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IMAGING OF BREAST LESIONS USING CONVENTIONAL MAGNETIC RESONANCE IMAGING AND DIFFUSION WEIGHTED IMAGING

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ABSTRACT: CONTEXT: Breast cancer is the second most common cancer in the world, and the second most common in cancer in Indian women. **AIMS:** The aims of this study were to differentiate between benign and malignant lesions using Diffusion Weighted Imaging, T2-weighted and T1-weighted imaging, and to set a cut off value of ADC to differentiate between benign and malignant lesions. **MATERIALS AND METHODS:** It included 51 patients between the ages of 15 and 75 years, coming to surgical OPD, Government Medical College, Kozhikode with USG/Mammogram proven breast lesions from January 2013 to September 2014. Non contrast MR Mammography was done using 1.5 T MR system. T1WI, T2WI and Diffusion weighted imaging (b= 0, 600) were done and ADC values were calculated for all the lesions. Validity parameters were assessed for each sequence and a combination of all the sequences. ROC curve was plotted and ADC cut off was chosen with a high sensitivity and specificity. **RESULTS:** Twenty nine lesions were categorized as benign and twenty two lesions were categorized as malignant based on the T1, T2 and DWI. By histopathological examination of these lesions, 2 lesions characterised as malignant turned out to be benign. T1WI was not found to be helpful in differentiating between benign and malignant lesions, whereas 95% of malignant lesions appeared either intermediate signal (90%) or hypointense (5%) in T2WI, conferring a sensitivity of 90.5% and specificity of 80.6% in detection of malignant lesions using T2WI. Applying an ADC threshold of 1.255×10^{-3} mm²/s benign and malignant lesions could be differentiated with 100% sensitivity and 93.5% specificity, with a PPV of 90.9% and NPV of 100%. Mean ADC value of malignant lesions was found to be 1.13 ± 0.007 mm²/s. **CONCLUSION:** Non contrast MRI using T2WI and DWI is a useful technique for characterizing breast lesions. It is also useful in the follow up of post lumpectomy irradiated breast to detect recurrence.

KEYWORDS: Non contrast MR mammography; diffusion weighted imaging; breast lesions.

MeSHterms:

Adult.
Breast/pathology*.
Breast Neoplasms/diagnosis*.
Diagnosis, Differential.
Female.
Humans.
Magnetic Resonance Imaging/methods*.
Middle Aged.
Predictive Value of Tests.

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Sensitivity and Specificity.
 Contrast Media.
 Diffusion Magnetic Resonance Imaging.
 Magnetic Resonance Imaging.
 Mammography.
 ROC Curve.

INTRODUCTION: Breast cancer is the second most common cancer in the world, and the second most common in cancer in Indian women. The state capital of Kerala- Thiruvananthapuram – has emerged as the nation's breast cancer capital, reporting the highest crude incidence rate 40 / 100,000 (as per 2012 statistics).

Conventional MRI is excellent for morphological assessment of the breast and its pathology. Newer modalities like Diffusion-weighted imaging, which are increasingly in vogue now, give assessment of the functional environment of water in tissues without the need for intravenous contrast material injection.

AIMS AND OBJECTIVES:

- To differentiate between benign and malignant lesions using T1, T2-weighted and Diffusion Weighted Imaging.
- To set a cut off value of ADC to differentiate benign and malignant lesions.

METHODS:

Study Design	Diagnostic test evaluation
Study Setting	Cases coming to Surgical OPD, Govt. Medical College Kozhikode, Kerala, India
Study Period	Jan 2013 to Sept 2014
Study method	MR examination in 3rd week of menstrual cycle.
Sample size	51 subjects
Inclusion Criteria	Women of the age group 15 to 75 years Breast lesions larger than 1cm detected by ultrasound/ mammogram. All patients to receive definite pathological diagnosis in our hospital
Exclusion Criteria	Previous history of breast surgery within preceding 18 months Chemotherapy within preceding 18 months Radiotherapy within preceding 18 months Lesions smaller than 1cm.
MRI protocols and imaging	MRI with a 1.5 T MR system (GE SIGNA HDXT) Axial T1, T2-weighted fast spin echo (FSE) pulse sequence Gradient echo planar image (EPI) DWI pulse, b-value 0, 600 second/mm ² . ADC values are calculated within the lesion - diameter of ROI - 31.2mm
Statistical Analysis	SPSS statistical software. P value < 0.05 → statistically significant difference

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ETHICS: The study was approved by the institutional research committee and ethics committee of Government Medical College, Kozhikode, Kerala, India.

STATISTICS: Validity parameters

- Sensitivity – ability of the test to detect true disease. It is the proportion of diseased patients who are reported as test positive. It is thus the True Positive rate.
 - Sensitivity= {True positive / True positive + False Negative}x 100
- Specificity – ability of the test to correctly detect disease free individuals, ie it is the True Negative rate.
 - Specificity –{True negative / True negative + False positive}x 100
- Positive predictive Value- indicates the probability that a patient with a positive result in fact has disease.
 - Positive predictive Value = {True positive / True positive + False Positive}x 100
- Negative predictive Value- indicates the probability that a patient with a negative result does not have the disease in question.
 - Negative predictive Value = {True negative / True negative + False negative}x 100

RECEIVER OPERATING CHARACTERISTIC CURVE: An ROC curve is a plot of test sensitivity (plotted on the y axis) versus its False Positive Rate (FPR) (or 1- specificity) (plotted on the x axis) using multiple cut points. Accuracy of a diagnostic test is measured using the area under the ROC curve. The ROC curve area can take on values between 0.0 and 1.0. A test with an area under the ROC curve of 1.0 is perfectly accurate because the sensitivity is 1.0 when the FPR is 0.0. In contrast, a test with an area of 0.0 is perfectly inaccurate. The practical lower bound for the ROC curve area is then 0.5; it is called the chance diagonal. Diagnostic tests with ROC curve areas greater than 0.5 have at least some ability to discriminate between patients with and those without disease. The closer the ROC curve area is to 1.0, the better the diagnostic test

To improve its performance ROC curve is used to estimate sensitivity at a fixed FPR. This measure of accuracy allows us to focus on the portion of the ROC curve that is of clinical relevance. This is what we have done in this study.

RESULTS:

Age group	Benign	%	Malignant	%	Total
20-29	5	83.3	1	16.6	6
30-39	10	58.8	7	41.2	17
40-49	12	70.5	5	29.4	17
50-59	3	75	1	25	4
60-69	1	14.3	6	85.7	7
Total	31	60.8	20	39.2	51

Table 1: Age Distribution of Benign and Malignant Breast Lesions

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Fig. 1

Fig. 2

Lesion histopathology	Number	%
Duct ectasia	2	3.9
Fibrocystic disease	11	21.6
Fibroadenoma	4	7.8
Galactocoele	1	2.0
Granulomatous mastitis	1	2.0
Infiltrating duct ca	19	37.3
Lipoma	2	3.9
Breast abscesses	1	2.0
Paget's disease of nipple	1	2.0
Phyllodes tumour	2	4.0
Scar	6	11.8
Seroma	1	2.0
Total	51	100.0

Table 2: Spectrum of lesions

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SIGNAL ON T1WI:

	Benign	%	Malignant	%
Hyperintense	2	6.5	0	0
Hypointense	29	93.5	18	90
Isointense	0	0	2	10

Table 3: Frequency of signal of lesions on T1WI

Fig. 3

SIGNAL ON T2WI:

	Benign	%	Malignant	%
Hyperintense	25	80.6	1	5.0
Hypointense	1	3.2	1	5.0
Intermediate	5	16.1	18	90.0
TOTAL	31		20	

Table 4: Frequency of Signal Intensity of Lesions on T2WI

Fig. 4

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DIFFUSION WEIGHTED IMAGING:

Fig. 5

	Benign	%	Malignant	%
No	28	90.3	0	0
Yes	3	9.7	20	100
TOTAL	31	100	20	100

Table 5: Frequency distribution of lesions (HPR diagnosis) on DWI

HPR	Benign	%	Malignant	%
MRI diagnosis				
Benign	29	93.5	0	0
Malignant	2	6.5	20	100
TOTAL	31		20	

Table 6: Correlation between MRI diagnosis and gold standard (HPR)

By non-contrast MRI using T1WI, T2WI and DWI, 100% of malignant lesions were correctly identified as malignancies, whereas 6.5% benign lesions were also incorrectly diagnosed as malignancy, thus conferring a sensitivity of 100% and specificity of 93.5% for the test.

Fig. 6

Area under the curve was 96.5%, (was found to be statistically significant- p value of <0.001), A cutoff of 1.255 was found to be the optimum with sensitivity of 100% and specificity of 93.5%. 100% of malignant lesions in the study had ADC value less than 1.255. Among benign lesions, 93.5 % had ADC value >1.255.

Validity parameter	Value
Sensitivity	100%
Specificity	93.5%
Positive predictive value	90.9%
Negative predictive value	100%

Table 7: Validity parameters on using ADC cut-off value of $1.255 \times 10^{-3} \text{ mm}^2/\text{s}$

	Number	Mean ADC value ($\times 10^{-3} \text{ mm}^2/\text{s}$)	Standard Deviation
Malignant	20	1.13	0.0704
Benign	31	2.08	0.4363

Table 8: mean ADC value

CONCLUSIONS:

1. Diffusion Weighted Imaging at b 0, 600 is useful to differentiate between benign and malignant lesions of breast.
2. According to this study an ADC value cut off of 1.255 can be used to differentiate between benign and malignant lesions at b value of 0 and 600 with good sensitivity and specificity.

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3. There is considerable overlap between lesions in T1 signal hence can-not help in differentiating benign and malignant lesions.
4. T2WI can be help to differentiate between benign and malignant lesions. Malignant lesions are more often hypointense or intermediate signal, while benign lesions are mostly hyperintense, though some overlap can occur in this criterion.
5. DWI is useful in follow up of post-operative or irradiated breast to look for recurrent disease.

DISCUSSION: The study evaluated 51 breast lesions with Non Contrast MR Mammography using T1WI, T2WI and Diffusion weighted imaging. Just over 1/3rd of the malignant lesions were in the age group 30-39 years. The maximum proportion of malignant lesions was seen in the age group 60-69 years (85.7% of breast lesions detected in the age group were malignant) and the minimum proportion in 20-29 years (16.6%); i.e., the distribution of malignant lesions increased with increasing age. Maximum number of benign lesions was seen in the age group 40- 49 years while maximum proportion of benign lesions were detected in the age group 20-29 years (83.4%). Most common benign lesion detected in the study was uncomplicated fibrocystic disease and most common malignant lesion was infiltrating duct carcinoma.

SIGNAL INTENSITY ON TIWI: Both benign and malignant lesions showed similar signal on non-contrast T1WI, hence benign and malignant lesions could not be differentiated using T1WI. Non contrast T1WI is useful in demonstrating high signal hemorrhagic cysts and high protein containing cysts as well as high signal within dilated ducts.

SIGNAL INTENSITY ON T2WI: This study showed that 90% malignant lesions showed intermediate signal on T2WI, and 5% appeared hypointense. Thus sensitivity of T2WI to detect malignant lesions was found to be 95%, specificity being 80.6%. This is in accordance with studies conducted by Kuhl et al,⁽¹⁾ in which majority (87%) malignant lesions were isointense or hypointense on T2WI. Malich et al,⁽²⁾ concluded that most malignant lesions were hypointense on T2WI. Buadu et al studied 54 cases, of which 57% tumours showed iso to hyperintensity, rather than iso to hypointensity. Certain histopathological variants like mucinous and medullary carcinoma have been reported to have hyperintense signal on T2WI, and may also be well defined simulating radiological appearance of benign fibroadenoma. All of the malignant lesions evaluated in the study were infiltrating duct carcinoma, hence the high sensitivity of T2WI.

DIFFUSION WEIGHTED IMAGING AND ADC VALUE: In this study, all malignant lesions showed diffusion restriction, conferring 100% sensitivity. The specificity of DWI to detect malignancy was found to be 90.3%.

However three histopathologically proven benign lesions (viz one case each of breast abscess, phyllode's tumour and granulomatous mastitis) showed diffusion restriction.

A case of phyllodes tumour, which appeared hypointense in T1WI, intermediate signal in T2WI with multiple cystic areas, showed diffusion restriction (ADC value of $1.18 \times 10^{-3} \text{ mm}^2/\text{s}$) was reported as malignant by MRI, however turned out to be benign by histopathological examination. MR features which help to identify malignant phyllodes tumour are size >3cm, irregular cyst wall, tumour signal less than normal tissue on T2WI, hyperintensity on T1WI, and low ADC value. However

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Liberman et al,⁽³⁾ have found significant overlap in the MR characteristics of benign and malignant phyllodes tumour.

A case of granulomatous mastitis, which appeared hypointense in T1WI, intermediate signal in T2WI with illdefined borders and diffusion restriction (ADC value $1.35 \times 10^{-3} \text{ mm}^2/\text{s}$) was erroneously classified as malignant. Granulomatous mastitis is a very rare breast inflammatory disease of unknown origin that can clinically and radiologically mimic carcinoma breast.

However a case of breast abscess, though showed diffusion restriction (ADC value $1.05 \times 10^{-3} \text{ mm}^2/\text{s}$), was correctly diagnosed as benign by virtue of T2 signal (hyperintense) and multiplicity. Abscesses can show central diffusion restriction due to high cellularity and viscosity of pus.⁽⁴⁾

The mean ADC for malignant lesions was $1.13 \times 10^{-3} \text{ mm}^2/\text{s} \pm 0.07 \text{ mm}^2/\text{s}$. ROC curve was plotted and area under the curve was 96.5%. Since the purpose of the study was to identify true positives, i.e. all malignancies, a cutoff value with high sensitivity was selected. An ADC threshold of $1.255 \times 10^{-3} \text{ mm}^2/\text{s}$ to differentiate between benign and malignant gives 100% sensitivity and 93.5% specificity, with a PPV of 90.9% and NPV of 100%.

A similar study by Partridge et al,⁽⁵⁾ at b value of 0, 600 revealed mean ADC value of malignant lesions $1.29 \pm 0.29 \times 10^{-3} \text{ mm}^2/\text{s}$. To attain 100% sensitivity to detect malignant lesions, positive predictive value was found to be 47%, with a 100% negative predictive value. The cutoff value of ADC to differentiate between benign and malignant lesions as per this study was $1.81 \times 10^{-3} \text{ mm}^2/\text{s}$.

Sana Parsian et al,⁽⁶⁾ evaluated 175 benign lesions with DWI, calculated ADC values at b 0, 600. The mean ADC value of the benign lesions in was $1.77 \pm 0.45 \text{ mm}^2/\text{s}$

Partridge et al, ⁽⁵⁾		Present study	
Benign	Malignant	Benign	Malignant
1.70±0.44	1.29±0.29	2.08±0.43	1.13±0.07

Table 7.1: Table comparing mean ADC values of breast lesions ($\times 10^{-3} \text{ mm}^2/\text{s}$) of present study and previous study

Partridge et al, ⁽⁵⁾	Present study
1.81	1.255

Table 7.2: Table comparing ADC threshold ($\times 10^{-3} \text{ mm}^2/\text{s}$) of present study and previous study

Validity parameter	Partridge et al, ⁽⁵⁾ %	Present study %
Positive predictive value	47	90.9
Negative predictive value	100	100

Table 7.3: Table comparing validity parameters of present and previous study for a sensitivity of 100%

F Kelcz et al,⁽⁷⁾ in a study evaluating cases of post lumpectomy irradiated breast have found a mean ADC value of 1.89 (range 1.43–2.20). These findings are well correlating with our study - there were 6 cases, all of which showed unrestricted diffusion. Mean value obtained is 2.26 (range 1.95- 2.26).

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These results are in concordance with findings of Palle lalitha et al,⁽⁸⁾ on 200 patients with breast lesions using MR Mammography with DWI at b value of 0, 500, 1000. According to this study, the sensitivity of ADC values for the detection of malignant lesions was 97.22% and the specificity was 100% and the positive predictive value was 100% and the negative predictive value was 99%.

Zhang Yili et al,⁽⁹⁾ on evaluating 57 breast lesions, the threshold value of ADC to differentiate benign and malignant lesions at b-1000 was $1.20 \pm 0.25 \times 10^{-3} \text{mm}^2/\text{s}$. They found that ADC values of malignant lesions were statistically much lower than benign lesions and peritumoral tissues.

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CASE 1: Well defined smooth margined lesion in right breast which appears hypointense in T1WI and hyperintense in T2WI, with no diffusion restriction, ADC value 1.96×10^{-3} .

HPE showing showing proliferation of intralobular stroma compressing and distorting the epithelium – Fibroadenoma.

Figure 1

CASE 2: Multiple lobulated mixed signal intensity lesions, predominantly hypointense in T1WI and intermediate signal in T2WI with multiple cystic areas which had smooth regular walls, some areas of hyperintensity in T1WI suggestive of hemorrhage were seen within the larger lesion. Diffusion restriction was seen. ADC value – 1.18×10^{-3} .

HPR- Leaf like projections seen into dilated lumen. Increased stromal cellularity also seen Benign phyllodes tumor-Benign Phyllodes tumour.

Figure 2

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CASE 3: Irregular spiculated mass in right breast appearing hypointense in T1WI, hypointense in T2WI, with diffusion restriction. ADC value $0.933 \times 10^{-3} \text{ mm}^2/\text{s}$. HPR- infiltrating duct carcinoma.

Figure 3

CASE 4: 32 year old lady with complaints of right breast lump .There is a mixed solid cystic lesion in right breast with solid areas appearing hypointense in T1WI, intermediate signal in T2WI, with significant diffusion restriction. ADC value is 1.18×10^{-3} . Cystic areas appear hyperintense in T1 and T2WI. - Infiltrating duct carcinoma.

Figure 4

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CASE 5: Paget's disease of nipple -A subareolar lesion hypointense in T1WI, isointense in T2WI, with diffusion restriction ADC Value 1.16×10^{-3} .

Figure 5

CASE 6: Case of stage I IDC left breast post lumpectomy and RT 2years back, on follow up. MRI shows diffuse skin thickening of left breast which appears hypointense in T1WI, intermediate signal in T2WI, with no diffusion restriction, ADC value 2.4×10^{-3} . No focal lesions seen in breast parenchyma. Architectural distortion noted in left breast - Consistent with post radiation changes.

Figure 6

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