Original Research Article

Diffusion weighted MR Imaging of breast for differentiation of benign from malignant lesions and histopathological correlation

Eesha Rajput[1*], Rochan Pant[2]

[1]MD, DNB Radiodiagnosis, INHS Kalyani, Andhra Pradesh, India
[2]HOD Department of Imaging and Interventional Radiology, Cardiothoracic centre (CTC) Pune, Maharashtra, India
[*]Corresponding author email: **eesharajput84@gmail.com**

International Archives of Integrated Medicine, Vol. 5, Issue 7, July, 2018.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 09-05-2018 **Accepted on:** 16-06-2018
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Eesha Rajput, Rochan Pant. Diffusion weighted MR Imaging of breast for differentiation of benign from malignant lesions and histopathological correlation. IAIM, 2018; 5(7): 8-16.

Abstract

The article highlights utility of Diffusion Weighted MR Imaging of breast in differentiating benign and malignant lesions along with correlation with histopathological findings. DWI of breast lesions can help predict nature of lesion with reasonable confidence limit.

Key words

Breast lump, Diffusion weighted imaging, Malignant lesion.

Introduction

Breast cancer is most prevalent and is the leading cause of cancer related deaths among women worldwide. It is estimated that in India, one out of every 20 women has the risk of developing breast cancer especially in cities like Delhi and Mumbai. The early and accurate diagnosis of breast cancer is crucial for successful treatment and to improve the quality of life [1-3].

Diffusion weighted imaging (DWI) is a new magnetic resonance technique that provides imaging based on diffusion properties in biological tissues. Rapid changes in diffusion characteristics can be observed by calculating the diffusion coefficient. However, in biological tissues the apparent diffusion coefficient (ADC) is usually used as a diffusion measurement instead of diffusion coefficient because the

diffusion is also dependent on factors other than Brownian motion, such as microcirculation represented by perfusion [4-6].

Apparent diffusion coefficient (ADC) is a quantitative parameter calculated from DWI and is a measure of diffusion in biological system. Diffusion weighted (DWI) MR imaging, combined with apparent diffusion coefficient (ADC) measurement is an important method for in-vivo quantification of the combined effects of capillary perfusion and diffusion [7].

Diffusion weighted MR imaging is found to have ability to detect and characterize a lot many benign and malignant tumors and is being evaluated as an important non-invasive imaging tool in oncology. It has been reported to have potential for characterization of focal breast lesions based on their apparent diffusion coefficient (ADC) value. Recently, several studies have reported that the ADC, one of the calculated parameter of DWI, is useful for differential diagnosis of the benign and malignant breast lesions, being significantly lower in malignant tumors than in benign breast lesions and normal tissue [9, 11].

DWI is non-invasive, requires no contrast injection, and can be performed within a single breath-hold or with free breathing. According to various studies, use of DWI with ADC value measurement has been found to be a reliable imaging method for characterization of benign and malignant breast lesions [8].

Aim and objectives

The purpose of this study was

- To determine ADC values for benign and malignant breast lesions.
- To determine usefulness of DWI combined with ADC values in characterization of breast lesions into benign and malignant lesions.
- To correlate the findings with histopathological results.

Materials and methods

From December 2012 to April 2017, all patients with focal breast lesions were also subjected to breast MRI following a period time sampling technique. This included diffusion-weighted MR sequences, provided they fulfilled the inclusion criteria for this study. The protocol used in this study was approved by our institutional review board and medical ethics committee.

Inclusion criteria

- All the patients with a palpable breast lump, a suspected breast lesion detected on mammography or sonomammography, or diagnosed cases of carcinoma breast with suspected recurrence.
- Informed consent was obtained in all cases.

Exclusion criteria

- Patients with lesions less than 1 cm on diffusion weighted images – These lesions will not allow a region of interest (ROI) to be placed entirely within the lesion for calculation of ADC values accurately.
- Patients who could not lie prone for the examination due to fungating mass lesions or painful etiology.
- Any patients in which MRI was contraindicated or DWI could not be done due to any other reasons were excluded from study.

Patients

The patients included in the study were those with palpable breast lump or lesions detected on USG and/or mammography. A total of 104 cases were studied in which the final diagnosis was confirmed on histopathological analysis after FNAC or surgery.

All the patients had at least one lesion detected on any of the imaging modality mentioned. Those patients, who had more than one lesion, the lesion with largest size was taken in to consideration. These cases also included 4 cases

of recurrent carcinomas after breast conservation surgery (BCS) and a single case of cystosarcoma phyllodes. Hence a total of 104 breast lesions were studied in a series of 97 patients.

In all cases patients, clinical background, history of any similar conditions in the family members (mother, sister, aunts) was sought for. Any previous imaging available was also compared wherever required.

MRI techniques

The scanning system used was 1.5 T (Symphony, Siemens Medical Solutions System) with a bilateral 8-channel breast coil.

DWI Parameters

DWI was performed using an axial single shot echo-planar imaging sequence centered on the lesions (b = 0, 500 and 1,000 s/mm^2); 1,800/93.8; echo-train length, 1; bandwidth, 25 MHz; matrix size, 160 × 192; field of view, 360 mm; number of signals averaged, 16; number of slices, 10; slice thickness, 5 mm; intersection gap, 0 mm; acquisition time, 2.0 minutes with three b values were used).

T2-weighted MR imaging

Sagittal fat suppressed T2-weighted fast spin-echo sequence(4,200/85; echo-train length, 19; bandwidth,22.7 MHz; matrix size, 320 × 224; field of view,220 mm; number of signals averaged, 2; slice thickness, 5 mm; intersection gap, 0 mm),

T1- weighted MR imaging

T1-weighted spin-echo sequence (TR/TE,370/15; echo-train length, 2; bandwidth, 41.67 MHz; matrix size, 512 × 256; field of view, 340mm; number of signals averaged, 1; slice thickness,5 mm; intersection gap, 1 mm),

A**xial STIR sequence**

(4,100/85; inversion time, 150 milliseconds; echo-train length, 17; bandwidth, 41.67 MHz; matrix size, 512 × 256; field of view, 340 mm; number of signals averaged, 2; slice thickness, 5 mm; intersection gap, 1 mm),and

Axial T1-weighted 3D fat-suppressed fast spoiled gradient-echo sequence (flip angle, 15°; bandwidth, 62.5 MHz; matrix size, 352 × 352; field of view, 350 mm; slice thickness, 1 mm; intersection gap, 0 mm).

Image analysis

All images were transferred to a workstation and the DWI sequence was post processed to obtain ADC maps. The ADC maps of each lesion were calculated using three b values (0, 500, and 1,000 s/mm^2). To achieve standardized conditions for analyses and to avoid contamination of the data by adjacent structures, two circular regions of interest (ROIs) having a mean diameter of 61 mm^2 (range, 40–94 mm2) were individually placed in the target lesion in the same location as the three ADC maps cited above, and the average ADC was acquired for each b value combination. Apparent necrotic or cystic components were avoided by referring to conventional MR images.

For each patient, the number, size and location of lesions visible in various sequences were noted. The characteristics on various MR sequences used were interpreted as follows:

On DWI: Various lesions of every patient were assessed as following:

- **Qualitative/ Visual Assessment:** i.e. for true restriction of diffusion with increasing '*b'* values.
- **Quantitative Assessment:** i.e. by calculating mean ADC value of Region of Interest (ROI). For this purpose single ROI was drawn over the lesion and values were calculated.
- **Qualitative / Visual Assessment: 0**

The signal intensity of the various breast lesions on DWI were assessed using three point scale system as follows:

0- iso to hypointense,
1- Moderately hyperintense,
2- Hyperintense, to that of breast parenchyma.

The visual grading used for true restriction of diffusion was as per **Table – 1**.

Table – 1: Visual grading for true restriction of diffusion.

	Low b value	*b* 500	*ADC Map*
No restriction of diffusion			
True restriction of diffusion			
T2 shine through effect			

Black circles - hypointense, white circles – hyperintense, Gray circles-intermediate signal that was hyperintense than that on ADC map.

Quantitative Assessment

After evaluation of imaging findings, we measured ADC values of masses detected on conventional MRI sequences and as well as those detected on DW MRI. Analysis and measurements of DWI data were done using the commercial Workstation (Syngo, Siemens Medical Solutions) and Pixel-based ADC maps were obtained. Image interpretation was started with conventional breast MRI. If a lesion was visualized in the conventional scan, it was identified in the corresponding slice of the diffusion weighted images. As a second step, a region-of-interest (ROI) was drawn in the centre of the lesion on the b-1000 DWI and copied to the ADC map. The scanner software then provides the mean value within the ROI which equals the ADC value (multiplied by10^{-3} mm^2/s). If the lesion is not visible in the *b*-1000 images the ADC value cannot be evaluated.

ADC values were measured through gray-scale ADC maps from each lesion at *b* 0, *b* 500, and *b* 1000 s/sq mm gradient values. ADC values were calculated by drawing a region of interest (ROI) over the lesion. ADCs were measured over the largest mass detected in patients with multiple lesions. All ROIs (round shape) were placed within the confines of the lesion. Necrotic portions of solid lesions detected on contrast enhanced MRI were not included in measurements. The scanner software calculates the ADC based upon a linear regression analysis of the function:

S/S0 = Log10 (-*b* X ADC) or ADC = AntiLog10 [(S/S0)] / (-b)

The formula is applied as follows, when there are 2 different b values (138):

ADC = [AntiLog10 (S1/S2)] /(*b*2-*b*1)

Where S0 is the signal intensity without the diffusion weighting, S is the signal with the gradient (*b*=1000 sec/ sq mm), S1 is the signal with the gradient *b*1 and S2 with that of *b*2, ADC is the Apparent diffusion-coefficient. The resultant values were expressed in Mean ± SD.

Assessment on other MR images:

The various criteria used while evaluating the breast lesions on MR imaging sequences were as follows:

Breast Cancer

Invasive ductal carcinomas (IDCs) demonstrate higher signal intensity and lower ADC values than do benign tumors and normal breast parenchyma on diffusion-weighted images. In addition, there is occasionally central hypointensity in IDCs on T1 and T2 WI which is thought to represent necrosis or fibrosis.

Mucinous carcinoma has a specific appearance at diffusion-weighted imaging [10]. It contains a mucin lake compartment, so that its signal intensity remains hyperintense on diffusion-weighted images (obtained at a low *b* value) and hyperintense on T2-weighted images. At a higher *b* value, the signal intensity of mucinous carcinoma will decrease at diffusion-weighted imaging due to T2 shine-through. The ADC value of mucinous carcinoma is generally higher than that of IDC

Benign Tumors

Cyst, fibroadenoma, fibrocystic disease and intraductal papilloma demonstrate high signal intensity on T2-weighted MR images; however, the signal intensity of benign tumors may be influenced by *b* value much more than the signal intensity of malignant tumors because of T2 shine-through. These benign tumors may display high signal intensity on DWI obtained at lower *b* values; than those at higher *b* values or they may become isointense and may not be identified .

Simple cyst

The signal intensity of cysts remains high at *b* values of 1000 sec/mm2 or lower, which are commonly used in breast MR imaging. However, a cyst with condensed or proteinaceous content sometimes has high signal intensity, even at higher *b* values. Following fluid signal intensity on all sequences, thin imperceptible walls.

Fibroadenomas

They have intermediate to low signal intensity relative to IDC at higher *b* values, and may have lower signal intensity than that of the surrounding breast parenchyma due to myxomatous change. The ADC value of fibroadenoma is generally higher than that of IDC. In large fibroadenomas, a low-signal-intensity septum may be observed on diffusion-weighted images.

Phyllodes tumor

It may manifest with a lobulated shape and a hypointense septum, appearing similar to fibroadenoma.

Fibrocystic disease

It is at DWI is variable, with diffuse, bilateral nodular, or segmental high signal intensity being typical. In addition, in the majority of cases, the signal intensity of fibrocystic disease decreases as *b* value increases, thus, imaging at a higher *b* value may be useful in differentiating between DCIS and fibrocystic disease.

Abscess and mastitis

They both have low ADC values similar to those of malignant tumors. The area of low ADC value within an abscess usually has high signal intensity on T2-weighted images, which indicates the high water content and high viscosity of the abscess.

Hematomas

They are containing intracellular components (intracellular oxyhemoglobin, or methemoglobin) show significantly reduced diffusion compared with hematomas containing lysed red blood cells (extracellular methemoglobin). Some hematomas have high signal intensity on precontrast T1-weighted images; therefore, T1-weighted images should be evaluated together with diffusion-weighted images to avoid misdiagnosis.

Final diagnostic criteria

The final diagnosis of the breast lesions was based on following as applicable:

- Histopathology/ Cytology and Contributory laboratory findings.
- Diagnostic radiological findings.
- Operative findings, Clinical follow up and contributory clinical history.

Tests for Statistical Analysis

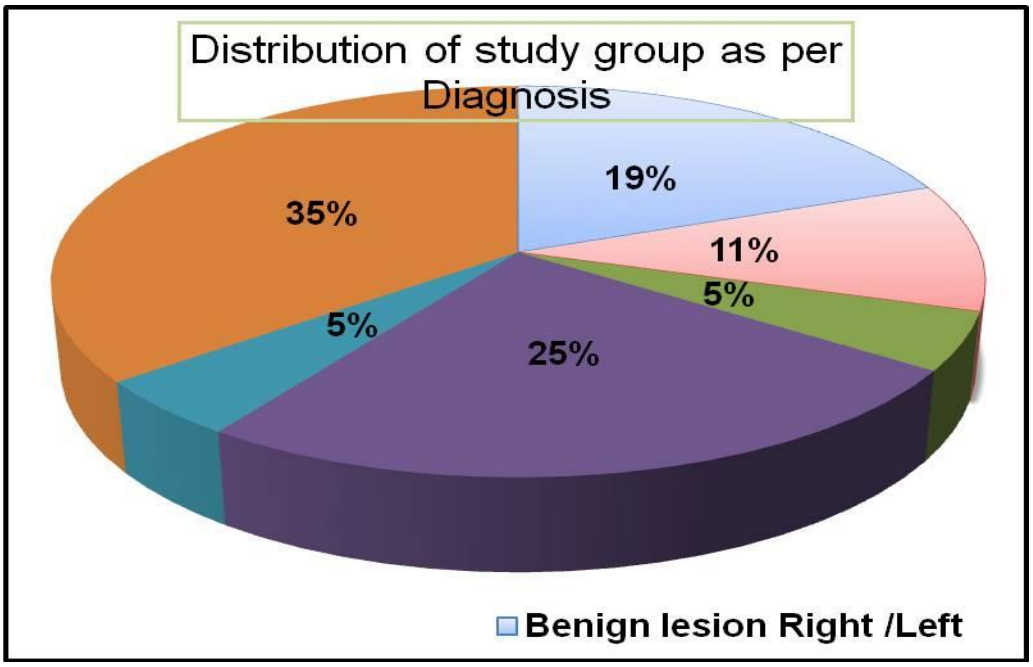
The various ADC values of individual lesions were analyzed using ROC curve to calculate the threshold ADC value with which we could differentiate maximum number of lesions with

high specificity and sensitivity. ROC curves were drawn for ADC values at all *b* values as well as for mean ADC values.

Results and Discussion

Distribution of study group as per diagnosis was as per **Graph – 1**. Distribution of study group as per Restriction was as per **Table – 2**. HPE findings among study group were as per **Graph – 3**. Association among study group between, Restriction and HPE findings were as per **Table – 3**.

Graph – 1: Distribution of study group as per diagnosis.



Graph – 2: HPE findings among study group.

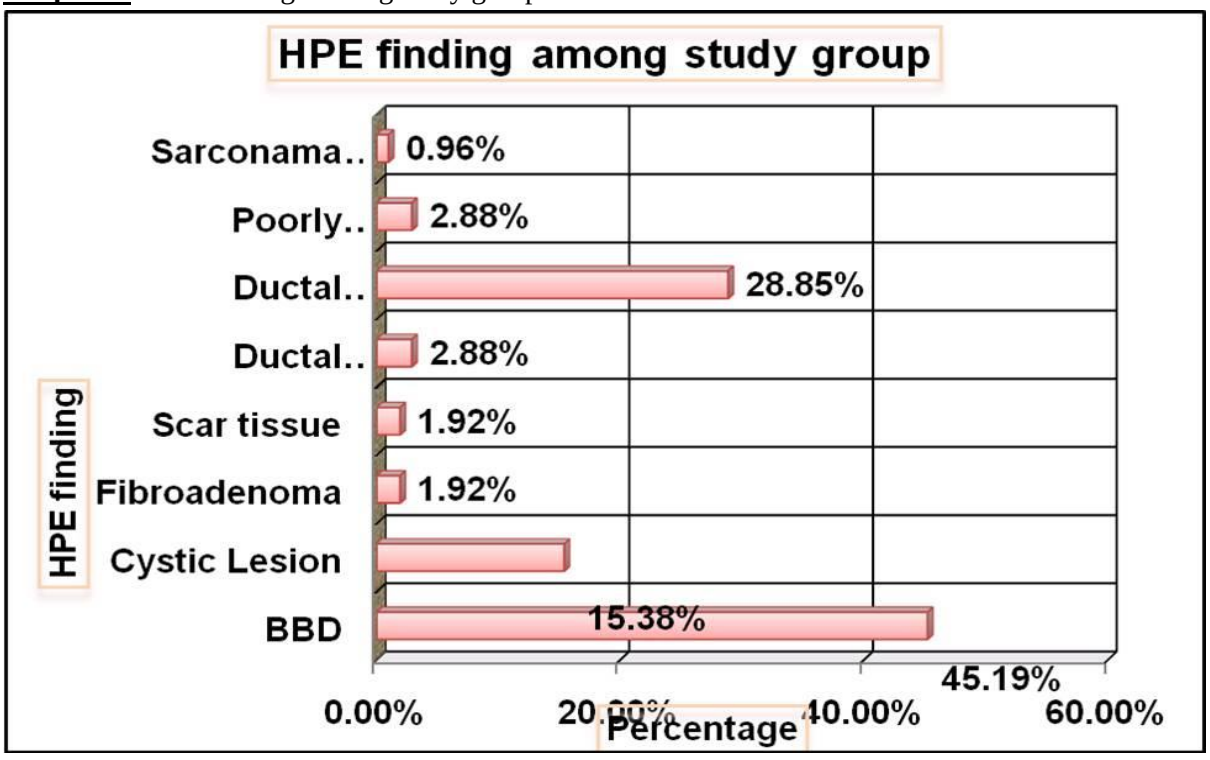


Table - 2: Distribution of study group as per, Restriction.

RESTRICTION	Percentage
Yes	40.38%
No	59.62%
Total	100.00%

Table - 3: Association among study group between, Restriction and HPE finding.

	HPE finding		Total
RESTRICTION	**Malignant**	**Benign**	
Malignant	100.0%	7.5%	40.4%
Benign	0.0%	92.5%	59.6%
Total	37	67	104
	100.0%	100.0%	100.0%

Chi-Square Tests	df	P Value	Association is
Pearson Chi-Square	1	0.000	Significant
Fisher's Exact Test		0.000	Significant

The malignant lesions showed low ADC values than that of benign lesions. The range of ADCs of benign lesions was 0.95x10-3mm^2/sec to 1.28x10-3mm^2/sec, mean value 1.17 x10-3mm^2/sec and malignant lesions were 0.88X 10-3mm^2/sec to 0.95 X 10-3mm^2/ sec, mean 0.93 x10-3mm^2/sec respectively. The difference between the ADC values of benign and malignant lesions was statistically significant ($p < 0.05$).

- Using a threshold value of 0.95 X 10^{-3} sq mm/s for ADC we could differentiate maximum number of malignant from benign lesions with sensitivity and specificity of 97.3% and 95.5%, respectively.

However, our study was restricted to determine role of DWI in differentiating benign from malignant ones. In our set of total 104 lesions studied the results that we got for differentiation between the benign and malignant breast lesions were similar to that noted in various published studies. For the differentiation of benign and malignant breast lesions on DWI, in our study we evaluated the signal intensity change between DWI using a *b*-value of 0, 500 and a high *b* value (1000s /mm^2). Although a suboptimal signal-to-noise ratio and artefacts may hinder detection of the focal lesions with high *b*-value DWI, it facilitates differentiation of malignant lesions from hemangiomas and cysts: malignant lesions showed high signal intensity because of restricted diffusion of extracellular water molecules. In contrast, cystic lesions such as hemangiomas and cysts showed decreased signal intensity at increasing *b*-values owing to a high fluid content. The malignant lesions showed true restriction of diffusion on DWI and ADC map. Benign lesions showed no true restriction of diffusion on DWI and ADC map except in two cases. The two cases in which false positive results were fibroadenomas showing central area of restricted diffusion on DWI and ADC map that turned out to be atypical fibroadenomas.

When ADC values were taken in to consideration the benign lesions showed higher ADC values in comparison to the malignant lesions, primary or recurrent. Though, ADC values are often variable from a study to another, partially related to different equipment and different b-values. ADCs tend to be larger when using small *b*-values, because the signal attenuation due to diffusion plays only a minor role in that case, and ADC values are contaminated by microperfusion. When higher *b*-values are used, ADCs tend to decrease, in relation with less perfusion contamination.

In our study there was a significant difference ($p < 0.05$) noted between mean ADCs of benign and malignant lesions when three b values were used (b = 0, 500 and 1000 s/sq mm; respectively) and average ADC value was calculated. Using a threshold mean ADC value of 0.95 X 10-3 sq mm^2/sec we were able to differentiate benign from malignant lesions with 97.30% sensitivity and 95.52% specificity, respectively. The pooled sensitivity and specificity from various studies has been found to be near to 86% and 84%, respectively.

Potential limitations that we encountered included atypical fibroadenomas where ADC was found to be lower (though we noted lower ADC values only along the margins of these lesions). The diagnosis in these cases then relied upon HPE/ Cytology and follow up imaging findings.

As far as lesion detection is concerned, DWI could detect all benign and malignant lesions visualized on other imaging modalities and other MR sequences including dynamic CEMRI. The sensitivity was 100 % in our study. Better lesion detection with DW imaging by using a small *b* value (100 sec/sq mm) is attributed to suppression of background vessels, equivalent to that achieved with black-blood images, with better contrast-to-noise ratio and better lesion conspicuity.

A limitation of our study was, in recent studies, image quality has been improved with faster parallel imaging methods (e.g., sensitivity encoding = SENSE) and so EPI-related artifacts have been reduced. Additionally, there are publications that report improved image quality in diffusion MRI studies with 3 Tesla MRI devices. The latest improvements to fusion software make it possible to superimpose diffusion-weighted MRI images onto routine MRI images, automatically or manually, overcoming difficulties in the localization of lesions.

Conclusion

To summarise in our set of 104 lesions that we studied using DWI for a total of 97 patients we got following outcomes:

- All malignant lesions (n= 37) showed true restriction of diffusion on DWI and ADC map.
- Out of 67 benign lesions, 62 showed no restriction of diffusion on DWI and ADC map, while 5 lesions showed areas of restricted diffusion on DWI and ADC map.
- Out of 4 cases of recurrent breast carcinoma – post BCS, all the lesions showed area of restricted diffusion on DWI and ADC map.

The malignant lesions showed low ADC values than that of benign lesions. The range of ADCs of benign lesions was 0.95x10-3mm^2/sec to 1.28x 10-3mm^2/sec, mean value 1.17 x10-3mm^2/sec and malignant lesions were 0.88X 10-3mm^2/sec to 0.95 X 10-3mm^2/ sec, mean 0.93 x10-3mm^2/sec respectively. The difference between the ADC values of benign and malignant lesions was statistically significant ($p < 0.05$).

- Using a threshold value of 0.95 X 10^{-3} sq mm/s for ADC we could differentiate maximum number of malignant from benign lesions with sensitivity and specificity of 97.3% and 95.5%, respectively.

Based upon these outcomes following conclusion could be reached:

a) Malignant lesions shows true restriction of diffusion on DWI and have low ADC value than that of benign lesions ,the difference between mean ADC values of the two being statistically significant ($p<0.05$).
b) The diffusion-weighted MRI sequence is a useful diagnostic tool since it can be obtained in free breathing, there is no need to use contrast media, and it can contribute to accurate diagnosis for

discrimination of benign and malignant breast masses.

c) This study recommends threshold value of 0.95 × 10-3 sq mm^2/s for mean ADC to differentiated maximum number of benign and malignant lesions with sensitivity and specificity of 97.3% and 95.5%, respectively.

d) DWI done at low b value has high sensitivity in detection of lesions which is comparable to standard T2WI.

e) Hence, DWI combined with ADC can be used as screening tool for detecting breast lesions and as diagnostic tool for characterizing them as benign or malignant. This has been correlated with histopathological findings.

References

1. Macura KJ, Ouwerkerk R, Jacobs MA, et al. Patterns of enhancement on breast MR images: interpretation and imaging pitfalls. Radiographics, 2006; 26: 1719-1734.
2. Schnall MD, Blume J, Bluemke DA, et al. Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. Radiology, 2006; 238: 42-53.
3. Szabo BK, Aspelin P, Wiberg MK, et al. Dynamic MR imaging of the breast. Analysis of kinetic and morphologic diagnostic criteria. Acta Radiol., 2003; 44: 379-386.
4. Bluemke DA, Gatsonis CA, Chen MH, et al. Magnetic resonance imaging of the breast prior to biopsy. Jama, 2004; 292: 2735-2742.
5. Wiener JI, Schilling KJ, Adami C, et al. Assessment of suspected breast cancer by MRI: a prospective clinical trial using a combined kinetic and morphologic analysis. AJR Am J Roentgenol., 2005; 184: 878-886.
6. Bedrosian I, Mick R, Orel SG, et al. Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. Cancer, 2003; 98: 468-473.
7. Heywang-Kobrunner SH, Bick U, Bradley WG, Jr., et al. International investigation of breast MRI: results of a multicentre study (11 sites) concerning diagnostic parameters for contrast-enhanced MRI based on 519 histopathologically correlated lesions. Eur Radiol., 2001; 11: 531-546.
8. Kaiser WA. Magnetic resonance tomography of the breast. The results of 253 examinations. Dtsch Med Wochenschr., 1989; 114: 1351-1357.
9. Kinkel K, Helbich TH, Esserman LJ, et al. Dynamic high-spatial-resolution MR imaging of suspicious breast lesions: diagnostic criteria and inter observer variability. AJR Am J Roentgenol., 2000; 175: 35-43.
10. Kuhl CK, Mielcareck P, Klaschik S, et al. Dynamic breast MR imaging: are signal intensity time course data useful for differential diagnosis of enhancing lesions? Radiology, 1999; 211: 101-110.
11. Fischer U, Kopka L and Grabbe E. Breast carcinoma: effect of preoperative contrast-enhanced MR imaging on the therapeutic approach. Radiology, 1999; 213: 881-888.