate tissues under compression. Ultrason imaging 1998; 20:260-274.
16. Hall TJ Zhu Y, Spalding CS. In vivo real- time freehand palpation imaging. Ultrasound Med Biol 2003;29:427-435.
17. Tardivon A, El Khoury C, Thibault F, Wyler A, Barreau B, Neuenschwander S. Elastography of the breast: a prospective study of 122 lesions J Radiol. 2007;88:657-62.
18. Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology 2006;239:341-350.
19. Garra BS, Cespedes EL, Ophir J, et al. Elastography of breast lesions: initial clinical results. Radiology 1997;202:79-86.
20. Hall T. AAPM/RSNA Physics Tutorial for Residents: Topics in US Beyond the basics:elasticity imaging with US. Radiographics 2003;23:1657-1671.
21. Itoh A. Review of the techniques and diagnostic criteria of breast ultrasound elastography. Medix Hitachi Supplement 2007:8-11.
22. Giuseppetti GM, Martegani A, Di Cioccio B, Baldassarre S. Elastosonography in the diagnosis of the nodular breast lesions: preliminary report. Radiol Med 2005;110:69-76.
23. Harms SE, Flamig DP, Hesley KL et al. MR imaging of the breast with rotating delivery

of excitation of resonance: clinical experience with pathological correlation. *Radiology* 1993;187:493-501.

24. Kaiser WA, Zeitler E. MR imaging of the breast: fast imaging sequences with and without Gd-DTPA. Preliminary observations. Radiology 1989;170(3 pt 1): 681-686.
25. Kuhl CK, Mielcareck P, Klaschik S, et al. Dynamic breast MR imaging are signal intensity time course data useful for differential diagnosis of enhancing lesions? Radiology. 1999;211:101-110.
26. Guo Y, Cai YQ, Gao YG et al. Differentiation of clinically benign and malignant breast lesions using diffusion-weighted imaging. J Magn Reson Imaging 2002;16:172-178.
27. Harms SE, Flamig DP, Hesley KL et al.Fat-suppressed three- dimensional MR imaging of the breast. *Radiographics*1993;13:247-267.
28. Orel SG, Schnall MD. MR imaging of the breast for the detection, diagnosis and staging of breast cancer. Radiology. 2001;220:13-30.
29. Kristoffersen Wiberg M, Aspelin P, Perbeck L, Bone B. Value of MR imaging in clinical evaluation of breast lesions. Acta Radiol 2002; 43:275-281.
30. Lilien D. Personal communication. Newport Beach, Calif., 1993.
31. Tse NY, Hoh CK, Hawkins RA, et al. The application of positron emission topographic imaging with fluorodeoxyglucose to the evaluation of breast disease. *Ann Surg* 1992;216:27-34.
32. Schirrmeister H, Kuhn T, Guhlmann A, Santjohanser C, Horster T, Nussle K, Koretz K, Glatting G, Rieber A, Kreienberg R, et al. Fluorine-18 2-deoxy-2-fluoro-D-glucose PET in the preoperative staging of breast cancer: Comparison with the standard staging procedures. Eur J Nucl Med 2001; 28:351-358.
33. Carter CL, Allen C, Henson DE. Relation of tumour size, lymph node status and survival in 24,740 breast cancer cases. Cancer 1989;63:181-187.
34. Flanagan FL Dehdashti F, Siegel BA. PET in breast cancer. Semin Nucl Med 1998;28:290-302.
35. Gallowitsch HJ, Kresnik E, Gasser J et al. F-18 fluorodeoxyglucose positron emission tomography in the diagnosis of tumour recurrence and metastases in the follow-up of patients with breast carcinoma; a comparison to conventional imaging. Invest Radiol 2003;38:250-256.
36. Schelling M, Avril N, Nahrig J et al. Positron emission tomography using 18F fluorodeoxyglucose for monitoring primary chemotherapy in breast cancer. J Clin Oncol 2000; 18:1689-1695.
37. Avril N, Menzel M, Dose J, Schelling M, Weber W, Janicke F, Nathrath W, Schwaiger M: Glucose metabolism of breast cancer assessed by 18F-FDG PET: histologic and immunohistochemical tissue analysis. J Nucl Med 2001,42:9-16.
38. Hisada K, Tonami N, Miyamae T, et al. Clinical evaluation of tumour imaging with ^{201}Tl chloride. *Radiology* 1978;129:497-500.
39. Sluyser M , Hoefnagel CA. Breast carcinomas detected by thallium-201 scintigraphy. *Cancer Lett* 1988;40:161-168.
40. Waxman AD, Ramanna L, Memsic LD, Foster CE, Silberman AW. Thallium scintigraphy in the evaluation of mass abnormalities of the breast. *J Nucl Med* 1993;34:18-23.