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Original Research Article

Role of diffusion weighted imaging and quantification of ADC values in Characterizing breast lesions on MR mammography with histopathological correlation

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Abstract:

Background: Dynamic contrast enhanced MRI (DCE MR) has high sensitivity to evaluate breast lesions with variable specificity. Diffusion weighted imaging (DWI) is added to increase the specificity of DCE MR in differentiating benign and malignant lesions.

Objectives: To characterize breast lesions by the DWI and to quantify ADC values to differentiate benign and malignant lesions.

Methods: This prospective study was done over period of one year on 3Tsiemens Magnetom Vida MRI machine. Thirty female patients with thirty-three breast lesions were included in this study. Diffusion weighted images of breast were obtained at b values 0 and 800. Qualitative & quantitative assessment of breast lesions was done on DWI and ADC map.

Results: Out of total thirty-three lesions, twenty-three were malignant and ten were benign. All malignant lesions showed restricted diffusion. Out of total ten benign lesions, three were non restricted while seven were showing restricted diffusion. Mean ADC value of malignant lesions was $1.01 \pm 0.24 \times 10^{-3}$ mm^2/sec and for benign lesions was $1.48 \pm 0.29 \times 10^{-3}$ mm^2/sec. The ADC cut off value of 1.22×10^{-3} mm^2/sec differentiated malignant lesions from benign with a sensitivity and specificity of 86.96% and 90% respectively.

Conclusion: Diffusion weighted imaging and quantitative analysis with ADC values can be used with DCE MR to differentiate benign and malignant breast lesions with high sensitivity and specificity.

Keywords: Breast Lesions, Dynamic Contrast Enhanced MRI, Diffusion Weighted Imaging, ADC.
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Introduction

Breast cancer is the second most common cause of cancer deaths after lung carcinoma in females worldwide [1]. The risk factors for breast cancer are aging (>35yrs), genetic abnormality (BRCA 1 & BRCA 2), family history of breast cancer, early menarche & late menopause, nulliparity, late first full-term pregnancy, radiation exposure of breast during development [2]. Breast lesions are evaluated by self-examination, clinical breast examination, x ray mammography, ultrasound, magnetic resonance imaging and positron emission tomography.

Dynamic contrast enhanced MRI (DCE MRI) is a problem-solving imaging modality. It has role in differentiating benign and malignant lesions, scar tissue and recurrent cancer, determine degree of invasion in surrounding soft tissues, multifocality and multicentricity of breast tumorand evaluate breast implants. MR imaging has high sensitivity 89-100% in detection of breast tumors but variable specificity 50-90% [3-6]. To improve the specificity of DCE MRI in differentiating benign and malignant breast lesion's role of diffusion weighted imaging (DWI) has been studied.

Previous Studies reported that DWI improved the specificity of DCE MRI without any significant increase in time [7-11]. Due to availability of limited literature regarding the usefulness of DWI and ADC values in differentiation of benign and malignant breast lesions, we studied the role of diffusion weighted imaging and ADC values in both mass and

non-mass breast lesions. We also calculated ADC cut off value to differentiate benign and malignant lesions in this study.

Materials and Methods

Prospective observational study was done at tertiary level hospital over a period of one year on 3T Siemens Magnetom Vida MRI scanner using dedicated phased array 8 channel breast coil. Patients with suspected breast lesions on mammography and ultrasound were included. After the Informed consents from the patients, DCE MRI with standard sequences of axial T1W, axial T2W and STIR were acquired in prone position. Additional Diffusion weighted imaging was done at b value 0 and 800. Then dynamic post contrast images were acquired. Contrast was injected by pressure injector using 20 ml of gadoversatamide 0.1 mmol/kg dose followed by 25 ml of saline flush at a rate of 2 ml/sec. Breast lesions were divided into mass and non-mass lesions. Mass lesions were evaluated for morphology including the shape, margins, T2W signal intensity, internal enhancement patterns. Non mass breast lesions were evaluated for their distribution and internal enhancement patterns. Breast lesion enhancement curves were obtained. DWI provides biological information about the composition of tissues, microstructure, their physical properties and architectural organization. This does not require contrast administration. DWI is based on the water molecules movement which is affected by pathological process. Lesions with restricted diffusion show high signal on DWI and low signal on ADC map. Quantitative assessment is done by calculating ADC values by placing ROI on the region of interest (as shown in figure 1).

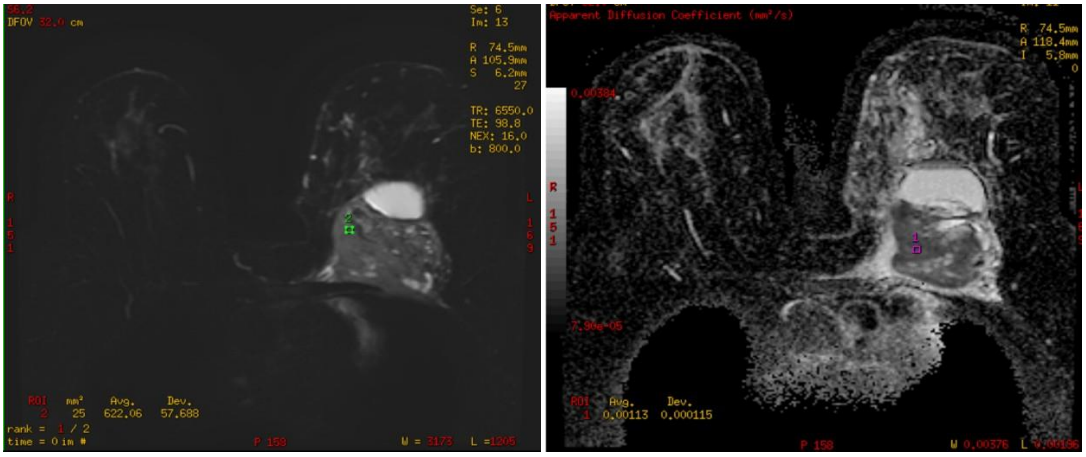

Fig 1. DWI and ADC map showing breast mass lesion with ROI placement giving ADC value of 1.13 x 10^{-3} mm^2/sec.

Areas of hemorrhage, necrosis and adipose tissues should be avoided during ADC value calculation. Diagnosis of breast lesions were confirmed by histopathology. Quantitative variables were compared using independent t test between benign and malignant and Anova test to compare mean ADC value among various diagnosis. Receiver operating characteristics curve was used to calculate cut off value of mean ADC value for benign and malignant. A p value of <0.05 was considered statistically significant.

Results

This study prospectively studied thirty female patients with thirty-three breast lesions aged between 28 to 74 years. The mean age was 48.39 ± 13.17 years. On histopathology seventy percent (23) of lesions were malignant and thirty percent (10) were benign. In this study out of total twenty-three malignant lesions sixteen were mass and seven were showing non mass like enhancement. Distribution of breast lesions according to histopathological diagnosis as shown below in table 1.

Table 1: Distribution of lesions according to diagnosis

Diagnosis	No of lesions	Percentage
Infiltrating ductal carcinoma	18	54.6
Ductal carcinoma in situ	3	9.1
Leiomyosarcoma	1	3.0
Ductal papilloma	2	6.1
Fibroadenoma	5	15.2
Benign phyllodes	1	3.0
Duct ectasia and fat necrosis	1	3.0
Chronic granulomatous inflammation	1	3.0
Pagets with DCIS	1	3.0

Breast lesions were assessed on DWI for restricted diffusion as shown in table 2.

Table 2. Distribution of lesions according to restricted and non-restricted

	Benign	Malignant	Percentage	p value
Restricted	7	23	90.9%	
Non restricted	3	0	9.1%	0.0212

Mean ADC value of benign and malignant lesions was calculated as shown in table 3.

Table 3. Mean ADC value of benign and malignant lesions

	Mean ADC value mm^2/sec	p value
Benign	1.48 ± 0.29	
Malignant	1.01 ± 0.24	<0.005

In this study statistically significant difference ($p < 0.005$) was found between the mean ADC value of malignant and benign breast lesions.

The mean ADC value was also calculated for benign and malignant mass and non-masslesions separately as shown in table 4 and table 5.

Table 4. Mean ADC value of benign and malignant mass lesions

	Sample size	Mean	Min-max	p value
Benign	8	0.9-1.89	1.51 ± 0.32	
Malignant	16	0.68-1.54	0.98 ± 0.24	<0.0005

Table 5. Mean ADC value of non-mass benign and malignant breast lesions

	Sample size	Min-max	Mean	p value
Benign	2	1.35 -1.42	1.39± .05	
Malignant	7	0.82-1.5	1.07 ±0.24	0.117

The difference between mean ADC value of benign and malignant non mass lesion was not statistically significant with p value <0.117. However non mass benign lesions showed higher ADC values compared to malignant non mass lesions.

ADC cut off values to differentiate benign and malignant breast lesions were calculated using ROC curve analysis. Four different ADC cut off values to differentiate malignant from benign were evaluated. At ADC cut off value of 1.03 x $10^{-3}mm^2/sec$, sensitivity and specificity were 60.57% & 90% respectively. At ADC cut off value of 1.15 x $10^{-3}mm^2/sec$, sensitivity and specificity obtained were 73.91% & 90% respectively. The ADC cut off valueof 1.22x 10^{-3} mm^2/sec had 86.96% sensitivity and 90.00% specificity in differentiating malignant and benign lesions. The ADC cut value calculated 1.30x 10^{-3} mm^2/sec had 86.96% sensitivity and 80% specificity. Out of these ADC cut off values 1.22x $10^{-3}mm^2/sec$ had highest sensitivity and specificity of 86.96% & 90% respectively.

Separate ADC cut off values were calculated for mass and non-mass lesions. For mass breast lesions ADC cut off value of 1.22x $10^{-3}mm^2/sec$ and for non-mass breast lesions ADC cut off value 1.20 x $10^{-3}mm^2/sec$ was calculated. This ADC cut off value had sensitivity& specificity of 87.50% each in mass lesions and sensitivity & specificity of 85.71% &100 %in non-mass lesions.

Discussion

In this study age group 46-55 years showed highest number of breast lesions and most commonly diagnosed breast lesion in this study was infiltrating ductal carcinoma (55%) followed by fibroadenoma (15%). In this study most malignant lesions (65%) showed hypointense signal followed by intermediate signal (35%). All hyperintense lesions were benign and only 30% benign lesions were hypointense. However, mucinous, medullary carcinoma and tumors with necrotic component may show hyperintense signal on T2 W imaging [12].

For quantitative analysis of diffusion weighted imaging ADC values of both benign and malignant lesions were calculated. Benign breast lesions were showing higher mean ADC values compared to malignant lesions. In this study we found significant difference between the mean ADC values of benign and malignant lesions with p value <0.005.

In this study the ADC cut off value of 1.22 x $10^{-3}mm^2/sec$ was obtained which has highest sensitivity and specificity of 86.96% &90.00% respectively in differentiating benign and malignant lesions. The positive predictive value was 95.24%and negative predictive value was 75.00%. In this study one out of two duct papillomas showed mean ADC value of 0.90 x 10^{-3} mm^2/sec in malignant range. Woodhams R et al and Tozaki M et al also reported that duct papilloma can be misdiagnosed due to low ADC value [13-14].

In this study breast lesions were divided into mass and non-mass type. In mass lesions benign lesions showed higher ADC values compared to malignant

lesions. The mean ADC value in mass lesions was1.51 ±0.32× 10^{-3} mm^2/s for benign and 0.98 ± 0.24× 10^{-3} mm^2/s for malignant lesions. There was statistically significant difference between the mean ADC values of benign and malignant mass lesions as p value <0.0005 was found. For mass breast lesions ADC cut off value 1.22 × 10^{-3} mm^2/s was calculated which has 87.50% sensitivity and 87.50 % specificity.

The mean ADC value of benign and malignant non mass lesions was1.39±0.05 × 10^{-3} mm^2/sand 1.07 ±0.24× 10^{-3} mm^2/s. Separate ADC cut off value for non-mass lesions was calculated. The ADC cut off value 1.20 × 10^{-3} mm^2/s was obtained to differentiate benign and malignant non mass lesions which gave 100 % sensitivity and 85.71% specificity. No statistically significant difference was found in the ADC values of non-mass benign and malignant breast lesions as p value was 0.117. This study corroborates with the previous studies as there is statistically significant difference is present between the mean ADC values of benign and malignant breast lesions.

Thus, Diffusion weighted imaging with the enhancement patterns and dynamic studies may increase the overall accuracy of MRI. It may be useful as a screening tool in young patients specially in the high-risk patients and in patients with contraindications to intravenous contrast agents. It is also less time-consuming sequence. ADC maps must also be studied together with DWI to eliminate the T2 shine through effect.

Limitations of this current study are small sample size and a smaller number of benign lesions. Hand drawn Region of interest (ROI) is difficult to reproduce, may not always be accurate. Patient movement may also affect the ADC value. Further studies with a larger sample size and wider spectrum of cases are recommended.

Conclusion

Diffusion weighted imaging and quantitative analysis with ADC values can be used with conventional DCE MRI to differentiate benign and malignant breast lesions with high sensitivity and specificity.

DWI does not require contrast administration and is relatively fast. The ADC cut off value is important to differentiate benign and malignant mass breast lesions. No statistically significant difference was found in mean ADC value of benign and malignant non mass lesions. However non mass benign lesions showed higher ADC values compared to malignant non mass lesions.

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