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Research Article

Role of Diffusion weighted MR Imaging in adding to the specificity of Breast MRI

Authors
Dr Sumod Mathew Koshy MD, FRCR, Dr Sonia Abraham MD,
Dr Anil Prahladan DNB, EDiR, Dr Krishnankutty Nair Ramachandran MD
Division Of Imageology, Regional Cancer Centre, Medical College Campus, Trivandrum, Kerala, India
PIN 695011
Corresponding Author
Dr Sumod Mathew Koshy MD, FRCR
Division of Imageology, Regional Cancer Centre, Medical College Campus, Trivandrum, Kerala, India
PIN 695011 +91 471 252 2604, +91 9446810833
Email: *sumodmk@gmail.com*

Abstract
MRI is known for its high sensitivity, but only moderate specificity for the characterization of breast lesions. Efforts have been made to develop newer sequences and tools that improve the specificity of lesion characterization without compromising sensitivity significantly. DW imaging with ADC quantification has shown promise in this regard. This study evaluates the role of DW MRI in improving the diagnostic accuracy of Dynamic Contrast Enhanced MRI in characterizing breast lesions and to set a cut off ADC value to differentiate benign and malignant lesions. The study is a prospective analytical study. 61 subjects with 132 MRI detected lesions, with final diagnosis confirmed pathologically were included. MRI was performed on a 1.5 T scanner (GE SIGNA HDX) using a dedicated eight channel phased array breast coil. Sequences studied were Axial T1W, T2W, STIR, post contrast axial VIBRANT, dynamic sagittal VIBRANT and diffusion weighted images with ADC maps. Out of the 132 lesions, 62 were benign and 70 malignant. The area under ROC curve for MRI based on dynamic contrast enhanced imaging alone, and combined with Diffusion Weighted Imaging were 0.935 and 0.991 respectively. Sensitivity increased from 90.0% to 98.6% and specificity from 83.9% to 96.8%. Setting a cut off value for Absolute ADC at < 1.21 x 10^3 mm^2/ sec could diagnose malignant lesions with a sensitivity and specificity of 91.43% and 98.39% respectively.Addition of quantitative DW imaging to conventional Dynamic Contrast Enhanced MRI significantly improved diagnostic accuracy, especially specificity of breast MR imaging.

Introduction

Carcinoma of the breast is the most common malignancy in women in both developed as well as developing countries. In India, it is the leading site of cancer in females in 6 major cities between 2001 and 2004 according to the national cancer registry. [1] Though mammography is the mainstay for screening, its limitations have made MRI, the diagnostic investigation of choice. [2,3,4] Dynamic contrast enhanced MRI has an inherently high sensitivity but a low and variable specificity for characterization of breast lesions.[5,6,7,8,9,10] Hence,

efforts are being directed towards new sequences and methods that improve specificity of lesion characterization, DWI imaging being the most promising currently. The advantage of DWI is that the degree of diffusion restriction in a region of interest can be quantified by calculating the ADC values, reduced values in malignancy reflecting high cellularity which inhibits free diffusion of water molecules. [11,12] DWI holds potential as an adjunct to reduce false positives, thereby improving the diagnostic accuracy, especially specificity of breast MRI. [13,14,15] Two meta-analyses evaluating quantitative DWI demonstrated consistent and overall better specificity than DCE MR alone. [16,17] Some studies have suggested possible correlation of ADC values with prognostic pathological markers such as tumour grade, hormone or receptor status. [18,19] Several studies have also shown that serial ADC quantification can help in assessing treatment response, post neoadjuvant chemot-herapy. Baseline ADC values have also shown to be lower in responders, with change in ADC being significantly higher, thereby predicting treatment outcome.[20]

Aims and Objectives

Primary objective: To evaluate the role of diffusion weighted imaging (DWI) in improving the diagnostic accuracy of dynamic contrast enhanced MRI breast.

Secondary objective: To calculate a cut off ADC value to differentiate benign and malignant breast lesions.

Materials and Methods

The study was designed as a prospective analytical one. 132 breast lesions in 61 of the 130 consecutive patients referred for clinically indicated MRI breast imaging in our department who satisfied the following criteria were included in the study.

- All patients who underwent MR imaging with both dynamic contrast enhanced and diffusion weighted sequences.
- The diagnosis was confirmed by histopathological analysis.

All MR studies were done on 1.5Tesla MR Scanner. Images were obtained using bilateral dedicated eight channel phased array breast coil with the patient in prone position. Sequences studied included axial T1W, T2W, DWI with corresponding ADC, VIBRANT and Post Contrast multiphase sagittal VIBRANT sequences. In all MR examinations, DW imaging was done with B values 0 and 700 and the corresponding ADC maps were obtained using standard post processing software. All images were reviewed on PACS imaging workstations using 6MP fusion monitors.(Figs 1-4). The MRI detected lesions were classified as mass or non mass like enhancement and the morphology of the tumours were analysed with respect to their size, margins, shape and enhancement pattern using the BIRADS MRI lexicon. Time signal intensity curves were obtained using software provided by placing and ROI within the lesion.

Absolute apparent diffusion coefficient (ADC) was measured from the lesion and from normal glandular parenchyma in the same breast at least 2 cm away from the lesion. Normalised ADC was calculated as: Normalised ADC = Absolute ADC / Breast parenchymal ADC.

Standard statistical evaluation tools were used. ROC curves were plotted for BIRADS categorization of lesions with and without combining DWI with dynamic contrast enhanced MRI.

Results

ROC curves were also plotted for absolute and normalized ADC values and area under curves were calculated. Youden selected cut off absolute and normalized ADC values for differentiating benign and malignant lesions and corresponding sensitivity and specificity were obtained from ROC curves.

ROC curves were plotted for the diagnostic ability of MRI using morphology and contrast kinetics alone and combined with DWI and AUC was calculated.(Table 1). The AUC for the latter

(0.991) was significantly higher than the former (0.935) (Fig. 5). Sensitivity increased from 90% to 98.6% and specificity increased from 83.9% to 96.8%.(Table 2) The difference in area under curve for MRI accuracy after adding DWI was 0.055 and is statistically significant with a p value of 0.0017 (Table 3).

ROC curves were plotted for absolute and normalized ADC values and area under curves were calculated. Absolute ADC was statistically better than normalized ADC, area under ROC curve (AUC) for absolute and normalized ADC being 0.981 and 0.954 respectively, p value = 0.02 Fig. 6 . However both ADC's were statistically significant independently with p value<0.0001.

Youden selected cut off absolute and normalized ADC values for differentiating benign and malignant lesions and corresponding sensitivity and specificity were obtained from ROC curves. Setting a cutoff value for absolute ADC at </= 1.21 x 10^{-3} could diagnose malignant lesions with a sensitivity and specificity of 91.43% and 98.39% respectively. (Table 4)

Table 1: ROC statistics of conventional MRI and with DWI added

	BIRADS-MORPHOLOGY+ DCE	BIRADS- MORPHOLOGY+ DCE + DWI
Area under the ROC curve (AUC)	0.935	0.991
Standard Error	0.0177	0.00621
95% Confidence interval	0.879 to 0.971	0.956 to 1.000
z statistic	24.552	78.997
Significance level P (Area=0.5)	<0.0001	<0.0001
Sensitivity	90.00%	98.6%
Specificity	83.9%	96.8%
Positive predictive value	86.4%	97.2%
Negative predictive value	88.1%	98.4%

Table 2: Comparative analysis - statistical significance

MORPHOLOGY+ DCE vs MORPHOLOGY+ DCE + DWI	
Difference between AUC	0.0555
Standard Error	0.0177
95% Confidence Interval	0.0209 to 0.0902
z statistic	3.142
Significance level	P = 0.0017

Table 3: Change in statistical indices with the application of quantitative ADC data.

Diagnostic category	Conventional MRI	Final HPR	Coventional MRI + DWI	Change
Benign	59	62	61	2
Malignant	73 (sens 90% spec 83.9%)	70	71 (sens 98.6% spec 96.8%)	2
Total	132	132	132	

Table 4: Suggested cut-off ADC value for optimal sensitivity and specificity.

Absolute ADC value	Sensitivity	Specificity
<0.53	0.00	100.00
≤1.19	87.14	100.00
≤1.2	88.57	98.39
≤1.21	**91.43**	**98.39**
≤1.25	91.43	93.55
≤1.28	95.71	93.55
≤1.41	95.71	69.35
≤1.42	97.14	66.13
≤1.43	98.57	62.90
≤1.46	98.57	58.06
≤1.48	100.00	56.45
≤2.33	100.00	0.00

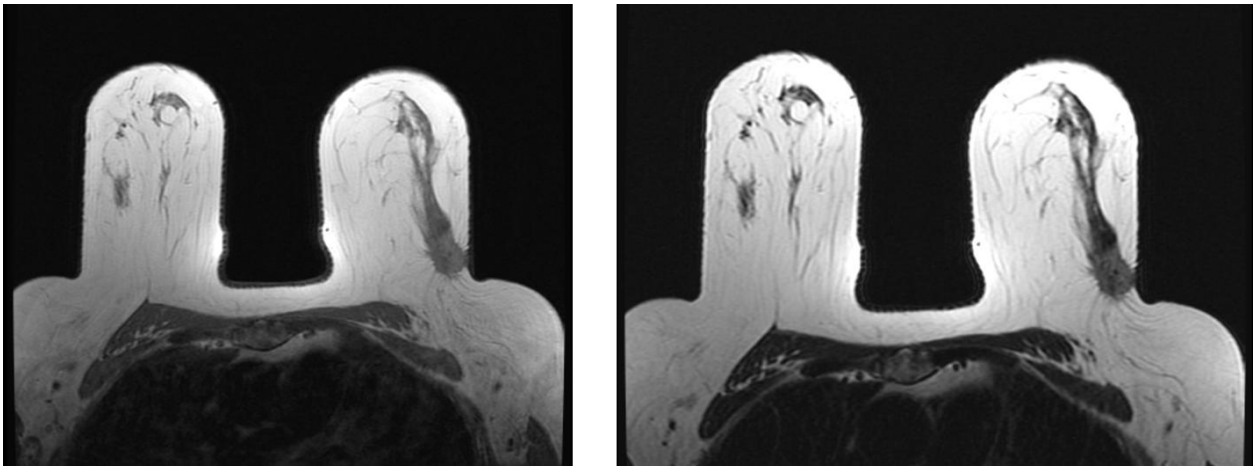

Fig 1 Axial T1, T2 weighted image showing an irregular heterogeneous hyperintense lesion in the upper outer quadrant of left breast infiltrating skin. Spiculated strands of tumour intensity extending to the adjacent breast parenchyma.

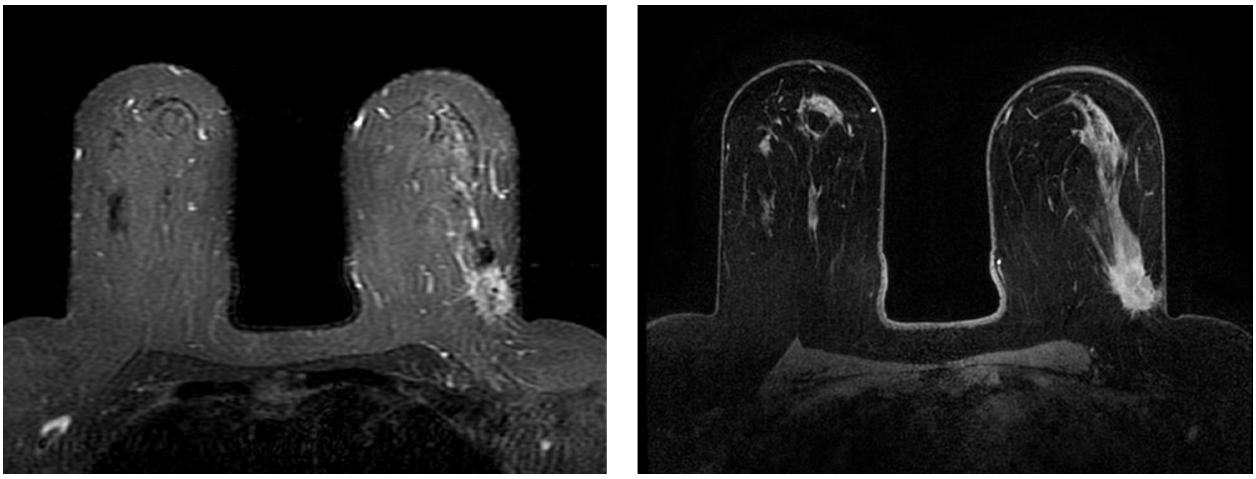

Fig. 2: STIR and post contrast images show the spiculated lesion becoming more conspicuous with fat suppression and contrast enhancement.

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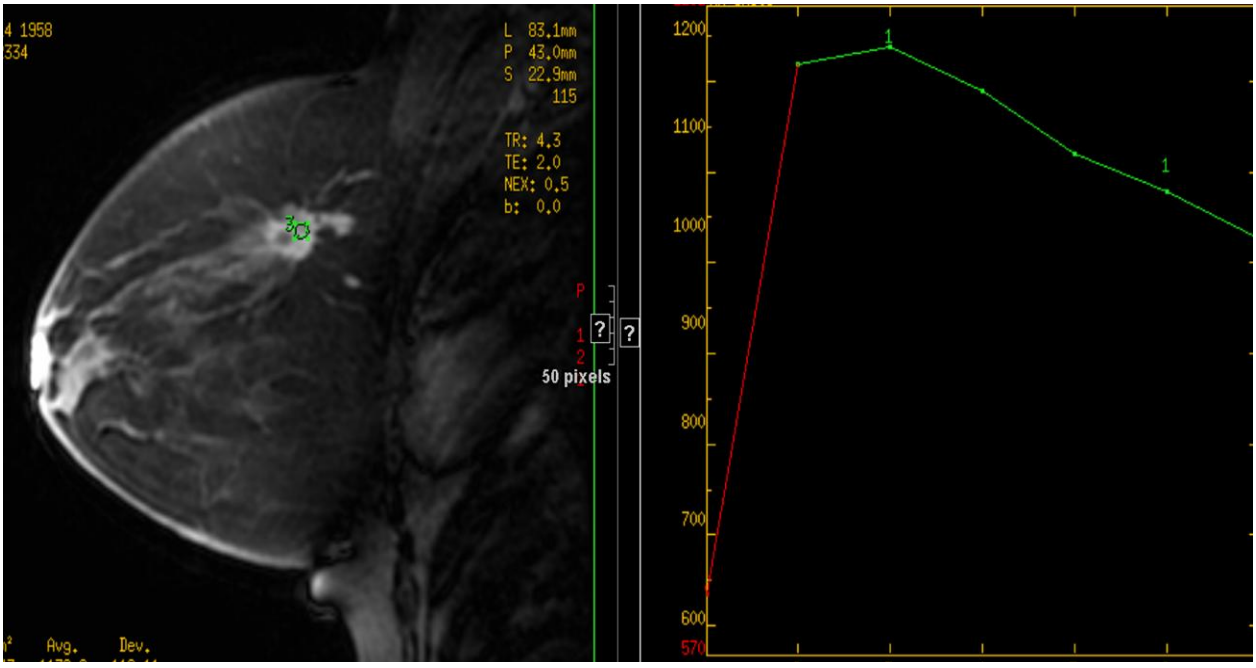

Fig 3 TIME SIGNAL INTENSITY CURVE demonstrating type III (washout) pattern of enhancement.

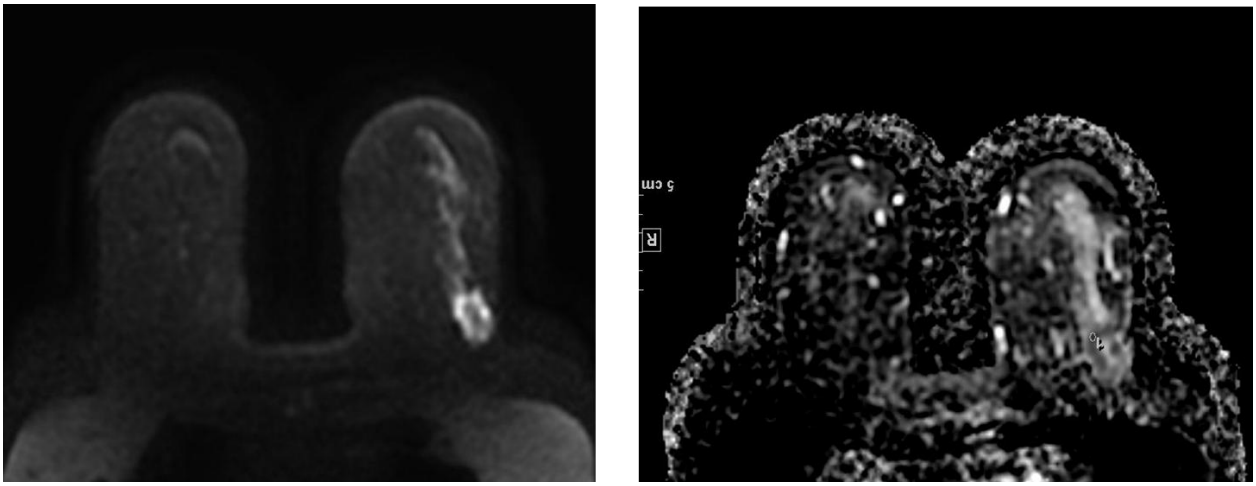

Fig 4 DWI demonstrate peripheral hyperintense areas in the lesion and corresponding areas in ADC maps shows hypointense areas. ROI placed in the hypointense area in ADC maps shows the Apparent Diffusion Coefficient of the lesion.

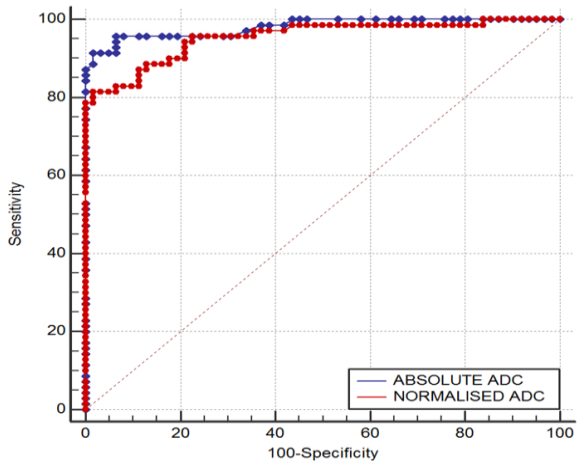

Fig 5 ROC curves of BIRADS categorisation (MR accuracy)with conventional DCE MRI (blue) and diffusion weighted imaging combined with conventional protocol (red). AUC of the latter (0.991) is higher than the former (0.935) and statistically significant with p value < 0.001.

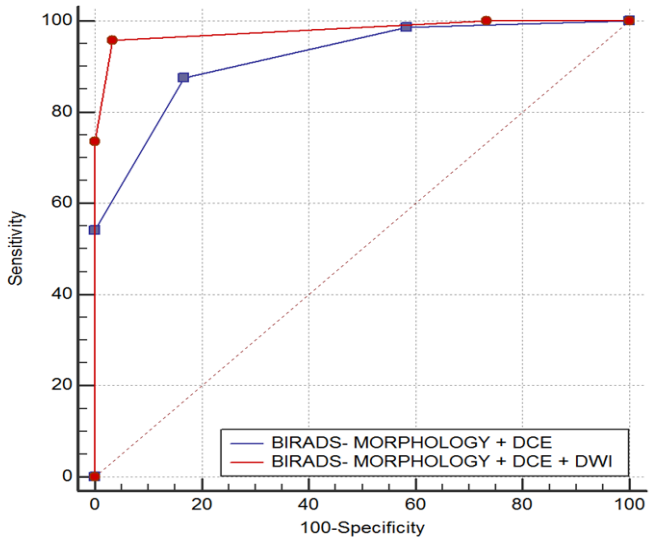

Fig 6 ROC curves of absolute (blue) and normalised (red) ADCs. AUC of absolute ADC was higher than normalised ADC

Conclusion

Our study has shown that addition of DWI with ADC quantification to conventional morpho-logical and contrast kinetic assessment, signific-antly improves the specificity and diagnostic accuracy of breast MRI. We were also able to suggest a cut off ADC value for differentiation of benign and malignant lesions with significantly better sensitivity and specificity. More studies on DWI in breast MRI can potentially develop this technique as a predictive marker for tumour grade, hormonal and receptor status, obviating the need for an invasive pretreatment biopsy. Also, further studies can establish DWI's role in predicting response to neoadjuvant chemotherapy, thereby resulting in treatment protocol optimization.

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