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BREAST

Can enhancement types on preoperative MRI reflect prognostic factors and surgical outcomes in invasive breast cancer?

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Abstract

Objectives This study was conducted in order to evaluate whether enhancement types on preoperative MRI can reflect prognostic factors and surgical outcomes in invasive breast cancer.

Methods Among 484 consecutive patients who underwent preoperative breast MRI from October 2014 to July 2017 for biopsy-proven breast cancer, 313 patients with 315 invasive breast cancers who underwent subsequent surgery were finally included in this study. Two radiologists retrospectively reviewed preoperative MRI findings of these 315 lesions and categorized them to mass, nonmass, and combined type according to enhancement features. Combined type was defined as coexisted mass and nonmass enhancement. Histopathologic results focusing on prognostic factors and surgical outcomes were compared among the three types of lesion using Pearson's chi-square, linear-by-linear association, Kruskal–Wallis, one-way ANOVA test, and multinomial logistic regression.

Results Of the cancers analyzed, 198 (62.9%) were mass, 59 (18.7%) were nonmass, and 58 (18.4%) were combined type. The nonmass type showed the smallest invasive tumor size ($p < 0.001$) and the most common positive HER2 receptor status ($p = 0.001$). The combined type had the most frequent lymphovascular invasion ($p = 0.011$), axillary lymph node–positive status ($p = 0.031$), operation changes ($p < 0.001$), and first resection margin–positive status ($p < 0.001$). Initial operation of mastectomy was more frequent in the nonmass and combined types than that in the mass type ($p < 0.001$). But HER2 receptor status and operation changes showed no statistical significance on multivariate analysis.

Conclusions Enhancement types on preoperative MRI reflect different prognostic factors and surgical outcomes in invasive breast cancer.

Key Points

- *Morphologic features of contrast media uptake on contrast-enhanced MRI may be related with fundamental biological differences of invasive breast cancers.*
- *Mass or nonmass enhancement type on preoperative MRI might reflect different prognostic factors and surgical outcomes in invasive breast cancer.*
- *The combined mass and nonmass enhancement type might be associated with poorer prognosis and worse surgical outcomes.*

Keywords Magnetic resonance imaging · Breast neoplasms · Prognosis · Surgical oncology

Abbreviations

AJCC	American Joint Committee on Cancer
BCS	Breast-conserving surgery
DCIS	Ductal carcinoma in situ
ER	Estrogen receptor
HER2	Human epidermal growth factor receptor 2
IDC	Invasive ductal cancer
IHC	Immunohistochemical
LVI	Lymphovascular invasion
ME	Mass enhancement
MRI	Magnetic resonance imaging
NME	Nonmass enhancement
PR	Progesterone receptor

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Introduction

Contrast-enhanced MRI is a widely accepted complementary method for diagnosing breast cancer. It yields important information on morphologic and functional aspects reflected by the temporal and spatial uptake of contrast medium [1, 2]. Many researchers have reported that morphologic features of rim enhancement or functional features of high enhancement rate and washout are associated with poor prognostic factors of breast cancers [3–6]. Invasive breast cancers mainly present as mass enhancement (ME) on contrast-enhanced MRI. However, some invasive breast cancers may reveal pure nonmass enhancement (NME) or ME combined with NME on contrast-enhanced MRI [7]. Previous studies reported that a clustered ring pattern in NME was significantly associated with invasiveness in breast cancer [8, 9]. These basic morphologic differences of contrast media uptake might provide valuable information about their biologic features associated with prognosis of invasive breast cancers. Few studies have reported the association of prognostic factors with ME or NME in invasive breast cancer, and according to Lee et al, there were no significant differences in prognostic factors between ME and NME [3, 10]. However, previous studies included small numbers of lesions, and the combined type of ME with NME was not considered in their statistical analyses [3, 10]. Invasive breast cancer can occur in conjunction with in situ component in the same lesion. Thus, accompanying NME is frequently detected on preoperative breast MRI in clinical practice. Its biologic features can be different from those of pure mass or nonmass type invasive cancers. Therefore, larger and more detailed studies including combined ME and NME are needed to determine the relationship of prognostic factors between breast cancers with different enhancement types.

Meanwhile, NME exhibits poorly defined boundaries, unlike ME. It is difficult to perform breast-conserving surgery (BCS) with margin safety for breast cancer presenting as NME. Therefore, NME can be one of the important factors associated with positive margin in women undergoing BCS. However, studies comparing surgical outcomes of breast cancers showing ME and NME on MRI are lacking.

The purpose of this study was to compare prognostic factors and surgical outcomes between invasive breast cancers showing ME, NME, and combined ME and NME on preoperative MRI.

Materials and methods

The Institutional Review Board approved this study, and informed consent was waived.

Study population

According to our radiologic database collected from October 2014 to July 2017, 484 consecutive women with biopsy-proven breast cancers underwent breast MRI. We reviewed their electronic medical records and excluded 114 women who received neoadjuvant chemotherapy ($n = 70$) or were referred to other hospitals ($n = 44$). Of the remaining 370 women, after excluding 55 women with pure ductal carcinoma in situ (DCIS), 313 women with 315 invasive cancers were finally included in this study. Two women had synchronous bilateral invasive cancers. All 313 women underwent breast cancer surgery within 2 weeks after MRI examinations. The mean age of these women was 53.7 ± 9.2 years (range 30 to 81 years).

MRI examinations

Preoperative MRI examination was performed at 3.0 T (Signa HDxt, GE Healthcare) with a dedicated 8-channel surface breast coil for patients in prone position. MRI protocols included an axial fat-suppressed T2-weighted image (T2WI; TR/TE 5400/85 ms; FOV 30 × 30 cm; section thickness 0.5 cm), a sagittal fat-suppressed T2WI (TR/TE 4000/85 ms; FOV 18 × 18 cm; section thickness 0.4 cm), and a dynamic contrast-enhanced fat-suppressed T1-weighted gradient echo sequence (TR/TE 4.8/2.3 ms; FOV 30 × 30 cm; section thickness 0.2 cm) after intravenous injection of 0.1 mmol/kg of gadoteridol (ProHance®, Bracco Diagnostics) over 20 s with an injector at a flow rate of 2 mL/s. Subtracted images were generated from the dynamic sequences. Maximum intensity projection reconstruction was obtained from the subtraction images 1–8 min after injection.

Image analysis

In the first session, two fellowship-trained breast imaging radiologists with 4–14 years of clinical experience of breast imaging retrospectively and individually interpreted preoperative MRI features of each cancer blinded to final pathologic results. Mammography and ultrasound findings were informed. Each lesion was designated as ME or NME. ME was defined as enhancing lesion that occupied space, had a convex-outward contour, and was oval, round, or irregular in shape regardless of size. NME was defined as lesion that was not a mass and in which internal enhancing characteristics are discrete from the normal surrounding background parenchymal enhancement. When lesions were multiple in each breast, the largest lesion was reviewed as a main lesion. These cases were recorded as multiplicity. When suspicious NME was accompanied around the index lesion of ME, it was regarded as combined ME and NME. Accordingly, lesions were classified as follows: (a) pure ME (mass type), (b) pure NME (nonmass type), and (c) combined ME and NME (combined type).

In the second session, the readers decided whether each lesion should be classified into mass, nonmass, or combined type in consensus. Combined type lesions were correlated with final pathologic results, and when the accompanying

NME was not confirmed as malignancy, it was reclassified as mass type. And then, the readers assessed size, shape, margin, and internal enhancement for ME and size, distribution, and internal enhancement for NME according to the BI-RADS lexicon [11]; in combined type cases, ME and NME were evaluated, respectively. Breast tissue composition and background parenchymal enhancement were reviewed.

Pathology analysis

Histopathologic features interpreted by one of the four pathologists with 8–15 years of experience in breast pathology were retrospectively evaluated through chart review. Tumor type, size, histologic grade, and axillary lymph node status were assessed as classical prognostic factors. Tumor size was decided based on invasive cancer size. Microinvasive carcinoma was designated as ≤ 0.1 cm of invasion according to The American Joint Committee on Cancer (AJCC) classification [12]. Immunohistochemical (IHC) analysis results were evaluated to determine the expression of estrogen receptor (ER), progesterone receptor (PR), c-erbB-2 receptor (HER2), the p53 tumor suppressor gene, and Ki-67 as prognostic factors. A recut of the corresponding paraffin block had been immunostained with commercially available antibodies to ER, PR, and HER2.

Surgical outcomes

Surgical outcomes were assessed by retrospective chart review. Initial operation such as mastectomy or BCS, first resection margin status, and operation changes such as conversion to mastectomy after initial BCS were evaluated. During surgery, intraoperative frozen biopsy for evaluation of the resection margin was routinely performed, and immediate re-excision was performed for positive margins at frozen biopsy. The positive resection margin status was defined as that there were tumor cells on inked margin. Delayed re-excision or operation change was performed for positive margins at a permanent histopathology report. After surgery, additional therapy such as irradiation, chemotherapy, or hormone therapy was offered to patients according to tumor and patient characteristics.

Statistical analysis

The interreader reliability for enhancement type classification was assessed using the intraclass correlation coefficient (ICC). Based on the terminology proposed by Landis and Koch [13], an ICC value from 0.6 to 0.8 indicated substantial agreement and from 0.8 to 1.0 almost full agreement. To test whether there were differences in prognostic factors and surgical outcomes among mass, nonmass, and combined types, Kruskal–Wallis test and one-way ANOVA test were performed for continuous variables, while Pearson's chi-square test and linear-by-linear association test were performed for categorical variables. Additionally, Bonferroni correction was used to reduce the chances of obtaining false-positive results when multiple pairwise tests were performed on a single set of data. Multivariate analysis was performed using multinomial logistic regression. All statistical analyses were performed with SPSS software package version 20.0 (IBM Corporation). All tests were two sided and a statistical significant difference was set at $p < 0.05$.

Results

Of the 315 cancers analyzed, 198 (62.9%) in 195 women (age range 35–75 years, mean age 53.9 ± 10.28 years) were mass type (Fig. 1), 59 (18.7%) in 59 women (age range 39–70 years; mean age 53.5 ± 10.23 years) were nonmass type (Fig. 2), and 58 (18.4%) in 58 women (age range 43–

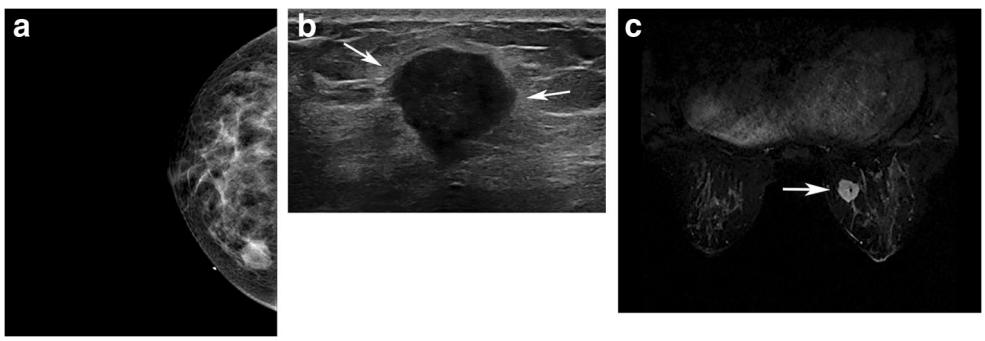

Fig. 1 A 45-year-old patient with a palpable right breast lump. **a** Right mammography showed a hyperdense nodular density at the palpable region (BB marker). **b** The palpable lesion was an irregular, microlobulated, and hypoechoic mass (arrows) on ultrasound, and it was diagnosed as invasive ductal cancer by ultrasound-guided core biopsy. **c** Mass enhancement (arrow) was revealed by preoperative breast MRI. It was finally confirmed as a 2.2-cm invasive ductal cancer with intermediate histologic grade and negative axillary lymph node status. Partial mastectomy was performed, and first resection margin was negative. Results of immunohistochemistry were ER-positive/PR-positive/HER2-negative, 50% Ki-67, and p53-positive

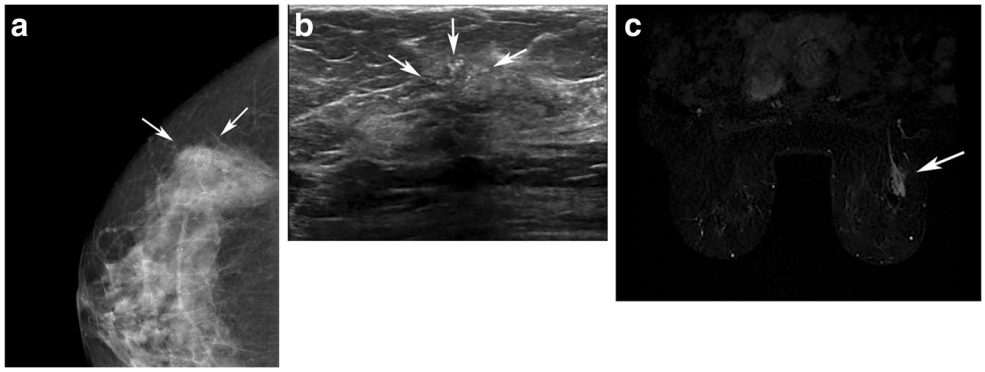

Fig. 2 A 60-year-old patient with right breast microcalcifications. **a** Right mammography showed grouped fine pleomorphic microcalcifications (arrows). **b** Microcalcifications were visible on targeted ultrasound (arrows), and it was diagnosed as ductal carcinoma in situ by ultrasound-guided core biopsy. **c** Preoperative breast MRI revealed segmental nonmass enhancement (arrows) at the right breast. The lesion was finally diagnosed as 450 μm microinvasive ductal carcinoma in 2.7 cm ductal carcinoma in situ (intermediate grade, solid and comedo type). There were no metastatic axillary lymph nodes. Partial mastectomy was performed, and the first resection margin was positive. Results of immunohistochemistry were ER-negative/PR-negative/HER2-positive, CK5/6-negative, 50% Ki-67, and p53-positive

70 years; mean age 53.2 ± 10.27 years) were combined type (Fig. 3). Multiple lesions were noted in 49 (24.7%) mass lesions, 18 (30.5%) nonmass lesions, and 43 (74.1%) combined lesions.

Enhancement type classification

There was disagreement in 20 (6.3%; 1 mass type, 10 nonmass type, and 9 combined type) of 315 lesions between two readers. The ICC showed almost perfect agreement (0.954). In consensus, the readers decided that 186 (59%) were mass type, 59 (18.7%) were nonmass type, and 70 (22.3%) were combined type. Of the 70 combined type lesions, 12 (17.1%) lesions were reclassified as mass type because the accompanying NME was finally confirmed as benign findings (fibrocystic changes, $n = 6$); usual ductal hyperplasia, $n = 3$; papillary ductal hyperplasia, $n = 2$; atypical ductal hyperplasia, $n = 1$).

General MR findings

The size, enhancement type, and morphologic features of lesions are summarized in Table 1. Irregular shape (201, 80.9%) and poorly circumscribed margin (208, 91.6%) were frequently noted in 227 mass lesions, and linear or segmental distribution (76, 86.4%) was a common finding in 88 nonmass lesions.

Prognostic factors

Table 2 summarizes the comparisons of pathologic results among mass, nonmass, and combined types. Tumor size

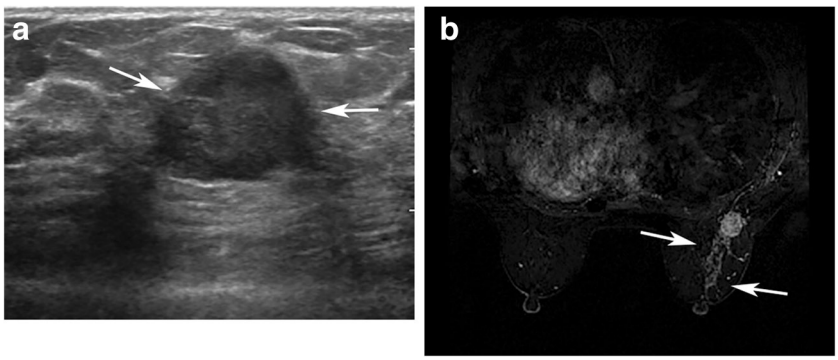

Fig. 3 A 60-year-old patient with a right breast lump. **a** On ultrasound, there were an irregular nodule (arrows) and duct ectasia at the palpable region of the right breast. The nodule was diagnosed as invasive ductal cancer by ultrasound-guided core biopsy. **b** Preoperative breast MRI revealed mass enhancement and accompanying segmental nonmass enhancement (arrows) at the right breast. According to final pathologic results, the lesion was 1.8-cm-sized invasive ductal cancer with high histologic grade, lymphovascular invasion, and ductal carcinoma in situ (intermediate grade). Initial operation was partial mastectomy. Additional modified radical mastectomy was performed due to positive resection margin by ductal carcinoma in situ. Four of the axillary lymph nodes were metastatic. Results of immunohistochemistry were ER-negative/PR-negative/HER2-positive and 65% Ki-67

Table 1 MRI descriptive analysis

MR findings	Numbers
Breast density	315
Fatty	3 (1.0)
Scattered fibroglandular	83 (26.3)
Heterogeneously dense	207 (65.7)
Extremely dense	22 (7.0)
BPE	315
Minimal	147 (46.7)
Mild	96 (30.5)
Moderate	57 (18.1)
Marked	15 (4.7)
Size (mean, mm)	26.7
Type of lesion	315
Mass	198 (62.9)
Nonmass	59 (18.7)
Combined	58 (18.4)
Shape (mass)*	227*
Round or oval	23 (10.1)
Irregular	204 (89.9)
Margin (mass)*	227*
Circumscribed	19 (8.4)
Not circumscribed	208 (91.6)
Internal enhancement (mass)*	227*
Homogeneous	58 (25.6)
Heterogeneous	130 (57.2)
Rim enhancement	39 (17.2)
Distribution (nonmass)**	88**
Focal	3 (3.4)
Linear or segmental	76 (86.4)

Numbers in parentheses are percentage

BPE, background parenchymal enhancement

*198 of mass type lesions + 29 of combined type lesions

**59 of nonmass type lesions + 29 of combined type lesions

($p < 0.001$), tumor pathology type ($p < 0.0005$), lymphovascular invasion ($p = 0.011$), comedo necrosis ($p < 0.001$), Paget's disease ($p < 0.001$), and axillary lymph node status ($p = 0.031$) were significantly different among mass, nonmass, and combined types. The nonmass type (12.8 ± 13.10 mm) showed significantly smaller invasive cancers than the mass (19.6 ± 15.60 mm) or combined type (19.4 ± 12.94 mm). Total tumor size including DCIS was larger in the nonmass type (mean, 36.4 ± 15.64 mm) than that in the mass type (mean, 19.6 ± 15.60 mm) or combined type (22.5 ± 15.84 mm). The main tumor pathology type was invasive ductal cancer (IDC) (162/198, 81.8%) for mass type. It was IDC with DCIS for nonmass type (34/59, 57.6%) and combined type (33/58, 56.9%). Microinvasive ductal carcinomas were more common in the nonmass type (9/59, 15.3%) than those in the mass type (2/198, 1.0%) or combined type (1/58, 1.7%). Small-size (2–5 mm) invasive cancer was also more frequent in the nonmass type (23/59, 39.0%) than that in the mass type (1/198, 0.5%) or combined type (3/58, 5.2%). Lymphovascular invasion (LVI) and axillary lymph node metastases were detected more in the combined type than those in the mass or nonmass type (23/58, 39.7% vs. 41/198, 20.7% or 14/59, 23.7%, $p = 0.011$ and 23/58, 39.7% vs. 50/198, 25.3% or 11/59, 18.6%, $p = 0.031$, respectively).

Table 3 summarizes the comparisons of immunohistochemical prognostic factors among mass, nonmass, and combined types. HER2 positivity was significantly more common in the nonmass type (26/59, 44.1%) and in the combined type (19/58, 32.8%) than that in the mass type (39/198, 19.7%) ($p = 0.001$). ER/PR-negative HER2-positive subtype was more frequent in the nonmass type (16/59, 27.1%) and in the combined type (10/58, 17.2%) than that that in the mass type (17/198, 8.6%) ($p = 0.0009$, Table 4).

On multivariable analysis, tumor size ($p < 0.0001$), tumor pathology type ($p < 0.0001$), LVI ($p < 0.001$), and axillary lymph node status ($p = 0.006$) were significantly different prognostic factors between the three types (Tables 3 and 4).

Surgical outcomes

Table 5 summarizes the comparisons of surgical outcomes among mass, nonmass, and combined types. Initial mastectomy was more commonly performed for the nonmass type (39/59, 66.1%) and the combined type (39/58, 67.2%) than that for the mass type (65/198, 32.8%) ($p < 0.001$). The first positive resection margin status was the most frequent in the combined type (24/58, 41.4%) ($p < 0.001$). Operation change to mastectomy after initial BCS was also the most common in the combined type (7/58, 12.1%) ($p < 0.001$). Multinomial logistic regression models showed that initial operation ($p < 0.001$) and first resection margin status ($p = 0.014$) only were significantly different surgical outcomes between the three types.

Discussion

Compared to the previous studies on the association of prognostic factors with ME and NME in invasive breast cancer [3, 10], the strength of this study was the relatively larger lesion numbers and more detailed analysis on enhancement type. Thus, this study would provide more reliable results. Lee et al reported that no significant association has been found with prognostic factors including tumor size between 170 (88%) ME type and 24 (12%) NME type IDCs [3]. In the

Table 2 Comparisons of pathologic results between mass, nonmass, and combined types

Variable	Mass (198)	Nonmass (59)	Combined (58)	*p* value	
Age				0.736*	
(Mean)	53.9 ± 10.28	53.5 ± 10.23	53.2 ± 10.27		
Lesion size				< 0.001**	< 0.0001[¶]
(Mean)	19.6 ± 15.60	12.8 ± 13.10	19.4 ± 12.94		
Pathology type				0.0005[§]	< 0.0001[¶]
IDC (194)	81.8% (162)	16.9% (10)	37.9% (22)	< 0.0001[‡]	
IDC with DCIS (74)	3.5% (7)	57.6% (34)	56.9% (33)	< 0.0001[‡]	
Microinvasive DCIS (12)	1.0% (2)	15.3% (9)	1.7% (1)	0.1039[†]	
ILC (15)	5.1% (10)	8.5% (5)	0 (0)	0.0940[†]	
Other invasive cancer (21)	8.6% (17)	3.4% (2)	3.5% (2)	0.2103[†]	
Histologic grade				0.183[‡]	
Low (60)	21.7% (43)	10.2% (6)	18.9% (11)		
Intermediate (136)	38.9% (77)	54.2% (32)	46.6% (27)		
High (119)	39.4% (78)	35.6% (21)	34.5% (20)		
Lymphovascular invasion				0.011[‡]	< 0.001[¶]
Present (78)	20.7% (41)	23.7% (14)	39.7% (23)		
Absent (237)	79.3% (157)	76.3% (45)	60.3% (35)		
Comedo necrosis				< 0.001[‡]	0.103[¶]
Present (52)	6.6% (13)	49.2% (29)	17.2% (10)		
Absent (260)	93.4% (185)	50.8% (30)	77.6% (45)		
Paget disease				< 0.001[‡]	0.069[¶]
Present (32)	4.5% (9)	20.4% (12)	19.0% (11)		
Absent (283)	95.6% (189)	79.6% (47)	81.0% (47)		
Axillary lymph node status				0.031[‡]	0.006[¶]
Positive (84)	25.3% (50)	18.6% (11)	39.7% (23)		
Negative (231)	74.7% (148)	81.4% (48)	60.3% (35)		

Numbers in parentheses are the numbers of patients unless otherwise indicated

IDC, invasive ductal cancer; *DCIS*, ductal carcinoma in situ; *ILC*, invasive lobular cancer

*Statistical analysis was performed using Kruskal–Wallis test

**Statistical analysis was performed using Kruskal–Wallis test and one-way ANOVA test

[§] The critical *p* value was 0.0001 but was modified using Bonferroni correction

[†] Statistical analysis was performed using Pearson's chi-square test

[‡] Statistical analysis was performed using linear-by-linear association test

[¶] Statistical analysis was performed using multinomial logistic regression

present study, invasive tumor size was significantly smaller in the nonmass type ($p < 0.001$), and coexisting DCIS was significantly more common in the nonmass and combined types ($p = 0.005$). These results were reasonable and expected because most malignant NME was associated with DCIS, while micro- or small-sized invasive cancer might be shown as NME without distinct ME on MRI. Jiang et al [10] have compared prognostic factors between 69 ME type and 19 NME type IDCs and found that nonmass type cancers were more correlated with lower patients' age, larger tumor size, DCIS, and lower histologic grade. Regarding tumor size, they used tumor size including DCIS, while we analyzed invasive tumor size. For histologic grade, our data showed no statistical significance.

We found that LVI and axillary lymph node metastases were more common in the combined type ($p < 0.001$ and $p = 0.006$, respectively). To our knowledge, these findings have never been reported. LVI is the pathologic finding of tumor emboli present within peritumoral vascular channels and is associated with increased risk of axillary lymph node metastases as well as local and distant recurrence [3–5]. The presence of axillary node metastases is prognostically significant for overall and disease-free survival [3–5]. Therefore, although the mechanism is

Table 3 Comparisons of immunohistochemical results between mass, nonmass, and combined types

Variable	Mass (198)	Nonmass (59)	Combined (58)	*p* value*	
ER status				0.167	
Positive (219)	71.7% (142)	59.3% (35)	72.4% (42)		
Negative (96)	28.3% (56)	40.7% (24)	27.6% (16)		
PR status				0.0641	
Positive (171)	56.1% (111)	40.7% (24)	62.1% (35)		
Negative (144)	43.9% (87)	59.3% (35)	37.9% (23)		
HER2 status				0.001	0.650§
Positive (84)	19.7% (39)	44.1% (26)	32.8% (19)		
Negative (231)	80.3% (159)	55.9% (33)	67.2% (39)		
p53**	(183)	(56)	(56)	0.242	
Positive (156)	55.2% (101)	50% (28)	48.2% (27)		
Negative (139)	44.8% (82)	50% (28)	51.8% (29)		
CK5/6**	(186)	(55)	(54)	0.619	
Positive (40)	15.1% (28)	10.9% (6)	11.1% (6)		
Negative (255)	84.9% (158)	89.1% (49)	88.9% (48)		
Ki-67**	(189)	(57)	(54)	0.986	
Positive (220)	73% (138)	26.3% (15)	25.9% (14)		
Negative (80)	27% (51)	73.7% (42)	74.1% (40)		

Numbers in parentheses are the numbers of patients unless otherwise indicated

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

*Statistical analysis was performed using Pearson's chi-square test

**Immunohistochemical analysis was not available for p53 (= 20), CK5/6 ($n = 20$), and Ki-67 ($n = 15$)

§ Statistical analysis was performed using multinomial logistic regression

unclear, our results might provide meaningful information for predicting prognosis of invasive breast cancer showing combined ME and NME. Previous studies investigated the significance of accompanying NME in IDC on preoperative MRI, and accompanying NME showed malignant pathologic results in 55–83% [14, 15]. In this study, 58 (82.9%) of 70 suspicious accompanying NME were malignant. Gweon et al compared clinicopathologic features between 163 IDCs with NME and without NME, and HER2-positive IDC was more frequently associated with malignant accompanying NME [14]. Nodal status was not evaluated in their study [14]. Meanwhile, HER2-positive or ER-negative IDC was related with NME in other previous studies [16, 17]. Even though multivariate analysis showed no statistical significance, our results were consistent with those of previous studies [14, 16, 17]. The value of HER2 as a prognostic factor is controversial, but previous data suggest that positive HER2 is an adverse prognostic factor [18, 19]. Therefore, our results suggest that additional NME might be associated with poor prognosis such as positive nodal status and HER2 positivity in invasive breast cancer.

Surgical outcomes were also different among the three types in this study. Mastectomy was planned more as an initial operation for nonmass or combined type cancers than that for mass type cancers (39/59, 66.1% or 39/58, 67.2% vs. 65/198, 32.8%, $p < 0.001$). Decision-making on initial breast cancer surgery is multifactorial. Previous studies have found that younger age, larger tumor size, positive lymph node status, invasive lobular cancer, and preoperative MRI were associated with higher rates of mastectomy [20]. Preoperative MRI frequently can detect additional lesions not found on mammography or breast ultrasound. These lesions could be multiple lesions with larger tumor extent or accompanying NME. Particularly, NME exhibits poorly defined boundaries. It tends to be associated with microcalcifications, random distribution, and extensive disease. According to our data, NME was mostly due to DCIS. Total tumor size including DCIS was the largest in the nonmass type, followed by that in the combined type and the mass type. Therefore, the higher rate of mastectomy for nonmass or combined type cancers is understandable.

To determine complete tumor resection in BCS, the margin of healthy tissue was evaluated by histologic examination because inadequate tumor resection margin could increase the risk of local recurrence of the tumor. In these cases, additional resection is recommended to obtain total tumor clearance. Prior studies have reported that factors associated with positive margin in BCS are multifocality,

Table 4 Comparisons of molecular subtypes between mass, nonmass, and combined types

Variable	Mass (198)	Nonmass (59)	Combined (58)	*p* value	
				0.020§	0.796†
ER+PR+HER2− (182)	62.1% (123)	44.1% (26)	56.9% (33)	0.1129*	
ER+PR−HER2− (41)	11.1% (22)	16.9% (10)	15.5% (9)	0.4145*	
ER−PR−HER2+ (43)	8.6% (17)	27.1% (16)	17.2% (10)	0.0009*	
Triple negative (49)	18.2% (36)	11.9% (7)	10.3% (6)	0.0947**	

Numbers in parentheses are the numbers of patients unless otherwise indicated

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

§ The critical *p* value was 0.005 but was modified using Bonferroni correction

*Statistical analysis was performed using the Pearson's chi-square test

**Statistical analysis was performed using linear-by-linear association test

† Statistical analysis was performed using multinomial logistic regression

lobular subtype, large tumor size, NME on MRI, and the presence of DCIS [21–24]. Our data showed that positive resection margin after lumpectomy was significantly more common in the combined type (24/58, 41.4%) and in the nonmass type (17/59, 28.8%) than that in the mass type (20/198, 10.1%) ($p < 0.001$). Our results were consistent with those of previous studies [21–24], but the combined type showed worse surgical outcomes. Jia et al [25] have reported that ER-negative/HER2-positive status is associated with an increased risk of positive cavity margin after lumpectomy and an independent prognostic factor for local recurrence. They suggested that the increased risk of local recurrence in HER2-positive breast cancer was due to an increased microscopic invasive tumor burden indicated by margin status after lumpectomy [25]. As described earlier, HER2 status was more associated with the nonmass or combined type than with the mass type in the present study, consistent with their results.

The present study has several limitations. First, as there is no clear categorization of MR findings of ME or NME, there could be selection bias in the classification of enhancement type. But interreader reliability was almost perfect, and the readers finally decided the type in consensus. Second, although this study included larger numbers of subjects compared to the previous studies for similar investigation, the numbers of each enhancement type of cancer were small. This study had 198 mass type, 59 nonmass type, and 58 combined type cancers. A larger and multicenter study should be performed to validate our results.

Table 5 Comparisons of surgical outcomes between mass, nonmass, and combined types

Variable	Mass (198)	Nonmass (59)	Combined (58)	*p* value	
Second-look US				0.023*	0.087§
Yes (58)	15.7% (31)	15.3% (9)	31.0% (18)		
No (257)	84.3% (167)	84.7% (50)	69% (40)		
Initial operation				< 0.001*	< 0.001§
BCS (172)	67.2% (133)	33.9% (20)	32.8% (19)		
Mastectomy (143)	32.8% (65)	66.1% (39)	67.2% (39)		
Operation change				< 0.001**	0.775§
Yes (13)	0.5% (1)	8.5% (5)	12.1% (7)		
No (302)	99.5% (197)	91.5% (54)	87.9% (51)		
First resection margin				< 0.001*	0.014§
Positive (61)	10.1% (20)	28.8% (17)	41.4% (24)		
Negative (254)	89.9% (178)	71.2% (42)	58.6% (34)		

Numbers in parentheses are the numbers of patients unless otherwise indicated

US, ultrasound; *BCS*, breast-conserving surgery

*Statistical analysis was performed using Pearson's chi-square test

**Statistical analysis was performed using linear-by-linear association test

§ Statistical analysis was performed using multinomial logistic regression

In conclusion, mass, nonmass, or combined enhancement type on preoperative MRI reflects different prognostic factors and surgical outcomes in invasive breast cancer. The results of our study may contribute to an appropriate treatment for patients with invasive breast cancers.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Hae Kyoung Jung.

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- retrospective
- observational
- performed at one institution

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