Section: Radiodiagnosis

Original Research Article

ROLE OF DW-MRI IN DIFFERENTIATING BENIGN AND MALIGNANT BREAST LESIONS

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ABSTRACT

Background: Aim: To evaluate the role of DW-MRI in differentiating benign and malignant breast lesions.
Materials and Methods: Fifty-five female subjects with sixty-five breast lesions underwent MR with T2W fat sat and DWI of the breasts using b (0,600) value. The computed mean apparent diffusion coefficients (ADC's) of the breast lesions were correlated with histopathology. Statistical analysis was done by independent variable t test and ROC curves.
Results: Mean ADC values of those with benign lesions was $1.47 \pm 0.21 \times 10^{-3}$ mm^2 /sec and those with malignant lesions was $0.85 \pm 0.28 \times 10^{-3}$ mm^2 /sec. There was significant difference in mean ADC between benign and malignant lesions. ADC was high in benign lesions and low in malignant lesions. By considering ADC cut off as 1.131×10^{-3} mm^2 /sec the sensitivity and specificity in the differentiating malignant from benign breast lesions was 90.48% and 95.65%, respectively.
Conclusion: DWI with ADC values is easy to obtain in short scan time and can differentiate between benign and malignant breast lesions with high sensitivity and specificity.
Keywords: MRI, Malignant breast lesions, Breast Cancer, tissues.

INTRODUCTION

Breast cancer is the most common type of tumour affecting females worldwide with its incidence increasing in India.[1] Early diagnosis and treatment can reduce the mortality and increase survival and improve quality of life. The key to survival is early detection for which accurate and precise diagnostic imaging is mandatory.

MRI is accepted as an adjuvant to mammography, ultrasonography and in high risk cases.[2] Several studies are investigating Multi-parametric MRI analysis of Breast lesions. Diffusion-weighted MRI sequence is a useful diagnostic tool since it can be obtained in short time, without use of contrast agent. DWI measures the mobility of water molecules within tissues. Diffusion can be evaluated by using apparent diffusion coefficient (ADC) values. Restriction of movement of water molecules is more in tissues with high cellularity. Malignant breast lesions have more cell density which in turn corresponds to lower ADC values. It can contribute to accurate discrimination of benign and malignant breast masses when used along with conventional MRI sequences.[3]

MATERIALS AND METHODS

This was a hospital-based time bound prospective study, conducted for a period of 18 months, from August 2016 to August 2018 in the department of Radiodiagnosis and imaging, Kasturba medical college and hospital, Manipal. Institutional ethics committee approval (IEC: 716/2016) was obtained and informed consent is taken from the patient prior to the procedure.

A total of 55 women with 65 solid breast lesions were subjected to DW-MRI of b values (0,600) and T2W fat sat sequences using Philips 1.5T MRI machine with patient in prone position. 8 channel phased array breast coil was used. On T2w fat saturated sequence lesion is confirmed to be solid

and more than 1cm. On DWI; ADC values were measured by using three point ROIs and 6 point ROIs for lesions less than 3.0 cm and more than 3.0 cm in its largest dimension respectively. The computed mean apparent diffusion coefficients of the breast lesions were correlated with histopathology.

MRI protocol: Philips MRI 1.5T Achieva, class IIA, model no 7812-96, series 16 channel system using dedicated 8-channel phased-array breast coil ; slice thickness: 2.0mm; recon voxel size: 1.75; TR(ms) : 1000; TE(ms); b-value (0,600) ; matrix : 112 x 110 ; FOV: 242mm; NEX:1; Diffusion weighting directions : 15; Imaging mode: EPI ; EPI factor:59; scan time: 4min; flip angle: 90degrees; Fat suppression :SPIR ; SAR : <10%.

Inclusion Criteria

- Solid breast lesions of more than 1 cm on T2W fat sat.
- Patients with histopathological and / or imaging follow up.

Exclusion Criteria

- Breast lesion less than 1 cm.
- Predominantly cystic/necrotic breast lesions.
- Post- operative patients / patients on neoadjuvent chemotherapy.
- Patients without histopathological and imaging follow up.

Statistical Analysis

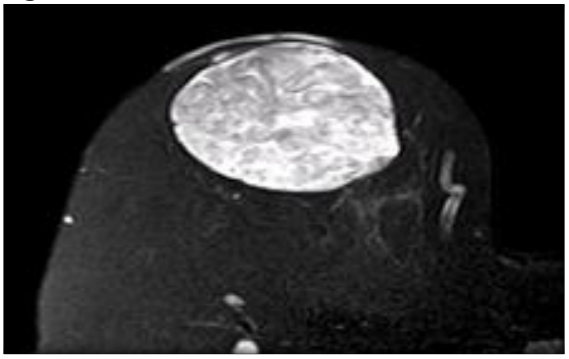
Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions whereas continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

Graphical representation of data: Microsoft Excel and Microsoft word were used to obtain various types of graphs such as bar diagram, Pie diagram and ROC curve.

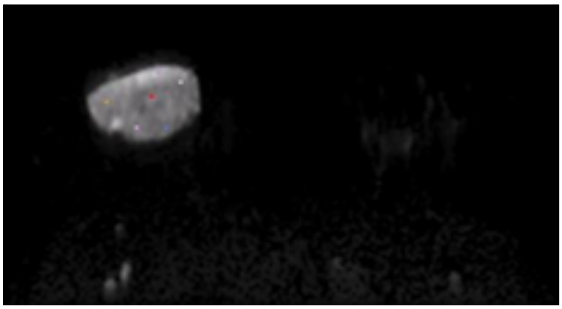
p value: (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

IMAGE GALLEY

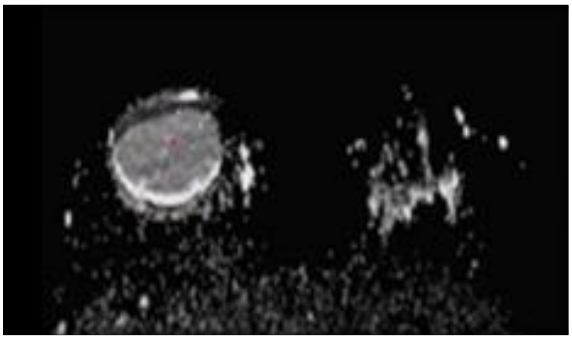
Figure 1



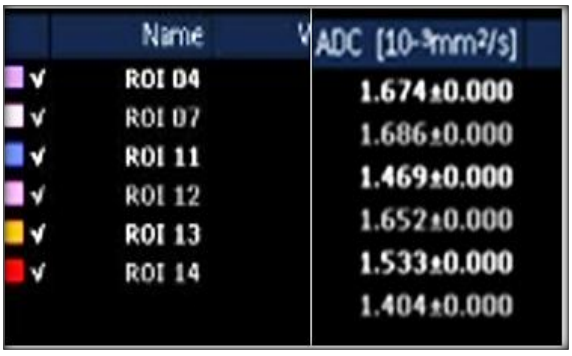
[A]. T2W fat sat showed a well-defined hyper intense lesion with smooth margins measuring more than 3.0cm.



[B]. DWI shows a low signal intensity lesion, in which 6 point ROI's are placed.

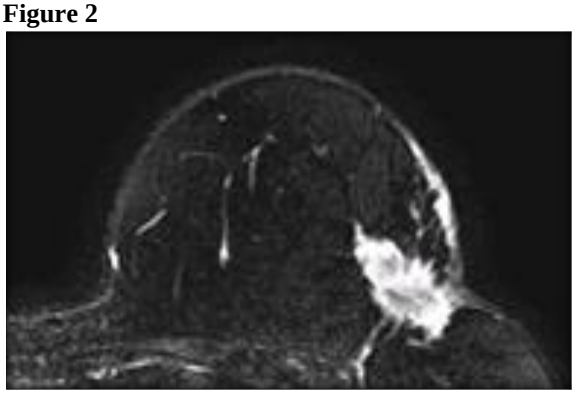


[c]. Corresponding ADC shows a low signal intensity lesion with point ROI's.
ADC values were obtained using inbuilt software and the mean was calculated.

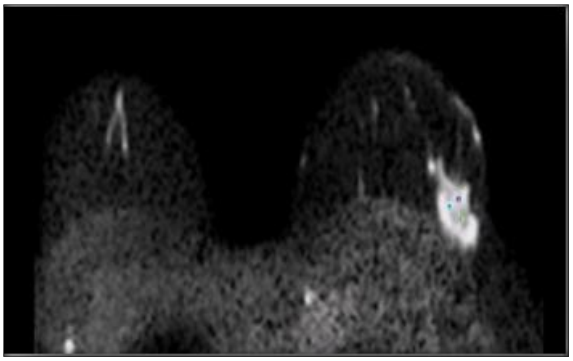


[D]. ADC values were obtained and mean was calculated, mean ADC value was found to be 1.569 x 10-3 mm2/s. (Histopathology came as fibro adenoma)

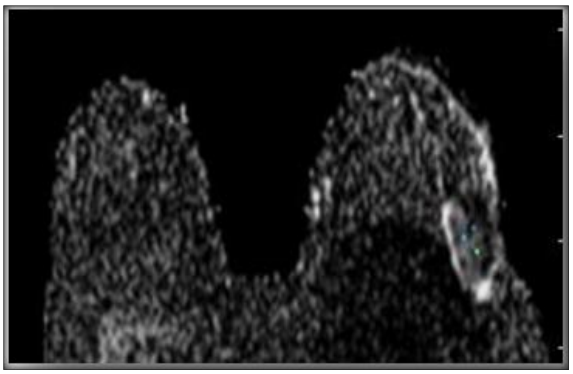
Figure 2



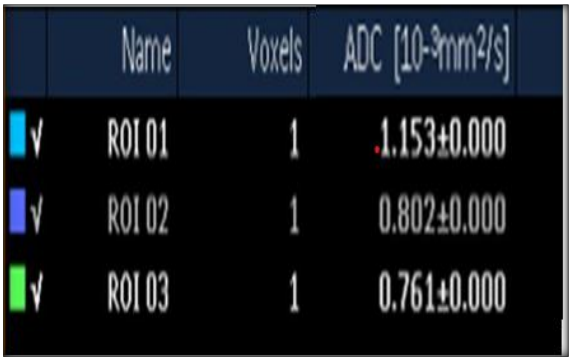
[A]. T2W fat sat showed an ill –defined heterogenous lesion with spiculated margins and measuring less than 3.0cm.



[B]. DWI shows a high signal intensity lesion, in which 3 point ROI's were placed.



[C]. Corresponding ADC showed a low signal intensity lesion with point ROI's.



[D]. ADC values were obtained and mean was calculated, mean ADC value was found to be 0.905 x 10-3 mm2/s (Histopathology came as infiltrating ductal carcinoma.)

RESULTS

In the study 55 cases with breast lesions were included. However a total of 65 lesions were studied. Few subjects had multiple lesions.

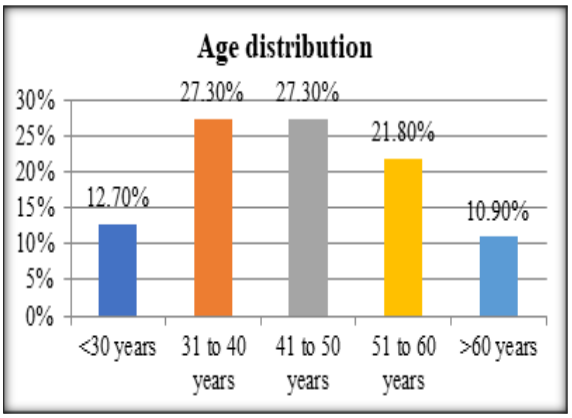


Figure 1: Bar diagram showing Age distribution of subjects

Table 1: Age distribution of subjects

Data		Count	%
Age	<30 years	7	12.7%
	31 to 40 years	15	27.3%
	41 to 50 years	15	27.3%
	51 to 60 years	12	21.8%
	>60 years	6	10.9%
	Total	55	100.0%

Mean age of subjects was 44.91 ± 12.374 years. 12.7% were in the age group <30 years, 27.3% were in the age group 31 to 40 years and 41 to 50 years respectively, 21.8% were in the age group 51 to 60 years and 10.9% were in the age group >60 years.

Table 2: Size of the lesions distribution

Data		Count	%
Size	<3 cm	46	70.80%
	>3 cm	19	29.20%

In the study 70.8% had lesions size <3 cm and 29.2% had lesion size >3 cm.

Table 3: Mean size of lesion value comparison between benign and malignant lesions

Data		Size	
		Mean	SD
Histopathology diagnosis	Benign	2.24	1.61
	Malignant	2.83	1.67
P value		0.172	

Mean Size of lesions among those with benign lesions was 2.24 ± 1.61 cm and those with malignant lesions was 2.83±1.67cm. There was no significant difference in mean size of lesion between benign and malignant lesions. Size was minimally high in malignant lesions and low in benign lesions.

Table 4: Shape of lesions distribution

Data		Count	%
Shape	Irregular	30	46.2%
	Oval	9	13.8%
	Round	26	40.0%

In the study 46.2% had irregular lesions, 40% had round lesions and 13.8% had oval lesions.

Table 5: Association between HPE diagnosis and Shape of the lesion

Data		Histopathology diagnosis			
		Benign		Malignant	
		Count	%	Count	%
Shape	Irregular	7	30.4%	23	54.8%
	Oval	7	30.4%	2	4.8%
	Round	9	39.1%	17	40.5%

χ 2 = 8.987, df = 2, p = 0.011*

In the study among benign lesions, 30.4% had irregular shape, 30.4% had oval shape and 39.1% had round shape. Among malignant lesions, 54.8% had irregular shape, 4.8% had oval shape and 40.5% had round shape.

Table 6: Margins of lesion distribution

Data		Count	%
Margins	Lobulated	18	27.6%
	Smooth	9	13.8%
	Spiculated	28	43.0%

In the study 21.5% had lobulated margins, 40% had smooth margins and 38.5% had Spiculated margins.

Table 7: Association between HPE diagnosis and Margins of the lesion

Data		Histopathology diagnosis			
		Benign		Malignant	
		Count	%	Count	%
Margins	lobulated	7	30.4%	11	26.1%
	Smooth	15	65.2%	4	9.5%
	Spiculated	1	4.3%	27	64.2%

χ 2 = 14.201, df = 2, p = 0.001*

In the study among those with benign lesions, 30.4% had lobulated margins, 65.2% had smooth margins and 4.3% had Spiculated margins. Among those with malignant lesions, 26% had lobulated margins, 9.5% had smooth margins and 64.2% had Spiculated margins. There was significant association between margins and HPE diagnosis.

Table 8: Signal intensity of lesions distribution

Data		Count	%
Intensity	Heterogeneous	42	64.6%
	Hyper intense	17	26.2%
	Hypo intense	6	9.2%

In the study 64.6% had heterogeneous intensity, 26.2% had hyper intense lesions and 9.2% had hypo intense lesions.

Table 9: Association between HPE diagnosis and Signal Intensity of the lesion

Data		Histopathology diagnosis			
		Benign		Malignant	
		Count	%	Count	%
Intensity	Heterogeneous	10	43.5%	32	76.2%
	Hyperintense	12	52.2%	5	11.9%
	Hypointense	1	4.3%	5	11.9%

χ 2 = 12.595, df = 2, p = 0.002*

In the study among those with benign lesions, 43.5% had Heterogeneous intensity, 52.2% had Hyperintense intensity, 4.3% had Hypointense intensity. Among those with malignant lesions, 76.2% had Heterogeneous intensity, 11.9% had Hyperintense intensity, 11.9% had Hypointense intensity.

Table 10: Validity of ADC in differentiating malignant and benign breast tumors

Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	**0.957**
Standard Error[a]	0.0256
95% Confidence interval[b]	0.875 to 0.992
z statistic	17.830
Significance level P (Area=0.5)	<0.0001

Youden index

Youden index J	**0.8613**
Associated criterion	≤1.131

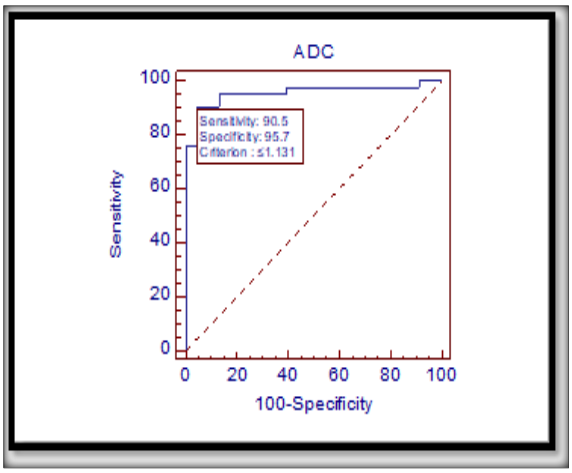


Figure: ROC Curve showing Area under the Curve for ADC in differentiating malignant and benign lesion

Criterion values and coordinates of the ROC curve

Criterion	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**	**+LR**	**-LR**	**+PV**	**-PV**
<0.308	0.00	0.0 - 8.4	100.00	85.2 - 100.0		1.00		35.4
≤0.9942	76.19	60.5- 87.9	100.00	85.2 - 100.0		0.24	100.0	69.7
≤1.021	76.19	60.5 - 87.9	95.65	78.1 - 99.9	17.52	0.25	97.0	68.7
≤1.131	**90.48**	**77.4 - 97.3**	**95.65**	**78.1 - 99.9**	**20.81**	**0.100**	**97.4**	**84.6**
≤1.1847	90.48	77.4 - 97.3	86.96	66.4 - 97.2	6.94	0.11	92.7	83.3
≤1.2593	95.24	83.8 - 99.4	86.96	66.4 - 97.2	7.30	0.055	93.0	90.9
≤1.3573	95.24	83.8 - 99.4	60.87	38.5 - 80.3	2.43	0.078	81.6	87.5
≤1.361	97.62	87.4 - 99.9	60.87	38.5 - 80.3	2.49	0.039	82.0	93.3
≤1.703	97.62	87.4 - 99.9	8.70	1.1 - 28.0	1.07	0.27	66.1	66.7
≤1.745	100.00	91.6 - 100.0	8.70	1.1 - 28.0	1.10	0.00	66.7	100.0
≤1.86	100.00	91.6 - 100.0	0.00	0.0 - 14.8	1.00		64.6	

ADC value of ≤1.131, had highest sensitivity (90.48%), specificity (95.65%), Positive predictive value (97.4%) and negative predictive value (84.6%). Other cut off values of ADC with respective sensitivity and specificity is shown in above table.

Table 11: Lesions classification based on ADC Cut off

Data		**Count**	**Column N %**
ADC Cut off	Benign (>1.31)	26	40.0%
	Malignant (<1.31)	39	60.0%

Based on the ADC Cutoff, 40% were benign and 60% were malignant.

Table 12: Lesions following ADC Cut off in the study

Data		**Histopathology diagnosis**			
		Benign		**Malignant**	
		Count	**%**	**Count**	**%**
ADC Cut off	Benign	22	95.7%	4	9.5%
	Malignant	1	4.3%	38	90.5%

χ 2 = 45.93, df = 1, p <0.001*

In the study out of 23 benign lesions in HPE, 95.7% were diagnosed as benign by ADC (Following the diagnosis) and 4.3% was diagnosed as malignant (Not following the cutoff). Similarly out of 42 malignant lesions, 90.5% were diagnosed by ADC (i.e. following the diagnosis) and 9.5% was diagnosed as benign (not following the cutoff). There was significant association between ADC Cutoff diagnosis and HPE diagnosis.

Table 13: Mean ADC value comparison between benign and malignant lesions

Data		ADC Mean	
		Mean	SD
Histopathology diagnosis	Benign	1.47	0.21
	Malignant	0.85	0.28
P value		<0.001*	

Mean ADC among those with benign lesions was 1.47 ± 0.21 and those with malignant lesions was 0.85 ± 0.28. There was significant difference in mean ADC between benign and malignant lesions. ADC was high in Benign lesions and low in malignant lesions.

Table 14: Histopathology diagnosis of lesions

Data		Count	%
Histopathology diagnosis	Benign	23	35.40%
	Malignant	42	64.60%

On HPE, 35.4% of lesions were diagnosed to be benign lesions and 64.6% had malignant.

Table 15: Diagnosis of lesions distribution

Data		Count	%
Lesions	Infiltrating ductal carcinoma	34	52.3%
	Fibro adenoma	13	20.0%
	Follow up (benign)	5	7.7%
	Lobular carcinoma	4	6.2%
	Fibrocystic diseases	2	3.1%
	Benign phyllodes	2	3.1%
	Intraductal papillary carcinoma	1	1.5%
	Medullary carcinoma	1	1.5%
	Mucinous adenocarcinoma	1	1.5%
	Phyllodes	1	1.5%
	Proliferative breast diseases	1	1.5%
	Total	65	100.0%

In the study 52.3% were diagnosed to have Infiltrating ductal carcinoma, 20% had fibro adenoma, 7.7% suggested follow up, 6.2% had lobular carcinoma, 3.1% had Fibrocystic diseases and Benign phyllodes respectively, 1.5% had Intraductal papillary carcinoma, Medullary carcinoma, Mucionus adenocarcinoma, Phyllodes and Proliferative breast diseases respectively.

DISCUSSION

Presently breast cancer is responsible for significant mortality and morbidity worldwide. Increased awareness of this fact has led to frequent physical examinations and diagnostic imaging procedures among the affected population. Amongst the several diverse techniques used; Breast MRI has been widely accepted as diagnostic approach for evaluating breast, to improve specificity and sensitivity in detecting breast cancer.[4] One amongst them being dynamic – enhanced MRI, though it has some drawbacks in terms of time consumption, cost and incompatibility in few patients. To overcome these disadvantages diffusion weighted imaging with apparent coefficient values can be used as an alternative.

Diffusion weighted imaging mainly represents random movement of water molecules within a voxel which is expressed as apparent diffusion coefficient values. Malignant lesions have high cellularity thereby lower apparent diffusion coefficient values in comparison to benign lesions.[5] Characterization of the lesions was mainly by using T2W fat sat, however imaging features have shown to demonstrate considerable overlap between benign and malignant lesions. Hence, in these circumstances, an additional feature to characterize suspicious lesions could be helpful in order to decrease the number of invasive breast procedures.

DWI measures random movement of molecules also known as Brownian motion. DWI is quantified using ADC values, which measures diffusion of water molecules through the tissues.

Values vary between malignant and benign breast masses, ADC values of malignant breast lesions was usually lower than those of benign lesions, indicating restricted water diffusion and increased cellularity. The ADC values of benign lesions are higher, reflecting normal cellularity and no restriction of water movement.

In our study 55 patients with 65 lesions were included for which DWI with b value of 600 and T2W fat sat images were taken. T2W fat sat sequence was mainly used to characterize the lesion. DWI was quantified using ADC values. ADC values were obtained for both benign and malignant lesions and they were correlated with histopathology. For few of the benign lesions imaging follow up was done.

Characterization of lesion using T2W fat sat

Size: Among 65 lesions 46 lesions were less than 3.0cm and 19 lesions were more than 3.0cm. Mean size among benign lesions were 2.24cm and malignant were 2.83cm. Hence there is no significant difference in mean size of benign and malignant lesions.

Shape: Out of 65 lesions 7 benign lesions were oval, 7 were irregular and 9 of them were round. 23 malignant lesions were irregular, 2 were oval and 17

were round. Thus according to our study shape of the lesion cannot differentiate between benign and malignant lesions.

Margins: Among 65 lesions 7 benign were lobulated, 1 was spiculated margins and 15 of them were showing smooth margins. Among malignant lesions 27 of them were showing spiculated margins, 4 were showing smooth margins and 11 were with lobulated margins.

Hence we can conclude most of the benign lesions were showing smooth margins and most of the malignant lesions were showing spiculated margins.

Signal intensity: Among 65 lesions 12 benign lesions were hyper intense, 10 of them were heterogeneous and 1 of them was showing Hypo intense signal intensity. Among malignant lesions 32 were heterogeneous, 5were hyper intense and 5 of them were hypo intense.

There is no significant difference in signal intensity of benign and malignant lesions, but most of the malignant lesions showed heterogenous signal intensity.

Wael Abd Ulghaffara et al,[6] - Analyzed 51 patients with breast lesions, to study the use of diffusion-weighted imaging and apparent diffusion coefficient in distinguishing benign from malignant lesions.

Data	WaelAbd Ulghaffara et al	Our study
1.No of patients	51 (63 lesions)	55(65 lesions)
2.b-value used	800	600
3.ADC cut off used	1.25	1.131
4.Malignant	21	39
5.Benign	39	26
6.Sensitivity	95.40%	90.48%
7.Specificity	97.50%	95.65%

Compared to above study we included more number of malignant lesions than benign lesion. We used b-value of 600 and by plotting ROC curve we got 1.131 as ADC cut off, where above mentioned study used b –value 800 and ADC cut off as 1.25. Our study showed slightly less sensitivity (90.48%) and specificity (95.65%) when compared to above mentioned study.

Qinghua Min et al-2015,[7] evaluated about 52 female patients to assess the use of DWI in finding out difference between various lesions.

Data	Qinghua Min et al	Our study
1.No of patients	52(49 lesions)	55(65 lesions)
2.b-value used	800	600
3.ADC cut off used	1.23	1.131
4.Malignant	29	39
5.Benign	20	26
6.Sensitivity	88.00%	90.48%
7.Specificity	90.00%	95.65%

Our study population was more when compared to above mentioned study. We used b-value of 600 and by plotting ROC curve we got 1.131 as ADC cut off, where above mentioned study used b –value 800 and ADC cut off as 1.23. Our study showed slightly better sensitivity (90.48%) and specificity (95.65%) when compared to above mentioned study.

Palle L, et al evaluated about 200 female patients to assess the use of DWI in finding out difference between various lesions

Data	Palle L, et al	Our study
1.No of patients	200(280 lesions)	55(65 lesions)
2.b-value used	800	600
3.ADC cut off used	1.3 to 1.5 &0.8-1.1	1.131
4.Malignant	72	39
5.Benign	208	26
6.Sensitivity	97.20%	90.48%
7.Specificity	98%	95.65%

Our study population was less when compared to above mentioned study. We used b-value of 600 and by plotting ROC curve we got 1.131 as ADC cut off, whereas the above mentioned study used different b-value of 800 and different ADC cut off values. Our study showed less sensitivity (90.48%) and specificity (95.65%) when compared to above mentioned study.

Fernanda Philadelpho Arantes Pereira et al,[8]– Conducted study on 45 women with 52 focal mass lesions.

Data	Fernanda Philadelpho Arantes Pereira et al	Our study
1.No of patients	45(52 lesions)	55(65 lesions)

2.b-value used	750	600
3.ADC cut off used	1.24	1.131
4.Malignant	26	39
5.Benign	26	26
6.Sensitivity	92.30%	90.48%
7.Specificity	96.20%	95.65%

Above mentioned study used equal number of benign and malignant lesions, where as in our study there were more number of malignant lesions. We used b-value of 600 and by plotting ROC curve we got 1.131 as ADC cut off, where above mentioned ADC value of ≤ 1.131 had highest sensitivity (90.48%), specificity (95.65%), Positive predictive value (97.4%) and negative predictive value (84.6%). ADC value of ≤1.2593, had sensitivity (95.24%), specificity (86.96%), Positive predictive value (93.0%) and negative predictive value (90.9%).

In the study out of 23 benign lesions in HPE, 22 were diagnosed as benign by ADC (Following the diagnosis) and 1 was diagnosed as malignant (Not following the cutoff). Similarly out of 42 malignant lesions, 38 were diagnosed by ADC (i.e. following the diagnosis) and 4 was diagnosed as benign (not following the cutoff).

Errors might be due to false sampling of adjacent parenchyma/tiny cystic and necrotic areas within the lesions.

CONCLUSION

DWI with ADC values are easy to obtain and require less scan time.

- DWI with ADC values can differentiate benign and malignant lesions with high sensitivity and specificity, however DWI cannot be used to differentiate between various histological types.
- DWI can be utilized in MRI protocol, when contrast is contraindicated.

study used different b –value of 750 and different ADC cut off 1.24. Our study got similar sensitivity (90.48%) and specificity (95.65%) as above mentioned study.

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