Original Article

Can MRI Features Predict Histopathology and Molecular Subtypes of Breast Cancer?

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Objective: To evaluate the relationship between magnetic resonance imaging (MRI) findings and histopathologic findings, including histologic type, histologic grade, extensive intraductal component (EIC), estrogen receptor (ER), progesterone receptor (PR), Ki-67, P53, and molecular subtypes in breast cancer.

Materials and Methods: The present data was a retrospective review of the patients that underwent breast MRI at King Chulalongkorn Memorial Hospital between January 1, 2014 and December 31, 2016. MRI was assessed for shape, margin, and internal enhancement of the mass lesion, distribution and internal enhancement of the non-mass enhancement lesions, and kinetic curve type and restricted diffusion of both mass and non-mass enhancement lesions. The association between MRI findings and histologic type, histologic grade, EIC, ER, PR, human epidermal growth factor receptor 2 (HER2), Ki-67, P53, and molecular subtypes were evaluated.

Results: One hundred seven patients with invasive breast cancers were included in the present study with 99 mass lesions and 8 non-mass enhancement lesions. Rim enhancement of the mass was a significant independent predictor of grade III (high) histologic grade (p=0.001, odd ratio 4.552), negative ER (p=0.001, odd ratio 4.644), negative PR (p=0.021, odd ratio 2.679), and positive Ki-67 status (p=0.022, odd ratio 3.373). Internal enhancement was significantly associated with molecular subtypes such as luminal A subtype appearing as heterogeneous enhancement for 78.3%, HER2-overexpressed and triple negative subtypes dominantly presented with rim enhancement for 76.9% and 75%, respectively. The authors found that spiculated tumor margin of the mass was significantly associated with negative EIC (p=0.006). Restricted diffusion of all lesions was also a significant independent predictor of negative EIC (p=0.022, odd ratio 7.417) and Ki-67 positive (p=0.028, odd ratio 7.182).

Conclusion: The consistency of the association between rim enhancement and high histologic grade, negative ER/PR, positive Ki-67 statuses in the present study may help to determine that rim enhancement was likely to predict poor pathologic prognosis of breast cancer. Rim enhancement may also predict poor molecular subtypes including HER2-overexpressed and triple negative subtypes. These results suggest that rim enhancement is the most useful MRI finding to predict histopathology and molecular subtypes of breast cancer.

Keywords: MRI, Breast cancer, Histopathology, Grade, ER, PR, HER2, Ki-67, EIC, Molecular subtypes

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Magnetic resonance imaging (MRI) has been increasing its role in the diagnosis of breast cancer and screening in patients with increased risk of breast cancer. Prediction of tumor grading, immunohistochemical status, and molecular subtypes from pre-operative MRI would suggest disease prognosis and treatment planning. Furthermore, breast cancer divided into four major molecular subtypes including luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)-overexpressed, and triple-negative or basal-like, according to the 2011 St. Gallen International Expert Consensus[(1)] in Table 1. There are different types of treatment and prognosis in each subtype. The presence of estrogen receptor (ER) and progesterone receptor (PR) in luminal A indicates a good prognosis. The luminal B subtype has a higher

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Table 1. Definitions of intrinsic subtypes of breast cancer[1]

Intrinsic subtypes	Clinico-pathologic definition
Luminal A	ER and/or PR positive, HER2 negative, and Ki-67 <14%
Luminal B	ER and/or PR positive, HER2 positive, or Ki-67 ≥14%
HER2-overexpressed	HER2 amplified, ER, and PR negative
Triple-negative or basal-like	ER, PR, and HER2 negative

ER=estrogen receptor; PR=progesterone receptor; HER2=human epidermal growth factor receptor 2

tumor cell proliferation and a poorer prognosis than the luminal A subtype. HER2-overexpressed and triple negative subtypes have the worse prognosis compared to the luminal subtypes.

Correlation between MRI features and histopathological features of breast cancer, including histologic type, tumor grade, ER, PR, HER2, and Ki-67, have been studied with various outcome in the past decade[2-13].

Thus, the purpose of the present study was to evaluate the relationship between MRI features and histopathologic findings, including histologic type, histologic grade, extensive intraductal component (EIC), ER, PR, Ki-67, P53, and molecular subtypes.

Materials and Methods

Patients

The authors retrospectively reviewed the patients that underwent breast MRI in King Chulalongkorn Memorial Hospital, Chulalongkorn University, Thailand between January 1, 2014 and December 31, 2016. Eight hundred fifty-two cases were included in the present study. Then, the authors reviewed the MRIs of the patients done pre-operatively and the pathology records of the breast cancer that was found in 175 cases. The patients were excluded from the analysis if they received neoadjuvant chemotherapy before the MRI study (3 cases), diagnosed with recurrent breast cancer (17 cases) or had incomplete MRI or pathological data (48 cases). Therefore, the present study was performed in 107 patients with invasive breast cancer. Case records were composed of patient characteristics, tumor characteristics, MRI findings, and histopathologic findings.

MRI technique

MRI was obtained using a 1.5T MR systems (Siemens MAGNETOM Espree-Pink). All patients were examined in the prone position using a breast array coil. The routine MRI were obtained using a standard protocol, including axial T2-weighted image, sagittal T2-weighted image with fat-suppressed, coronal T1-weighted image and axial T1-weighted image with fat suppressed. Contrast-enhanced axial T1-weighted image with fat-suppressed was obtained, using a bolus injection of 0.1 mmol/kg gadobutrol (Gadovist; Bayer Healthcare Pharmaceuticals, Inc., Whippany, NJ, USA). Standard subtraction images were created from the non-enhanced and the early and late contrast-enhanced images. Multiplanar reconstruction (MPR) and maximum intensity projection (MIP) reconstruction images were also obtained. Axial T1-weighted FLASH 3D high-resolution sequence, diffusion weighted image (DWI) sequence are obtained. Apparent diffusion coefficient (ADC) maps were created automatically by using b values of 800 second/mm^2.

Imaging analysis

The authors reviewed the MRI features according to the American College of Radiology, Breast Imaging Reporting and Data System (ACR BI-RADS) MR lexicon edition 2013. The MRI was reviewed to define patient with mass or non-mass enhancement. If the lesion was a mass, then, it was assessed for shape (oval, round, or irregular), margin (circumscribed, irregular, or spiculated), and internal enhancement (homogeneous, heterogeneous, or rim enhancement). If the lesion was a non-mass enhancement, the authors assessed the distribution (focal, linear, segmental, regional, multiple regions, or diffuse) and internal enhancement (homogeneous, heterogeneous, clumped, or cluster ring). The kinetic curve type (I, II, or III) and restricted diffusion were assessed in both mass and non-mass enhancement lesions. A threshold value of ADC to define restricted diffusion is 1.23×10^{-3} mm^2/second or less, according to the 2009 meta-analysis by Tsushima et al[14].

Histopathologic analysis

The histopathology of the biopsy or surgical specimens with the records in hospital information systems (HIS) were reviewed, including size, histologic type, histologic grade in routine histopathological examination, ER, PR, Ki-67, and P53 statuses in immunohistochemistry (IHC) result, and HER2 status in IHC or fluorescence in situ hybridization (FISH) results. According to the American Society of Clinical Oncology and the College of American Pathologists (ASCO/CAP), the cutoff point of ER and PR positivity was staining of 1%, and positive HER2/neu was immunohistochemical staining of 3+

Table 2. Baseline tumor characteristics (n=107)

Tumor Characteristics	n (%)
Histologic type	
IDC NST	98 (91.6)
ILC	7 (6.5)
Other*	2 (1.9)
Histologic grade	
Grade I, II (low, intermediate)	70 (65.4)
Grade III (high)	37 (34.6)
Size (cm)	
<2	39 (36.4)
2 to 5	47 (43.9)
>5	7 (6.5)
Associated DCIS component	
Present	50 (46.7)
Absent	57 (53.3)
EIC	
Present	15 (14.0)
Absent	92 (86.0)
ER	
Positive	74 (69.2)
Negative	33 (30.8)
PR	
Positive	66 (61.7)
Negative	41 (38.3)
HER2	
Positive	35 (32.7)
Negative	72 (67.3)
P53	
Positive	40 (37.4)
Negative	67 (62.6)
Ki-67	
Positive	81 (75.7)
Negative	26 (24.3)
Subtype	
Luminal A	27 (25.2)
Luminal B	50 (46.7)
HER2-overexpressed	14 (13.1)
Triple negative	16 (15.0)

IDC NST=invasive ductal carcinoma with no special type; ILC=invasive lobular carcinoma; DCIS=ductal carcinoma in situ; EIC=extensive intraductal component; ER=estrogen receptor; PR=progesterone receptor; HER2=human epidermal growth factor receptor 2

* Other including aprocrine differentiation, tubular carcinoma, mucinous carcinoma, secretory carcinoma, solid papillary carcinoma, invasive breast carcinoma with neuroendocrine features

or FISH result of HER2/neu gene amplification. The cutoff point for Ki-67 and P53 positivity were staining of 14% and 10%, respectively.

Statistical analysis

For mass lesions, shape, margin, internal enhancement, kinetic curve type, and restricted diffusion of MRI findings were correlated with pathological breast cancer type, histologic grade, EIC, ER, PR, HER2, Ki-67, P53, and molecular subtypes, using a chi-square test or Fisher's exact test.

For non-mass enhancement lesions, distribution and internal enhancement of MRI findings were correlated with pathological breast cancer type, histologic grade, EIC, ER, PR, HER2, Ki-67, P53, and molecular subtypes, using a chi-square test or Fisher's exact test.

Kinetic curve type and restricted diffusion of both mass and non-mass enhancement lesions were correlated with pathological breast cancer type, histologic grade, EIC, ER, PR, HER2, Ki-67, P53, and molecular subtypes, using a chi-square test or Fisher's exact test.

The parameters found to be significant by chi-square test or Fisher's exact test were entered and examined using binary logistic regression to identify the relationship. The types of internal enhancement in mass lesion were grouped into rim enhancement and non-rim enhancement due to a small number of homogeneous enhancement group (3/99 lesions, 3.03%).

The analysis was performed using the IBM SPSS Statistics software, version 22 (IBM Corp., Armonk, NY, USA), and p-value less than 0.05 was considered statistical significance.

The present study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. The IRB number was 091/60.

Results

Of the 107 breast cancer patients, 99 lesions (92.5%) were mass and 8 lesions (7.5%) were non-mass enhancement. The mean patient age was 51.2 years (range 28 to 75 years). Baseline tumor characteristics are shown in Table 2.

According to the correlation between MRI findings of mass and histopathologic findings in Table 3, rim enhancement of the mass was significantly associated with grade III (high) histologic grade ($p<0.001$), negative ER status ($p=0.001$), negative PR status ($p=0.032$), and positive Ki-67 status ($p=0.027$) (Figure 1).

Furthermore, internal enhancement of the mass was also significantly associated with molecular subtype ($p=0.003$), which luminal A subtype was seen

Table 3. Correlation between MR imaging findings of mass and histopathologic findings and molecular subtypes in breast cancer

MRI findings	Histologic type (n=99); n (%)				Histologic grade (n=99); n (%)			EIC (n=99); n (%)			ER (n=99); n (%)			PR (n=99); n (%)		
	IDC NST	ILC	Other	p-value	Grade I, II	Grade III	p-value	Positive	Negative	p-value	Positive	Negative	p-value	Positive	Negative	p-value
Shape				1.000			0.122			0.187			0.431			0.413
Oval	3 (3.2)	0 (0.0)	0 (0.0)		1 (1.6)	2 (5.6)		0 (0.0)	3 (3.4)		3 (4.4)	0 (0.0)		3 (5.0)	0 (0.0)	
Round	6 (6.5)	0 (0.0)	0 (0.0)		2 (3.2)	4 (11.1)		2 (16.7)	4 (4.6)		3 (4.4)	3 (9.7)		3 (5.0)	3 (7.7)	
Irregular	84 (90.3)	5 (100)	1 (100)		60 (95.2)	30 (83.3)		10 (83.3)	80 (92.0)		62 (91.2)	28 (90.3)		54 (90.0)	36 (92.3)	
Margin				1.000			0.650			0.006*			0.561			0.494
Circumscribed	2 (2.2)	0 (0.0)	0 (0.0)		1 (1.6)	1 (2.8)		2 (16.7)	0 (0.0)		2 (2.9)	0 (0.0)		2 (3.3)	0 (0.0)	
Irregular	46 (49.4)	2 (40.0)	0 (0.0)		29 (46.0)	19 (52.8)		7 (58.3)	41 (47.1)		31 (45.6)	17 (54.8)		27 (45.0)	21 (53.8)	
Spiculated	45 (48.4)	3 (60.0)	1 (100)		33 (52.4)	16 (44.4)		3 (25.0)	46 (52.9)		35 (51.5)	14 (45.2)		31 (51.7)	18 (46.2)	
Internal enhancement				0.132			<0.001*			0.220			0.001*			0.032*
Homogeneous	2 (2.2)	1 (20.0)	0 (0.0)		2 (3.2)	1 (2.8)		1 (8.3)	2 (2.3)		2 (2.9)	1 (3.2)		3 (5.0)	0 (0.0)	
Heterogeneous	44 (47.3)	3 (60.0)	0 (0.0)		38 (60.3)	9 (25.0)		7 (58.3)	40 (46.0)		40 (58.8)	7 (22.6)		33 (55.0)	14 (35.9)	
Rim	47 (50.5)	1 (20.0)	1 (100)		23 (36.5)	26 (72.2)		4 (33.3)	45 (51.7)		26 (38.2)	23 (74.2)		24 (40.0)	25 (64.1)	

MRI findings	HER2 (n=99); n (%)			Ki-67 (n=99); n (%)			P53 (n=99); n (%)			Molecular subtype (n=99); n (%)				
	Positive	Negative	p-value	Positive	Negative	p-value	Positive	Negative	p-value	Luminal A	Luminal B	HER2-overexpressed	Triple negative	p-value
Shape			0.303			0.321			0.735					0.302
Oval	2 (6.3)	1 (1.5)		2 (2.6)	1 (4.5)		1 (2.7)	2 (3.2)		1 (4.3)	2 (4.3)	0 (0.0)	0 (0.0)	
Round	1 (3.1)	5 (7.5)		6 (7.8)	0 (0.0)		1 (2.7)	5 (8.1)		0 (0.0)	3 (6.4)	0 (0.0)	3 (18.8)	
Irregular	29 (90.6)	61 (91.0)		69 (89.6)	21 (95.5)		35 (94.6)	55 (88.7)		22 (95.7)	42 (89.4)	13 (100)	13 (81.3)	
Margin			1.000			0.215			0.778					0.635
Circumscribed	0 (0.0)	3 (3.0)		1 (1.3)	1 (4.5)		0 (0.0)	2 (3.2)		1 (4.3)	1 (2.1)	0 (0.0)	0 (0.0)	
Irregular	16 (50.0)	32 (47.8)		40 (51.9)	8 (36.4)		18 (48.6)	30 (48.4)		8 (34.8)	24 (51.1)	6 (46.2)	10 (62.5)	
Spiculated	16 (50.0)	33 (49.3)		36 (46.8)	13 (59.1)		19 (51.4)	30 (48.4)		14 (60.9)	22 (46.8)	7 (53.8)	6 (37.5)	
Internal enhancement			0.622			0.027*			0.261					0.003*
Homogeneous	1 (3.1)	2 (3.0)		3 (3.9)	0 (0.0)		1 (2.7)	2 (3.2)		0 (0.0)	3 (6.4)	0 (0.0)	0 (0.0)	
Heterogeneous	13 (40.6)	34 (50.7)		31 (40.3)	16 (72.7)		14 (37.8)	33 (53.2)		18 (78.3)	22 (46.8)	3 (23.1)	4 (25.0)	
Rim	18 (56.3)	31 (46.3)		43 (55.8)	6 (27.3)		22 (59.5)	27 (43.5)		5 (21.7)	22 (46.8)	10 (76.9)	12 (75.0)	

IDC NST=invasive ductal carcinoma with no special type; ILC=invasive lobular carcinoma; EIC=extensive intraductal component; ER=estrogen receptor; PR=progesterone receptor; HER2=human epidermal growth factor receptor 2

* Identifies a statistically significant correlation

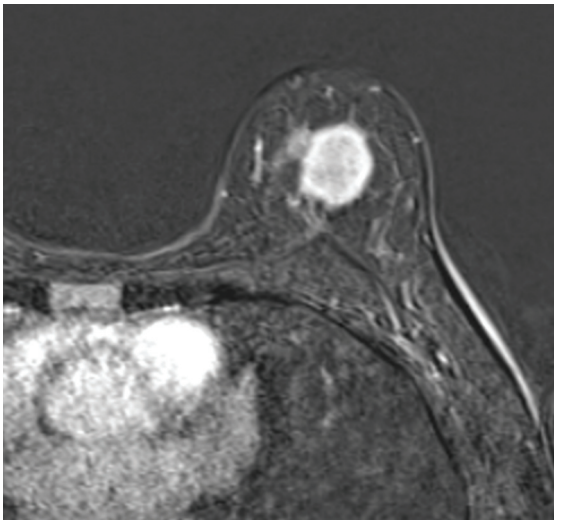

Figure 1. Triple negative invasive ductal carcinoma in a 41-year-old woman.

Pathological result showed IDC grade III, ER negative, PR negative, HER2 negative, Ki-67 positive and P53 negative. MRI fat-suppressed T1-weighted post-contrast axial image with subtraction shows an irregular shaped, irregular margin, and rim enhancing mass in the left breast.

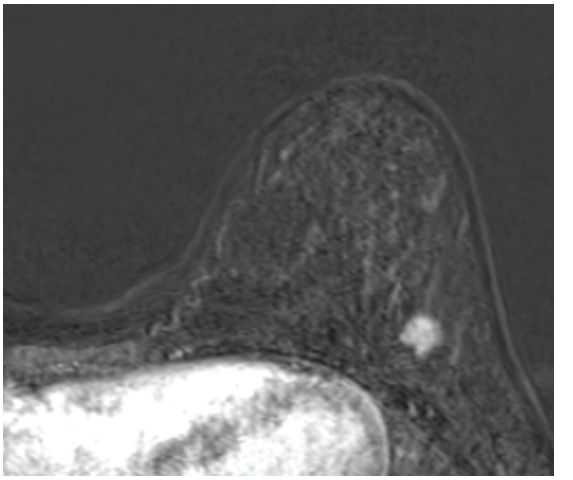

Figure 2. Luminal A invasive ductal carcinoma in a 47-year-old woman.

Wide excision specimen showed IDC grade II, DCIS 5%, ER 20%, PR 80%, HER2 1+, Ki-67 10%, P53 5%. MRI fat-suppressed T1-weighted post-contrast axial image with subtraction shows an irregular shaped, irregular margin, and heterogeneous enhancing mass at upper outer quadrant of the left breast.

with heterogeneous enhancement for 18/23 lesions (78.3%) (Figure 2) and HER2-overexpressed subtype was found with rim enhancement for 10/13 lesions (76.9%) as well as triple negative subtype appeared with rim enhancement for 12/16 lesions (75.0%).

Shape and margin of the mass were not significantly correlated with molecular subtypes. However, spiculated tumor margin of the mass was significantly associated with negative EIC (p=0.006) (Figure 3).

Moreover, the correlation between kinetic curve type, restricted diffusion of both mass and non-mass enhancement lesions with histopathologic findings is shown in Table 4. There were significant associations between restricted diffusion and EIC negative (p=0.035) as well as restricted diffusion and Ki-67 positive (p=0.030) (Figure 4).

There was no significant correlation between MRI findings of the non-mass enhancement with histopathologic findings and molecular subtypes.

Additionally, there was also no significant relationship between HER2 positive and MRI findings of mass lesions, non-mass enhancement lesions, kinetic curves, and diffusivity of water molecules in the present study.

According to univariate analysis (Table 5), rim enhancement of the mass was a significant independent predictor of grade III histologic grade

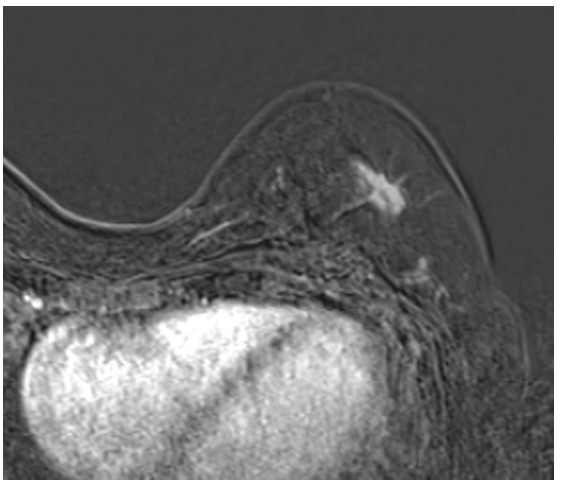

Figure 3. Invasive ductal carcinoma with negative EIC of in a 47-year-old woman.

Pathological result showed IDC grade II, DCIS 10%, ER 80%, PR 60%, HER2 negative, Ki-67 5% and P53 negative. MRI fat-suppressed T1-weighted post-contrast axial image with subtraction shows an irregular shaped, spiculated margin and heterogeneous enhancing mass at upper outer quadrant of the left breast.

(p=0.001, odd ratio 4.552), negative ER (p=0.001, odd ratio 4.644), negative PR (p=0.021, odd ratio 2.679), and positive Ki-67 status (p=0.022, odd ratio 3.373). In addition, restricted diffusion of mass and non-mass enhancement lesions were significant independent predictors of negative EIC (p=0.022, odd ratio 7.417), and positive Ki-67 status (p=0.028, odd ratio 7.182)

Table 4. Correlation between MR imaging findings of kinetic curve type, restricted diffusion and histopathologic findings in breast cancer

MRI findings	Histologic type (n=107); n (%)				Histologic grade (n=107); n (%)			EIC (n=107); n (%)			ER (n=107); n (%)			PR (n=107); n (%)		
	IDC NST	ILC	Other	p-value	Grade I, II	Grade III	p -value	Positive	Negative	p -value	Positive	Negative	p -value	Positive	Negative	p-value
Kinetic curve type				0.446			0.799			0.141			0.549			0.374
Type I	6 (6.1)	0 (0.0)	0 (0.0)		5 (7.1)	1 (2.7)		2 (13.3)	4 (4.3)		5 (6.8)	1 (3.0)		2 (3.0)	4 (9.8)	
Type II	45 (45.9)	5 (71.4)	0 (0.0)		32 (45.7)	18 (48.6)		9 (60.0)	41 (44.6)		32 (43.2)	18 (54.5)		32 (48.5)	18 (43.9)	
Type III	47 (48.0)	2 (28.6)	2 (100)		33 (47.1)	18 (48.6)		4 (26.7)	47 (51.1)		37 (50.0)	14 (42.4)		32 (48.5)	19 (46.3)	
Restricted diffusion				1.000			0.662			0.035*			0.664			0.403
Present	92 (93.9)	7 (100)	2 (100)		65 (92.9)	36 (97.3)		12 (80.0)	89 (96.7)		69 (93.2)	32 (97.0)		61 (92.4)	40 (97.6)	
Absent	6 (6.1)	0 (0.0)	0 (0.0)		5 (7.1)	1 (2.7)		3 (20.0)	3 (3.3)		5 (6.8)	1 (3.0)		5 (7.6)	1 (2.4)	

MRI findings	HER 2 (n=107); n (%)			Ki-67 (n=107); n (%)			P53 (n=124); n (%)			Molecular subtype (n=128); n (%)				
	Positive	Negative	p -value	Positive	Negative	p -value	Positive	Negative	p -value	Luminal A	Luminal B	HER2-overexpressed	Triple negative	p -value
Kinetic curve type			0.496			0.308			0.221					0.729
Type I	2 (5.7)	4 (5.6)		3 (3.7)	3 (11.5)		2 (5.0)	4 (6.0)		3 (11.1)	2 (4.0)	1 (7.1)	0 (0.0)	
Type II	19 (54.3)	31 (43.1)		38 (46.9)	12 (46.2)		23 (57.5)	27 (40.3)		11 (40.7)	24 (48.0)	8 (57.1)	7 (43.8)	
Type III	14 (40.0)	37 (51.4)		40 (49.4)	11 (42.3)		15 (37.5)	36 (53.7)		13 (48.1)	24 (48.0)	5 (35.7)	9 (56.3)	
Restricted diffusion			0.661			0.030*			0.407					0.082
Present	34 (97.1)	67 (93.1)		79 (97.5)	22 (84.6)		39 (97.5)	62 (92.5)		23 (85.2)	49 (98.0)	13 (92.9)	16 (100)	
Absent	1 (2.9)	5 (6.9)		2 (2.5)	4 (15.4)		1 (2.5)	5 (7.5)		4 (14.8)	1 (2.0)	1 (7.1)	0 (0.0)	

IDC NST=invasive ductal carcinoma with no special type; ILC=invasive lobular carcinoma; EIC=extensive intraductal component; ER=estrogen receptor; PR=progesterone receptor; HER2=human epidermal growth factor receptor 2

* Identifies a statistically significant correlation

Table 5. Univariate logistic regression analysis

Variables	B	SE	Odd ratio (95% CI)	p-value
Association with high histologic grade				
Rim enhancement	1.509	0.455	4.552 (1.854 to 11.029)	0.001*
(vs. non-rim enhancement)			1	
Association with ER negative				
Rim enhancement	1.536	0.480	4.644 (1.811 to 11.907)	0.001*
(vs. non-rim enhancement)			1	
Association with PR negative				
Rim enhancement	0.985	0.425	2.679 (1.164 to 6.165)	0.021*
(vs. non-rim enhancement)			1	
Association with Ki-67 positive				
Rim enhancement	1.216	0.531	3.373 (1.191 to 9.547)	0.022*
(vs. non-rim enhancement)			1	
Association with EIC negative				
Spiculated	0.962	0.723	2.618 (0.635 to 10.793)	0.183
(vs. irregular margin)			1	
Association with EIC negative				
Restricted diffusion	2.004	0.872	7.417 (1.341 to 41.008)	0.022*
(vs. no restricted diffusion)			1	
Association with Ki-67 positive				
Restricted diffusion	1.972	0.899	7.182 (1.233 to 41.824)	0.028*
(vs. no restricted diffusion)			1	

B=coefficient for the constant in the null model; SE=standard error around the coefficient for the constant; CI=confidence interval; EIC=extensive intraductal component; ER=estrogen receptor; PR=progesterone receptor

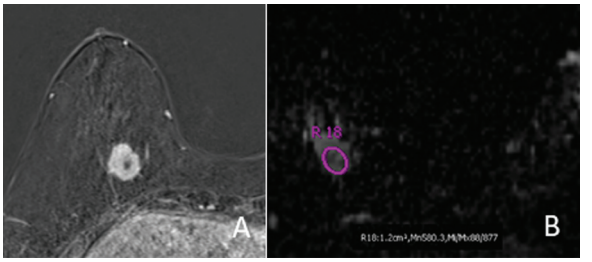

Figure 4. Invasive ductal carcinoma with negative EIC and positive Ki-67 in a 64-year-old woman.

Mastectomy specimen showed IDC grade II, DCIS negative, ER 95%, PR 95%, HER2 negative, Ki-67 20%, P53 negative. (A) MRI fat-suppressed T1-weighted post-contrast axial image with subtraction shows an irregular heterogeneous enhancing mass at lower inner quadrant of the right breast with restricted diffusion (circle in B).

Discussion

The present study showed that rim enhancement of the mass was 4.55 times more likely to predict histologic grade III, 4.64 times more likely to predict negative ER, 2.68 times more likely to predict negative PR, and 3.37 times more likely to predict positive Ki-67 statuses.

Many previous studies reported similar result to the present study that rim enhancement of the mass in dynamic contrast-enhanced MRI was an important imaging finding to predict the histologic grade, ER, PR, and Ki-67 status. They published that exhibition of higher microvessels in tumor periphery and tumor center ratio was seen in malignant lesions, and visible rim enhancement was the most accurate prognostic enhancement criterion for negative ER, PR statuses, and high tumor grade[3,10,15]. Another study also stated that rim enhancement was significantly correlated with high histologic grade and increased Ki-67 index[9].

Moreover, the present study results showed that internal enhancement was significantly associated with molecular subtypes such as many lesions of luminal A subtype appeared as heterogeneous enhancement for 78.3%. HER2-overexpressed and triple negative subtypes were dominantly presented with rim enhancement for 76.9% and 75%, respectively. As the knowledge of HER2-overexpressed and triple

negative subtypes have a worse prognosis, thus, this implied that rim enhancement may predict poor molecular subtypes of breast cancer.

The authors also found spiculated tumor margin of the mass was also significantly associated with negative EIC status. In addition, restricted diffusion of all lesions in the present study showed 7.42 times more likely to predict negative EIC status and 7.18 times more likely to predict positive Ki-67 status.

On the contrary, shape and margin of the mass were not significantly correlated with molecular subtypes.

For non-mass enhancement lesions, the authors found distribution and internal enhancement had no significant association with histopathologic findings. These results had been confirmed in the previous report of the 19 non-mass enhancement cases[16]. There was no significant correlation between morphologic enhancement type and ER, PR, HER2, P53, or Ki-67 status as well as no correlation between the distribution of the non-mass enhancement and prognostic factors.

Furthermore, no association between all HER2 positive lesions and MRI findings was noted in the present study. In correspondence with the former study in 78 histologically proven IDC patients (30 HER2 positives and 48 HER2 negatives), they found no significant difference regarding lesion shape, lesion margin, internal enhancement pattern, and enhancement kinetics patterns between HER2-positive and HER2-negative breast cancer[12].

There was also no association between kinetic curve types of the lesions and histopathologic findings. Like the prior study reported, no statistical significance was seen for hormone receptor subtypes and histologic tumor grades when compared against the most suspicious kinetic curves[17].

Limitations of the present study were a small number of patients with non-mass enhancement and incomplete MRI or pathological data from retrospective study design. Further investigation in a large population with non-mass enhancement lesions would allow more precise answers to the relationship between distribution and internal enhancement of non-mass enhancement lesions with histopathology and molecular subtypes of breast cancer.

Conclusion

The consistency of the association between rim enhancement and high histologic grade, negative ER or PR, positive Ki-67 statuses may help to determine that rim enhancement was likely to predict poor pathologic prognosis of breast cancer. Rim enhancement may also predict poor molecular subtypes including HER2-overexpressed and triple negative subtypes. These results suggest that rim enhancement is the most useful MRI finding to predict histopathology and molecular subtypes of breast cancer.

What is already known on this topic?

Correlation between rim enhancement and high histologic grade, negative ER or PR, positive Ki-67 statuses were agreed in the former studies. None of them had clearly stated the molecular subtypes.

What this study adds?

Rim enhancement of the mass lesions may predict poor molecular subtypes including HER2-overexpressed and triple negative subtypes. Rim enhancement would be the most useful MRI finding to predict histopathology and molecular subtypes of breast cancer.

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Conflicts of interest

The authors declare no conflict of interest.

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