

# Diagnostic investigation of breast magnetic resonance imaging in malignant and benign mass lesions

Masoumeh Gity<sup>1,2</sup>, Ali Arabkheradmand<sup>3</sup>, Elham Taheri<sup>1</sup>, Madjid Shakiba<sup>1</sup>

<sup>1</sup>Advanced Diagnostic and Interventional Radiology Research Center (ADIR), Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Radiology, Medical Imaging Center, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Surgery, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran

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## Corresponding author:

Dr. Elham Taheri  
Advanced Diagnostic  
and Interventional Radiology  
Research Center (ADIR)  
Medical Imaging Center  
Keshavarz Blvd.  
Tehran, 1419733141, Iran  
Phone: +98-912 6200762  
E-mail: [elhamtaheri.md@gmail.com](mailto:elhamtaheri.md@gmail.com)

## Abstract

**Introduction:** Breast magnetic resonance imaging (BMRI) has been identified as a valuable modality in the diagnosis of breast cancer and monitoring the response to chemotherapy. The aim of this study was to evaluate the relative importance of different descriptors of breast masses in contrast-enhanced breast MRI.

**Material and methods:** In a database of pathologically proven breast lesions, in total 433 masses in 312 patients detected by contrast-enhanced breast MRI were selected. All images were assessed according to the MRI BI-RADS lexicon and those with significant positive MRI findings (BI-RADS categories 3, 4, 5) were enrolled in the study.

**Results:** Mean age of patients was  $45.09 \pm 10.5$  years. The most frequent BI-RADS score was 4 (60.7%), followed by 3 (27%). Among the morphologic descriptors of the enhancing masses, the findings most strongly associated with malignancy included spiculated margin (60.6%) and irregular shape (38%). Considering the dynamic descriptors, a wash-out pattern in the time-intensity curve was the most powerful finding associated with malignancy (27.9%). Among all breast MRI descriptors, the best odds ratio (OR) in association with malignancy was noted for spiculated margin (OR = 10.2) followed by wash-out or plateau curves (OR = 6.1), size greater than 1 cm (OR = 4.3) and irregular shape (OR = 3.1).

**Conclusions:** It seems that morphologic descriptors of MRI BI-RADS for enhancing masses are quite specific, while dynamic descriptors of the masses are highly sensitive. Appropriate consideration and combination of different BI-RADS findings could help in better characterization of enhancing masses on breast MRI, lowering the rate of false positive reports and avoiding unnecessary biopsies.

**Key words:** breast, magnetic resonance imaging, mass, diagnosis, biopsy.

## Introduction

Breast magnetic resonance imaging (BMRI) has been identified as a valuable modality in the diagnosis of breast cancer [1, 2], and monitoring the response to chemotherapy [3–5]. The sensitivity of breast MRI for diagnosing invasive breast cancer has been reported between 88% and 100%, surpassing all other conventional modalities such as mammog-

raphy and ultrasound [6]. However, its specificity in discriminating malignant from benign lesions is highly varied, reported in the range of 35% to 90% [7, 8]. Different lesions found in breast MRI include enhancing masses, non-mass-like enhancing lesions and enhancing foci.

The MRI BI-RADS lexicon has been developed in order to obtain a standard system of reporting. This lexicon defines morphologic and kinetic descriptors for assessing breast lesions and finally scores the lesion in a range of BI-RADS categories from 0 to 6. Although some paradigms for interpretation and scoring of the lesions in the BI-RADS system have been proposed, the final scoring is somewhat subjective. As the assessment is based on different morphologic and dynamic criteria, a critical question is the relative importance of each descriptor in the final assessment of breast MRI which could optimize the accuracy of the MRI report. A review of the literature shows that there have been similar studies with different approaches in this issue [9–12].

In this study, our goal was to evaluate the importance of each BI-RADS descriptor of “enhancing masses” and its relation to benign outcome or malignant pathology among a group of patients with a final assessment of BI-RADS categories 3–5.

## Material and methods

### Patient enrolment

The study was approved by the ethics committee of the Tehran University of Medical Sciences. In a database of patients referred from September 2007 until March 2013, for breast MRI, we included patients with a final assessment BI-RADS categories 3, 4 and 5 who had a pathological examination of MRI-detected breast lesions. Tissue sampling included core needle/vacuum-assisted image guided biopsy before the operation, post-operative pathologic examination, or both. We excluded patients with a previous biopsy-proven malignancy (BI-RADS category 6), any history of neo-adjuvant chemotherapy or those who showed a discrepancy between the pre-operative and post-operative pathology results. We included the follow-up of patients who did not have surgery, and those without follow-up MRI for at least 12 months were excluded. In addition, as we did not have access to MRI-guided biopsy in that period, we excluded patients who were referred to other centers for MRI-guided biopsy.

Finally, 433 enhancing mass lesions (in 312 patients) were enrolled in the study. Among these masses, 117 had a BI-RADS category of 3 (probably a benign finding), 263 had a BI-RADS category of 4 (suspicious lesions) and 53 had a BI-RADS category of 5 (highly suggestive of malignancy)

(Figures 1 and 2). In addition to evaluation of the recent mammography, second look ultrasound examination was obtained for all BI-RADS 4 and 5 category enhancing masses on MRI.

In case of positive ultrasound or mammographic findings that could be correlated with the MRI enhancing mass, core needle biopsy with a 14-gauge needle or vacuum-assisted biopsy with a 9- or 12-gauge needle was performed.

A small group of enhancing masses with BI-RADS 3 category assessment that could not be localized on ultrasound examination or mammography was followed by a 6- and 12-month MRI. Also some patients with BI-RADS 4 category masses who did not undergo MRI-guided biopsy and had follow-up MRI in our institute were included.

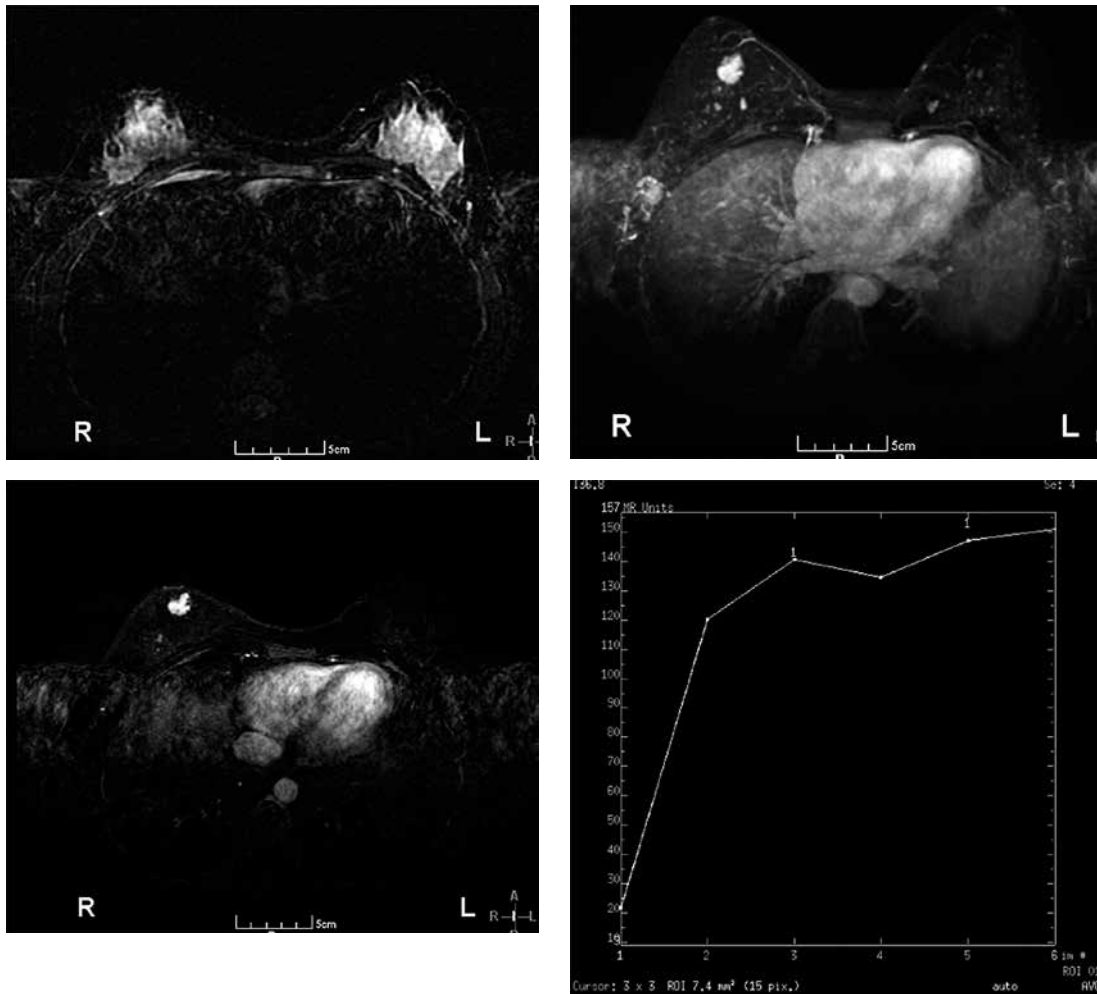
All 53 patients with BI-RADS 5 category masses underwent image-guided biopsy, finally confirmed by surgery. The masses with a stable or downgraded BI-RADS score after 12 months were considered as benign and were scheduled for follow-up by sonography and/or screening mammography depending on the patient's age.

### Magnetic resonance imaging protocol

Magnetic resonance imaging was conducted using a 1.5T Signa system (General Electric Medical Systems, USA) with a bilateral phased-array 4-channel breast coil. All patients were scanned in the prone position. Among the premenopausal patients, MRI was conducted during the second week of their menstrual cycle, whenever possible. Axial T1-weighted and axial STIR images were obtained, followed by six series of axial dynamic T1-weighted three-dimensional, fat-suppressed spoiled gradient-echo, one set prior to and five series after the rapid bolus injection of 0.1 mmol/kg gadolinium-DTPA (Dotarem, Guerbet), followed by a 15 ml saline injection.

The axial T1-weighted sequence was obtained with the following parameters: TR/TE: 400/10; BW: 31.25 Hz/pixel; FOV: usually 32 mm; slice thickness: 5.0 mm; matrix size: 384 × 256; NEX: 1. The parameters of axial STIR were as follows: TR/TE: 4500/63; bandwidth: 62.50; FOV: usually 32; slice thickness: 5.0 mm; matrix size: 320 × 256; NEX: 1. A dynamic T1-weighted three-dimensional, fat-suppressed spoiled gradient-echo sequence with the following parameters was obtained: TR/TE: 9/4; BW: 31.25; FOV: 32; slice thickness: 4.0 mm with no intersection gap; matrix size: 352 × 288; NEX: 1; FA: 300.

The dynamic series were obtained every 60–90 s, so all six series were performed within 9 min of *i.v.* contrast injection. MR mammograms were interpreted by a dedicated, sub-specialized, expert radiologist with more than 15 years of experience in breast imaging. The assessment of morphologic



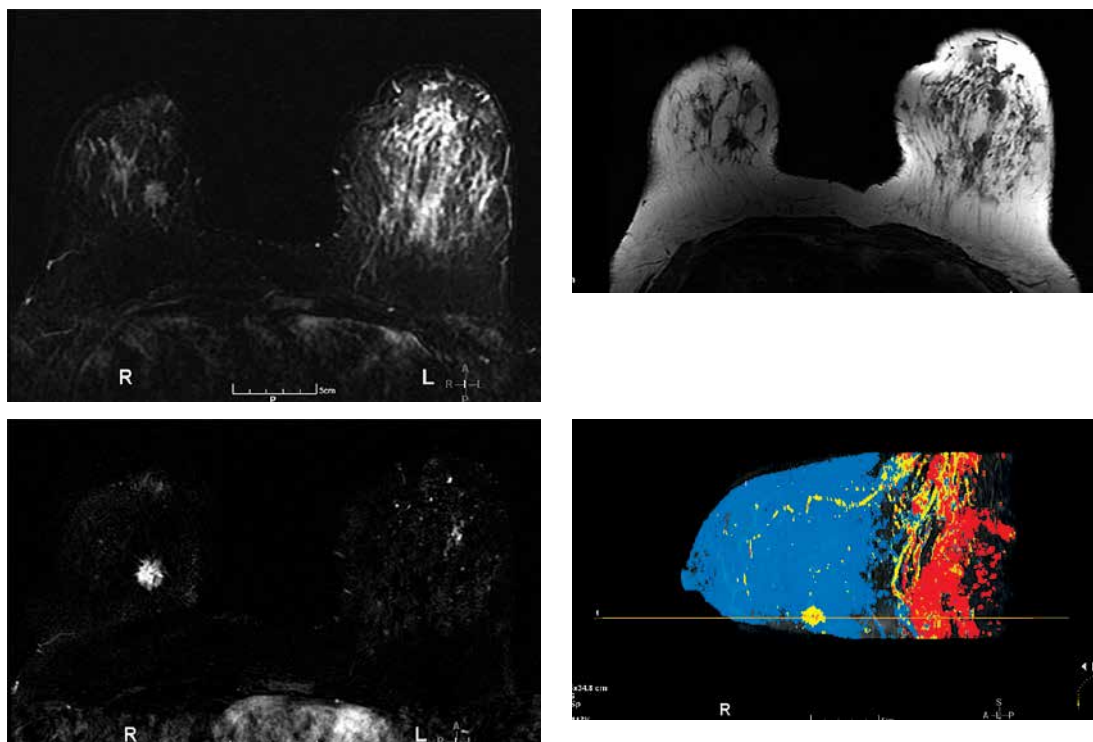
**Figure 1.** A 45-year-old female patient with screening detected borderline appearing mass in LIQ of right breast on ultrasound examination, in breast MRI, a low T1, low STIR, enhancing mass was detected in the right lower inner quadrant, which showed irregular shape and borders, heterogeneous internal pattern and type 2 curves assessed as BI-RADS category type 4. The mass proved to be a complex fibroadenoma on core needle biopsy

configuration and kinetic enhancement was based on the American College of Radiology BI-RADS MRI lexicon version 4. We used CAD-STREAM for a systematized interpretation of MR mammograms and five series of three-dimensional subtracted images were processed by CAD-stream Confirma. The morphologic configurations included focus/foci (punctuate dots of enhancement smaller than 5 mm), mass (enhancing masses that had space-occupying features larger than 5 mm) and non-mass-like enhancement (areas of enhancement that had neither tri-dimensional shape nor typical mass characteristics) [13]. Lesions showing slow initial contrast enhancement (less than 50% enhancement in the first 60–90 s) were excluded, and those with 50–100% and more than 100% initial rise of the time-intensity curve were named as intermediate (non-rapid) and rapid type of curves respectively. Among three types of time-intensity curves including persistent, plateau and rapid-wash out, the most concerning curve type

in each lesion was considered for interpretation. Based on morphologic and kinetic enhancement characteristic results, all patients were assigned a BI-RADS-category score of 0–6 [14].

#### Statistical analysis

We reviewed enhancing masses on breast MRI with BI-RADS 3, 4, and 5 assessment categories, and compared different MRI findings descriptors with final outcome of the patients. We used the  $\chi^2$  test for assessment of statistical difference of categorical variables among malignant and benign lesions. In order to calculate diagnostic indices including sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio, we used the cross tabulations in dichotomized variables, and we also calculated the odds ratios based on these tables. In addition, multivariate logistic regression analysis was used for assessment of malignancy as the dependent variable and different



**Figure 2.** A 45-year-old high-risk female patient presented with a palpable mass in the right lower part, referred for preoperative staging, after suspicious mammography and ultrasound. Breast MRI on workstation as reviewed by radiologist showed: **A** – A round enhancing mass with speculated borders, dark on T1W, and isosignal on STIR images. **B** – The mass shows heterogeneous internal pattern with type 2 and type 3 dynamic curves (as yellow and red colors); final BI-RADS assessment was category 5. The mass proved to be invasive ductal carcinoma

descriptors to find the independent MRI descriptors which could predict the malignancy.

All data were analyzed using SPSS ver. 16 for Windows (SPSS Inc., Chicago, IL, USA). A  $p$ -value  $< 0.05$  was accepted to be statistically significant.

## Results

In a retrospective study we searched a database of pathologically proven breast lesion patients who underwent dynamic contrast-enhanced breast MRI examination before operation or biopsy, and finally 433 masses among 312 patients were evaluated. The mean age of the patients was  $45.1 \pm 10.5$  years (range: 18 to 83 years). Among breast lesions, 198 (45.7%) were positioned in the right breast and 235 (54.3%) were detected in the left breast. The most common location was upper outer quadrant (UOQ) (21.7%) followed by lower outer quadrant (LOQ) (20.8%). In total, 88 (20.3%) observed masses were malignant. The most frequent BI-RADS score was 4 ( $n = 263$ , 60.7%), followed by 3 ( $n = 117$ , 27%). Distribution of other imaging characteristics of the mass lesions is summarized in Table I. Keeping in mind the fact that early background enhancement may obscure some details, the reported early background enhancement was observed in 89 (26.7%) of 312 patients. The most

common shape of the masses was an oval/lobulated shape that was seen in 288 lesions (66.5%) (Table I).

The mean diameter of the enhancing masses was  $12.4 \pm 6.1$  mm (range: 5–40), and 117 (33.6%) lesions had a diameter less than 10 mm. The mean diameter of benign and malignant masses was  $11.6 \pm 5.4$  mm and  $15.7 \pm 7.5$  mm, respectively ( $p < 0.0001$ ). The association of different BI-RADS descriptors with malignancy was assessed. In our study group selected based on mentioned inclusion and exclusion criteria, masses greater than 10 mm were more associated with malignancy (26.4% vs. 7.7%,  $p$ -value  $< 0.001$ ).

The frequency of malignant and benign pathologies in each descriptor is presented in Table II. In all descriptors except for enhancement type, the distribution of malignancy was statistically different in subgroups.

In the cross tabulation, in each descriptor group, the subclass that showed the highest association with malignancy was determined. For example, among all subclasses of shape (including round, oval/lobulated and irregular shapes), the frequency of malignancy was higher in irregular masses (38% in irregular, 16.7% in oval/lobulated and 15.2% in round masses). Based on the highest association with malignancy, we categorized each descriptor into two groups, the first group with the highest

Table I. Distribution of MRI descriptors in patients with breast mass lesions

Data characteristics	Categorization	Number	Percent
BI-RADS	3	117	27
	4	263	60.8
	5	53	12.2
Early background enhancement	Yes	89	26.7
	No	244	73.3
Descriptors:			
Shape	Round	66	15.2
	Oval/lobulated	288	66.5
	Irregular	79	18.2
Margin	Circumscribed	229	52.9
	Noncircumscribed	204	47.1
Internal enhancement	Central enhancement	1	0.2
	Dark internal septation	28	6.5
	Homogeneous	198	45.7
	Rim enhancement	38	8.8
	Heterogeneous	163	37.6
	Enhanced internal septation	3	0.7
Enhancement type	Rapid	409	94.5
	Non-rapid	24	5.5
Curve type	Persistent	98	22.6
	Plateau	106	24.5
	Wash-out	229	52.9
T2 Finding	Hypo-signal	34	12
	Iso-signal	63	22.3
	Hyper-signal	186	65.7
Size	< 10 mm	117	33.6
	≥ 10 mm	231	66.4

frequency of malignancy and the second group consisting of other descriptors. For example, regarding shape, the irregular subclass was considered as the first group and the two other subclasses (including oval/lobulated and round masses) were integrated in one group as the second group. We cross-tabulated these two new groups of BI-RADS descriptors with the pathology results and calculated the odds ratio and diagnostic indices including sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio (Tables III and IV).

In a multivariate logistic regression analysis in which the pathology result was considered as the

dependent variable and the above-mentioned dichotomized BI-RADS descriptors were considered as the independent variables, the Cox model R square was 0.23 and the size, margin, enhancement type and curve type remained significant in the model, while the shape and internal enhancement did not have a significant *p*-value in the model (Table V).

## Discussion

Magnetic resonance imaging can detect breast cancers that are occult in other imaging modalities or physical examination. The sensitivi-

**Table II.** Distribution of malignant and benign features according to each descriptor and BI-RADS of MRI

Descriptors	Categorization	Malignant, n (%)	Benign, n (%)	P-value
Shape	Round	10 (15.2)	56 (84.8)	< 0.001
	Oval/lobulated	48 (16.7)	240 (83.3)	
	Irregular	30 (38)	49 (62)	
Margin	Circumscribed	18 (7.9)	211 (92.1)	< 0.001
	Non circumscribed	70 (34.3)	134 (65.7)	
Internal enhancement	Central enhancement	0 (0)	1 (100)	0.041
	Dark internal septation	1 (3.6)	27 (96.4)	
	Homogeneous	35 (17.7)	163 (82.3)	
	Rim enhancement	9 (23.7)	29 (76.3)	
	Heterogeneous	42 (25.8)	121 (74.2)	
	Enhanced internal septation	1 (33.3)	2 (66.7)	
Enhancement type	Non-rapid	2 (8.3)	22 (91.7)	0.133
	Rapid	86 (21)	323 (79)	
Curve type	Persistent	5 (5.1)	93 (94.9)	< 0.001
	Plateau	19 (17.1)	87 (82.1)	
	Wash-out	64 (27.9)	165 (72.1)	
Size	< 10 mm	9 (7.7)	108 (92.3)	< 0.001
	≥ 10 mm	61 (26.4)	170 (73.6)	
BI-RADS	3	4 (3.4)	113 (96.6)	< 0.001
	4	41 (15.6)	222 (84.4)	
	5	43 (81.1)	10 (18.9)	

ty of MRI for breast cancer is higher than 90% (94–99%), while regarding overlapping features among malignant and benign lesions; its specificity is significantly lower and remains variable, leading to considerable false positive results and unnecessary invasive diagnostic procedures [2, 3, 14–16].

Most malignant breast tumors are highly vascular and are easily discovered in contrast-enhanced MRI. In addition, there are many benign lesions that are hypervascular and may cause difficulty in interpretation of the breast MRI. Some benign lesions such as fibrocystic changes and sclerosing adenosis have been presented as misleading pathologies in recent articles [17–19]. In this study, we observed similar overlapping with a wide range of benign lesions in our false positive results, especially in the BI-RADS 4 category. Accordingly, any improvement in the imaging methods and interpretation leading to higher specificity of breast MRI without sacrificing the sensitivity would be a considerable achievement. Since in the MRI BI-RADS reporting system, the radiologist is dealing with multiple morphologic

and kinetic descriptors, defining the relative importance of each descriptor seems to be useful for this purpose.

In this article, we assessed the odds ratio (OR) and also diagnostic indices of each MRI descriptor in enhancing breast masses. Based on our proposed grouping for descriptors, the highest odds ratio was seen for margin, followed by the dynamic curve type, mass size, and shape.

On the other hand, we assessed diagnostic indices of each descriptor individually in malignant breast masses that showed high sensitivity and low specificity in the type of enhancement, curve type, and size, while this analysis showed high specificity (fewer unnecessary procedures) and a low sensitivity for shape and margin. In addition, for internal enhancement, both sensitivity and specificity were in a medium range. These findings mean lower false positive results could be achieved by considering morphologic indices, while lower false negative results are obtained in dynamic curves and lesion size.

Some other studies have focused on the rate of false positive and false negative results of the

**Table III.** Odds ratio for differentiating benign and malignant features of breast masses in each MRI descriptor

Descriptors	Categorization	Malignant, n (%)	Benign, n (%)	P-value	OR (95% CI)
Shape	Irregular	30 (38)	49 (62)	< 0.001	3.1 (1.8–5.3)
	Other	58 (16.4)	296 (83.6)		
Margin	Non circumscribed (only spiculated)	40 (60.6)	26 (39.4)	< 0.001	10.2 (5.7–18.3)
	Circumscribed and other non circumscribed	48 (13.1)	319 (86.9)		
Internal enhancement	Heterogeneous/rim/enhancing septa	52 (25.5)	152 (74.5)	0.013	1.8 (1.1–2.9)
	Other	36 (15.9)	191 (84.1)		
Enhancement type	Rapid	86 (21)	323 (79)	0.133	2.9 (0.7–12.7)
	Non-rapid	2 (8.3)	22 (91.7)		
Curve type	Wash-out or plateau	83 (24.8)	252 (75.2)	< 0.001	6.1 (2.4–15.6)
	Persistent	5 (5.1)	93 (94.9)		
Size	≥ 10 mm	61 (26.4)	170 (73.6)	< 0.001	4.3 (2.1–9)
	< 10 mm	9 (7.7)	108 (92.3)		

**Table IV.** Diagnostic indices of the BI-RADS descriptors for malignancy

Descriptor	TP	FN	TN	FP	Sen. (95% CI)	Spec. (95% CI)	PPV (95% CI)	NPV (95% CI)	PLR (95% CI)	NLR (95% CI)
Size (≥ 10 mm)	61	9	108	170	87 (77–94)	39 (33–45)	26 (21–33)	92 (86–96)	1.4 (1.3–1.6)	3 (1.6–5.7)
Shape (irregular)	30	58	296	49	34 (24–45)	86 (82–89)	38 (27–50)	84 (79–87)	2.4 (1.6–3.5)	1.3 (1.1–1.5)
Margin (spiculated non-circumscribed)	40	48	319	26	45 (35–56)	92 (89–95)	61 (48–72)	87 (83–90)	6 (3.9–9.3)	1.7 (1.4–2.1)
Internal enhancement (heterogeneous /rim/enhancing septa)	52	36	191	152	59 (48–69)	56 (50–61)	25 (20–32)	84 (79–89)	1.3 (1.1–1.6)	1.4 (1–1.8)
Enhancement type (rapid)	86	2	22	323	98 (92–99)	6 (4–10)	21 (17–25)	92 (73–99)	1.04 (1–1.09)	2.8 (0.67–11.7)
Curve type (Wash-out and plateau)	83	5	93	252	94 (87–98)	27 (22–32)	25 (20–30)	95 (88–98)	1.3 (1.2–1.4)	4.7 (2–11.3)
BI-RADS (4,5)	84	4	113	232	95 (89–99)	33 (28–38)	27 (22–32)	97 (91–99)	1.4 (1.3–1.5)	7.2 (2.7–19)

NLR – neutrophil to lymphocyte ratio, PPV – positive predictive value.

**Table V.** Multivariate logistic regression model for estimating malignancy according to BI-RADS descriptors

Variable	B	Sig.	Exp (B)	95% CI for Exp (B)	
				Lower	Upper
Size (≥ 10 mm)	1.1	0.012	2.9	1.3	6.8
Shape (irregular)	0.61	0.11	1.8	0.87	3.9
Margin (spiculated non-circumscribed)	2.6	< 0.0001	13.0	5.4	31.5
Internal enhancement heterogeneous/rim/enhancing septa	0.15	0.65	1.2	0.6	2.3
Enhancement type (rapid)	2.5	0.03	12.1	1.3	116.1
Curve type (Wash-out and plateau)	2.6	0.002	14.0	2.7	72.9
Constant	-14.845	< 0.0001	0.000		

MRI BI-RADS final assessment. They have also assessed the relative importance of each descriptor in MRI BI-RADS. Mahoney *et al.* reported 29% of their BI-RADS 5 and 79% of their BI-RADS 4 lesions as benign pathologies positive predictive value (PPV) equal to 71% and 21%, respectively [9]. In another study, 33% and 81% of BI-RADS 5 and 4 lesions were benign (PPV equal to 67% and 19%, respectively) [20]. In our series, 18.9% of BI-RADS 5 and 84.4% of BI-RADS 4 lesions were benign (PPV equal to 81.1% and 15.6%, respectively).

As observed in different studies, the rate of false positive cases is considerable, especially in BI-RADS 4 lesions. This means that the current policy of breast lesion management has been adjusted based on a conservative set point to decrease the cancer-missing rate at the cost of performing unnecessary invasive procedures.

In the review of the literature, we found some studies focusing on the efficacy of each descriptor of breast MRI [9–12, 21–26]. In spite of somewhat different designs and settings, the general goal of these studies is to assess the relative importance of each descriptor in the diagnosis of malignant breast lesions.

In an overall view, our results showed a good sensitivity (and thus a low cancer-missing rate) for size, enhancement type and curve type of kinetic assessment, while it showed a good specificity (and thus a decreased false positive rate leading to fewer unnecessary invasive procedures) among patients for morphologic descriptors of shape and margin. In addition, the best OR was seen for margin and curve type, then for size and shape, and other descriptors showed lower ORs. Findings of other studies were quite similar to our study; however, there were different results among other studies. These differences were related to stronger or weaker diagnostic indices in different descriptors; as mentioned, these differences are partly related to inhomogeneous settings and patient enrollment settings among these studies. Gutierrez *et al.* reported ORs of 2.8–4.6 for size, shape, margin and internal enhancement in diagnosis of malignancy [20]. However, they considered only BI-RADS 4 and 5 lesions. This could lower the indices, as the most lesions that lower diagnostic indices are BI-RADS 4 lesions, and excluding BI-RADS 3 lesions could decrease the diagnostic indices and ORs. The positive likelihood ratio of morphologic characteristics (including irregular shape, spiculated margin and heterogeneous internal enhancement) in the study of Baltzer *et al.* was similar to our study [10]. Mahoney *et al.* reported that among 121 enhancing masses, irregular shape, spiculated and irregular margins and rapid internal enhancement were most predictive of malignancy [9]. In the study of Wedegärtner

*et al.*, irregular lesion contour (margin) had the best efficacy in determining malignancy (sensitivity and specificity of 83% and 76%, respectively) [12]. Thus, compared to our findings, in somewhat lower specificity, they obtained a significantly better sensitivity for margin. Considerable power of spiculated margin presence for malignancy was reported by Schnall *et al.* [11]. In addition, they stated that kinetic characteristics are among the most reliable criteria suggestive for malignancy. Tozaki *et al.* reported a spiculated margin to be suggestive of malignancy in all masses and an irregular shape to be related to malignancy in 97% of cases [21].

To find independent MRI descriptors that could predict malignancy, we performed a multivariate analysis, in which margin, size and kinetic characteristics were statistically significant variables. Similarly, Gutierrez *et al.* found shape as a less significant descriptor of BI-RADS in the multivariate model [20]. Although more powerful variables such as “margin” do not exclude the less powerful descriptors such as “shape” from the multivariate model in the current study, based on our results, neither morphology nor kinetic characteristics have been completely excluded from the model in our study. We can conclude that both morphologic and kinetic descriptors bear a valid weight in the diagnosis of masses and neither could be ignored.

Finally, the new BI-RADS lexicon seems to be more efficient in discrimination of malignant and benign lesions and may increase sensitivity while not sacrificing specificity, and as a result reduces unnecessary biopsy and patient anxiety. Future studies should compare the results.

In conclusion, it seems that morphologic descriptors of MRI BI-RADS are highly specific while kinetic related descriptors are highly sensitive in diagnosis of malignant masses of the breast. Appropriate consideration and combination of different BI-RADS findings could help in better interpretation of MRI BI-RADS and lowering the rate of false reports.

### Conflict of interest

The authors declare no conflict of interest.

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