



## EFFICACY OF X-RAY MAMMOGRAPHY, SONOMAMMOGRAPHY AND MR MAMMOGRAPHY FOR EVALUATION OF BREAST LESIONS IN WOMEN

### KEYWORDS

X-Ray mammography, Sonomammography, MR mammography, BIRADS

#### Pooja Gupta

MD, DNB Radiodiagnosis, Assistant Professor, Department of Radiodiagnosis and Imaging, Armed Forces Medical College, Pune -411040, India.

#### Samar Chatterjee

MD Radiodiagnosis, Professor, Department of Radiodiagnosis and Imaging, Armed Forces Medical College, Pune -411040, India.

#### Vivek Sharma

MD, DNB Radiodiagnosis, Professor & Head of Department, Department of Radiodiagnosis and Imaging, Armed Forces Medical College, Pune -411040, India.

#### Kamlesh Kumar Singh

MD Pathology, Assistant Professor, Department of Pathology and Laboratory Science, Armed Forces Medical College, Pune -411040, India.

#### Devika Gupta

MD, DNB , Pathology, Assistant Professor, Department of Pathology and Laboratory Science, Armed Forces Medical College, Pune -411040, India.

### ABSTRACT

**Aims & Objectives** The purpose of this article is to compare the effectiveness of X-Ray mammography, Sonomammography and MR mammography for evaluation of breast lesions in women.

**Materials and Methods:** This prospective study has been carried out on 50 patients presenting with breast lump or nipple discharge who were subjected to mammography and sonomammography. The high BIRADS lesions (III and above) then underwent MRI mammography. All patients underwent ultrasound guided FNAC of the breast lesions. The diagnostic sensitivities, specificities, positive predictive values and negative predictive values of the three imaging modalities were compared. The imaging features of suspicious malignant breast lesions on all three modalities were then correlated with final histopathological diagnosis.

**Result:** The sensitivity and negative predictive values of MR mammography was significantly higher than those of mammography or sonomammography. The specificity and positive predictive value of sonomammogram was significantly higher than those of mammography and MR mammography.

**Conclusion:** Our results indicate that the sensitivity of breast imaging can be increased by complementary use of MRI, especially for patients in whom the status of breast lesion remains unclear. MRI though more cost prohibitive, may help to reduce the number of unnecessary biopsies and diagnostic ambiguities.

### Introduction:

Breast cancer is the leading cause of cancer related deaths in women. Breast cancer, however is a curable disease in that, 20 to 30 % of patients diagnosed as having early breast cancer will enjoy a normal life span without further morbidity, following treatment. The high prevalence and need for early treatment of breast malignancy emphasizes the importance of early and accurate diagnosis. Breast symptoms of pain and lumpiness are frequent manifestations of normal cyclical changes and also of benign diseases such as cysts, benign breast change and inflammatory processes. These symptoms however become worrisome as women enter a higher age group. It is here that breast imaging makes an important contribution.

X-ray mammography is of greatest advantage due to its ability to detect micro-calcifications which often are the earliest signs of malignancy. It is the standard investigation in routine screening of patients for breast disease. It has high specificity in detecting invasive breast carcinomas. Mammography has been evaluated in large randomized controlled trials and in smaller nonrandomized studies [1, 2].

Breast ultrasound is invaluable in characterizing masses as cystic or solid. It is the only modality employed during lactation and pregnancy and in painful conditions where mammographic compression is not possible. It is also valuable for evaluation of the post surgical and irradiated breast. Stavros et al have reached high sensitivities for the ultrasound differentiation between benign and malignant breast nodules [3].

MRI, a powerful tool for evaluating patients with a high risk of having

breast cancer, can detect a significant number of lesions not found on x-ray mammography and sonomammography. The excellent soft tissue resolution and the lack of ionizing radiation makes MRI an attractive imaging modality.

It is very important to detect breast cancer at the earliest possible stage when it is curable. In order to achieve this, it is necessary that we select the appropriate modality for investigation which would not only yield more specific results but would also go a long way in minimizing patient discomfort and cost. With this background, this study has been carried out to evaluate, correlate and compare the role of x-ray mammography, sonomammography and MRI mammography in breast imaging.

### Materials and Methods:

This prospective study has been carried out on 50 patients presenting with breast lump or nipple discharge who were subjected to mammography and sonomammography. The high BIRADS lesions (III and above) were evaluated with bilateral contrast-enhanced MR mammography between July 2010 to June 2012 at our institution which is a tertiary care hospital. Patients who were excluded from the study were those who underwent chemotherapy or radiotherapy for malignant breast lesions, claustrophobic patients and those with pacemakers or metallic implants. Patients were subjected to a detailed history and breast examination. This was followed by whole breast mammographic, sonomammographic and MRI mammographic evaluation.

For sonomammography a GE Logiq P5 machine with linear transducer of frequency 7-11 MHz was used. Evaluation was carried

out in grey scale mode. The use of a dedicated 7.5-10 MHz transducer has been recommended by Laing FC et al [4]. The patient was examined supine with arms raised above the head. Both the breasts were examined with overlapping scans in a radial pattern from the nipple to the periphery in two orthogonal planes and in craniocaudal plane. The retroareolar region was separately scanned with angled views to ensure complete coverage of the entire breast tissue. Both axillae were examined for presence of lymphadenopathy. The x-ray mammography was performed on a Siemens Mammomat 3000 Nova digital radiography unit with automatic optimization parameters (AOP) settings. Mammographic evaluation was carried out initially using the two basic projections, the mediolateral oblique (MLO) and the cranio-caudal (CC). Proper compression of the breast tissue was ensured. Care was taken to include the axillary fold, the pectoralis muscle and the inframammary fold in the mediolateral oblique projection and the pectoralis muscle in the cranio-caudal projection. The breast MR imaging was performed with a 1.5-T magnet (Siemens) with the patient in the prone position, lying on a dedicated breast coil. Pre contrast gradient echo T1W1 imaging was checked carefully to ensure adequate breast coverage and lack of artifacts. Post contrast imaging began immediately after the intravenous gadolinium bolus (0.1 mmol Gd/kg) and saline flush were completed. Five post contrast sequences were taken, the first sequence taken 20 seconds after the bolus injection followed by all the other sequences, each separated by an interval of 20 seconds. In addition to the standard dynamic gadolinium enhanced 3DT1W1 imaging (1 pre & 5 post contrast-Slices 120, thickness 1mm, TR 4.42ms, TE 1.62ms, Flip 12°, FOV 490mm), the breast MR imaging

examination was supplemented with the following sequences: T1W1 axial (Slices 25, thickness 4mm, TR 437ms, TE 14ms, Flip 15°, FOV 300mm), T1W1 coronal (Slices 25, thickness 4mm, TR 447ms, TE 14ms, Flip 15°, FOV 300mm), T2 STIR (Short T1 Inversion Recovery) axial (Slices 25, thickness 4mm, TR 9000ms, TE 70ms, TI 150ms, FOV 320mm), TRUFI (True Fast Imaging with Steady state free precession) (Slices 40, thickness 4mm, TR 3.8ms, TE 1.6ms, Flip 60°, FOV 400mm).

MR images were evaluated by two radiologists in consensus. MR pre and post contrast images, subtracted images (post contrast minus pre contrast images) and maximum intensity projection reconstructions were evaluated. The semi quantitative analysis of the signal intensity-to-time relation was performed with the region-of-interest technique. The region of interest (2-5 pixels) was placed within the tumor area with the highest signal intensity enhancement. The evaluation criterion was by the signal intensity-time curves obtained at up to four regions of interest placed on enhancing regions within the lesion. The signal intensity curves were of three types, type I to III depending on shape [5-6] (Fig 1). Mammograms were retrospectively reviewed at time of MR mammographic interpretation to determine breast density according to the four-point scale from I to IV of the Breast Imaging Reporting and Data System classification [7].

Following the imaging all the patients underwent ultrasound guided fine needle aspiration cytology (FNAC) of the breast lesions.

#### Statistical analysis:

The diagnostic sensitivities, specificities, positive predictive values and negative predictive values of the three imaging modalities were compared. The imaging features of suspicious malignant breast lesions on all three modalities were then correlated with final histopathological diagnosis.

#### Results:

Findings in our study (Table 1) showed that the majority of cases were in age group 51 to 60yrs (38%), 14 (28%) cases were in age group 41 to 50yrs, 6(12%) cases were in age group 31 to 40yrs and 10(20%) cases were in the age group 61yrs and above. In this study the youngest patient was 30yrs and the oldest 76yrs. The mean age of patients was 53.10 yrs (Table 2). Out of the 50 patients, 5 patients (10%) had history

of hormonal replacement therapy (HRT) and 6 patients (12%) had history of benign breast disease. 02(4%) of the patients gave family history of breast cancer and both had first degree relatives with breast cancer. Patients with history of early menarche and late menopause constitute 20% of the study population. Out of 50 women 27(54%) did not have any associated factors (Table 3).

On histopathological examination the majority of the cases were malignant (82%) with benign pathology seen in 18% of cases (Table 4).

Most common location of malignant tumor was in the outer upper quadrant in women of both <55 yrs (12 cases) and >55 yrs (08 cases) of age group (Table 5). Thus statistically the upper outer quadrant had a significantly higher incidence of tumor involvement compared to the other three quadrants in both groups.

On sonomammogram most benign lesions were wider than taller (L/AP Ratio >1.4) while malignant lesions were taller than wider (L/AP <1.4). This however is applicable to lesions smaller in size; it does not apply to the larger malignant lesions. Most benign lesions were round to oval in shape with smooth or lobulated margins. One benign lesion however had irregular shape. Malignant lesions were found to be irregular in shape and margins with the exception of 12 malignant lesions which were round to oval in shape. Spiculated margin was the feature most consistently associated with malignancy. However, one benign lesion was also found to have spiculated margins. Most of the malignant lesions had heterogeneous echotexture. Only 07 malignant lesions were hypoechoic in echotexture. Most of the benign lesions were hypoechoic. Only one benign lesion exhibited heterogeneous echotexture. There was a predominant display of posterior acoustic shadowing by majority of malignant lesions, neither shadowing or enhancement was seen in eleven malignant lesions, however enhancement was seen in one malignant lesion. Only one of the benign lesions showed posterior acoustic attenuation, three exhibited enhancement and there was no sound transmission in four benign lesions (Table 6).

On x-ray mammography the majority of the benign lesions had lobulated margins (05) and smooth margins (02); however one of the benign lesions had spiculated margins. Most of the malignant lesions were found to have spiculated margins; however, 06 of the malignant lesions had lobulated margins (Table 7). Micro calcification was seen in 11 cases, out of which 09 were malignant and 02 were benign. Both micro and macro calcifications were seen in 02 malignant cases (Table 7). There was a significant increase in the sensitivity of mammography in non dense breasts as compared to dense breasts (Table 8). Architectural distortion was seen in one case on mammogram and was associated with an irregular mass, which on histopathology was an invasive ductal carcinoma, thus indicating that this distortion was due to invasion into surrounding breast parenchyma. Skin involvement was seen in 03 and nipple retraction in 02 of the malignant cases (Table 9).

One case showed only clustered micro calcifications on mammogram and was considered as high risk for malignancy. However, no lesion was visualized on mammogram and sonomammogram and MRI mammogram and biopsy from that site was found benign.

On MR mammogram the majority of the benign lesions were found to have smooth or lobulated margins with the exception of one lesion with spiculated margins. Most malignant lesions had spiculated margins; however, 10 malignant lesions had lobulated margins. Spiculation was the feature most consistently associated with malignancy. Involvement of skin/pectoralis was seen in 10 lesions all of which were malignant (Table 10). Type I signal intensity curve was seen in 06 benign lesions whereas Type II signal intensity curve was seen in 05 lesions out of which, 04 were malignant and 01 was benign. Type III signal intensity curve was seen in 38 lesions out of which 37

were malignant and 1 was benign (Table 11).

While assessing the accuracy of cancer detection by individual modalities (Table 12), lesions that were BIRADS I, II and III on that modality were included under 'negative' (for malignancy) and lesions that were BIRADS IV and V on that modality were included under positive (for malignancy). The sensitivity, specificity, positive and negative predictive values of X-ray mammography noted in this study were 80.5%, 88.8%, 97.06% and 50% respectively. The values for sonomammogram was 78.05%, 100%, 100%, 50% and that of MR mammogram was 100%, 88.8%, 97.6%, 100% respectively. The sensitivity of MR mammography was significantly higher than those of mammography or sonomammography. The specificity and positive predictive value of sonomammogram was significantly higher than those of mammography and MR mammography. The negative predictive values for MR mammography were significantly higher than X-ray mammogram and sonomammogram (Table 13).

**Discussion:**

In our study, the range of ages of the patients was 30 yrs to 76 yrs. The mean age of our study was 53 yrs and the commonest age group of patients was 51 yrs to 60 yrs. In a study of Eren Yeh et al [8] who did a comparison of mammography, sonomammography, and MRI in patients undergoing neo adjuvant chemotherapy for palpable breast cancer the range of patients was 31-65 yrs and mean age was 45 yrs. In a study of Warner et al [9] of 196 women, which compared efficacy of breast Magnetic Resonance Imaging, mammography and ultrasound for surveillance of women at high risk for hereditary breast cancer, the age range was 26 to 59 yrs and the mean age group was 43 yrs. Mean age of our study was in consensus with the findings of various authors as mentioned above.

The location of cancer according to quadrants in patients younger than 55yrs and in those 55yrs and older in our study was similar to the distribution in series of Tellum et al [10]. Most studies have shown the upper outer quadrant has a greater risk of cancer than the other quadrants.

Sonomammography proved to be the modality used to measure mass lesions, so as to obtain maximum accuracy. This in accordance to the observations of Fornage et al [11] who have shown that real time sonomammography as compared with physical examination or mammography yields the most accurate pre-operative determination of breast cancer size. In our study most malignant lesions were taller than wider. This in accordance to the observations of Fornage et al [11]. In our study most benign lesions showed round-oval shape with smooth or lobulated margins with posterior acoustic enhancement. Most malignant lesions were irregular in shape and margins, heterochoic with posterior acoustic shadowing. This was in accordance with studies done earlier by Vlajavljjevic [12] and Tzu-Chieh Chao [13]

Mammographic sensitivity is lower in radiographically dense breasts [14, 15]. Mammographic sensitivity was found to be 100% in non dense breasts and only 62% in dense breasts. These findings are similar to various other studies. Rosenberg et al [16] found that in all age groups, women with dense breasts had a lower mammographic sensitivity than those with fatty breasts. The sensitivity of mammography to the index cancer ranges from 63% to 98% [17] and has been reported to be as low as 30%-48% in dense breasts [18].

In our study micro calcifications were most commonly associated with malignant lesions. The commonest pattern was of clustered pleomorphic or branching and linear pattern. Mammography was found to be the best modality for detecting micro calcifications. This was in accordance with other studies.

In our study on MRI most malignant lesions showed either spiculated (30 lesions) or lobulated (10 lesions) margins. 37 malignant lesions showed type III SI curve and 4 showed type II curve. Most benign

lesions showed smooth/lobulated margins with type I SI curve. This was in accordance with previous study done by Kinkel K et al [19].

In our study there was discordance in the results among all the three imaging modalities in 13 cases. Out of these 12 cases were found as malignant on histopathology. 7 of these 12 cases were correctly diagnosed by MRI and considered low risk for malignancy by mammogram and sonomammogram (Fig 2). 2 of the 12 cases were considered low risk for malignancy on mammogram only (Fig 3). These 2 lesions had well defined, lobulated margins with no micro calcifications. 3 of the 12 cases were considered low risk for malignancy on sonomammogram only. These 3 lesions had well defined lobulated margins with no distal shadowing on sonomammogram.

The sensitivity, specificity, positive and negative predictive values of mammography noted in this study was 80.5%, 88.8%, 97.06% and 50%, respectively, of sonomammogram was 78.05%, 100%, 100%, 50% and of MR mammogram was 100%, 88.8%, 97.6%, 100%. The sensitivity of MR mammography was significantly higher than those of mammography or sonomammography. The specificity and positive predictive value of sonomammogram was significantly higher than those of mammography and MR mammography. The negative predictive values for MR were significantly higher than mammogram and sonomammogram. This was in accordance with study done by Sabine Malur et al (20) and Berg WA et al (21).

**CONCLUSION:**

Our study findings indicate that sensitivity and negative predictive value of MR mammography was significantly higher than those of mammography or sonomammography. The specificity and positive predictive value of sonomammogram was significantly higher than those of mammography and MR mammography. Thus the sensitivity of breast imaging can be increased by complementary use of MRI, especially for patients in whom the status of breast lesion remains unclear

**Tables:**

**Table 1: Age group wise distribution of cases:**

Age Group (Yrs)	Number of cases	Percentage
21-30	01	2%
31-40	06	12%
41-50	14	28%
51-60	19	38%
61 and above	10	20%
Total	50	100%

**Table 2: Age distribution of cases**

No of cases	Minimum age	Maximum age	Range	Mean	Std. Deviation
50	30	76	46	53.10	10.80

**Table 3: Other associated factors in the patients**

S. No	Associated Factors	No of Patients	Percentage
1.	HRT	5	10%
2.	Benign breast disease	6	12%
3.	Family h/o breast cancer	2	4%
4.	Early menarche	7	14%
5.	Late menopause	3	6%
6.	No risk factors	27	54%

**Table 4: Distribution of benign and malignant cases**

Histopathology	Number of cases	Percentage
Malignant cases	41	82%
Benign cases	09	18%
Total	50	100%

**Table 5: Gross quadrant location of malignant tumor**

Quadrant	Age distribution of the patients	
	<55yrs	>55yrs
Outer Upper	12	8
Inner upper	4	2
Outer lower	0	1
Inner lower	1	5
Retroareolar	2	4
>1 quadrant	1	1
Total	20	21

**Table 6: Features of the lesions on sonomammogram**

Sonomammographic features		No of lesions	Benign	Malignant
Size	L/AP> 1.4	23	8	15
	L/AP<1.4	26	1	25
Shape	Round	10	3	7
	Oval	09	4	5
	Irregular	30	1	29
Margins	Smooth	02	2	0
	Lobulated	17	5	12
	Spiculated	30	1	29
Echotexture	Hypoechoic	14	7	7
	Heteroechoic	35	1	34
Posterior sound transmission	Shadowing	30	1	11
	Enhancement	4	3	1
	No change	15	4	11

**Table 7: X-ray mammographic features of breast lesions**

X-ray mammographic features		No of lesions	Benign	Malignant
Margins	Smooth	6	2	4
	Lobulated	11	5	6
	Spiculated	32	1	31
Calcifications	Micro	11	2	9
	Macro	7	3	4
	Mixed	2	0	2

**Table 8: Effect of breast density on sensitivity of X-ray mammography**

X-ray mammographic density	True positive	False positive	True negative	False negative	Sensitivity
Dense breasts (>25% glandular)	13	1	4	8	62%
Non dense breasts (<25% glandular)	19	0	4	0	100%

**Table 9: Other associated findings on X-ray mammography**

X-ray mammographic features	No of lesions	Benign	Malignant
Architectural distortion	1	0	1
Skin involvement	3	0	3
Pectoralis involvement	0	0	0
Nipple retraction	2	0	2

**Table 10: MR mammographic features of breast lesions**

MR mammographic features		No of lesions	Benign	Malignant
Margins	Smooth	2	2	0
	Lobulated	16	6	10
	Spiculated	31	1	30
Skin thickening / Pectoralis invasion		10	0	15

**Table 11: Time intensity curve on contrast enhanced MR mammography**

Type of time intensity curve	Number	Benign	Malignant
Type I	6	6	0

Type II	5	1	4
Type III	38	1	37

**Table 12: Accuracy of cancer detection by imaging modalities used**

Modality	True positive	False positive	True negative	False negative
Sonomammogram	32	0	9	9
X-ray mammogram	33	1	8	8
MR mammogram	41	1	8	0

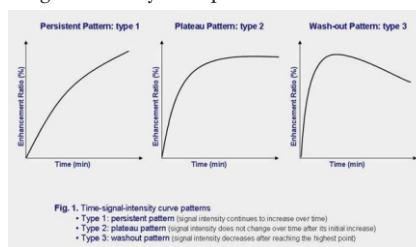
**Table 13: Performance characteristics of each screening modality**

Modality	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Sonomammogram	78.05%(95%CI=62.0-88.9)	100%(95%CI=62.9-100)	100%(95%CI=86.7-100)	50%(95%CI=26.8-73.2)
Mammogram	80.5%(95%CI=64.6-90.6)	88.8%(95%CI=50.7-99.4)	97.06%(95%CI=82.9-99.8)	50%(95%CI=25.5-74.5)
MR mammogram	100%(95%CI=89.3-100)	88.8%(95%CI=50.7-99.4)	97.6%(95%CI=85.9-99.9)	100%(95%CI=59.8-100)

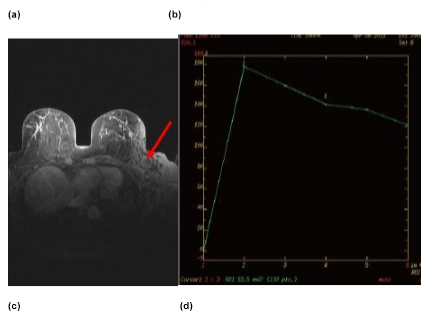
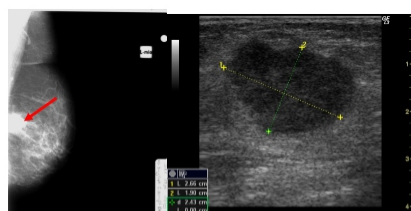
CI=confidence interval

**Figures:**

**Fig. 1:** Time signal intensity curve pattern



**Fig 2:** A 58-year-old woman with positive family history of breast cancer presented with lump in the left breast. (a) X-Ray mammography (mediolateral oblique view) shows a well defined soft tissue density lesion with lobulated margins in the superolateral quadrant of the left breast - BIRADS III (Probable benign lesion). (b) Sonomammography shows a well defined hypoechoic lesion with lobulated margins with distal enhancement at 3'o clock position in left breast - BIRADS III. (c) MRI mammogram (3DT1W1 post contrast image) shows a well defined lesion with lobulated margins in lateral quadrant of the left breast. (d) The lesion shows heterogeneous contrast enhancement with early sharp rise with early washout (Type III curve) - BIRADS V. Histopathological examination proved it to be an Invasive ductal cell carcinoma

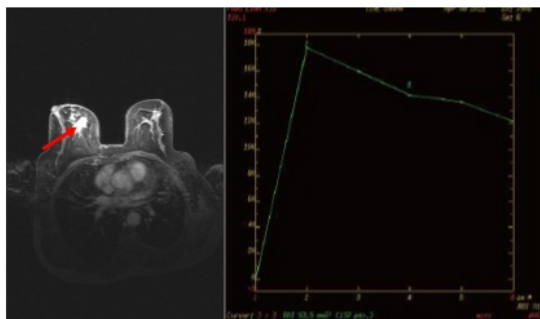




**Fig 3:** A 50-year-old woman with history of benign breast disease presented with lump in the right breast. (a) X-Ray mammography (mediolateral oblique view) shows an ill defined lesion? glandular tissue in the superomedial quadrant of the right breast - BIRADS III (Probable benign lesion). (b) Sonomammography shows a well defined hypoechoic lesion with spiculated margins and distal shadowing at 2'o clock position in right breast - BIRADS IV. (c) MRI mammogram (3DT1WI post contrast image) shows a well defined lesion with irregular margins in the superomedial quadrant of the right breast. (d) The lesion shows heterogeneous contrast enhancement with early washout (Type III curve) - BIRADS V. Histopathological examination proved it to be an Invasive ductal cell carcinoma



(a) (b)



(c) (d)

**References:**

1. Roberts MM, Alexander FE, Anderson TJ, et al. Edinburgh trial of screening for breast cancer: mortality at 7yrs. *Lancet* 1990;335:241-246
2. Frisell J, Eklund G, Hellstrom L, et al. Randomized study of mammography screening: preliminary report on mortality in the Stockholm trial. *Breast Cancer Res Treat* 1991; 18:49-56
3. Stavros AT, Thickman D, Rapp CL, et al. Solid breast nodules: use of ultrasonography to distinguish between benign and malignant lesions. *Radiology* 1995; 196:123-134
4. Laing FC, Jeffrey RB, Minagi H. Ultrasound localization of occult breast lesions. *Radiology* 1984;151 (3):795-796
5. Orel SG. Differentiating benign from malignant enhancing lesions identified at MR imaging of the breast: are time-signal intensity curves an accurate predictor? *Radiology* 1999;211:5-7
6. 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
7. American College of Radiology. *Breast Imaging Reporting and Data System Atlas (BIRADS Atlas)*. 4th ed. Reston, Va: American College of Radiology; 2003
8. Erenyeh, Priscilla Slanetz, Daniel B. Kopans, et al. Prospective Comparison of Mammography, Sonography, and MRI in Patients Undergoing Neoadjuvant Chemotherapy for Palpable Breast Cancer *AJR* March 2005;184:868-877
9. E. Warner, D. B. Plewes, R.S. Shumak, et al. Comparison of Breast Magnetic Resonance Imaging, Mammography, and Ultrasound for Surveillance of Women at High Risk for Hereditary Breast Cancer. *Journal of Clinical Oncology*, August 2001:3524-3531
10. Milton Tellum, Lucien Prive and David R. Meranze. Four quadrant study of breasts removed for carcinoma. *Cancer* 1962; 15:10-15
11. Fomage BD, Lorigan JG, Andry E. Fibroadenoma of the breast: sonographic appearance. *Radiology* 1989; 172:671-675
12. Vlasisavljevic V. Differentiation of solid breast tumors on the basis of their primary echographic characteristics as revealed by real-time scanning of the uncompressed breast. *Ultrasound Med Biol* 1988;14[suppl 1]:75-80
13. Tzu-Chieh Chao, Yung-Feng Lo, Shin-Cheh Chen, Miin-Fu Chen. Prospective Sonographic Study of 3093 Breast Tumors 1999 by the American Institute of Ultrasound in Medicine. *J Ultrasound Med* 1999; 18:363-370
14. Bird RE, Wallace TW, Yankaskas BC. Analysis of cancers missed at screening mammography. *Radiology* 1992; 184:613-617
15. Ma L, Fishell E, Wright B et al. Case control study of factors associated with failure to detect breast cancer by mammography. *J Natl Cancer Inst* 1992; 84:781-785
16. Rosenberg RD, Hunt WC, Williamson MR et al. Effects of age, breast density, ethnicity,

and estrogen replacement therapy on screening mammographic sensitivity and cancer stage at diagnosis: review of 183,134 screening mammograms in Albuquerque, New Mexico. *Radiology* 1998;209:511-518

17. Burhenne HJ et al. Interval breast cancers in Screening Mammography Program of British Columbia: analysis and classification. *AJR* 1994;162:1067-1071
18. Mandelson Mt et al. Breast density as a Predictor of Mammographic Detection: *J Natl Cancer Inst* 2000;92:1081-1087
19. Kinkel K, Helbich TH, Esserman LJ, et al. Dynamic high-spatial-resolution MR imaging of suspicious breast lesions: diagnostic criteria and interobserver variability. *AJR Am J Roentgenology* 2000; 175:35-43
20. Sabine Malur, Susanne Wurdinger, Andreas Moritz, Wolfgang Michels, Achim Schneider, et al. Comparison of written reports of mammography, sonography and magnetic resonance mammography for preoperative evaluation of breast lesions, with special emphasis on magnetic resonance mammography. *Breast Cancer Res.* 2001;3(1):55-60
21. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. *Radiology*. 2004 Dec; 233(3):830-49