



Journal Homepage: - www.journalijar.com
**INTERNATIONAL JOURNAL OF
 ADVANCED RESEARCH (IJAR)**

Article DOI: 10.21474/IJAR01/9645
 DOI URL: <http://dx.doi.org/10.21474/IJAR01/9645>



RESEARCH ARTICLE

ROLE OF DIFFUSION WEIGHTED MRI IN EVALUATION OF BIRADS3 AND BIRADS4 BREAST LESIONS.

Heba Ahmed Mostafa¹, Sahar Mansour², Sahar M abd Elsalam¹ and Soha.t.Hamed².

1. Department of Radiology, Faculty of Medicine, Beni suef University, Egypt.
2. Department of Radiology, Faculty of Medicine, Cairo University, Egypt.

Manuscript Info

Manuscript History

Received: 04 July 2019

Final Accepted: 06 August 2019

Published: September 2019

Key words:-

Breast cancer, DCE-MRI, DWI, BI-RADS, Sensitivity.

Abstract

Background: Precise diagnosis of suspicious breast lesions helps in better assessment and management. The aim of this study is to explore the role of DCE-MRI and DWI in evaluation of suspicious breast lesions (BI-RADS 3 and 4).

Subjects and Methods: A total of 50 patients with suspicious breast lesions (BI-RADS 3 and 4) participated in the study. After giving informed consent, all patients were subjected to DWI and DCE-MRI, and their findings were compared to histopathology results. DCE-MRI curves, borders, and enhancement were described, and DWI findings were also extracted. Factors predicting distinction of cancerous tissue from benign tissue by DCE-MRI and DWI according to histopathology reference have been analyzed.

Results: Using DCE-MRI, out of 19 patients proven by histopathology to have benign lesions, 12 (63.2%) showed mass lesions and out of 29 patients with malignant lesions 21 (72.4%) had mass lesions ($p < 0.001$). Curves of benign lesions were mostly persistent (83.3%) whenever malignant curves were either plateau or wash out; (47.6%) each ($p < 0.001$). ADC brightness was more frequent in benign lesions ($p < 0.05$). The best cut-off of ADC that can differentiate between malignant and benign lesions was 1.19 (sensitivity 94.7% and specificity 67.7%). DCE-MRI had a sensitivity of 75.8% and specificity of 73.7%, while DWI had a sensitivity of 82.8% and specificity of 73.7%. No statistically significant differences have been noticed between benign and malignant breast non-mass lesions regarding any of the studied measures ($p > 0.05$).

Conclusion: DCE-MRI and DWI are crucial in distinction of suspicious breast mass lesions. The sensitivity and specificity of DCE-MRI and DWI as diagnostics have been determined.

Copy Right, IJAR, 2019, All rights reserved.

Introduction:-

Magnetic resonance imaging (MRI) of breast is suggested to be adjunct to mammography in screening women with higher risk to develop breast cancer.¹ Although mammography is crucial in clinical practice especially in assessment of nodal status and mass sizes, and guiding needle biopsies, its function is restricted by lower sensitivity, presence of dense tissue and architectural distortion that could mask the detection of breast cancer.² On the other hand,

Corresponding Author:-Heba Ahmed Mostafa.

Address:-Department of Radiology, Faculty of Medicine, Beni suef University, Egypt.

dynamic contrast-enhanced MRI (DCE-MRI) and diffusion-weighted imaging (DWI) have the ability to differentiate between normal and diseased breast tissue with higher sensitivity. Such distinction could minimize the number of biopsies, especially in suspicious lesions. Therefore it is gaining popularity in clinical practice as a complementary diagnostic tool for breast cancer.³

Breast DCE-MRI includes typically multiple sequences of post-contrast recorded at different times after injecting a contrast agent. The time-signal intensity curves resulting from these sequences reflect the intensity changes induced by contrast uptake over different periods. These kinetic curves can be categorized according to the voxel level to persistent, plateau and washout, and may help in diagnosing breast cancer, expecting cancer recurrence, and measuring chemotherapeutic response. Other kinetic characteristics such as enhancement pattern in addition to shape of lesion may be of diagnostic value in detecting breast cancer and its subtypes.⁴⁻⁸

However, specificity of DCE-MRI is still questionable in screening and characterization, because the interpretation of breast DCE-MRI depends on many factors such as expertise of the radiologist and adequate use of visualization techniques, which could result in substantial amount of false positive results.^{8,9} Further, DCE-MRI is an expensive technique, and could not be available in most health-settings. Also, it cannot be used for patients with previous reaction to contrast agents or those with renal dysfunction.^{8,9}

On the other hand, DWI measures the mobility of water in tissue. The movement of water is more restricted in tissues with a higher cellular content and numerous intact cell membranes such as those in malignant breast lesions. DWI is considered sensitive to disrupted characteristics that could indicate malignancy such as cell organization, density, extracellular space, and cell membrane permeability. This advantage may help in more precise discrimination between benign and cancerous breast lesions.⁸

In this regard, the objective of this study is to investigate the role of DCE-MRI and DWI in evaluation of suspicious breast lesions (BI-RADS 3 and 4).

Subjects and Methods:-

In this observational study, a total of 50 patients with suspicious breast lesions, and categorized according to Breast Imaging Reporting and Data System (BI-RADS) as BI-RADS 3 and 4, using full-field digital mammography and ultrasonography, were recruited for this study. Exclusion criteria were history of breast implants, lactating, benign breast surgery within 1 year, and ineligibility for breast MRI.

Then, all included patients were referred for further DWI and DCE-MRI examination. For premenopausal women; MRI was ideally scheduled the 2nd week of the menstrual cycle.

DWI was performed before the DCE-MRI acquisition using a diffusion-weighted echo-planar imaging (EPI) sequence with parallel imaging (Philips Intera); reduction factor 2, 7000/71.5, number of excitations 2, matrix 240 × 240, field of view 34 cm, slice thickness 3 mm, and gap 0. Diffusion gradients were applied in 6 directions with $b = 0, 300, 600$ and 1500 s/mm^2 , and the scanning time was 4 minutes. Respiratory triggering was used for better resolution.^{9,10}

A bolus of gadolinium-dimeglumine (Gd-DTPA) (Magnevist, Schering AG Berlin, Germany) was injected manually intravenous at a dose of (0.1 mmol/kg) followed by saline flush to ensure that contrast-enhanced images could be obtained immediately after contrast agent injection.^{9,10}

Dynamic T1 WIs was performed, using Gradient echo T1-weighted image, with fat suppression at the following time points: 1.27 minute, 2.55 minute, 4.21 minute, 5.47 minute and 7.13 minute.^{9,10}

Post processing image subtraction was obtained between the post contrast imaging showing maximum enhancement and pre-contrast images (in the same axial plane). Diffusion maps were formed. A noise-level threshold of 200 was applied to mask the $b = 0 \text{ s/mm}^2$ images before forming diffusion maps, and apparent diffusion coefficient (ADC) maps were obtained from the resulting DWIs.^{9,10}

Then, DCE-MRI was performed with high field strength 1.5 Tesla on Signa system (Philips Intera) using dedicated double breast coil. Coronal T1 weighted spin echo sequence was carried out for localization purpose and followed by

plain sequences using T1-weighted fast spin echo sequence (TR=501 msec., TE=10 msec.), in addition to T2-weighted fast spin echo sequence (TR=4131msec., TE=120msec.) in axial orientation.⁵

For each DCE-MRI-detected lesion at the corresponding location on the combined DWI series, a region of interest (ROI) was defined. The mean ADC of the voxels in the ROI was calculated for each lesion. Quantitative analysis was done by placing the ROI at the most enhanced part within the lesion result in automatically created time/signal intensity curve.¹⁰

Subtraction images were first examined to detect the presence or absence of lesion enhancement. In case of lesion enhancement the corresponding non subtracted pre-contrast and post contrast images in each time point was viewed together and lesions interpretation took place whether it a focus, mass or non-mass like enhancement. In case of mass enhancement evaluation was carried out as follow; shape, border, pattern of enhancement and dynamic behavior. In case of non-mass like enhancement, its distribution and enhancement pattern were evaluated.^{5,10}

DWIs and ADC maps were then examined regarding the signal intensity and the mean ADC of each lesion. BIRADS classification was applied for each lesion based on the combination of morphologic and kinetic criteria.^{5,10} Later, a surgical biopsy was performed for all patients and those with non-palpable lesions underwent radio-guided occult lesion localization (ROLL) prior to the biopsy. Haematoxylin and eosin stained slides of formalin-fixed and paraffin-embedded tissue blocks were assessed by a pathologist.

The study was conducted in Kasr El-Aini Hospital during the period between December 2015 and January 2017. Data entry, verification, and validation were carried out using standard computer software. Data were analyzed using the software, Statistical Package for Social Science (SPSS Inc. Released 2009, PASW Statistics for Windows, version 18.0: SPSS Inc., Chicago, Illinois, USA), then processed and tabulated. Frequency distribution with its percentage and descriptive statistics with mean and standard deviation were calculated. Chi-square, t-test, correlations were done whenever needed. P values of less than 0.05 were considered significant.

The study was conducted in full accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki, and data for each patient were collected only after obtaining that patient's signed written data release forms.

Results:-

Out of the 50 included patients with suspicious breast lesions, 2 patients were considered free by both MRI and histopathology.

DCE-MRI showed that out of the 19 patients proven by histopathology to have benign lesions, 12 (63.2%) showed mass lesions and out of 29 patients with malignant lesions 21 (72.4%) had mass lesions, while focal lesions were more associated with benign lesions ($p < 0.001$). Malignant lesions were more likely to show Type III curves; 41.4% compared to 0% in benign lesions ($p < 0.001$) (Table 1).

For mass lesions, the margins of the benign lesions tended to be distinct (91.7%), while those of the malignant lesions were either indistinct (66.7%) or speculated (23.8%) ($p < 0.001$). Benign lesions were more likely to show homogenous enhancement (66.8%), while malignant lesions were more heterogeneous (47.7%) ($p < 0.05$). Curves of benign lesions were mostly persistent (83.3%) whenever malignant curves were either plateau or wash out; (47.6%) each ($p < 0.001$). Further, ADC was significantly higher in benign lesions compared to malignant lesions, and the brightness was more frequent in benign lesions ($p < 0.05$). Also, DWI of mass lesions showed that benign lesions were more likely to be bright ($p < 0.05$) (Table 1).

On the other hand, no statistically significant differences have been noticed between histopathology-proven benign and malignant lesions regarding enhancement, curve shape ADC or DWI ($p > 0.05$) (Table 1).

However, DCE-MRI and DWI did not show good ability in distinction between non-mass cancerous and benign lesions, since no statistically significant differences have been shown between both groups ($p > 0.05$) (Table 1).

DCE-MRI was accurate in diagnosing 75% of lesions with a sensitivity of 75.8% and specificity of 73.7%, while DWI achieved an accuracy of 77.6% with a sensitivity of 82.8% and specificity of 73.7% (Table 2).

The best cut-off of ADC that can differentiate between malignant and benign lesions stood at 1.19 (AUC 0.83, sensitivity 94.7%, and specificity 67.7%) (Figure1).

Table 1:-Assessment of MRI findings in regards to histopathological findings

MRI		Histopathology		
		Benign (n, %)	Malignant (n, %)	P value
Morphology (n=48)	Mass	12 (63.2)	21 (72.4)	<0.001*
	Non-mass	4 (21.0)	7 (24.1)	
	Focal areas	3 (15.8)	1 (3.5)	
Curve (n=48)	Type I	11 (57.9)	5 (17.2)	<0.001*
	Type II	8 (42.1)	12 (41.4)	
	Type III	0 (0.0)	12 (41.4)	
Mass Margin (n=33)	Distinct	11 (91.7)	2 (9.5)	<0.001*
	Indistinct	1 (8.3)	14 (66.7)	
	Speculated	0 (0.0)	5 (23.8)	
Mass Enhancement Pattern (n=33)	No	2 (16.6)	0 (0.0)	0.024*
	Homogenous	8 (66.8)	7 (33.3)	
	Heterogeneous	1 (8.3)	10 (47.7)	
	Ring	1 (8.3)	4 (19.0)	
Mass Curve Shape (n=33)	Persistent	10 (83.3)	1 (4.8)	<0.001*
	Plateau	2 (16.7)	10 (47.6)	
	Wash out	0 (0.0)	10 (47.6)	
Mass Diffusion (n=33)	Restricted	8 (66.8)	16 (76.2)	0.762
	Facilitated	4 (33.2)	5 (23.8)	
Mass Quantitative ADC (Mean±Sd)		1.3±0.4	1.0±0.3	0.048*
Mass Qualitative ADC (n=33)	Bright	7 (58.3)	1 (4.8)	0.001*
	Intermediate	3 (25.0)	13 (61.9)	
	Intermediate-Bright	2 (16.7)	0 (0.0)	
	Low	0 (0.0)	7 (33.3)	
Mass DWI (n=33)	Bright	8 (66.6)	0 (0.0)	0.123
	Intermediate	2 (16.7)	16 (76.2)	
	Intermediate-Bright	2 (16.7)	5 (23.8)	
Non-mass Enhancement Pattern (n=11)	Homogenous	2 (50.0)	1 (14.3)	0.279
	Heterogeneous	2 (50.0)	6 (85.7)	
Non-mass Curve Shape (n=33)	Persistent	0 (0.0)	3 (42.8)	0.073
	Plateau	4 (100.0)	2 (28.6)	
	Wash out	0 (0.0)	2 (28.6)	
Non-mass Quantitative ADC (Mean±Sd)		1.4±0.1	1.3±0.3	0.521
Non-mass Qualitative ADC (n=11)	Bright	2 (50.0)	1 (14.3)	0.378
	Intermediate	2 (50.0)	5 (71.4)	
	Low	0 (0.0)	1 (14.3)	
Non-mass DWI (n=11)	Bright	3 (75.0)	5 (71.4)	0.721
	Intermediate	1 (25.0)	2 (28.6)	

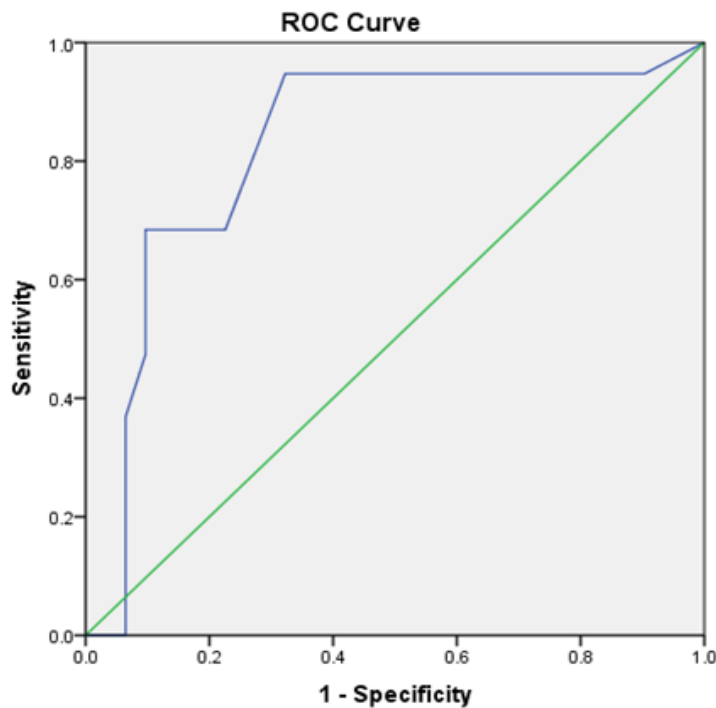
*p value is considered significant

Table 2:-The diagnostic accuracy of MRI compared to histopathological findings

Accuracy		Histopathology		
		Benign	Malignant	Total
DCE-MRI	Benign	14 (TN)	7 (FN)	21
	Malignant	5 (FP)	22 (TP)	27
	Total	19	29	48
Sensitivity=TP/TP+FN=				75.8%

Specificity= $TN / (TN + FP) =$				73.7%
Positive Predictive Value= $TP / (TP + FP) =$				81.5%
Negative Predictive Value= $TN / (TN + FN) =$				66.7%
Accuracy= $(TP + TN) / (TP + TN + FP + FN) =$				75%
Accuracy		Histopathology		
		Benign	Malignant	Total
DWI-MRI	Benign	14 (TN)	5 (FN)	19
	Malignant	5 (FP)	24 (TP)	29
	Total	19	29	48
Sensitivity= $TP / (TP + FN) =$				82.8%
Specificity= $TN / (TN + FP) =$				73.7%
Positive Predictive Value= $TP / (TP + FP) =$				82.8%
Negative Predictive Value= $TN / (TN + FN) =$				73.7%
Accuracy= $(TP + TN) / (TP + TN + FP + FN) =$				77.6%

TP; True Positive, TN; True Negative, FP; False Positive, FN; False Negative



Area under the curve (AUC): 0.83; 95%CI 0.70-0.95; Best Cut-off:1.19; Sensitivity: 94.7%, Specificity: 67.7%

Figure 1:-ROC curve for the best cut-off diagnostic value of ADC to malignancy

Discussion:-

Identifying precise and effective tools in screening for breast cancer in suspicious lesions is crucial. In the current study, the characteristics of cancerous mass lesions have been clearly differentiated from benign lesions, using DCE-MRI and DWI; due to the differences in type of kinetic curves, enhancement patterns, margins and borders. Both quantitative ADC and qualitative ADC have been also shown as predictors for cancerous lesions. Malignant lesions in our study were more likely to take mass shape and type III kinetic curves. Malignant mass lesions were commonly of indistinct margin, heterogeneous enhancement and plateau or washout curves. Quantitative ADC of malignant mass lesions was lower and qualitative ADC was less bright, compared to benign lesions. Also, when compared to histopathology as a reference DCE-MRI had a sensitivity of 75.8% and specificity of 73.7%, while DWI had a sensitivity of 82.8% and specificity of 73.7%.

In consistence with our findings, a recent systematic review over several studies using DCE-MRI for diagnosis of breast cancer showed that the kinetic and morphological features of mass lesions described by DCE-MRI can differentiate between cancerous and benign lesions with reasonable sensitivity and specificity.¹¹

A recent retrospective study over 51 patients with breast cancer and 51 controls showed that kinetic measures of DEC-MRI could distinct between breast cancer and benign lesions. The authors also concluded that the abnormal enhancement characteristics may represent biological progression of potential breast cancer.¹²

Other studies have also focused on the role of the morphological features, detected by DCE-MRI, in diagnosing breast cancer. The studies showed in details the indication of DCE-MRI in identifying and evaluating breast lesions, especially in high risk patients.^{13,14}

Also, DWI has been suggested to be useful in assessing the malignant suspicious mass lesions detected on screening mammograms and reduce unnecessary biopsies. DWI improves the diagnostic accuracy of breast MRI, since it provides information about the cellularity of the lesion.⁹

The accuracy of MRI in diagnosing suspicious lesions have been investigated by Sardanelli and colleagues who examined results of 19 patients with suspicious mammographic findings; 5 of these were malignant, 4 of which could be diagnosed by MRI achieving a sensitivity of 80%.¹⁵

Alike, Lee et al cited outcomes of MRI for 86 suspicious lesions, 9 of them were malignant; and there was 1 additional incidental malignancy reported among a total 12 MRI lesions.¹⁶ Similar studies on suspicious lesions, however on different sample sizes, have also reached the same conclusion.¹⁷⁻¹⁹

In the current study, we could not find statistically significant differences between benign and malignant non-mass breast lesions regarding morphological or enhancement kinetic features of DCE-MRI or DWI.

In agreement, a recently-published study over patients with non-mass lesions showed that DCE-MRI could not differentiate for sure between malignant and benign non-mass lesions. The authors concluded that DCE-MRI cannot show the subtle histological differences between non-proliferative lesions, proliferative lesions without atypia and proliferative lesions with atypia. They also recommended further histopathology specimens for such cases.²⁰ In contrary, DWI in one study was more specific than DCE-MRI in defining the nature of non-mass lesions.²¹

In our study, ADC values of benign mass lesions were significantly higher than those of malignant mass lesions. Previous studies have suggested the efficacy of ADC in the precise differentiation between benign and malignant breast lesions, yielding different calculated ADC values and cutoff points.^{6,22}

In conclusion, DCE-MRI and DWI are essential in distinction of suspicious breast mass lesions; however their ability to differentiate between malignant and benign non-mass lesions is still questionable. The sensitivity and specificity of DCE-MRI and DWI are comparable and their diagnostic ability has been determined.

References:-

1. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *Cancer J Clin.* 2007; 57:75–89.
2. Boyd NF, Martin LJ, Yaffe MJ, Minkin S. Mammographic density and breast cancer risk: current understanding and future prospects. *Breast Cancer Res.* 2011; 13(6):223.
3. Weinstein S, Rosen M. Breast MR imaging: current indications and advanced imaging techniques. *Radiol Clin N Am.* 2010; 48(5):1013–42.
4. Hylton N. Dynamic contrast-enhanced magnetic resonance imaging as an imaging biomarker. *J Clin Oncol.* 2006; 24(20):3293–8.
5. Kuhl CK, Mielcareck P, Klaschik S, Leutner C, Wardelmann E, Gieseke J, et al. Dynamic breast MR imaging: are signal intensity time course data useful for differential diagnosis of enhancing lesions? *Radiology.* 1999; 211(1):101–10.
6. El Khouli RH, Macura KJ, Jacobs MA, Khalil TH, Kamel IR, Dwyer A, et al. Dynamic contrast-enhanced MRI of the breast: quantitative method for kinetic curve type assessment. *Am J Roentgenol.* 2009; 193(4):295–300.

7. Partridge SC, Rahbar H, Murthy R, Chai X, Kurland BF, DeMartini WB, et al. Improved diagnostic accuracy of breast MRI through combined apparent diffusion coefficients and dynamic contrast-enhanced kinetics. *Magn Reson Med*. 2011; 65(6):1759–67.
8. Krammer J, Pinker-Domenig K, Robson ME, Gonen M, Bernard-Davila B, Morris EA, et al. Breast cancer detection and tumor characteristics in BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res Treat*. 2017; 163:565–71.
9. Mann RM., Kuhl CK, Kinkel K, Boetes C. Breast MRI: guidelines from the European society of breast imaging. *Eur Radiol* 2008; 18, 1307–18.
10. Ashraf AB, Gavenonis SC, Daye D, Mies C, Rosen MA, Kontos D. A multichannel Markov random field framework for tumor segmentation with an application to classification of gene expression-based breast cancer recurrence risk. *IEEE Trans Med Imaging*. 2013; 32(4):637–48.
11. Fusco R, Sansone M, Filice S, Carone G, Amato DM, Sansone C, et al. Pattern Recognition Approaches for Breast Cancer DCE-MRI Classification: A Systematic Review. *J. Med. Biol. Eng*. 2016; 36:449–59.
12. Wu S, Berg WA, Zuley ML, Kurland BF, Jankowitz RC, Nishikawa R, et al. Breast MRI contrast enhancement kinetics of normal parenchyma correlate with presence of breast cancer. *Breast Cancer Research* 2016; 18:76.
13. Lee CH. Problem solving MR imaging of the breast. *Radiol Clin North Am* 2004; 42:919–934.
14. Nunes LW, Schnall MD, Orel SG. Update of breast MR imaging architectural interpretation model. *Radiology* 2001; 219:484–494.
15. Sardanelli F, Melani E, Ottonello C. Magnetic resonance imaging of the breast in characterizing positive or uncertain mammographic findings. *Cancer Detect Prev* 1998; 22(1):39–42.
16. Lee CH, Smith RC, Levine JA, Troiano RN, Tocino I. Clinical usefulness of MR imaging of the breast in the evaluation of the problematic mammogram. *AJR Am J Roentgenol* 1999; 173(5):1323–9.
17. Spick C, Szolar DHM, Preidler KW, Tillich M, Reittner P, Baltzer PA. Breast MRI used as a problem-solving tool reliably excludes malignancy. *Eur J Radiol* 2015; 84(1):61–4.
18. Oztekin PS, Kosar PN. Magnetic resonance imaging of the breast as a problem-solving method: to be or not to be? *Breast J* 2014; 20 (6):622–31.
19. Strobel K, Schradling S, Hansen NL, Barabasch A, Kuhl CK. Assessment of BI-RADS category 4 lesions detected with screening mammography and screening US: utility of MR imaging. *Radiology* 2015; 274 (2):343–51.
20. Milosevic ZC, Nadrljanski MM, Milovanovic ZM, Gusic NZ, Vucicevic SS, Radulovic OS. Breast dynamic contrast enhanced MRI: fibrocystic changes presenting as a non-mass enhancement mimicking malignancy. *Radiol Oncol* 2017; 51(2): 130-6.
21. Ochi M, Kuroiwa T, Sunami S, Murakami J, Miyahara S, Nagaie T, et al. Diffusion-weighted imaging (b value = 1500 s/mm²) is useful to decrease false-positive breast cancer cases due to fibrocystic changes. *Breast Cancer* 2013; 20: 137-44.
22. Sinha S, Lucas-Quesada FA, Sinha U, DeBruhl N, Bassett LW. In vivo diffusion-weighted MRI of the breast: potential for lesion characterization. *J Magn Reson Imaging* 2002; 15(6):693–704.