

Original Article

Diagnostic potential of weight and identification values for magnetic resonance imaging-based parameters in BI-RADS for differentiating benign and malignant breast lesions

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Abstract: *Objective:* The aim of this study was to investigate whether weighting magnetic resonance imaging (MRI)-derived parameters in the descriptors defined by the breast imaging-reporting and data system (BI-RADS) can differentiate benign and malignant breast lesions. *Methods:* Retrospective analysis was conducted on 69 benign and 56 malignant breast lesions confirmed by pathology. MRI data taken before operation or biopsy were used to calculate weighting factors (weight values) for MRI parameters defined in the BI-RADS descriptors of morphology, kinetics, and molecular function. Correlation between the weight values of MRI parameters and frequencies of benign or malignant lesions presenting those parameters was investigated. The weight values were combined into identification values, whose ability to differentiate benign and malignant breast lesions was assessed using receiver operating characteristic (ROC) curves. *Results:* Among all MRI parameters tested, apparent diffusion coefficient $< 1.0 \times 10^{-3}$ mm²/s was assigned the highest weight value (1.122), while plateau pattern was assigned the lowest (-1.369). Weight values of parameters correlated positively with the frequencies of malignant lesions presenting those parameters ($r = 0.684, P < 0.001$) and negatively with the frequencies of benign lesions ($r = -0.671, P < 0.001$). Identification values showed good accuracy in differentiating benign and malignant breast lesions: at the optimal value of 1.575, the area under the ROC curve was 0.972, sensitivity was 84.1%, and specificity was 94.6%. *Conclusion:* Establishing weight values of MRI parameters in BI-RADS descriptors and combining them into identification values may help improve accuracy in differentiating benign and malignant breast lesions.

Keywords: Magnetic resonance imaging, apparent diffusion coefficient, benign, malignant, breast lesion, weight value, receiver operating characteristic curve

Introduction

Among women worldwide, breast cancer is the most frequent cancer and the leading cause of cancer-related death, with 1.7 million new cases recorded in 2012 [1]. Early detection, diagnosis and treatment are crucial for improving survival and quality of life among patients with breast cancer [2, 3]. The breast imaging-reporting and data system (BI-RADS) has proven useful for enhancing diagnostic accuracy of breast lesions [4-7]. This system integrates findings from magnetic resonance imaging (MRI) and other types of clinical and laboratory tests to characterize a patient's breast cancer

along several descriptors, including morphology, kinetics and molecular function.

BI-RADS descriptors assign different weights to MRI parameters depending on whether the lesion is benign or malignant. This raises the question of whether the various MRI parameters integrated into BI-RADS can be weighted in such a way that they can accurately differentiate the two types of lesion. Few studies have examined this possibility [8]. Some authors have examined the diagnostic accuracy of one or a few MRI parameters for differentiating benign and malignant lesions, but we are unaware of reports systematically assessing all

Weight analysis of MRI parameters of breast lesion from BI-RADS

MRI parameters currently integrated into BI-RADS [9].

Therefore we performed a retrospective study of patients with pathology-confirmed benign or malignant breast lesions and assigned weighting factors (weight values) to all MRI parameters in the BI-RADS descriptors of morphology, kinetics and molecular function. Then we combined the various weight values together into identification values, which we tested for the ability to differentiate benign and malignant lesions.

Methods

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of the Affiliated Tumor Hospital of Guangxi Medical University. Patients provided written informed consent for their clinical records to be used in this study.

Participants

Medical records were retrospectively analyzed from 117 patients (all women; median age, 49 yr; age range, 24 to 72 yr) with 125 breast lesions analyzed by MRI in the Department of Radiology at the Affiliated Tumor Hospital of Guangxi Medical University between February 2013 and March 2014. All patients were examined using MRI before breast surgery or biopsy, and diagnosis of benign or malignant breast lesion was confirmed by pathology. Of the total group of 117 patients, 50 patients (56 lesions) had the following types of benign lesions: breast fibroadenoma (21 patients), proliferative lesion (18), inflammatory lesion (7), intraductal papilloma (2), or benign phyllodes tumor (2). The remaining 69 patients (69 lesions) had the following types of malignant disease: breast cancer (64 patients), comprising 58 patients with invasive ductal carcinoma, 3 with invasive lobular carcinoma, 2 with *in situ* ductal carcinoma, and 1 with mucinous carcinoma; malignant phyllodes tumor (2 patients); and lymphoma (1 patient).

MRI

MRI was performed on a 1.5-T clinical MRI system (Magnetom Avanto, Siemens Healthcare,

Erlangen, Germany) equipped with a dedicated eight-channel phased array breast coil in the prone position. A transverse T1-weighted FLASH pulse sequence was performed with the following parameters: repetition time, 8.6 ms; echo time, 4.7 ms; section thickness, 1 mm; intersection gap, 0.2 mm; field of view, 32 × 32 cm; matrix dimensions, 323 × 448. A transverse T2-weighted TIRM pulse sequence was performed with the following parameters: repetition time, 5600 ms; echo time, 59 ms; inversion time, 180 ms; section thickness, 4 mm; intersection gap, 0.8 mm; field of view, 34 × 34 cm; matrix dimensions, 314 × 320. Diffusion-weighted MRI was conducted in the axial plane using an echo-planar imaging sequence involving the following algorithms and parameters: parallel imaging with sensitivity encoding (acceleration factor = 2); fat suppression via a spectrally selective, attenuated inversion-recovery sequence; volume shimming; b values, 0 and 800 s/mm²; repetition time, 5800 ms; echo time, 86 ms; inversion time, 180 ms; section thickness, 6 mm; intersection gap, 0.2 mm; field of view, 32 × 32 cm; matrix dimensions, 323 × 448.

Apparent diffusion coefficient (ADC) maps were created automatically from trace-weighted images with b values of 0 and 800. ADC values were calculated according to the following formula: $ADC = -(1/b) \ln(S_2/S_1)$, where S₂ and S₁ are the signal intensities at respective b values of 800 and 0. Contrast agent Gd-DTPA (0.1 mmol/kg body weight, MAGNEVIST, gadopentetate dimeglumine) was intravenously injected at 2.0 ml/s. For multiphase dynamic enhancement, masks were acquired before injection of contrast agent. At approximately 25 s after the start of injection, dynamic volume enhancement was performed. Five phases were continuously collected during an acquisition time of 55 s for each phase.

Image post-processing

A minimum of three ADC measurements in regions of interest (each measuring 0.2-0.4 cm²) at slightly different positions on ADC images were averaged to obtain a single ADC value for the lesion. Obviously necrotic, liquescent, hemorrhagic, cystic, or calcified areas were excluded based on T1- or T2-weighted images or based on dynamic contrast-enhanced images.

Weight analysis of MRI parameters of breast lesion from BI-RADS

Table 1. Weight values of MRI parameters in the BI-RADS descriptors of morphology, kinetics and molecular function

BI-RADS descriptor	MRI parameter	No. benign lesions	No. malignant lesions	Weight value
Kinetic descriptor (Curve pattern)	Plateau	19	1	-1.369
	Persistent	25	11	-0.447
	Washout	12	57	0.586
Molecular-function descriptor (ADC values)	$< 1.0 \times 10^{-3} \text{ mm}^2/\text{s}$	3	49	1.122
	$1.0\text{-}1.5 \times 10^{-3} \text{ mm}^2/\text{s}$	17	17	-0.091
	$> 1.5 \times 10^{-3} \text{ mm}^2/\text{s}$	36	3	-1.17
Indirect morphological descriptor (Presence)	Feeding arteries	8	39	0.567
	Nipple inversion	4	12	0.386
	Thick skin	5	17	0.441
	Perilesional edema in the lesion	4	29	0.77
	Shortest diameter of the lymph node $> 1.0 \text{ cm}$	3	17	0.663
Direct morphological descriptor (Shape of lesion)	Oval/Round	17	6	-0.543
	Lobular	20	29	0.071
	Irregular	19	34	0.162
Direct morphological descriptor (Margin of lesion)	Smooth	37	2	-1.358
	Irregular	19	42	0.254
	Spiculated	2	25	1.006
Direct morphological descriptor (Boundary of lesion)	Clear	30	46	0.095
	Obscure	26	23	-0.144
Direct morphological descriptor (Enhancement pattern and internal enhancement of lesion)	Homogeneous enhancement	6	2	-0.568
	Heterogeneous enhancement	35	56	0.113
	Rim enhancement	10	36	0.466
	With internal septation	9	1	-1.045
	Without internal septation	14	16	-0.033
	Clustered ring enhancement	15	24	0.113
	Centripetal enhancement	8	1	-0.994
	Centrifugal enhancement	3	23	0.794
	Blooming sign	1	5	0.608
Constant sharpness sign	17	1	-1.321	

Abbreviations: ADC, apparent diffusion coefficient; BI-RADS, breast imaging-reporting and data system; MRI, magnetic resonance imaging.

For analysis of kinetic enhancement, time-signal intensity curves (TICs) were plotted from the signal intensity values obtained in regions of interest (each measuring 10-30 mm²) on multiphase dynamic images. To assess the increase in signal intensity during the early phase, we evaluated the enhancement for the first contrast-enhanced image at 60 s after injection of contrast material. Standard subtraction images (early contrast-enhanced *minus* unenhanced) and reverse subtraction images (early contrast-enhanced *minus* last contrast-enhanced) were obtained on a pixel-by-pixel basis. These two types of subtraction image were used to create reformatted images with a maximum intensity projection.

Image analysis

Breast magnetic resonance images were analyzed according to BI-RADS [8] by two radiolo-

gists (GQJ, XNZ) with 10 and 12 years of experience with breast MRI. These clinicians were blinded to pathological diagnosis and clinical examinations. TICs were classified as indicating persistent, plateau, or washout according to the BI-RADS descriptor of kinetics. ADC values were classified as $< 1.0 \times 10^{-3} \text{ mm}^2/\text{s}$, $1.0\text{-}1.5 \times 10^{-3} \text{ mm}^2/\text{s}$ or $> 1.5 \times 10^{-3} \text{ mm}^2/\text{s}$ according to the BI-RADS descriptor of molecular function [9]. The following characteristics were determined as defined by the BI-RADS descriptor of morphology (indirect): presence of feeding arteries, nipple inversion, thick skin, perilesional edema in the lesion, and shortest diameter of the lymph node $> 1.0 \text{ cm}$. The following characteristics were determined as defined by the BI-RADS descriptor of morphology (direct) [10, 11]: shape (oval/round, lobular, irregular), margin (smooth, irregular, spiculated), boundary (clear, obscure), enhancement pattern, internal

Weight analysis of MRI parameters of breast lesion from BI-RADS

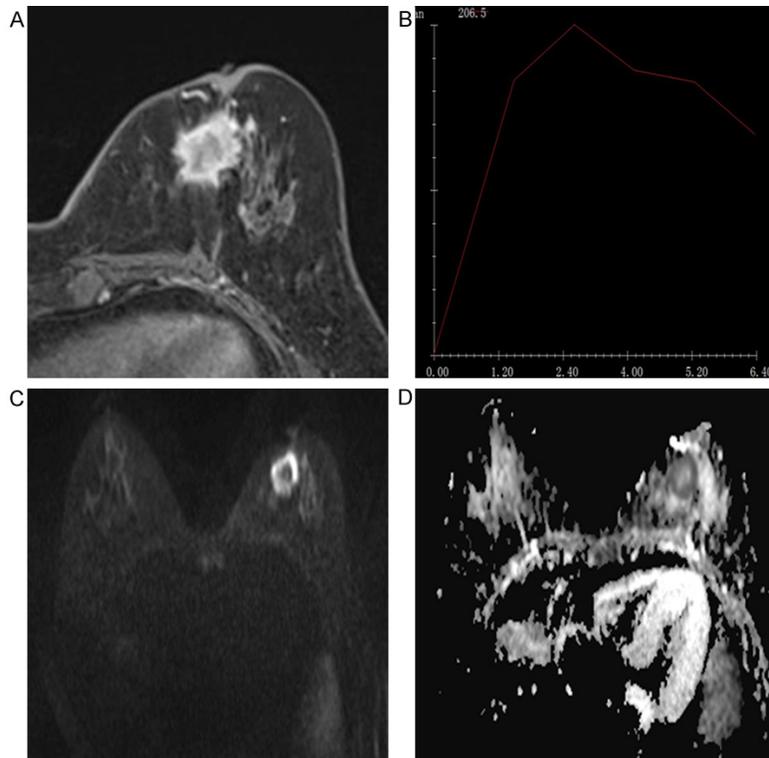


Figure 1. MRI findings for a 30-year-old woman with invasive ductal carcinoma in the left breast. A. The lesion showed irregular shape with peripheral and centripetal enhancement, spiculated margin, blooming sign and nipple inversion. B. The time-intensity curve showed a washout pattern. C. The lesion margin showed high signal in the diffusion-weighted image. D. The lesion margin showed low signal in the apparent diffusion coefficient map; the coefficient was $0.872 \times 10^{-3} \text{ mm}^2/\text{s}$. The identification value for this lesion (see Methods) was 5.792.

enhancement of lesion (homogeneous enhancement, heterogeneous enhancement, rim enhancement, with or without internal septation, clustered ring enhancement, centripetal enhancement, centrifugal enhancement, blooming sign, constant sharpness sign).

Calculation of frequency, weight value and identification value

The frequency of malignant lesions presenting a given MRI parameter was calculated as the number of malignant lesions showing that parameter, divided by the total number of malignant lesions in the sample (69). Similarly, the frequency of benign lesions presenting a given MRI parameter was calculated as the number showing that parameter, divided by the total number of 56.

The weight value for each MRI parameter_n was calculated according to Kaiser [11]: weight value_n = $\log M/B$ where M refers to the number of

malignant lesions presenting parameter_n, and B refers to the number of benign lesions presenting parameter_n. Parameters were assigned a value of 0 when absent or 1 when present. The various weight values were combined to give an identification value for a given lesion_x: identification value_x = weight value₁ × parameter value₁ + weight value₂ × parameter factor value₂ + ... weight value_n × parameter factor value_n.

Statistical analysis

All statistical analyses were performed using SPSS 19.0 (IBM, Chicago, IL, USA) using a significance threshold of $P < 0.05$. Spearman correlation analysis was used to analyze the potential relationship between weight values for a given MRI parameter and the frequencies of benign or malignant lesions presenting that parameter. The ability of identification values to diagnose lesions as benign or malignant was

assessed using receiver operating characteristic (ROC) curves. The optimal cut-off value was defined as the value maximizing the area under the ROC curve and was determined using the Youden index $J = \text{maximum} (\text{sensitivity} + \text{specificity} - 1)$ [12], assuming equal weighting for sensitivity and specificity. The level of accuracy based on the area under the ROC curve was classified as high if > 0.9 , moderate if 0.7-0.9, low if 0.5-0.7 and random if 0.5 [13].

Results

Correlation between weight values of MRI parameters and frequencies of benign or malignant lesions presenting those parameters

For all MRI parameters in the BI-RADS descriptors of morphology, kinetics and molecular function (Table 1), weight values were determined (Figures 1 and 2). Spearman correlation analysis showed that weight values correlated positively with the frequencies of malignant

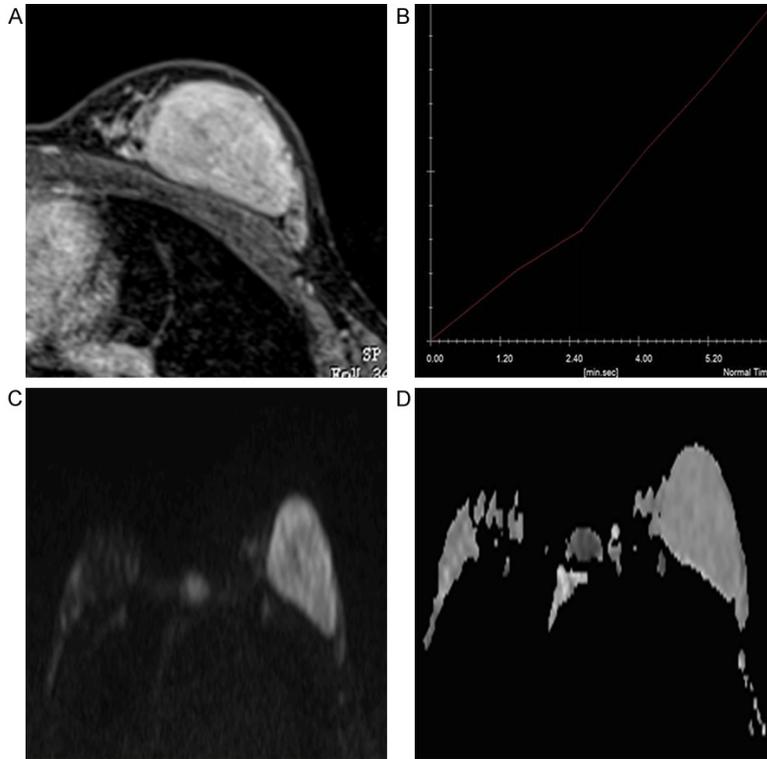


Figure 2. MRI findings for a 39-year-old woman with breast fibroadenoma in the left breast. A. The lesion showed an oval shape with heterogeneous enhancement, smooth margin and constant sharpness sign. B. The time-intensity curve showed a plateau pattern. C. The lesion margin showed high signal in the diffusion-weighted image. D. The lesion margin showed isointensity in the apparent diffusion coefficient map; the coefficient was $1.971 \times 10^{-3} \text{ mm}^2/\text{s}$. The identification value of the lesion was -4.038.

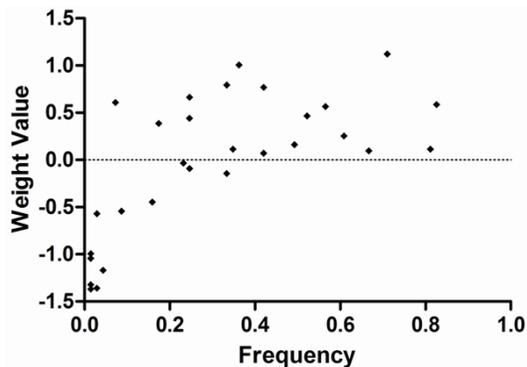


Figure 3. Scatter diagram illustrating the correlation between weight values of MRI parameters and the frequencies of malignant lesions presenting those parameters ($r = 0.684, P < 0.001$).

lesions presenting the corresponding parameter ($r = 0.684, P < 0.001$; **Figure 3**) and negatively with the frequencies of benign lesions presenting the corresponding parameter ($r = -0.671, P < 0.001$; **Figure 4**).

Diagnostic accuracy of identification values for differentiating benign and malignant breast lesions

The ROC curve indicating the accuracy of identification values for differentiating benign and malignant lesions among all 125 lesions in the data is shown in **Figure 5**. At the optimal cut-off value of 1.575, the area under the ROC curve was 0.972, sensitivity was 84.1% and specificity was 94.6%.

Discussion

Increasingly, MRI findings are being integrated into BI-RADS descriptors to enhance the diagnostic accuracy of breast lesions. The use of MRI findings has likely improved the ability of BI-RADS to reduce interference from subjective factors during breast exams [14-16]. However, how to weight MRI parameters relative to one another during diagnosis is unclear,

since some parameters may be less robust to inter-clinician variation and more prone to error or misjudgment, and some parameters may vary among patients more than others. In particular, the MRI parameters integrated into the BI-RADS descriptors of morphology, kinetics and molecular function vary substantially among individuals [17], so it is unclear whether the different weight values they are assigned in the case of benign or malignant lesions has diagnostic power to differentiate the two types of lesion [10]. Few studies have addressed this question, and most have looked at only one or a few MRI parameters [9]. In the present study, we use Kaiser's approach of weight value and identification value [11] to systematically assess the ability of MRI parameters in the three BI-RADS descriptors to differentiate between benign and malignant lesions. Our results suggest that a combination of identification values may be useful as part of a standardized scheme for differentiating the two

Weight analysis of MRI parameters of breast lesion from BI-RADS

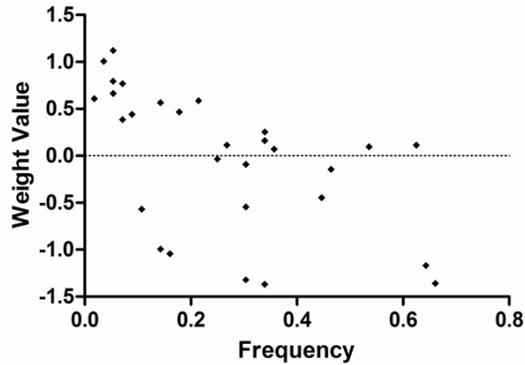


Figure 4. Scatter diagram illustrating the correlation between weight values of MRI parameters and the frequencies of benign lesions presenting those parameters ($r = -0.671$, $P < 0.001$).

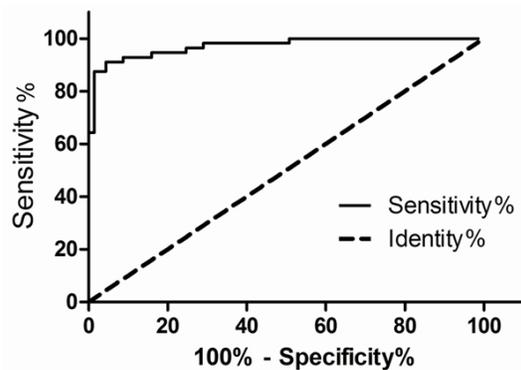


Figure 5. Receiver operating characteristic curve depicting the diagnostic accuracy of identification values for differentiating benign and malignant breast lesions. At the optimal cut-off value of 1.575, the area under the curve was 0.972, sensitivity was 84.1% and specificity was 94.6%.

types of lesions within the BI-RADS framework.

In our study, weight values correlated positively with the frequencies of malignant lesions presenting the corresponding MRI parameters. Among the MRI parameters, $ADC < 1.0 \times 10^{-3} \text{ mm}^2/\text{s}$ received the highest weight value and spiculated margin the second-highest; these weight values strongly indicated malignant lesions. These findings are consistent with studies suggesting that ADC is significantly higher in a benign lesion than in a malignant one [18], and that spiculated margin has a higher positive predictive value in a malignant lesion than in a benign one [10]. We also found that weight values correlated negatively with

the frequencies of benign lesions presenting the corresponding MRI parameters. Among the MRI parameters, a plateau pattern on the TIC was assigned the lowest weight value and smooth lesion margin the second-lowest weight value; these two weight values strongly indicated benign lesions. These findings are consistent with studies suggesting that a plateau shape for the kinetics curve shows higher positive predictive value for benign lesions [19, 20], and with studies associating smooth margin with benign lesions [10, 20].

When we combined the various weight values into identification values, we obtained relatively high sensitivity (84.1%) and specificity (94.6%) for differentiating benign and malignant breast lesions. This suggests that it may be possible to develop a quantitative diagnostic scoring system for differentiating the two types of lesions. Our results should be confirmed and extended in larger studies that include rare BI-RADS descriptors not analyzed here.

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Disclosure of conflict of interest

None.

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References

- [1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin* 2016; 66: 7-30.
- [2] Evans DG, Astley S, Stavrinou P, Harkness E, Donnelly LS, Dawe S, Jacob I, Harvie M, Cuzick J, Brentnall A, Wilson M, Harrison F, Payne K, Howell A. Improvement in risk prediction, early detection and prevention of breast cancer in the NHS breast screening programme and family history clinics: a dual cohort study. Southampton (UK): NIHR Journals Library 2016.
- [3] Kuhl CK, Strobel K, Bieling H, Leutner C, Schild HH, Schrading S. Supplemental breast MR im-

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- aging screening of women with average risk of breast cancer. *Radiology* 2017; 283: 361-370.
- [4] Trimboli RM, Carbonaro LA, Cartia F, Di Leo G, Sardanelli F. MRI of fat necrosis of the breast: the "black hole" sign at short tau inversion recovery. *Eur J Radiol* 2012; 81: 573-579.
- [5] Abramson RG, Li X, Hoyt TL, Su PF, Arlinghaus LR, Wilson KJ, Abramson VG, Chakravarthy AB, Yankeelov TE. Early assessment of breast cancer response to neoadjuvant chemotherapy by semi-quantitative analysis of high-temporal resolution DCE-MRI: preliminary results. *Magn Reson Imaging* 2013; 31: 1457-1464.
- [6] Luo N, Su D, Jin G, Liu L, Zhu X, Xie D, Liu Y. Apparent diffusion coefficient ratio between axillary lymph node with primary tumor to detect nodal metastasis in breast cancer patients. *J Magn Reson Imaging* 2013; 38: 824-828.
- [7] Kim TY, Kim SH, Kang BJ, Kim HS, Cha ES, Kim JY, Song BJ. Characterization of the enhancing lesions on dynamic contrast enhanced magnetic resonance imaging in patients with interstitial mammoplasty. *Eur J Radiol* 2013; 82: 2205-2211.
- [8] Tardivon AA, Athanasiou A, Thibault F, El Khoury C. Breast imaging and reporting data system (BIRADS) magnetic resonance imaging illustrated cases. *Eur J Radiol* 2007; 61: 216-223.
- [9] Jeong SJ, Lim HS, Lee JS, Park MH, Yoon JH, Park JG, Kang HK. Medullary carcinoma of the breast: MRI findings. *Am J Roentgenol* 2012; 198: W482-W487.
- [10] Tozaki M, Igarashi T, Fukuda K. Positive and negative predictive values of BI-RADS-MRI descriptors for focal breast masses. *Magn Reson Med Sci* 2006; 5: 7-15.
- [11] Kaiser, Werner A. Signs in MR-mammography. Springer Berlin Heidelberg 2008.
- [12] Akobeng AK. Understanding diagnostic tests 3: Receiver operating characteristic curves. *Acta Paediatrica* 2007; 96: 644-647.
- [13] Fischer JE, Bachmann LM and Jaeschke R. A readers' guide to the interpretation of diagnostic test properties: clinical example of sepsis. *Intensive Care Med* 2003; 29: 1043-1051.
- [14] Tardivon AA, Athanasiou A, Thibault F, El Khoury C. Breast imaging and reporting data system (BIRADS) magnetic resonance imaging illustrated cases. *Eur J Radiol* 2007; 61: 216-223.
- [15] Tozaki M, Fukuda K. High-spatial-resolution MRI of non-masslike breast lesions: interpretation model based on BI-RADS MRI descriptors. *AJR Am J Roentgenol* 2006; 187: 330-337.
- [16] Leach MO, Boggis CR, Dixon AK, Easton DF, Eeles RA, Evans DG, Gilbert FJ, Griebisch I, Hoff RJ, Kassar P, Lakhani SR, Moss SM, Nerurkar A, Padhani AR, Pointon LJ, Thompson D, Warren RM; MARIBS study group. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet* 2005; 365: 1769-1778.
- [17] Stines J. BI-RADS: use in the French radiologic community. How to overcome with some difficulties. *Eur J Radiol* 2007; 61: 224-234.
- [18] Luo N, Su D, Jin G, Liu L, Zhu X, Xie D, Liu Y. Apparent diffusion coefficient ratio between axillary lymph node with primary tumor to detect nodal metastasis in breast cancer patients. *J Magn Reson Imaging* 2013; 38: 824-828.
- [19] Szabó BK, Aspelin P, Wiberg MK, Boné B. Dynamic MR imaging of the breast. *Acta Radiol* 2003; 44: 379-386.
- [20] Kuhl CK, Mielcareck P, Klaschik S, Leutner C, Wardelmann E, Gieseke J, Schild HH. Dynamic breast mr imaging: are signal intensity time course data useful for differential diagnosis of enhancing lesions? *Radiology* 1999; 211: 101-110.