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ORIGINAL RESEARCH

Role of diffusion weighted imaging in characterisation of breast masses

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ABSTRACT
This prospective observational study explores the role of Diffusion Weighted Imaging (DWI) in characterizing breast masses and differentiating benign from malignant lesions. The study included 54 patients with 59 breast lesions, who met the inclusion criteria based on X-ray mammography and/or sonomammography. The aim was to assess the utility of DWI, measured via the apparent diffusion coefficient (ADC) values, in distinguishing between benign and malignant lesions. The results indicate that malignant lesions exhibit significantly lower ADC values than benign lesions. An optimal ADC threshold of 0.998 × 10^-3 mm²/s for minimum ADC values and 1.209 × 10^-3 mm²/s for mean ADC values were identified, demonstrating high sensitivity (92% and 96%, respectively) and specificity (94% and 91%, respectively). The findings suggest that DWI, particularly ADC value analysis, can be a reliable diagnostic tool in differentiating benign from malignant breast lesions, offering high diagnostic accuracy with minimal reliance on contrast media, and is especially beneficial for patients with contraindications to contrast agents.

Key words: Diffusion weighted imaging, breast masses, apparent diffusion coefficient, benign lesions, malignant lesions, MRI, breast cancer, sensitivity, specificity, ADC threshold

INTRODUCTION

Conventional MRI sequences, although have a major role in the differential diagnosis of breast lesions it has a low specificity. Diffusion-weighted imaging (DWI) is an active field of research for evaluating breast lesions. Diffusion can be quantified by measuring the apparent diffusion coefficient (ADC) value. Recent studies have shown that DW-MRI and ADC measurements have a high accuracy rate in differentiating benign and malignant lesions.

Hence, the aims of this study are to assess the role of DWI in differentiating benign from malignant breast lesions and to propose a cut-off ADC value for differentiating benign from malignant breast lesions.

METHODOLOGY: This prospective observational study was done for a period of 10 months. Both inpatients and outpatients who satisfy the inclusion and exclusion criteria were included in this study.

INCLUSION CRITERIA

1. Patients with breast masses of size more than 1 cm which fall under BIRADS-3, 4 or 5 after undergoing X-ray mammography and/or sonomammography.
2. Patients who will subsequently undergo biopsy of the breast mass.

EXCLUSION CRITERIA

1. Patients who fall under BIRADS-1 and 2.
2. Patients with mass lesions < 1.0 cm in size were excluded because the measurement of ADC values is difficult in such small lesions, due to difficulty in placement of a region of interest (ROI) entirely within the lesion.
3. Benign cysts, because they do not present a diagnostic difficulty and their high ADC would artificially increase the mean and range of benign values.
4. Neoadjuvant treatment before MRI, which could cause an increase in the ADC values.

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5. Patients with general contraindication to MRI such as claustrophobia, those with pace makers, cochlear implants and other electromagnetic implants in body.

Statistical analysis was performed with **SPSS** (Statistical Package for Social Sciences) software (Version 16). The t-test was used to calculate the significance of differences in the ADC values between benign and malignant lesions. A p-value of <0.05 was considered as significant. ROC curves were used to determine the ADC cut-off values.

RESULTS

Total number of patients included in our study were 54, with 59 breast lesions in the age group range of 17 to 70 years. Most common age group was 41-50 years. The results of our study are summarised below:

- Size of the lesions include were in the range of 1-7.5 cm.
- There were 34 benign lesions (58%) and 25 malignant lesions (42%).
- Of the total 34 benign lesions, 28 lesions were fibroadenoma.
- All the 25 malignant lesions were invasive ductal carcinoma.
- The mean ADC value of benign lesions were as follows (x 10^{-3} mm^2/s): fibroadenoma 1.536 ± 0.33, fibroadenolipoma 1.870 ± 0.66, fibrocystic disease 1.459, phylloides 2.423, abscess 0.489, mastitis 1.266. There was significant overlap between the ADC values of different types of benign lesions.
- The mean of minimum ADC values of benign lesions was 1.387 ± 0.383x 10^{-3} mm^2/s. The mean of minimum ADC values of malignant lesions was 0.830 ± 0.162 x 10^{-3} mm^2/s. The mean of minimum ADC values was significantly lower than that of benign lesions (p value < 0.001).
- The mean of mean ADC values of benign lesions was 1.541 ± 0.413 x 10^{-3} mm^2/s. The mean of minimum ADC values of malignant lesions was 0.940 ± 0.117 x 10^{-3} mm^2/s. The mean of minimum ADC values was significantly lower than that of benign lesions (p < 0.001).
- By ROC analysis of minimum ADC values, of benign and malignant lesions, an ADC cut-off of 0.998 x 10^{-3} mm^2/s was able to differentiate benign and malignant lesions with a sensitivity of 92% and a specificity of 94%. Positive predictive value was 92% and negative predictive value was 94%.
- By ROC analysis of mean ADC values, of benign and malignant lesions, an ADC cut-off of 1.209 x 10^{-3} mm^2/s was able to differentiate benign and malignant lesions with a sensitivity of 96% and a specificity of 91%. Positive predictive value was 88.9% and negative predictive value was 96.9%.

DISCUSSION

Breast MRI is a widely accepted diagnostic approach for evaluating the breast. To improve the sensitivity of detecting breast cancer, many diverse techniques are used for breast MRI. Dynamic contrast-enhanced MRI is useful in evaluating multiple foci of carcinoma in the breast and it displays extremely high sensitivity for identifying breast cancer. However, dynamic-enhanced breast MRI has some disadvantages like being time-consuming and costly, the possible side effects of the contrast media, and the relatively low specificity compared to mammography and ultrasonography [1].

The essential concept behind detecting malignancy with quantitative diffusion imaging is that malignant breast lesions have significantly lower ADCs than benign breast lesions [2,3]. This is due to increased tumor cellularity in malignant lesions, which restricts diffusion. Diffusion restriction is manifested by bright signal on diffusion weighted images and dark signal on corresponding ADC map.

Some recent studies showed the effectiveness of DWI for differentiating malignant from benign lesions (2-16). Consistent with these studies, malignant breast lesions revealed significantly lower ADC values than benign lesions in our study. The mean ADC of malignant lesions was 0.940 x 10^{-3} mm^2/sec and that of benign lesions was 1.529 x 10^{-3} mm^2/sec (significance< 0.001).

We calculated the mean of minimum ADC of benign and malignant lesions, which were 1.387 x 10^{-3} mm^2/sec and 0.830 x 10^{-3} mm^2/sec respectively (significance< 0.001). This was close to the mean of minimum ADC in studies conducted by Hirano *et al*. and Kul S *et al.*[4,15].

We calculated the optimal threshold for mean ADC value between benign and malignant lesions using ROC analysis, which was 1.029 x10^{-3} mm^2/sec. Lesions showing an ADC value greater than this threshold value were characterized as benign and those with lower ADC values were characterized as malignant. This ADC threshold value can differentiate benign and malignant lesions with a sensitivity of 96%, specificity of 91.2%, positive predictive value of 88.9% and negative predictive value of 96.9% which is close to similar other studies [17, 8].

The optimal threshold for minimum ADC value between benign and malignant lesions was also calculated using ROC analysis, which was 0.998 x 10^{-3} mm^2/sec. This ADC threshold value can differentiate benign and malignant lesions with a sensitivity of 92%, specificity of 94% positive predictive value of 92% and negative predictive value of 94%. This sensitivity and specificity of minimum ADC value was close to similar other studies [4,14].

The optimal mean and minimum ADC thresholds were calculated such that both sensitivity and specificity were optimized. In our study the sensitivity of mean ADC threshold (96%) was higher than the minimum ADC threshold (92%). But the specificity

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of minimum ADC threshold (94%) was higher than the minimum ADC threshold (91.2%).

With the mean ADC threshold value (1.209 x 10^{-3} mm^2/sec), only one lesion was false negative for malignancy. It showed an ADC of 1.215 x 10^{-3} mm^2/sec, which is greater than the mean ADC threshold value and so it was falsely characterized as benign lesion. Histopathological analysis proved it to be malignant. With this threshold, three lesions showed false positive for malignancy. Their mean ADC values were less than the threshold and so they were falsely characterized as malignant lesions. Two of these lesions were fibroadenomas and one lesion was abscess which showed the lowest mean ADC value (0.489 x 10^{-3} mm^2/sec) in our study.

With the minimum ADC threshold value (0.998 x 10^{-3} mm^2/sec), two lesions showed false negativity for malignancy. They showed ADCs of 1.166 x 10^{-3} mm^2/sec and 1.103 x 10^{-3} mm^2/sec,which are greater than the minimum ADC threshold value and so they were falsely characterized as benign lesions. Histopathological analysis proved them to be malignant lesions.

With this minimum ADC threshold, two lesions showed false positive for malignancy. Their mean ADC values were less than the threshold and so they were falsely characterized as malignant lesions. The lesions were histopathologically proved to be abscess and chronic mastitis.

In our study, inflammatory lesions like abscess and mastitis formed the common false positive lesions for malignancy, due to significant diffusion restriction in these lesions. Since our study included only two inflammatory lesions, studies with larger populations should be done, for documentation of the effect of DWI in the differentiation of benign inflammatory and malignant lesions.

Though DWI shows high sensitivity and specificity, it has some limitations too. It has low geometric resolution, a large field field of view requirement and limited matrix size, which limits detectability of small lesions. For optimal lesion localization and ROI placement on ADC maps, synchronization with contrast-enhanced images and diffusion weighted images may be helpful.

Table 1: Comparison of our study with other studies

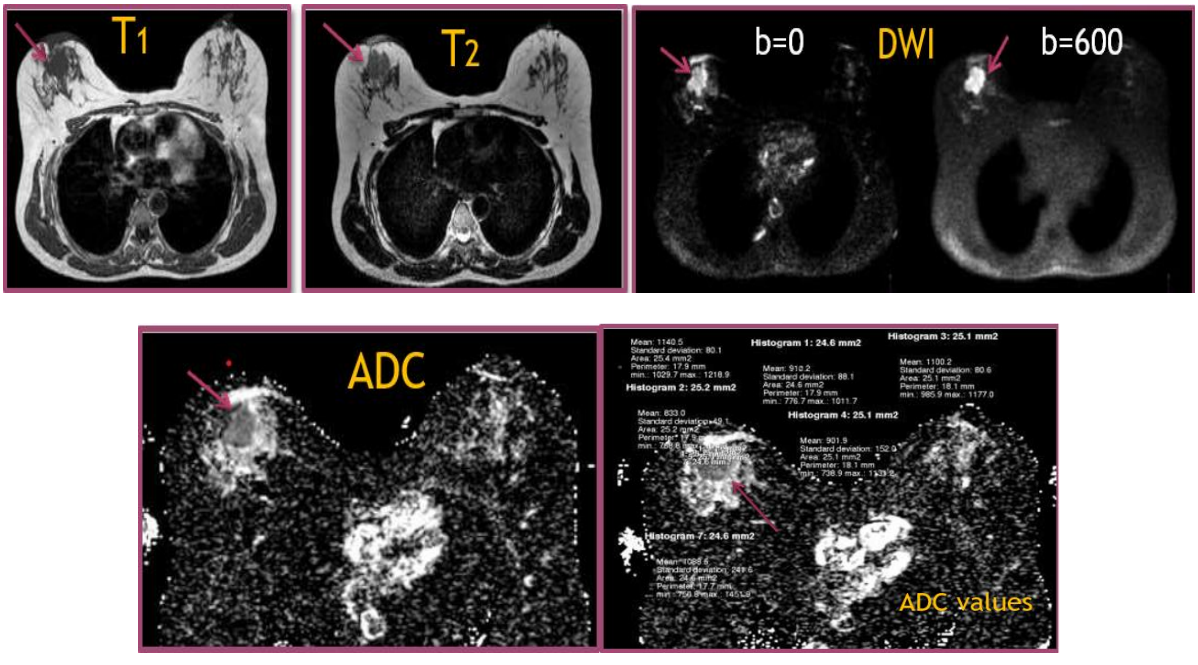
Authors	Baltzer (18)	Marini (19)	Woodhams (20)	Guo (2)	Jin (21)	Li (22)	Our study
b-values	0, 750, 1000	0, 1000	0, 750	0, 1000	0, 600	0, 1000	0,600
Mean ADC of malignant	1.05 ± 0.33	0.95 ± 0.18	1.22 ± 0.31	0.97 ± 0.20	1.33 ± 0.36	1.21 ± 0.26	0.940 ± 0.117
Mean ADC of benign	1.63 ± 0.42	1.48 ± 0.37	1.67 ± 0.54	1.57 ± 0.23	1.82 ± 0.31	1.49 ± 0.43	1.541 ± 0.413
Threshold(cut-off)	1.23	1.10	1.60	1.30	1.44	1.42	1.21

CASE 1

Right breast shows T1& T2 hypointense lesion,
Hyperintense on DWI and hypointense on ADC (Diffusion restriction).

Maximum ADC-1.140 x $10^{-3}$$mm^2$/s
Mean ADC-0.995 x $10^{-3}$$mm^2$/s.
Minimum ADC-0.833 x $10^{-3}$$mm^2$/s.
HPE-Invasive ductal carcinoma.

CASE 1 FIGURES



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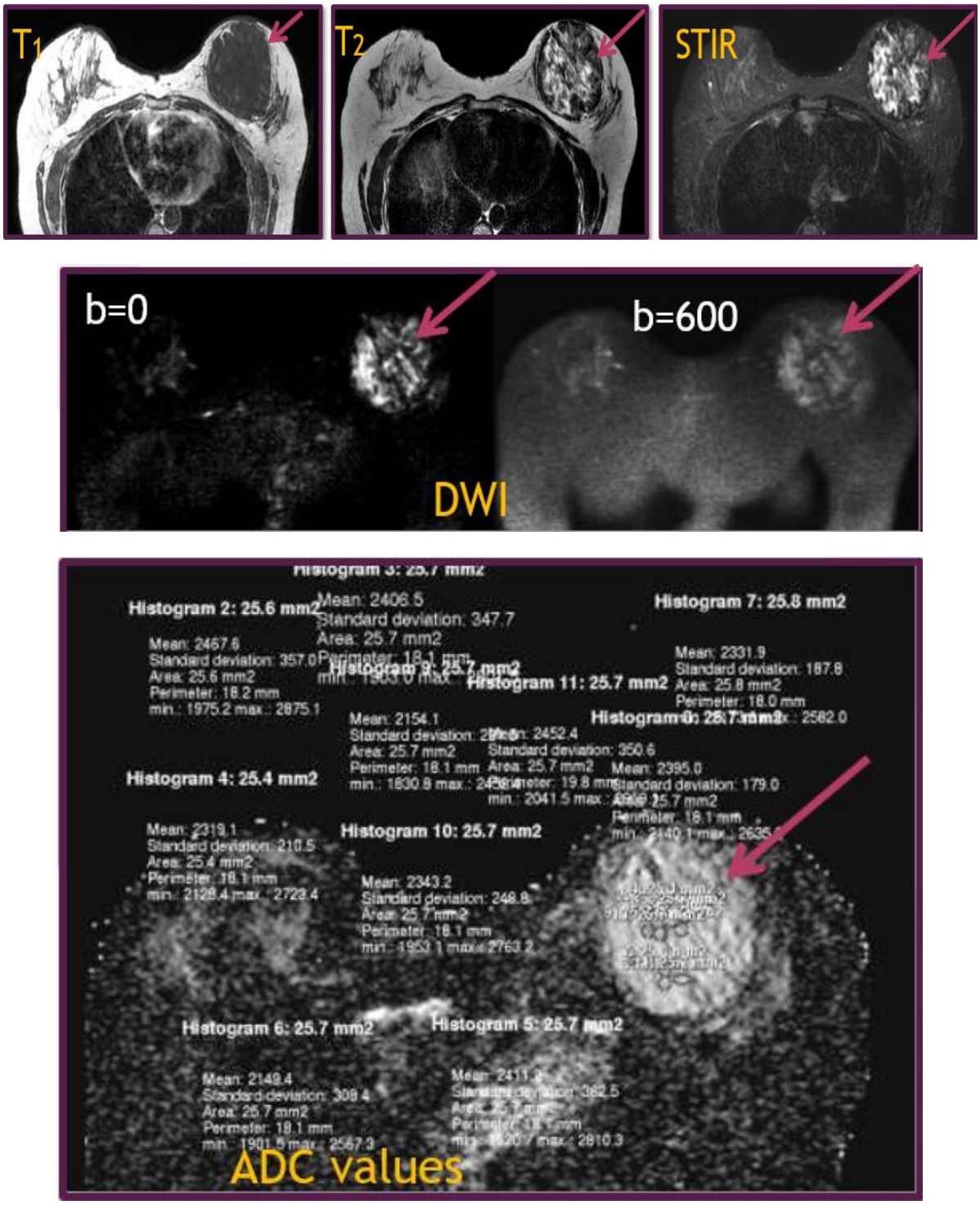
CASE 2

Left breast shows a large well-defined lesion, which is hypointense on T1, heterointense on T2 & DWI, hyperintense on ADC (no diffusion restriction).

Maximum ADC-2.467 x $10^{-3}mm^2/s$,
Mean ADC-2.342 x $10^{-3}mm^2/s$,
Minimum ADC-2.149 x $10^{-3}mm^2/s$
HPE diagnosis-Fibroadenoma.

CASE 2 FIGURES



CASE 3

Left breast shows a small well-defined lesion, Heterointense on T1&T2. The lesion shows internal fat intensities, which is suppressed on STIR (Short Tau Inversion Recovery)sequence. Shows no diffusion restriction. Maximum ADC value-1.538 x 10 -3mm2/s,
Mean ADC value-1.398 x 10 -3mm2/s. Minimum ADC value-1.258 x 10 -3mm2/s,
HPE DIASNOSIS-FIBROADENOLIPOMA.

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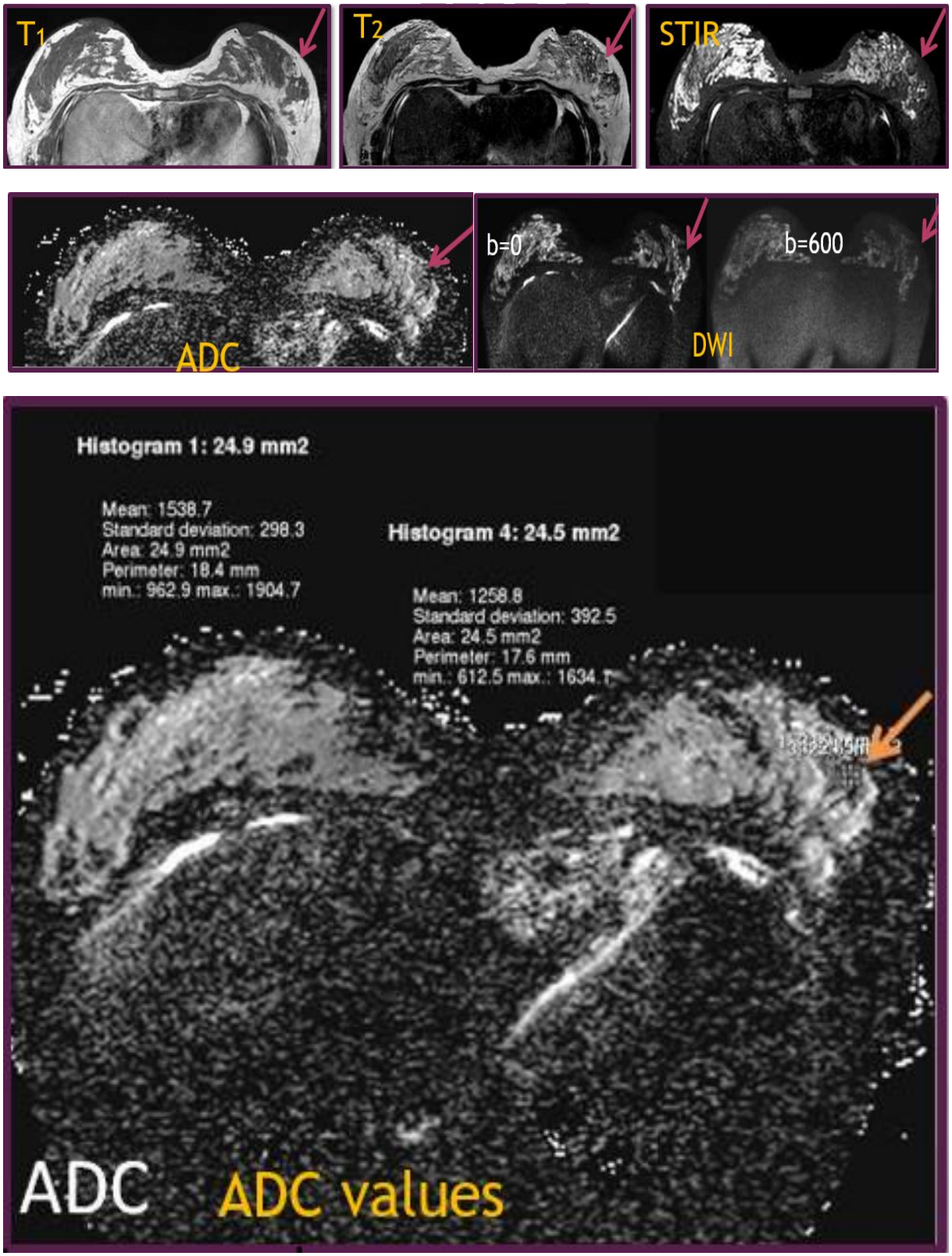
CASE 3 FIGURES



CASE 4

A case of post right mastectomy for malignancy. Left breast shows a lesion, which is hypointense on T1 & T2, hyperintense on STIR. The lesion shows diffusion restriction. Maximum ADCV value-0.726 x $10^{-3}mm^2/s$.
Minimum ADC value-0.607 x $10^{-3}mm^2/s$.
Mean ADC value-0.699 x $10^{-3}mm^2/s$.
HPE diagnosis-Invasive ductal carcinoma.

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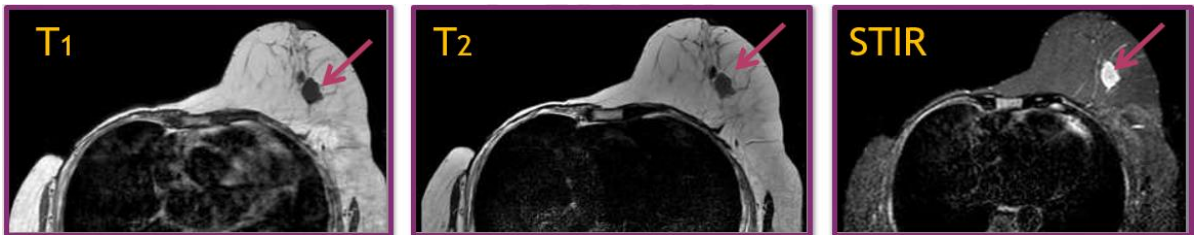
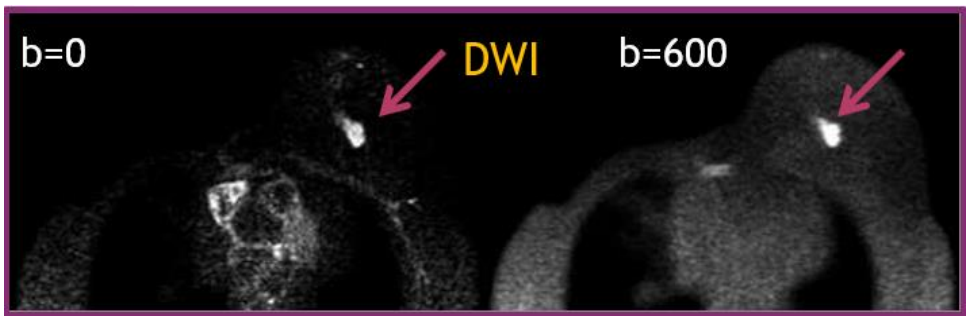
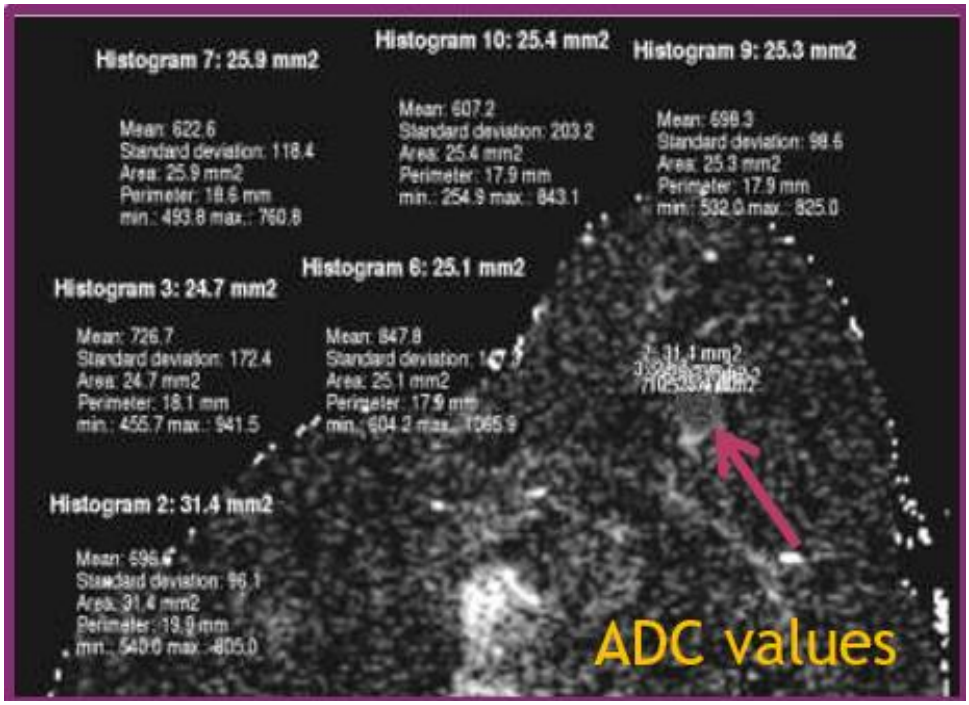
CASE 4 FIGURES







CASE 5

Right breast shows a T1 hypointense, T2 & STIR hyperintense lesion, showing severe diffusion restriction.

Maximum ADC value-0.542 x $10^{-3}mm^2/s$.
Minimum ADC value-0.441 x $10^{-3}mm^2/s$.
Mean ADC value-0.481 x $10^{-3}mm^2/s$.
HPE-Abscess.

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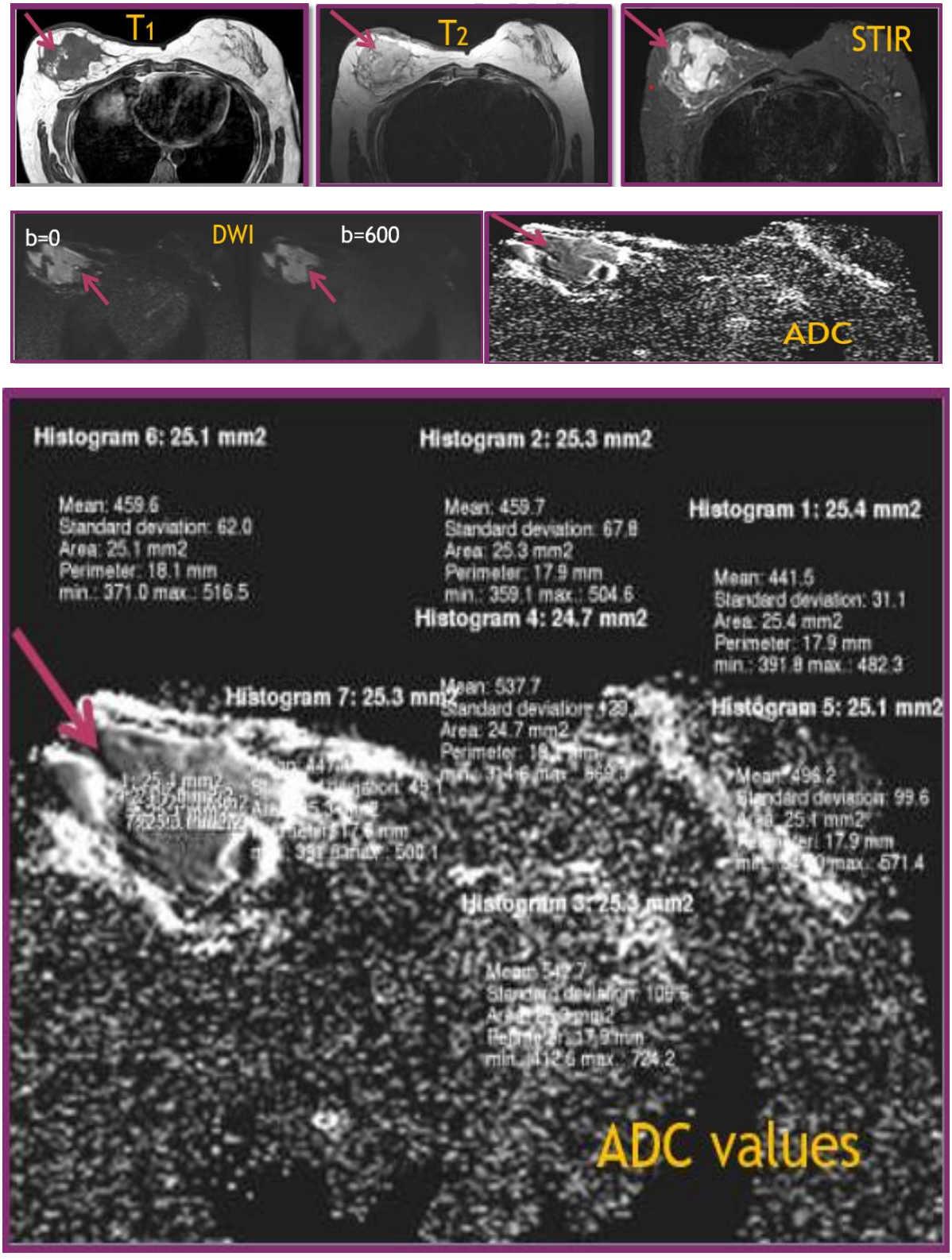
CASE 5 FIGURES



CASE 6

Left breast shows an irregular lesion, which is T1 hypointense, T2 & STIR hyperintense, showing diffusion restriction.

Maximum ADC-1.478 x 10 $^{-3}$mm^2/s.
Minimum ADC value-0.900 x 10 $^{-3}$mm^2/s.
Mean ADC value-1.120 x 10 $^{-3}$mm^2/s.
HPE-Chronic mastitis.

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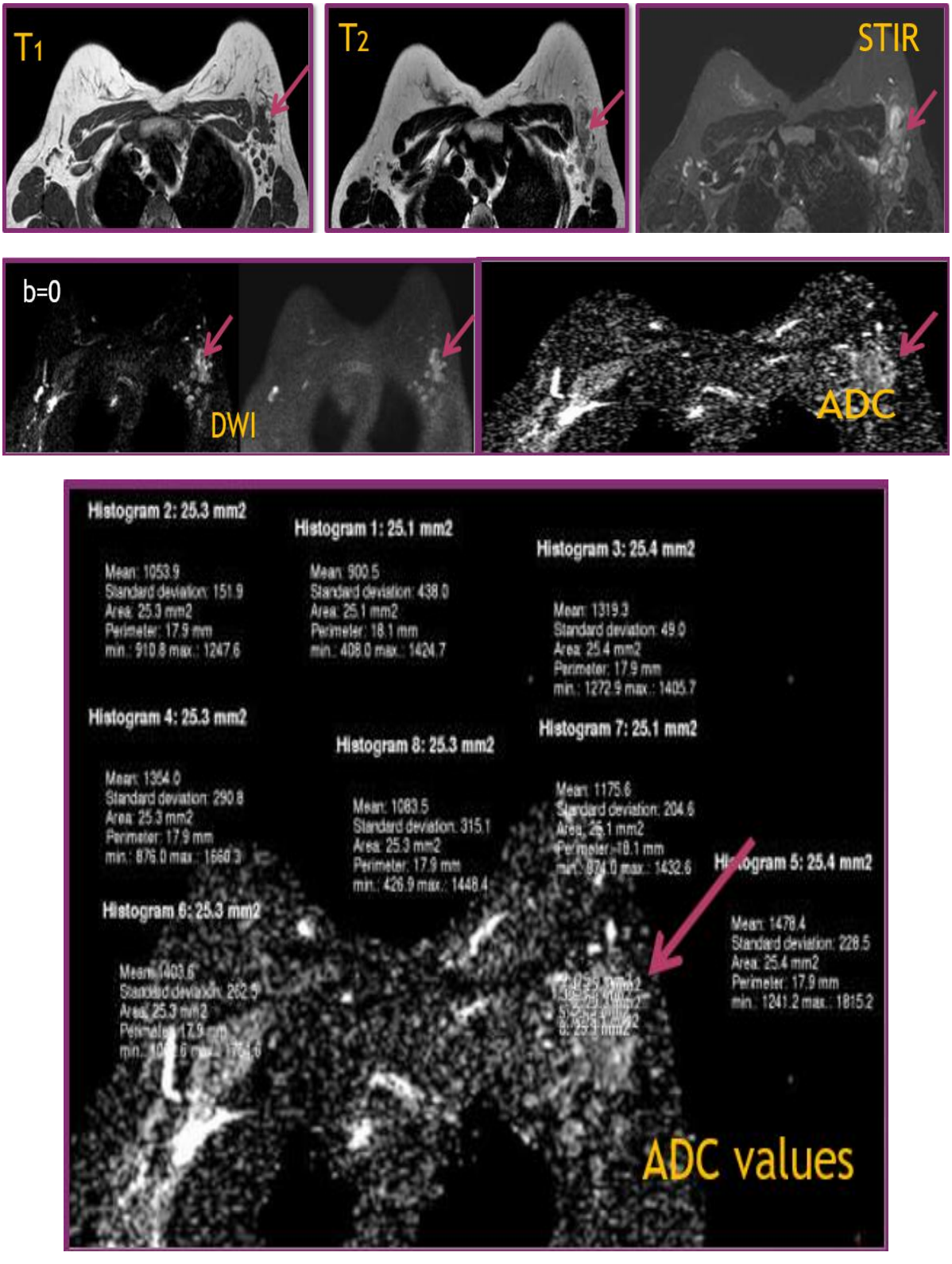
CASE 6 FIGURES



CASE 7

Left breast shows a small well-defined lesion, which is hypointense on T1, heterointense on T2 &hyperintense DWI & ADC (no diffusion restriction). The lesion shows a tiny cystic area(marked by small arrow),which is intensely hyperintense on T2,STIR,DWI& ADC(T2 shine through).This cystic area is avoided while placing the ROI.

Maximum ADC-1.697x $10^{-3}mm^2/s$.

Mean ADC-1.695 x $10^{-3}mm^2/s$.

Minimum ADC-1.693 x $10^{-3}mm^2/s$.

HPE DIAGNOSIS-FIBROADENOMA

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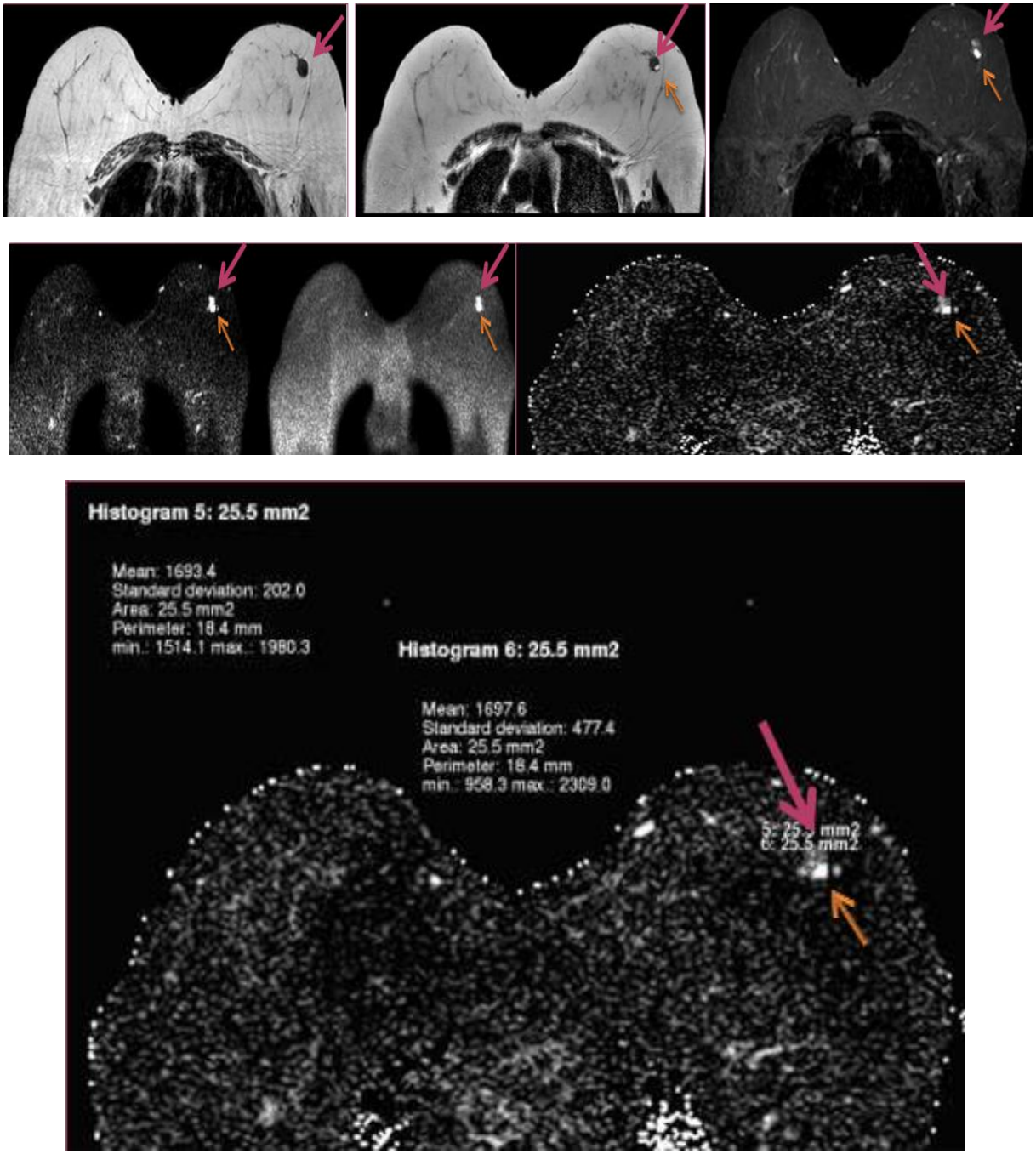
CASE 7 FIGURES



CASE 8

Two lesions seen in the same patient.

Lesion 1-In the right breast: T1, T2, STIR hypointense, isointense on DWI & ADC (No diffusion restriction).

ADC VALUES (x $10^{-3}mm^2/s$)

Max-1.413, min-1.260, mean-0.828.

HPE Diagnosis-Fibroadenoma.

Lesion 2-In the left breast: T1 hypo & T2 heterointense, STIR hypertense. Hyperintense on DWI and hypointense on ADC (Diffusion restricted).

ADC values (x 10-3mm2/s)

Max-0.887, Min-0.673, mean-0.828.

HPE-Invasive ductal carcinoma.

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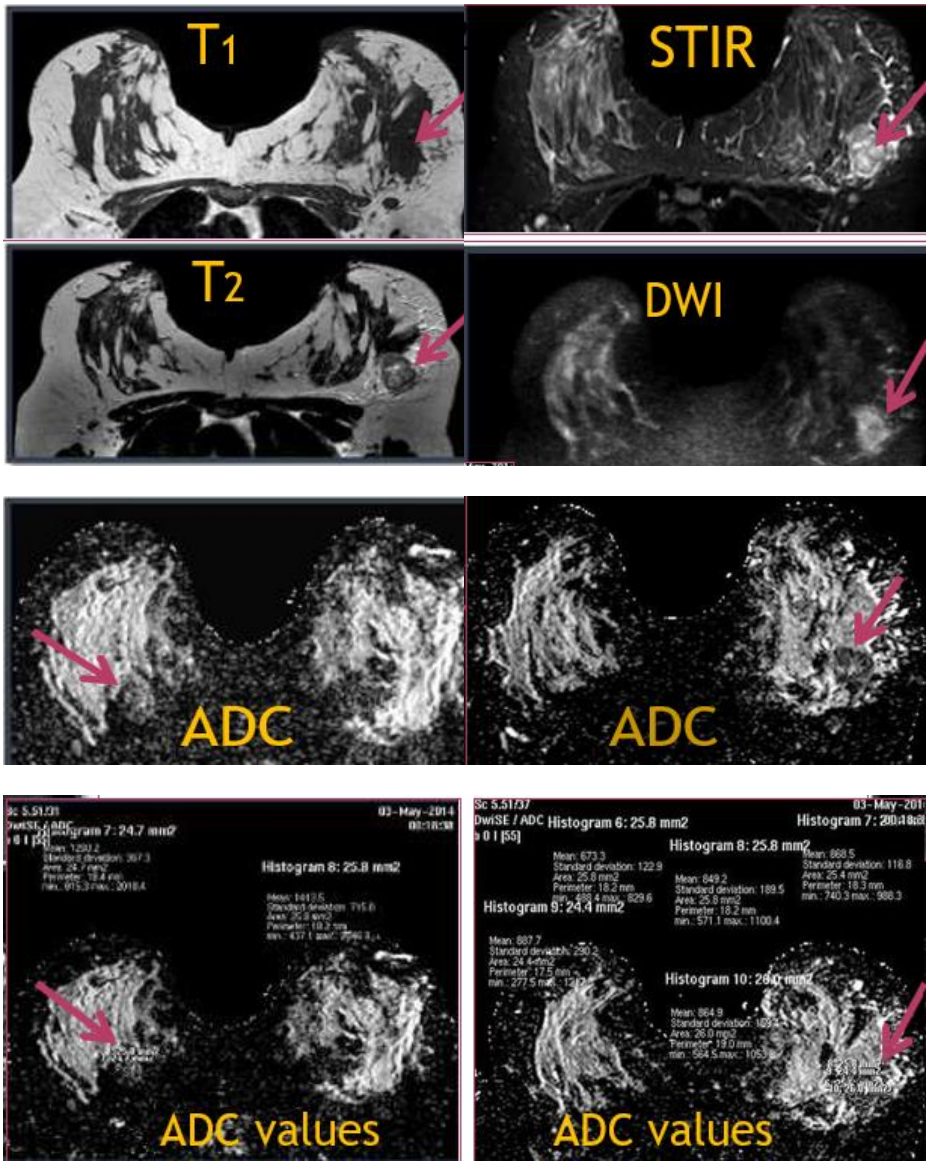
CASE 8 FIGURES



STATISTICAL ANALYSIS

A total of 54 patients (age range-17-68 yrs), with 59 breast lesions were included in our study.

Of the 59 lesions, 34 were benign and 25 were malignant.

Malignant lesions included: 23 invasive ductal carcinoma and 2 Invasive lobular carcinoma.

Benign lesions included: 28 fibroadenomas, 2 fibrodenolipoma,1 fibrocystic change,1 phyllodestumor,1 abscess & 1 chronic mastitis.

STATISTICAL ANALYSIS

TABLE 2

S. No	Lesion	No.of lesions	Mean ADC (min) value (x 10^{-3} mm^2 /s)	Standard deviation	p-value
1	Benign	34	1.387	0.383	<
2	Malignant	25	0.830	0.162	0.001

GRAPH 1

Comparing MINIMUM ADC VALUES between benign and malignant lesions.

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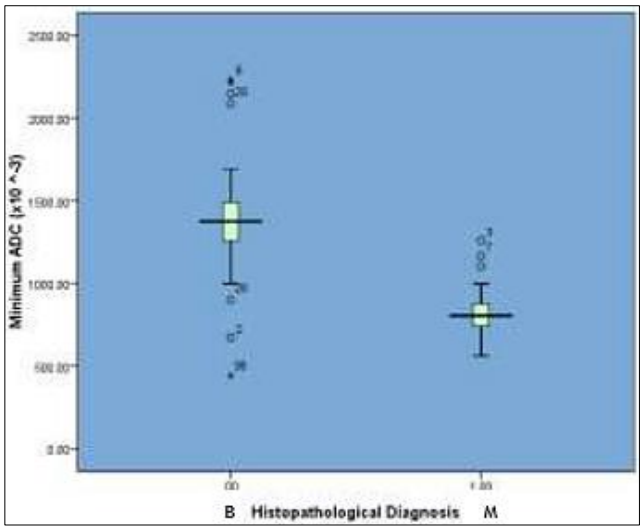
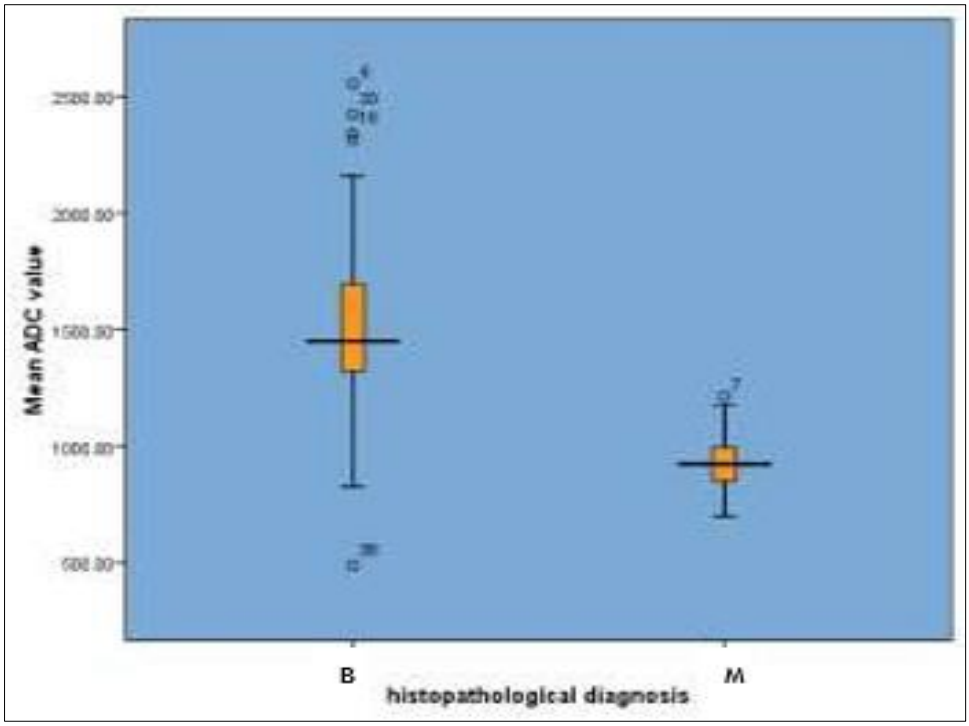


GRAPH 2

Comparing MEAN ADC VALUES between benign and malignant lesions.

The ADC Values of malignant lesions were statistically lower than the those of benign lesions.

S. No	Lesion	No.of lesions	Mean ADC value (x 10^{-3} mm^2 /s)	Standard deviation	p-value
1	Benign	34	1.541	0.413	<
2	Malignant	25	0.940	0.117	0.001



ROC CURVE ANALYSIS

Area under the curve (AUC) for mean ADC value is 96.6%.

The cut off mean ADC value, to differentiate benign and malignant lesions is 1.192 x 10-3 mm2/s, wherein the sensitivity is 96% and specificity is 94.1%.

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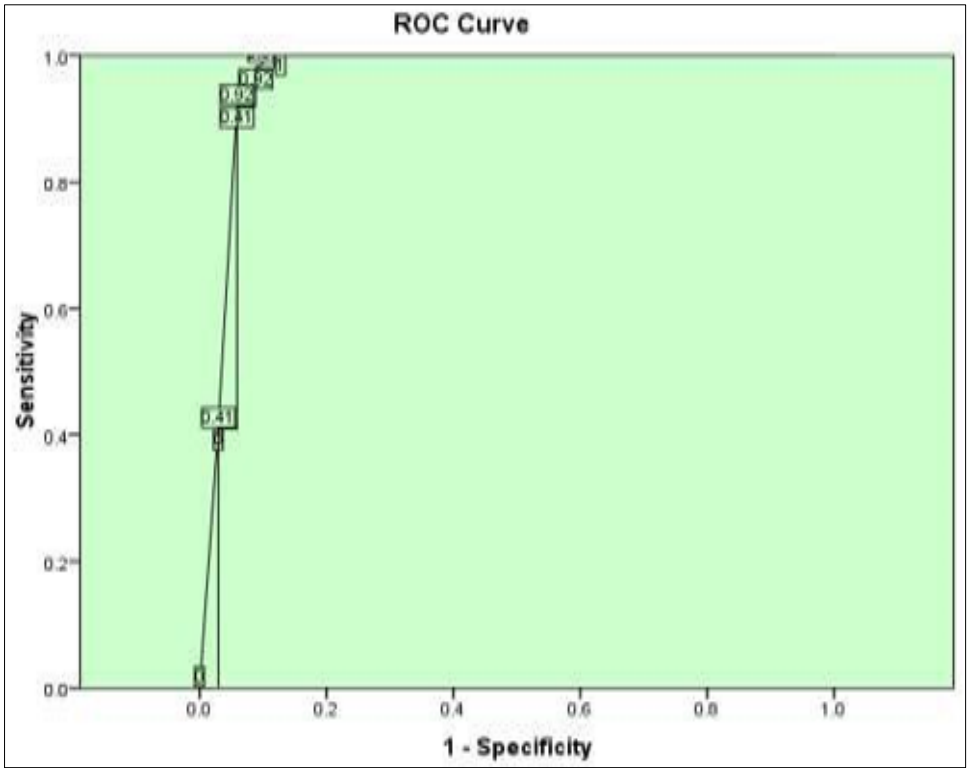
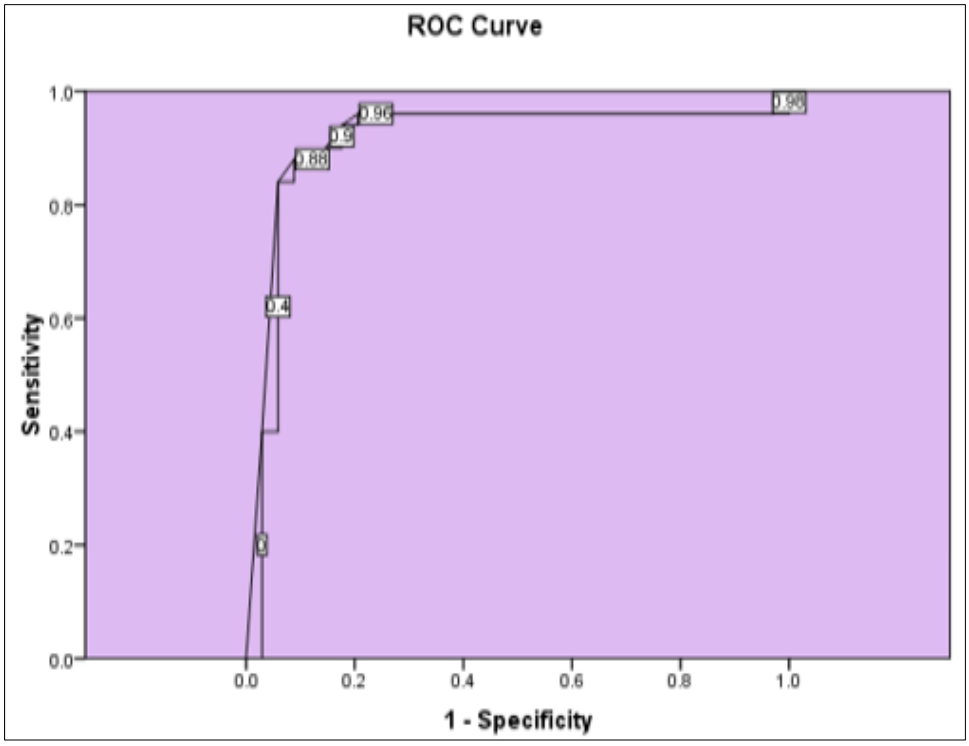
Area under the curve (AUC) for minimum value is 91.9%.

The cut off minimum ADC value, to differentiate benign and malignant lesions is 0.891x 10-3 mm2/s, wherein the sensitivity is 80% and specificity is 97%.

ROC CURVES ANALYSIS





CONCLUSION

The diagnostic performance of breast MRI can be improved by using different combined MR methods, including perfusion imaging, MR spectroscopy, diffusion-weighted imaging, and DCE-MRI. However, DWI has some important advantages for

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use in combined MRI protocols. It is available on most commercial MR scanners. It does not need secondary gadolinium use. It has a very short imaging time with the use of echo planar imaging (EPI). The evaluation of the images obtained is quantitative, using ADC values and rather easy. Our study has shown that, ADC values can differentiate between benign and malignant breast lesions with high sensitivity, specificity, positive predictive value and negative predictive value. Hence DWI can be a problem solving sequence in patients with contraindication to contrast media. However, studies with larger population are needed for more evaluation of DWI in breast lesions.

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