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MR mammography is useful in the preoperative locoregional staging of breast carcinomas with extensive intraductal component

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Abstract

Purpose: To determine the role of magnetic resonance (MR) mammography in detection and assessment of extent of tumors with extensive intraductal component (EIC+).

Material and methods: In a prospective study, 233 consecutive women with a suspicious lesion underwent preoperative MR mammography and 209 invasive ductal carcinomas were detected. We studied the prediction of intraductal spread on mammography (MX), ultrasound (US) and MR. We compared the size of the total lesion on MX, US and MR and correlated it with histopathology. Enhancement patterns on MR were described.

Results: Of 209 invasive ductal carcinomas, 50 were EIC+ (24%).

MX predicted intraductal spread in EIC+ carcinomas in 48.5%, US in 34.2% and MR in 68%. Compared to MX and US, MR was best in assessment of total tumor size.

On MR, ductal spread in EIC+ tumors presented as ductal or linear enhancement, long spicules, a regional enhancing area or nodules adjacent to a mass.

Conclusion: MR had the highest sensitivity to predict intraductal spread and was superior in assessing total tumor size.

Keywords: Invasive breast cancer; Extensive intraductal component; Ductal carcinoma in situ; MR mammography; Detection; Extent

1. Introduction

Locoregional staging of breast carcinoma is mandatory to select patients for breast conserving therapy and includes accurate assessment of tumor size, multifocality and presence of an extensive intraductal component (EIC+ tumors).

The presence of an extensive intraductal component results in a higher recurrence rate after conservative surgery, 26% in EIC+ patients compared with 7% without EIC [1]. However, if negative margins can be obtained, excellent outcome has been reported [2,3]. Recurrence is probably due to residual cancer [4]. Moreover, about 50% of recurrences after resection for ductal carcinoma in situ (DCIS) are invasive carcinomas [5]. In a study of Holland et al., 71% of patients with primary EIC+ tumors had residual intraductal carcinoma in the remainder of the breast, compared to 28% of patients without EIC+ [4].

Accurate preoperative measurement of the invasive cancer and ductal carcinoma in situ, on breast imaging is mandatory in therapy planning [6] and can limit reintervention for positive margins. The best estimate of tumor size results from correlating imaging and pathologic data [6].

MR mammography is most accurate in the estimation of extent of breast carcinoma [7–10]. Sensitivity of MR to detect DCIS with an invasive cancer varies between 54% and 100% [11–14]. EIC+ tumors are described as spiculated masses or masses with linear enhancement adjacent to it [7,13]. In this prospective study we tried to predict, on mammography, ultrasound and MR mammography, whether a suspicious mass had accompanying DCIS and the total size of the cancer, including

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the in situ component. We also studied MR features of EIC+ carcinomas.

2. Material and methods

2.1. Patients

In a prospective study, consecutive women with a lesion suspicious of breast cancer diagnosed on clinical examination, mammography and/or ultrasound underwent preoperative MR mammography. Exclusion criteria were pregnancy, prior breast surgery for malignancy in the same breast, neoadjuvant chemotherapy and being older than 80 years. Two hundred thirty three women entered the study, after they signed informed consent. The study was performed in two hospitals.

2.2. Imaging protocol

All patients had a clinical examination performed by a gynaecologist specialised in breast diseases. The examination included inspection and palpation of the breasts and examination of the axillae. Mammography (MX) was performed on a GE mammography unit Senographe DMR (GE Medical Systems). All patients had conventional oblique and cranio-caudal mammographic views, completed with tangential, profile, extra lateral or magnification views if routine views did not allow good evaluation of the border of a lesion or if evaluation or extent of microcalcifications was not possible. Mammographic examinations were interpreted by a radiologist specialised in breast imaging. Mammography interpretation was based on the Breast Imaging Reporting and Data System (BI-RADS) [15]. All patients underwent whole-breast ultrasound (US) of both breasts as initial work-up, with a high frequency probe (7.5–13 MHz), using a GE or ATL (HDI 3000, Washington) US equipment in centre A and a Sequoia, Acuson (Mountain View, California) in centre B. The ultrasound examinations were performed by the same radiologist who interpreted the mammography.

All patients underwent preoperative magnetic resonance (MR) mammography within 1 week after mammography and ultrasound examinations.

Both breasts were examined simultaneously by the use of a dedicated bilateral breast coil in the two centres. In both hospitals we used a 3D FLASH sequence. Sixty-four coronal images were obtained before and after 0.2 mmol/kg GD-DTPA administration and subtraction images were made.

Imaging was performed in centre A and on a 1.5 T Symphony Quantum system (Siemens). Parameters were respectively repetition time (TR) of 12 ms and 13 ms, echo time (TE) of 5.0 ms and 6.3 ms, time to acquisition (TA) of 1.27 min and 1.15 min, a field of view (FOV) of 320 mm, rec FOV 4/8 with a 87% phase resolution (matrix of 112×256) and FOV 320 mm, 50% FOV and 80% phase resolution (matrix 102×256) revealing 64 coronal sections of 2.0 mm slice thickness (SL). On both systems, a flip angle of 25° was used. On the Symphony Quantum system, an additional sequence with fat saturation with TR 32.0 ms, TE 6.3 ms, TA 6.07 min, SL 3.0 mm, FOV 160–320 mm and matrix 205×512 was performed.

In centre B examinations were performed on a 1 T Magnetom Impact Expert MRI machine (Siemens) and a 3D FLASH sequence with selective water excitation was used with TR 24.0 ms, TE 7.0 ms, TA 3.34 min, flip angle 30°, FOV 160–320 mm, 177×512 matrix and slice thickness of 3.2 mm.

Percentage of maximal enhancement and type of curve of the lesion were obtained in both centres, moment of maximal enhancement could only be achieved in centre A. The same kinetic data were obtained in the surrounding enhancing region in some of the cancers. To evaluate the curve in the enhancing surrounding structures, we chose a Region of Interest (ROI) that was small enough to avoid underestimation due to inclusion of non-enhancing environment.

As MR mammography is a complementary examination and should be interpreted regarding clinical examination, mammography and ultrasound results, all MR mammograms were interpreted by a radiologist specialised in breast disease, with knowledge of patient history and results of clinical examination, mammography and ultrasound images.

2.3. Imaging interpretation

On mammography, suspicious microcalcifications or prominent nodular pattern adjacent to a probably malignant mass were considered to be suspect for accompanying DCIS. On ultrasound, diagnosis of intraductal spread was made if duct dilatation with or without intraductal contents or if a tubular structure or an area of architectural distortion could be recognised next to a mass. On MR, accompanying DCIS was suggested if there were long spicules, ductal, linear or focal enhancement or small nodules adjacent to the mass. Kinetic data were not taken into account for the diagnosis.

The diameter of the mass and of the total pathologic area was measured on all three imaging modalities and sizes were given in millimetres.

2.4. Imaging-pathology comparison

Radiologist and breast surgeon discussed mammography, ultrasound and MR mammography examinations preoperatively and therapy planning was performed taking into account the diameter of the mass and the "diameter of the total lesion", described as diameter of the mass with surrounding abnormalities. All biopsy specimens were anatomically oriented and a drawing was made by the surgeon to show the origin of the specimen. The specimen was serially sectioned in 3–5 mm intervals and a radiograph of the slices was performed. Mastectomy specimens were sectioned at 5 mm intervals. Radiologist and pathologist jointly evaluated the tissue sections, mammography, ultrasound and MR.

On pathologic examination, the diameters of all malignant lesions, including invasive cancer and/or DCIS were measured and sizes were given in millimetres. If the difference in diameter measured on MR and on histopathology was larger than 2 mm, the lesion was called underestimated or overestimated on MR.

In tumorectomy (tumor excision with minimal tumor free margins) the in situ component was considered extensive if in the histological cross-section more than 25% of the tumor area consisted of DCIS and if DCIS was present in the surrounding breast tissue outside the margins of the invasive tumor. In lumpectomy (wide local excision with an estimated 1 cm margin of (macroscopically) normal breast tissue) specimens the in situ component was considered extensive if at least 15 ductulobular units around the invasive tumor were involved [16].

In our study, we considered three groups of invasive cancers: invasive carcinomas without surrounding DCIS are called "invasive cancers"; invasive cancers with local surrounding DCIS, but no EIC were called "invasive cancer with non-extensive DCIS" and invasive cancer with extensive DCIS in and around the cancer as defined above, were called "EIC+ carcinomas". The group of the DCIS carcinomas contains only pure DCIS carcinomas. The histologic grade of invasive cancer was scored by means of the Elston modification of the Boom and Richardson system [17,18]. To classify the type of DCIS, we used the pathologic classification of Van Nuys, determined by nuclear grade and necrosis: non-high grade without necrosis = I; non-high grade with necrosis = II; high grade with/without necrosis = III [19].

The lesion first detected on clinical examination, mammography or ultrasound was called the primary lesion, subsequent detected lesions were called second, third, …. Tumors and lesions only detected by MR were called additional foci.

We measured the extent of the DCIS component in EIC+ carcinomas by calculating the difference between the diameter of the total lesion and that of the invasive component on histopathology, in mm.

2.5. Data analysis

Categorical data were compared using an exact test. The distribution of continuous data was tested for normality by Shapiro Wilk's W. As normal distributions could not be accepted, even after log transformation, correlations were assessed by Spearman Rank correlation coefficient and groups were compared by non-parametric tests (Mann–Whitney *U*-test). Prevalences of confirmation in suspicious and non-suspicious for accompanying DCIS, were compared for the different imaging techniques by an exact test. Extension of the DCIS in EIC+ carcinomas that were not predicted on MR was compared with the extent of the EIC+ predicted on MR, using a Mann–Whitney *U*-test. Differences between diameters measured on MR and histopathology of less than 2 mm were considered correct, differences of more than 2 mm were called over- or underestimation. Finally, different morphologic features of invasive carcinomas with intraductal extent on MR were described. A Fisher exact test was used to study differences in features of EIC+ tumors and tumors with non-extensive DCIS.

3. Results

3.1. Detection of DCIS around a mass

Our study population consisted of 233 women with 403 lesions: 106 benign lesions, 1 Paget's disease of the nipple, 49 pure DCIS and 247 invasive carcinomas, 209 of them being invasive ductal carcinomas (IDA). Age range of the study population was 21–79 years (mean 55.5 years). Of the invasive ductal carcinomas, 50 were EIC+. Of them, 36 were primary lesions, 4 were second or third lesions and 10 were additional foci detected on MR only. The mean diameter was 20.5 mm for the invasive carcinomas and 41 mm for the total carcinomas (invasive + surrounding DCIS). Additionally, 61 invasive carcinomas had local DCIS but no EIC (called invasive cancer with non-extensive DCIS). Of these, 50 were primary lesions, 6 s or third lesions and 5 were additional foci. The mean diameter was 24.5 mm for the invasive carcinoma and

Table 1
Characteristics of different carcinomas

	Invasive, no DCIS	Invasive with local DCIS, no EIC+	Invasive, EIC+	*p*
Age				
Mean	58.6 years	53.5 years	55.7 years	0.0169
Range	(33–75 years)	(24–79 years)	(32–76 years)	
Tumor size				
Mean	18 mm	Mean 25 mm	20 mm	0.7455
Range	(2–100 mm)	(3–180 mm)	(5–75 mm)	
Total tumor size				
Mean	19 mm	Mean 31 mm	41 mm	
Range	(2–100 mm)	(8–180 mm)	(10–90 mm)	
Method of detection				
C.E. palpable	51%	64%	62%	0.33618
MX detection	65%	75%	66%	0.14843
US detection	64%	87%	76%	0.00389
MR detection	96%	100%	100%	0.02615
Grade invasive cancer				
High grade	33%	44%	55%	0.0002
Intermediate grade	17%	30%	22%	
Low grade	50%	26%	22%	

Table 2a
Prevalence of different pathologies for different mammographic diagnosis

Diagnosis on MX	Pathology				
	Benign ($n=106$)	Pure DCIS ($n=49$)	Invasive ca[a] ($n=136$)	Invasive ca + non-extensive DCIS[b] ($n=61$) (35 III, 8 II, 18 I)	IDA, EIC+ ($n=50$) (38 III, 4 II, 8 I)
Invasive ca + DCIS ($n=36$)	1 (3%)	3 (8%)	9 (25.0%)	9 (25%) 6 (17%) III 2 (6%) II 1 (3%) I	14 (39%)[*] 14 (39%) III
Invasive ca ($n=160$)	28 (17%)	1 (1%)	77 (48%)	37 (23%) 19 (12%) III 4 (2%) II 14 (9%) I	17 (11%)[*] 9 (6%)III 3 (2%) II 5 (3%) I
DCIS ($n=54$)	24 (44%)	26 (46%)	2 (4%)	0	2 (4%) 1 (2%) III 1 (2%) I
Benign ($n=9$)	5 (55%)	1 (11%)	1 (11%)	2 (22%)	0 (0%)
Not detected ($n=140$)	48 (34%)	16 (11%)	47 (34%)	13 (9%)	16 (11%)
Not defined		2			1

DCIS: ductal carcinoma in situ; ca: carcinoma; EIC: extensive intraductal component; I, II, III: pathology grades of DCIS according to Van Nuys (Ref. [23]); MX: mammography. n is the number of cases for which this diagnosis is made.

[*] $p=0.0001$ between prevalences of EIC+, when DCIS is or is not predicted (Fisher-exact).

[a] Ninety-eight invasive ductal carcinomas, 22 invasive lobular carcinomas, 16 other invasive carcinomas.

[b] Sixty invasive ductal carcinomas and one medullary carcinoma.

31.4 mm for the total lesion (invasive + surrounding DCIS) (Table 1).

If a lesion was considered malignant on mammography, ultrasound or MR mammography, we tried to predict on every imaging technique seperately whether it was a pure DCIS, an invasive carcinoma without surrounding DCIS or an invasive carcinoma with surrounding DCIS. Prevalences are given in Tables 2a–2c. Prevalences of EIC+ tumor were significantly higher when mammography, ultrasound or MR mammography predicted DCIS than when it was not predicted, $p=0.0001$, $p=0.0007$, $p<0.0001$, respectively (Fisher exact). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) to predict invasive cancer with DCIS around it were 20%, 96%, 64% and 76% for mammography, 14%, 94%, 48% and 74% for ultrasound and 50%, 90%, 65% and 82% for MR mammography.

On MX, 36 cases were predicted as invasive carcinoma with DCIS. The diagnosis was correct in 23 of them, 9 had non-extensive DCIS and 14 were EIC+. MX was false positive in predicting DCIS in 9 pure invasive cancers. MX predicted only

Table 2b
Prevalence of different pathologies for different diagnosis on US

Diagnosis on US	Pathology				
	Benign ($n=106$)	Pure DCIS ($n=49$)	Invasive ca[a] ($n=136$)	Invasive ca + non-extensive DCIS[b] ($n=61$) (35 III, 8 II, 18 I)	IDA, EIC+ ($n=50$) (38 III, 4 II, 8 I)
Invasive ca + DCIS ($n=33$)	2 (6%)	4 (12%)	11 (33%)	3 (9%) 2 (3%) III 1 (3%) II 0 (0%) I	13 (39%)[**] 12 (36%)III 1 (3%) II
Invasive ca ($n=190$)	32 (17%)	5 (3%)	78 (41%)	50 (26%) 29 (15%) III 5 (3%) II 16 (8%) I	25 (13%)[**] 18 (9%) III 2 (1%) II 5 (3%) I
DCIS ($n=5$)	3 (60.0%)	2 (40.0%)	0	0	0
Benign ($n=9$)	7	1	1	0	0
Not detected ($n=163$)	62	36	45	8	12
Not defined		1	1		

DCIS: ductal carcinoma in situ; ca: carcinoma; EIC: extensive intraductal component; I, II, III: pathology grades of DCIS according to Van Nuys (Ref. [23]); US: ultrasound. Ninety eight invasive ductal carcinomas, 22 invasive lobular carcinomas, 16 other invasive carcinomas. Sixty invasive ductal carcinomas, one medullary carcinoma. n is the number of cases for which this diagnosis is made.

[**] $p=0.0007$ between prevalences of EIC+, when DCIS is or is not predicted (Fisher-exact).

[a] Ninety-eight invasive ductal carcinomas, 22 invasive lobular carcinomas, 16 other invasive carcinomas.

[b] Sixty invasive ductal carcinomas and one medullary carcinoma.

Table 2c
Prevalence of different pathologies for different diagnosis on MR

Diagnosis on MR	Pathology				
	Benign ($n=106$)	Pure DCIS ($n=49$)	Invasive ca[a] ($n=136$)	Invasive ca + non-extensive DCIS[b] ($n=61$) (35 III, 8 II, 18 I)	IDA, EIC+ ($n=50$) (38 III, 4 II, 8 I)
Invasive ca + DCIS ($n=85$)	8 (9%)	8 (9%)	14 (17%)	23 (27%) 16 (19%) III 5 (9%) II 2 (2%) I	32 (38%)[***] 26 (31%) III 1 (1%) II 5 (6%) I
Invasive ca ($n=219$)	42 (19%)	9 (4%)	114 (52%)	38 (17%) 19 (9%) III 3 (1%) II 16 (7%) I	16 (7%)[***] 11 (5%) III 3 (1%) II 2 (1%) I
DCIS ($n=43$)	16 (37%)	23 (51%)	2 (5%)	0	2 (5%) 1 (2%) III 1 (2%) I
Benign ($n=17$)	15	1	1	0	0
Not detected ($n=38$)	25	8	5	0	0

DCIS: ductal carcinoma in situ; ca: carcinoma; EIC: extensive intraductal component; I, II, III: pathology grades of DCIS according to Van Nuys (Ref. [23]); MR: magnetic resonance mammography. *n* is the number of cases for which this diagnosis is made.

[a] Ninety eight invasive ductal carcinomas, 22 invasive lobular carcinomas, 16 other invasive carcinomas.

[b] Sixty invasive ductal carcinomas and one medullary carcinoma.

[***] $p=0.0001$ between prevalences of EIC+, when DCIS is or is not predicted (Fisher-exact).

invasive carcinoma in 54 of 111 cancers with DCIS, respectively in 37 of 61 with non-extensive DCIS and in 17 of 50 EIC+ carcinomas. US predicted DCIS in 33 lesions, in 16 cases the diagnosis was correct. US was false positive in predicing DCIS in 11 pure invasive carcinomas. On US only the invasive carcinoma was diagnosed in 75 of the 111 cancers with DCIS, respectively in 50 of 61 with non-extensive DCIS and 25 of 50 EIC+ cancers.

MR predicted DCIS with invasive carcinoma in 85 lesions: 23 were invasive with non-extensive DCIS, 32 were EIC+, 8 were pure DCIS and 8 were benign. Moreover, 14 were pure invasive cancers (=false positive on MR) and the surrounding enhancement was due to benign changes in most of the cases and corresponded with lymphovascular invasion in 1 cancer. On MR mammography the DCIS component was not predicted in 16 of 50 EIC+ tumors (2/8 grade I, 3/4 grade II and 11/38 grade III DCIS) and in 38 of 61 cancers with non-extensive DCIS (16/18 grade I, 3/8 grade II and 19/35 grade III) because only a mass was seen, without enhancing surrounding lesions.

Tables 3 and 4 show prediction of EIC+ tumors and tumors with non-extensive DCIS.

Mammography predicted DCIS around a mass in 42% EIC+ mammographically detected tumours and in 19.6% cancers surrounded by non-extensive DCIS, US in respectively 34.2% and 5.7% and MR in 64.0% and 37.7%.

3.2. Extent

Fig. 1 shows diameters as measured on MX, US and MR compared to measurements on histopathology of EIC+ tumors and Fig. 2 those of invasive carcinoma surrounded by non-extensive DCIS. For both groups, MR had the highest correlation coefficient (Spearman Rank) and gave the most accurate estimate of the total tumor. If EIC+ was not predicted on MR mammography, the DCIS component was significantly smaller (mean = 9.9 mm) than in the EIC+ carcinomas with predicted DCIS on MR (mean = 26.7 mm) ($p=0.0019$; Mann–Whitney *U*-test). In the16 EIC+ tumors where the DCIS was not predicted, the diameter of the lesion on MR corresponded with the total diameter (invasive and DCIS) on pathology in six cases and in one case MR even overestimated the carcinoma.

Table 5 shows therapy change after MR mammography of the primary cancers. A wider excision was performed after MR mammography in respectively in 42% of EIC+ carcinomas and in 31% of invasive carcinomas with non-extensive DCIS.

Table 3
Detection of carcinomas and prediction of intraductal spread in EIC+ carcinomas for different imaging techniques

EIC+ ($n=50$) (38 III, 4 II, 8 I)	MX	US	MR
Detection of carcinoma	33 (24 III, 3 II, 6 I) 66%	38 (30 III, 3 II, 5 I) 76%	50 (38 III, 4 II, 8 I) 100%
Prediction of DCIS	14 (14 III, 0 II, 0 I) 42% (58% III, 0% II, 0% I)	13 (12 III, 1 II, 0 I) 34.2% (25% III, 33.3% II, 0% I)	32 (26 III, 1 II, 5 I) 64.0% (68% III, 25% II, 62% I)

ca: Carcinoma; IDA: invasive ductal carcinoma; EIC: extensive intraductal component; I, II, III: pathology grades of DCIS according to Van Nuys (Ref. [23]); MX: mammography; US: ultrasound; MR: magnetic resonance mammography.

Table 4
Detection of carcinomas and prediction of ductal spread in carcinomas with non-extensive surrounding DCIS for different imaging techniques

DCIS ($n=61$) (35 III, 8 II, 18 I)	MX	US	MR
Detection of carcinoma	46 (25 III, 6 II, 15 I) 75%	53 (31 III, 6 II, 16 I) 87%	61 (35 III, 8 II, 18 I) 100%
Prediction ductal in situ component +	9 (6 III, 2 II, 1 I) 19.6% (23.1% III, 33.3% II, 6.7% I)	3 (2 III,1 II, 0 I) 5.7% (6.5% III, 16.7% II, 0% I)	23 (16 III, 5 II, 2I) 37.7% (45.7% III, 6.3% II, 11.1% I)

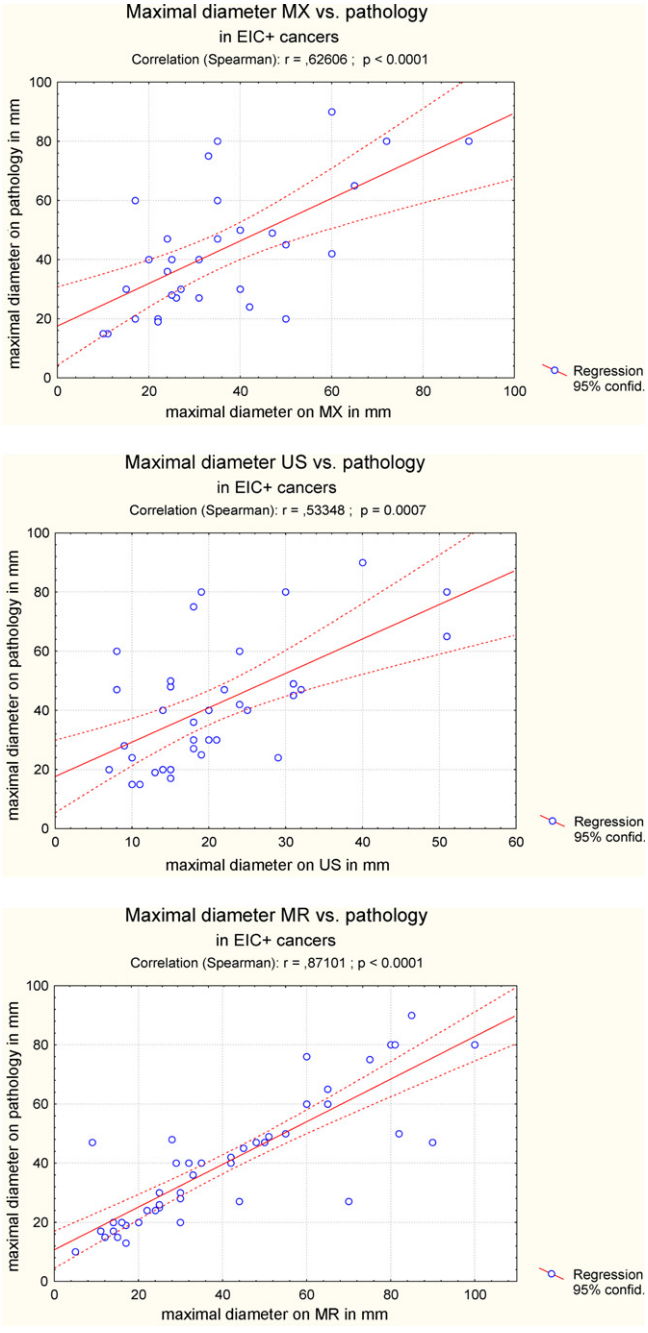

Fig. 1. Correlation of diameter of the total lesion measured on mammography (MX), ultrasound (US) and magnetic resonance (MR) mammography with measurements on histopathology, given in mm, in EIC+ carcinomas.

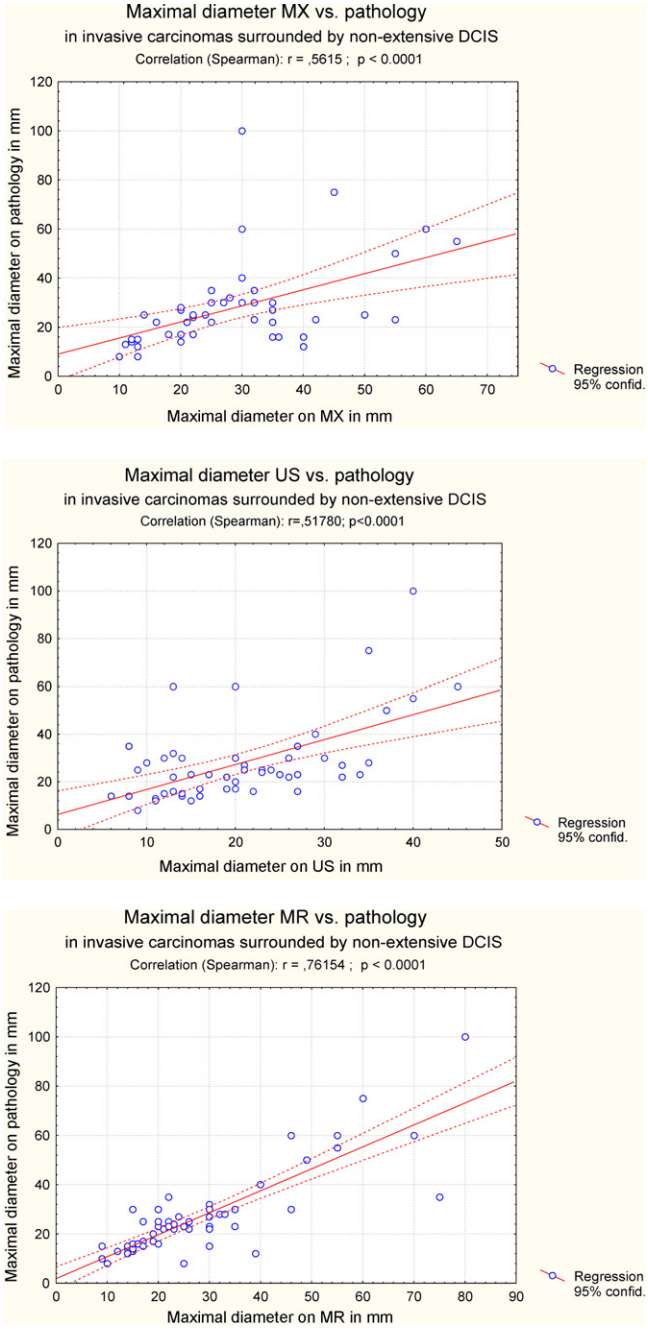

Fig. 2. Correlation of diameter of the total lesion measured on mammography (MX), ultrasound (US) and magnetic resonance (MR) mammography with measurements on histopathology, given in mm, in invasive carcinomas surrounded by non-extensive DCIS.

Table 5
Change in therapy after MR mammography for primary carcinomas

	Wider excision after MR	Wider excision after MR necessary	Wider excision after MR unnecessary
Invasive carcinoma + DCIS ($n=50$)	19 (31%)	14 (74%)	5 (26%)
Invasive carcinoma EIC+ ($n=36$)	21 (58%)	18 (86%)	3 (14%)

Table 6
MR features of invasive carcinomas with intraductal extent

MR features	EIC+ ($n=50$)	+DCIS ($n=61$)	Neither EIC or DCIS ($n=136$)	p	Spec (%)
Ductal or linear pattern	$n=23$ (46%)	$n=16$ (26.23%)	$n=15$ (11%)	0.000	89
Spicules	$n=14$ (28%)	$n=16$ (26.23%)	$n=23$ (17%)	0.152	83
Small nodules	$n=8$ (16%)	$n=8$ (13.11%)	$n=11$ (8%)	0.253	92
Regional enhancing area	$n=5$ (10%)	$n=4$ (6.65%)	$n=1$ (<1%)	0.009	99

DCIS: ductal carcinoma in situ; EIC: extensive intraductal component; Spec: specificity.

Histopathologic examination showed positive margins in 3 invasive carcinomas, in 0 carcinomas with non-extensive DCIS and in 2 EIC+ carcinomas.

3.3. MR features

Table 6 shows features on MR mammography of EIC+ tumors, compared to carcinomas surrounded by non-extensive DCIS and invasive carcinomas. Ductal or linear enhancement around a mass was seen in 23 EIC+ cancers, a mass with spicules in 14, small nodules or a regional enhancing area adjacent to a mass in respectively 8 and 5 EIC+ tumors (Figs. 3 and 4). Some had a combination of types of enhancement around the mass. Ductal or linear pattern is significantly more often seen in EIC+ tumors than in invasive cancers with non-extensive DCIS ($p=0.045$) and in both of them more then in invasive cancers without DCIS ($p=0.000$).

Table 7
Enhancement kinetics of surrounding enhancement in EIC+ tumors

	EIC+ (grade III, II, I DCIS) ($n=19$)	DCIS (grade III, II, I DCIS) ($n=12$)
SI increase		
<70%	3 (2, 0, 1)	0
70–100%	3 (2, 0, 1)	1 (1, 0, 0)
100–200%	5 (4, 0, 1)	5 (5, 0, 0)
>200%	8 (5, 0, 3)	6 (4, 1, 1)
Type of curve		
Wash out	4 (4, 0, 0)	4 (3, 0, 1)
Steady state	6 (4, 0, 2)	0
Continuous	7 (4, 0, 3)	5 (4, 1, 0)
Unknown	2	3
Time of max enhancement		
1–3 min	4 (3, 0, 1)	1 (0, 0, 1)
>3 min	10 (7, 0, 3)	8 (8, 0, 0)
Unknown	5	3

DCIS: ductal carcinoma in situ; EIC: extensive intraductal component; I, II, III: pathology grades of DCIS according to Van Nuys (Ref. [23]); SI: signal intensity; max: maximum.

Of 19 of EIC+ tumors and of 12 invasive cancers with non-extensive DCIS, we studied time intensity curves of the surrounding enhancing area after contrast administration (Table 7). Thirteen EIC+ tumors and 11 carcinomas with non-extensive DCIS showed more than 100% intensity increase. Continuous increase in time and maximal enhancement after 3 min was seen in most of the cases in both groups.

4. Discussion

If conservative surgery is performed on lesions with extensive intraductal spread, high risk of recurrence is reported [1,20,21]. EIC was an independent factor for ipsilateral recurrence for ages ≤ 55 years in a study of Freedman et al. of 912 women [22]. However, among the 30 of 181 patients with an EIC-positive tumor, the 5-year rate of recurrence at or near the primary site was 0% when margins were negative or close but 50% when margins were more than focally positive in a study of Schnitt et al. [2]. This was confirmed in a study of Gage et al. [3] on 343 EIC+ carcinomas.

Extensive intraductal spread is common in invasive ductal carcinoma. In our study, 110 of 209 (52.6%) invasive ductal cancers had an associated intraductal component, and 50 of them were EIC+ (23.9%). A higher incidence was seen in a study by Stomper et al.: 35% of 101 infiltrating ductal carcinomas had an extensive intraductal component [23]. Mumtaz et al. reported on 53 cancers of which 47% showed accompanying DCIS, 19 of them being EIC+ (35.9%) [7].

Preoperative detection of intraductal spread is important as exact measurement of a carcinoma on histopathology is difficult if the tumorectomy specimen had positive margins [7]. Positive margins are more frequent in EIC+ tumors than in tumors without EIC. In a study by Mai et al. of 62 lumpectomy specimens, 56% positive margins were found in EIC+ tumors compared with 18% in tumors with non-extensive DCIS. Smit et al. also reported that patient age and EIC were significant predictors of residual disease at reexcision [24].

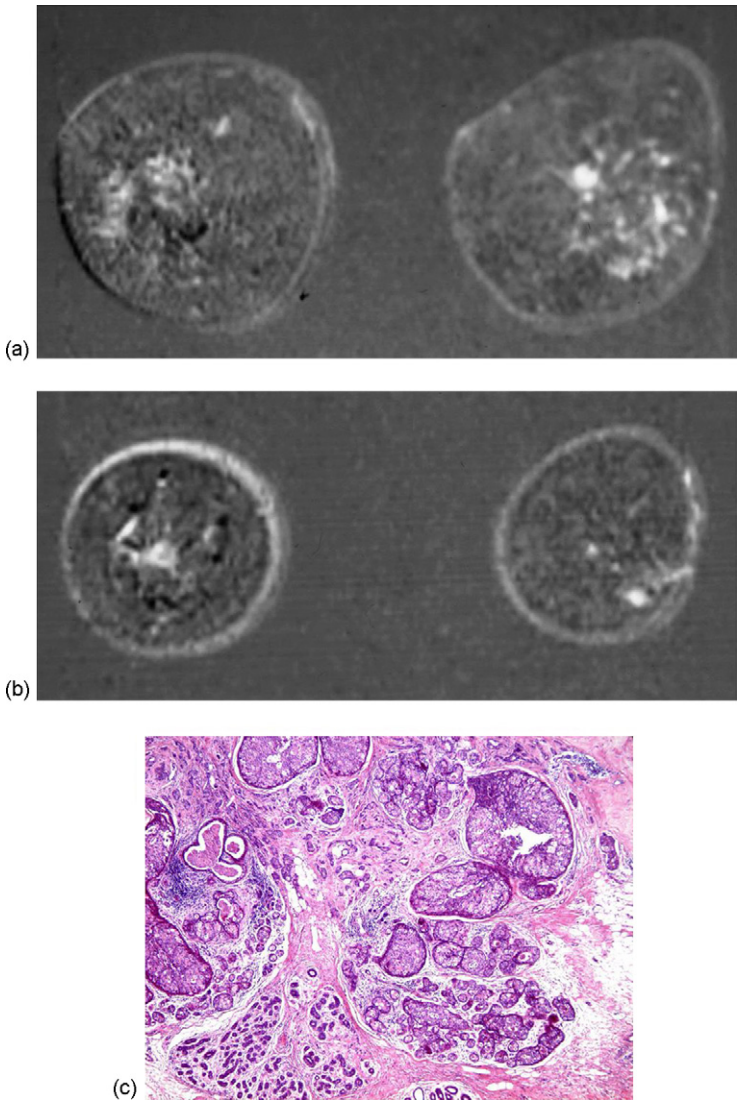

Fig. 3. Forty seven-year-old woman with in the lateral part of the left breast a palpable mass of 15 mm, fixed to the skin. MR: 4 masses are detected, between them there is a nodular pattern of enhancement. The total diameter is 60 mm. HP: multicentric carcinoma with high grade DCIS between the foci, EIC+. The total diameter is 60 mm.

4.1. Detection and extent

In our study, MR *predicted intraductal spread* in 34 of 50 (68%) of EIC+ tumors. If it was not predicted and if only a mass was seen, the DCIS component was limited to an area close to the invasive mass. Compared to mammography and ultrasound, *estimation of tumor extent was best on MR mammography* in our series. This is in concordance with other studies. Sensitivity of

Table 8
Reported figures of detection and estimation of extension of invasive carcinomas with DCIS

Authors	Number of patients	Histopathology	Sensitivity (%)	Diameter	MR features of enhancement
Boetes et al. [11]	8	Invasive + EIC	100	Underestimation (>1 cm)	Not available
Kerslake et al. [12]	13	Invasive + DCIS	54	Good	Not available
Soderstrom et al. [13]	11	Invasive + EIC	100	Concordant in 11	Spiculated, linear and clumped
Mumtaz et al. [7]	19	19 Invasive + DCIS	81	Good	EIC: diffuse, linear Invasive + minimal DCIS: focally enhancing mass
Satake et al. [14]	25	Invasive + DCIS; 13 comedo, 2 non-comedo	93	Overestimation	Linear; regional or segmental

DCIS: ductal carcinoma in situ; EIC: extensive intraductal component; I, II, III: pathology grades of DCIS according to Van Nuys (Ref. [23]).

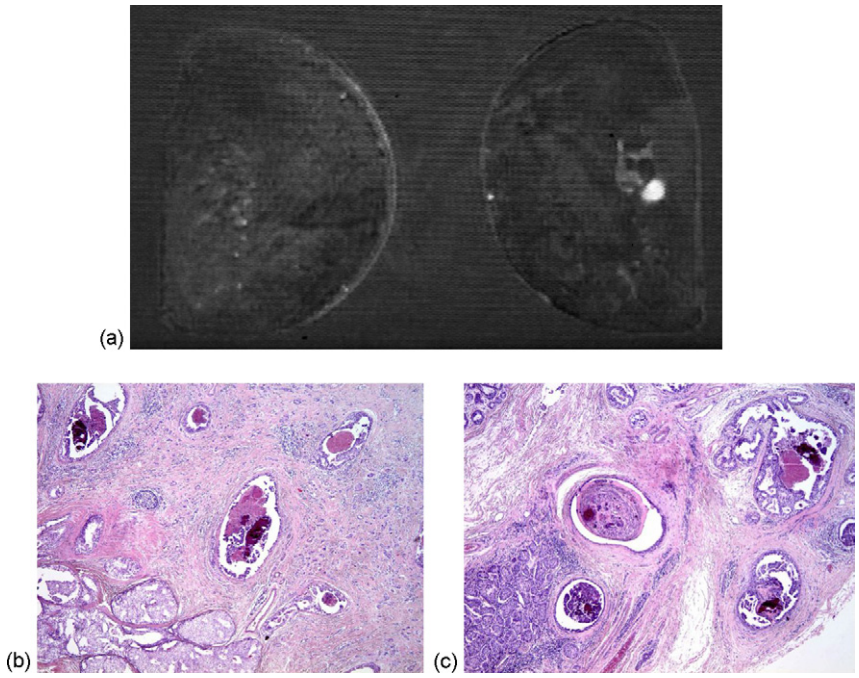

Fig. 4. Forty four-year-old woman with a palpable mass of 20 mm in the upper outer quadrant of the left breast. MR: enhancing mass of 12 mm. Next to the mass is an area of ductal enhancement, the total diameter of the enhancing region is 30 mm. HP: invasive ductal carcinoma, grade I, of 9 mm. Next to the tumor, non-high grade DCIS, not EIC+. The total diameter is 22 mm.

MR to detect DCIS with an invasive cancer varies between 54% and 100% (Table 8). Most authors reported a good correlation of tumor size on MR and histopathology [7,11–13].

In our study, overestimation of more than 1 cm was due to enhancement of normal glandular tissue, fibrocystic disease or adenosis and in four other cases a radial scar, fat necrosis, desmoplastic reaction or lymphovascular invasion were the cause of the overestimation. MR examination was performed within 1 week after diagnosis on MX and US, regardless of the menstrual cycle. In some of our patients, enhancement of normal breast tissue can result in overestimation.

Overestimation of the extent of the intraductal lesion due to fibrocystic disease was reported by Gilles et al. in some of their cases [25]. Date et al. reported a sensitivity of MR imaging for the detection of intraductal spread of DCIS of 82% and a specificity of 80%, due to enhancement of severe fibrocystic disease and higher enhancement during the second half of the normal menstrual cycle [26].

Boland et al. examined recently the validity of the Van Nuys Prognostic Index (VNPI) in a UK population of 237 patients who had breast conserving operations for DCIS. Excision margin width ($p < 0.001$) and tumor grade (by Van Nuys grading ($p = 0.014$) or simple nuclear grading ($p = 0.004$)) were the only independent risk factors for local recurrence. Excision margin width had three times more power than grade in predicting local recurrence [27]. In our study, MR predicted DCIS extent in 71% of the grade III EIC+ cancers, which carry the highest risk of recurrence [28]. Fischer et al. reported a sensitivity of 72% in a series of 35 patients with a significantly higher enhancement in the comedotype than in the non-comedotype [29].

4.2. MR features

The MR feature most frequently seen in EIC+ tumors was a mass surrounded by ductal or linear enhancement. Date et al. observed linear, band-like, branch-like, plate-like and minute ring enhancements [26]. Soderstrom et al. reported spiculated enhancement in 9 of 11 EIC+ carcinomas [13].

In cancers with a small rim of extensive DCIS, MR showed the DCIS component confined to the enhancing mass without abnormal enhancing surrounding area. This was also reported by Mumtaz et al. who described a focally enhancing mass in case of minimal DCIS confined to the margin, with combined histologic size of the invasive and intraductal cancer [7]. If EIC+ tumors were seen, MR showed an adjacent area of diffuse or linear enhancement around a mass. The extent of enhancement correlated well with the extent of EIC in their study and sensitivity of MR mammography (76%) for demonstration of DCIS was higher than mammography (52%).

A shortcoming of this study is that kinetic data of the enhancing surroundings are only obtained in a limited number of cancers. Most of them showed more than 100% signal increase and a continuous enhancement or maximal enhancement after 3 min.

5. Conclusion

MR mammography, performed together with mammography and ultrasound, surpasses mammography and ultrasound alone in the prediction of the presence and extent of DCIS around an invasive mass, especially in EIC+ cancers. MR is the best technique for the detection of DCIS with invasive carcinoma, despite

average results with false negative and false positive findings. Therefore, pathological examination must be performed before wider excision is performed. Moreover, more studies must be done to define the role of MR.

Most EIC+ carcinomas present as a mass surrounded by ductal or linear enhancement on MR. Other MR features are a mass surrounded by long spicules, small nodules or a regional enhancing area.

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References

[1] Boyages J, Recht A, Connolly JL, et al. Early breast cancer: predictors of breast recurrence for patients treated with conservative surgery and radiation therapy. Radiother Oncol 1990;19:29–41.
[2] Schnitt SJ, Abner A, Gelman R, et al. The relationship between microscopic margins of resection and the risk of local recurrence in patients with breast cancer treated with breast-conserving surgery and radiation therapy. Cancer 1994;74:1746–51.
[3] Gage I, Schnitt SJ, Nixon AJ, et al. Pathologic margin involvement and the risk of recurrence in patients treated with breast-conserving therapy. Cancer 1996;78(9):1921–8.
[4] Holland R, Connolly JL, Gelman R, et al. The presence of an extensive intraductal component following a limited excision correlates with prominent residual disease in the remainder of the breast. J Clin Oncol 1990;8:113–8.
[5] Silverstein MJ. Ductal carcinoma in situ of the breast: a surgeon's disease. Ann Surg Oncol 1999;6:802–10.
[6] American College of Surgeons. Special report: International consensus conference. Image-detected breast cancer: state of the art diagnosis and treatment. J Am Coll Surg 2001;3:297–302.
[7] Mumtaz H, Hall-Craggs M, Davidson T, et al. Staging of symptomatic primary breast cancer with MR imaging. AJR 1997;169:417–24.
[8] Harms S, Flamig D, Hesley K, et al. MR Imaging of the breast with rotating delivery of excitation off resonance: clinical experience with pathologic correlation. Radiology 1993;187:493–501.
[9] Hwang E, Kinkel K, Esserman L, Lu Y, Weidner N, Hylton N. Magnetic resonance imaging in patients diagnosed with ductal carcinoma-in-situ: value in the diagnosis of residual disease, occult invasion and multicentricity. Ann Surg Oncol 2003;10:381–8.
[10] Tillman G, Orel S, Schnall M, Schultz D, Tan J, Solin L. Effect of breast magnetic resonance imaging on the clinical management of women with early-stage breast carcinoma. J Clin Oncol 2002;20:3413–23.
[11] Boetes C, Mus R, Holland R, et al. Breast tumors: comparitive accuracy of MR imaging relative to mammography and US for demonstrating extent. Radiology 1995;179:743–7.
[12] Kerslake RW, Carleton PJ, Fox JN, et al. Dynamic gradient-echo and fat-suppressed spin-echo contrast-enhanced MRI of the breast. Clin Radiol 1995;50:440–54.
[13] Soderstrom C, Harms S, Copit D, et al. Three-dimensional RODEO breast MR imaging of lesions containing ductal carcinoma in situ. Radiology 1996;201:427–32.
[14] Satake H, Shimamoto K, Sawaki A, et al. Role of ultrasonography in the detection of intraductal spread of breast cancer: correlation with pathologic findings, mammography and MR imaging. Eur Radiol 2000;10:1726–32.
[15] American College of Radiology. Breast imaging reporting and data system (BI-RADS). 3rd ed. Reston, VA: American College of Radiology; 1998.
[16] European Organization for Research and Treatment of Cancer (EORTC) Breast Cancer Cooperative Group. EORTC manual for clinical research and treatment in breast cancer. EORTC breast cancer cooperative group. 4th ed. Almere, the Netherlands: Excerpta Medica; 2000.
[17] Elston CW. Grading of invasive carcinoma of the breast. In: Page DL, Anderson TJ, editors. Diagnostic histopathologiy of the breast. New York: Churchill Livingstone; 1987. p. 302–11.
[18] Bloom H, Richardson W. Histologic grade and prognosis in breast cancer. Br J Cancer 1957;11:359–77.
[19] Silverstein M, Poller D, Waisman J, et al. Prognostic classification of breast ductal carcinoma-in-situ. Lancet 1995;345:1154–7.
[20] Fodor J, Major T, Polgar C, Toth J, Nemeth G. The impact of radiotherapy on the incidence and time of occurrence of local recurrence in early-stage breast cancer after breast conserving therapy. Neoplasma 2000;47:181–6.
[21] Sinn HP, Anton HW, Magener A, von Fournier D, Bastert G, Otto HF. Extensive and predominant in situ component in breast carcinoma: their influence on treatment results after breast-conserving therapy. Eur J Cancer 1998;34:646–53.
[22] Freedman GM, Hanlon AL, Fowble BL, Anderson PR, Nicolaou N, Nicoloau N. Recursive partitioning identifies patients at high and low risk for ipsilateral tumor recurrence after breast-conserving surgery and radiation. J Clin Oncol 2002;20:4015–21.
[23] Stomper PC, Connolly JL. Mammographic features predicting an extensive intraductal component in early-stage infiltrating ductal carcinoma. AJR Am J Roentgenol 1992;158:269–72.
[24] Smitt MC, Nowels K, Carlson RW, Jeffrey SS. Predictors of reexcision findings and recurrence after breast conservation. Int J Radiat Oncol Biol Phys 2003;57(4):979–85.
[25] Gilles R, Zafrani B, Guinebretière JM, et al. Ductal carcinoma in situ: MR imaging-histopathologic correlation. Radiology 1995;196:415–9.
[26] Date S. Diagnosis of intraductal spread of breast cancer by high-resolution MR imaging: correlation between MR imaging and pathohistological findings. Nippon Igaku Hoshagen Gakkai Zasshi 1998;58:212–20.
[27] Boland GP, Chan KC, Knox WF, Roberts SA, Bundred NJ. Value of the Van Nuys Prognostic Index in prediction of recurrence of ductal carcinoma in situ after breast-conserving surgery. Br J Surg 2003;90:426–32.
[28] Healey EA, Osteen RT, Schnitt SJ, et al. Can the clinical and mammographic findings at presentation predict the presence of an extensive intraductal component in early stage breast cancer? Int J Radiat Oncol Biol Phys 1989;17:1217–21.
[29] Fischer U, Westerhof J, Brinck, Koabiowska M, Schauer A, Grabbe E. Das duktale in-situ-karzinom in der dynamischen MR-mammographie bei 1,5T. Fortschr Röntgenstr 1996;164:290–4.