Clinics of Oncology

Research Article

ISSN: 2640-1037 | Volume 5

Breast MR Imaging Helps Differentiate Malignant and Benign Mammographic Microcalcifications: A Study Based on the 5th Edition of BI-RADS

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Received: 27 June 2021
Accepted: 12 July 2021
Published: 17 July 2021

Citation:

Wang D, Breast MR Imaging Helps Differentiate Malignant and Benign Mammographic Microcalcifications: A Study Based on the 5th Edition of BI-RADS. Clin Onco. 2021; 5(3): 1-9

Keywords:

Breast; Microcalcification; Magnetic Resonance Imaging; Clinical Decision-Making

Key points

- The majority of mammographic suspicious microcalcifications requiring biopsy turned out benign.
- MRI improves PPV in patients with mammographic microcalcifications with no malignancy missed.
- MRI-BI-RADS category is superior to presence of enhancement

Abbreviations:

MRI: magnetic resonance imaging; BI-RADS: breast imaging reporting and data system; AUC: area under curve; LR: likelihood ratio; PPV: positive predictive value; MG: mammography; SVAB: stereotactic vacuum-assisted biopsy; DWI: diffusion weighted imaging; STIR: short tau inversion recovery; TR: repetition time; TE: echo time; TIC: time-intensity curve; ADC: apparent diffusion coefficient; NME: non-mass enhancement; DCIS: ductal carcinoma in situ; SD: standard deviation

1. Abstract

1.1. Objective: To investigate whether breast MR imaging could help in differentiating malignant from benign mammographic microcalcifications.

1.2. Methods: The study consecutively included 106 patients with 112 mammographic microcalcifications between January 2014 and April 2017 in our institute. Pre-operative mammograms and breast MR images were analyzed in a blind manner by two trained breast imaging subspecialists. Each lesion was described and categorized according to the 5th BI-RADS atlas. AUC, sensitivity, specificity, positive Likelihood Ratio (LR) were used to evaluate the value of MR imaging in differentiating malignancy from benignity.

1.3. Results: Of the 112 lesions, pathologic results revealed 81 benign, 12 pre-cancerous and 19 malignant (10 invasive cancers and 9 ductal carcinomas in situ) findings. The number of lesions assigned to BI-RADS 3, 4B, 4C, and 5 was 2, 92, 16, and 2, respectively, resulting in a PPV of 14.7% (17/108) for MG-BI-RADS 4 microcalcifications. The number of MRI classification 1-5 to the corresponding BI-RADS 4B microcalcifications were 37, 2, 33, 27, and 9 respectively. MR-BI-RADS criteria ruled out 72 benign MG-BI-RADS 4 lesions with none malignancy missed, while MRI enhancement criteria ruled out 46 benign lesions. MR-BI-RADS criteria were significantly better in AUC (0.896, P<0.0001), specificity (79.12%, P <0.0001), and positive LR (4.79) than mammography and MRI enhancement criteria.

1.4. Conclusion: Breast MR imaging is useful in the evaluation of BI-RADS 4 mammographic microcalcifications by avoiding 79.12% unnecessary biopsies with none false-negative diagnosis.

2. Introduction

Breast cancer is the most frequent cause of cancer death in women worldwide [1]. Screening mammography has been proved to

be effective in detecting breast cancer and decreasing the corresponding mortality [2]. Microcalcifications account for approximately 31% of abnormalities detected at screening mammography [3] and are seen in approximately 60 percent of cancers detected mammographically. The Positive Predictive Value (PPV) of mammographic microcalcifications is usually less than 30%, and varies from studies [4-6], which requires biopsy under the current guidelines [7, 8]. Although mammography remains the modality of choice for diagnosis of microcalcifications, the majority of suspicious microcalcifications turned out to be benign by biopsy. It would be desirable to refine the diagnostic workup for patients undergoing biopsy, which is essential to reducing the number of biopsies yielding benign results and to guaranteeing detection of malignancy at the same time. Breast Magnetic Resonance Imaging (MRI) has been considered a problem-solving method for equivocal mammogram findings, but its value in the further evaluation of suspicious mammographic calcifications is still under debate. The purpose of the present study was to find out whether breast MRI, as a non-invasive method, could play a part in the diagnostic workup for suspicious mammographic microcalcifications.

3. Materials and Methods

3.1. Patients

This retrospective study was approved by the Ethics Committee of Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. The requirement for Patients' written informed consent was waived.

Our study included consecutive patients who were detected as pure microcalcification on mammography, underwent preoperative breast MRI and mammographically-guided hook wire localization or Stereotactic Vacuum-Assisted Biopsy (SVAB) on the day of surgery from January 2014 to April 2017 in our department. There were 134 patients with 141 lesions underwent mammography-guided intervention during this time period. Cases with missing images (e.g., patients had diagnostic mammography or MR imaging in outside institutions, n = 3 patients and 3 lesions; patients had no preoperative MR imaging, n = 10 patients and 11 lesions), interval between preoperative MR imaging and breast intervention longer than 3 months (n = 4 patients and 4 lesions), and microcalcifications with an associated finding (e.g., mass, asymmetry, or architectural distortion, n = 11 patients and 11 lesions) were excluded. Finally, a total of 106 patients with 112 mammographic pure microcalcification lesions were eligible for this study, including 6 patients with bilateral breast lesions.

3.2. Mammography and Interventional Procedure

Bilateral digital full-filed diagnostic mammography was performed in standard projections (craniocaudal and mediolateral oblique) using a dedicated commercial device (GE Medical Systems) in our department before the mammography-guided procedure. All participants underwent either mammography guided hook wire localization and excisional biopsy or SVAB (SenoRx, Hologic). For all lesions, immediate specimen radiography was taken to confirm successful excision or biopsy of microcalcifications.

3.3. MR Imaging Protocol

All participants underwent breast MR imaging in a 3.0 T whole-body MRI scanner in the prone position with an 8-channel phase-array double breast-surface coil (Signa HDxt, GE Healthcare or Ingenia, Philips). We use a localization sequence prior, followed by axial STIR/T2WI sequence, diffusion weighted imaging (DWI), and dynamic imaging. For dynamic imaging, gadolinium-diehtylenetriamine pentaacetic acid (Gd-DTPA, Magnevist, Bayer-Schering Pharma AG) of 0.1 mmol/kg body weight was administered intravenously at a rate of 2 ml/s followed by a 20 ml normal saline flush.

The imaging protocol in Signa HDxt is as follows: axial short tau inversion recovery (STIR) (TR/TE, 7060/35.2ms; slice thickness, 4mm; gap, 1 mm; matrix, 320×192); axial DWI, b=600 s/mm2 (TR/TE, 5960/64.6ms; slice thickness, 4mm; gap, 1 mm; matrix, 160×160); axial Volume Image Breast Assessment (VIBRANT) sequence (GE Healthcare) with images obtained before and 5 times after Gd-DTPA injection (TR/TE, 4.3/2.1ms; slice thickness, 1.2mm; gap, 0mm; matrix, 416×320; temporal resolution, 54s).

Imaging protocol in Ingenia is as follows: axial T2WI-SPAIR with fat suppression (TR/TE, 5000/65 ms; slice thickness, 4mm; gap, 1mm; matrix, 320*371); axial DWI, b=800 s/mm2 (TR/TE, 5100/70 ms; slice thickness, 4mm; gap, 1 mm; matrix, 350×240); axial T1 high resolution isotropic volume excitation (eTHRIVE) sequence with images obtained before and 4 times after Gd-DTPA injection (TR/TE, 4.3/2.1ms; slice thickness, 2mm; gap, -1mm; matrix, 280×340; temporal resolution, 57s).

3.4. Image Interpretation

Two trained breast imaging subspecialists (reader 1: Dr. Lijun Wang with 7 years of experience; reader 2: Dr. Ran Luo with 5 years of experience) reviewed mammography of participants independently in a blind manner. They were informed of the location of microcalcification but blinded to the pathological diagnosis and MRI findings. They were required to describe the microcalcification in three dimensions: morphology, distribution and present or absent of associated abnormalities and record the results on a worksheet. Lesions described discordantly were settled by discussion till consensus were reached. Then MG-BI-RADS classification was assigned to each lesion based on the morphologic and distributive descriptors by reader 2 according to the 5th edition of Breast Imaging Reporting and Data System (BI-RADS) [9]. Suspicious microcalcifications were subdivided into 3 categories: 5(malignancy, PPV range >95%, fine linear/fine linear branching in with segmental distribution), 4C (high suspicion for malignancy, PPV range >50 and <95%, fine linear/fine linear branching in morphology or linear/segmental in distribution), and 4B (moderate

suspicion for malignancy, PPV range >10 and <50%, other suspicious microcalcifications). In addition, grouped punctate microcalcification without prior mammogram for reference was considered category BI-RADS 3.

The same two readers conducted the MRI image interpretation independently. Similarly, they were informed of the location of microcalcifications on mammography (quadrant and distance from nipple) but blinded of the mammograms, specific descriptors or pathologic diagnosis of the index lesion. They were asked to decide if there was any asymmetric enhancement at the corresponding location, then give descriptions including not only the lesion morphology (shape and internal enhancement for masses, distribution and internal enhancement for non-mass enhancement) but also the level of background parenchymal enhancement (minimal, mild, moderate or marked). Lesions described discordantly were also settled by discussion. Type of time-intensity curve (TIC) and apparent diffusion coefficient (ADC) value for every lesion were recorded. Then the MRI-BI-RADS category was assigned to each lesion according to the 5th edition of BI-RADS by reader 2. Category 1 was assigned for no abnormal findings. Category 2 was assigned to typical benign findings (e.g., intramammary lymph nodes, cysts and typical fibroadenomas). Category 3 was used for findings apart from category 4 or 5, including foci, focal or regional heterogeneous non-mass enhancement which was unable to tell from BPE (e.g., a menstruating patient with moderate or marked BPE, scanned at a suboptimal phase of her cycle) and masses with benign morphologic and kinetic features. Category 4 was assigned to suspicious findings apart from category 5, including NME (clumped, linear or segmental), enhancing focus or masses with suspicious morphologic or kinetic features. Category 5 was used for typical malignant findings with a combination of highly suspicious features.

3.5. Histologic Analysis

Histologic diagnoses were determined by one of three experienced pathologists. Patients with benign diagnosis were advised to undergo imaging follow-up for 6 months to rule out false-negative diagnosis and all complied. No calcification progression or additional biopsy recommended at post-intervention mammographic follow-up. Patients diagnosed with high-risk lesions (including atypical ductal hyperplasia, lobular carcinoma in situ and flat epithelial atypia) through SVAB were advised to have further surgery. Patients with ductal carcinoma in situ (DCIS) or invasive carcinoma were further treated with breast-conserving surgery or mastectomy. And for the latter two groups, the final pathologic diagnosis was obtained.

3.6. Statistical Analysis

All DCIS and invasive carcinoma were considered malignant and the others, including high-risk lesions, were considered benign in statistical analysis. Continuous variables were reported as means ± standard deviation (SD) for normally distributed data or medians with ranges for non-normally distributed data. Dichotomous variables are reported as frequencies. We used Mann-Whitney or Student's t-test for quantitative data and chi-square or Fisher's exact test for qualitative data. Fisher's exact test was used to analyze the differences in diagnostic performance parameters between mammogram and MRI criteria. All statistical analyses were performed using MedCalc Statistical Software version 17.9.5 (MedCalc Software bvba, Ostend, Belgium). All tests were two-sided and P values < 0.05 were considered statistically significant.

4. Results

4.1. Patient Cohort

We recruited 106 consecutive patients with 112 lesions in the present study. Cancer (including 9 DCIS and 10 invasive breast cancer) was found in 19 patients (all unilateral). The remaining 87 patients were diagnosed as benign (93 lesions, including 12 pre-cancerous findings and the remaining other benign diseases). The mean patient age was 47.8years (SD, 9.4 years). The median interval between MR imaging and mammographic guided intervention was 15.0 days (range, 0 and 91 days). Table 1 provides detailed characteristics of the patient cohort. No statistical difference was found in age, interval, menopausal status, personal history of breast cancer, uni/bi-laterality, referral reason for mammography, and biopsy methods between benign and malignant groups.

4.2. Mammographic and MRI Findings

Mammographic pure microcalcifications were described and classified in a combination of morphology and distribution descriptors according to the 5th BI-RADS atlas. Two lesions and patients were categorized as MG-BI-RADS 3 because of regional punctate calcifications, both were mastosis in pathology. One lesion was found absent of enhancement at the corresponding location in MRI and categorized as MRI-BI-RADS 1 (Figure 1). The other one had heterogeneous focal enhancement buried in marked background parenchymal enhancement, thus categorized as MRI-BI-RADS 3. Two lesions and patients were categorized as MG-BI-RADS 5 because of linear/linear branching calcification in segmental distribution, both of which had segmental heterogeneous enhancement on MR imaging and were graded as MRI-BI-RADS 5. Excisional pathology confirmed invasive carcinoma in both lesions. Contrast-enhanced MR imaging did not contribute to the diagnostic workup for these MG-BI-RADS 3 and 5 microcalcification lesions. So we focused on the remaining 108 MG-BI-RADS 4 lesions in statistical analysis when comparing diagnostic performance.

Of the 108 MG-BI-RADS 4 lesions, pathology revealed 9 DCIS (3 low-grade, 2 intermediate-grade, and 4 high-grade, 2 of which had comedo change), 8 invasive carcinomas, 12 high-risk lesions (9 atypical ductal hyperplasia, 2 lobular carcinomas in situ, and 1 flat epithelial atypia) and 79 benign lesions. Both high-risk and benign lesions were regarded as benign in statistical analysis. The

PPV of MG-BI-RADS 4 lesions was 0.16 (17/108). The detailed characteristic breakdown of microcalcifications is shown in Table 2. There were 92 lesions assigned to MG-BI-RADS 4B, including 13 malignancy, and 16 lesions were assigned to MG-BI-RADS 4C, including 4 malignancy. Resulting in a pre-MRI prevalence of 0.14 (13/92) and 0.25 (4/16), respectively, which were not statistically different (P = 0.501).

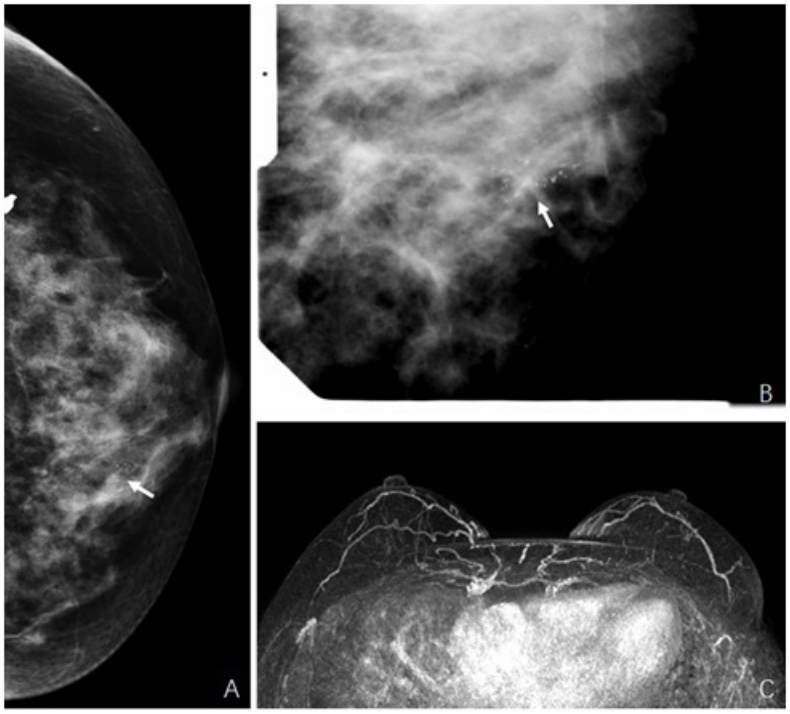


Figure 1: A 63-year-old female with a palpable mass in the left breast underwent diagnostic mammography and was detected with segmental fine pleomorphic calcification in the inner region of the left breast (A. craniocaudal projection and B. spot compression image, arrow) which was categorized as MG-BI-RADS 4C. The MIP image (C) derived from subtracted images of breast MRI found no abnormal enhancement at the indexed region and the patient was categorized as MRI-BI-RADS 1. Hook-wire localization and open-surgical biopsy of the microcalcification was performed for this patient. The final pathological analysis confirmed adenosis.

Table 1: Description of the study cohort (106 patients).

Characteristic	Total (n=106)	Benign (n=87)	Malignant (n=19)	P value
Age (Mean ± SD, years)	47.8±9.4	47.3±9.4	50.3±8.9	0.838
Interval (days)	15.0 (0,91)	22.0 (0,91)	11.0 (2,81)	0.062
Menopausal status				
Premenopausal	63	53	10	0.505
postmenopausal	43	34	9	
Personal history of Breast Cancer				
No	100	84	16	0.966
Yes	6	5	1	
Bi/Unilateral				
Unilateral	100	81	19	0.528
Bilateral	6	6	0	
Referral Reason for MG				
Screening	54	47	7	0.175
Symptomatic	52	40	12	
Biopsy method				
SAVB	17	16	1	0.286
MG-guided hook wire localization and excisional biopsy	89	71	18	

Note: SD, standard deviation; MG, mammography; SAVB, stereotactic vacuum-assisted biopsy.

Table 2: Characteristics of Mammographic pure microcalcification (112 lesions).

Morphology & Distribution	Total (n=112)	Benign (n=93)	Malignant (n=19)	PPV(%)
BI-RADS 3	**2**	**2**	**0**	**0**
Punctate & grouped	2	2	0	0
BI-RADS 4B	**92**	**79**	**13**	**14.1**
Amorphous & regional	11	10	1	9.1
Amorphous & grouped	50	44	6	12
Coarse heterogeneous & regional	1	1	0	0
Coarse heterogeneous & grouped	12	11	1	8.3
Fine pleomorphic & regional	3	2	1	33.3
Fine pleomorphic & grouped	15	11	4	26.7
BI-RADS 4C	**16**	**12**	**4**	**25**
Punctate & linear	2	2	0	0
Amorphous & segmental	3	3	0	0
Coarse heterogeneous & segmental	1	1	0	0
Fine pleomorphic & linear	2	1	1	50
Fine pleomorphic & segmental	4	4	0	0
Fine linear & regional	2	0	2	100
Fine linear & grouped	2	1	1	50
BI-RADS 5	**2**	**0**	**2**	**100**
Fine linear or fine linear branching & segmental	2	0	2	100

Note: PMC, pure microcalcification; PPV, positive predictive value;

All 17 malignant lesions were detected on breast MR imaging, the detailed description of these lesions was distributed on Table 3. BI-RADS criterion (MR-BI-RADS 4 or 5 was considered positive) ruled out 63 benign MG-BI-RADS 4B lesions and 9 benign MG-BI-RADS 4C lesions with none malignancy missed. Whilst enhancement criterion (present of enhancement was considered positive) ruled out 42 benign MG-BI-RADS 4B lesions and 4 benign MG-BI-RADS 4C lesions, also with none malignancy missed (Table 4 and 5). There were 26 enhancing lesions considered negative by MRI-BI-RADS criterion, including 6 focus, 3 oval and homogeneously enhanced masses, and 17 focal/regional heterogeneous NME, all of which categorized as MRI-BI-RADS 3.

Table 3: Description of 17 malignant lesions.

Lesion	Calcification	MG-BI-RADS	Enhancement	MRI-BI-RADS	Pathology
1	Amorphous & grouped	4B	Segmental & heterogeneous	4	Invasive carcinoma
2	Fine pleomorphic & linear	4C	linear	4	DCIS (high-grade)
3	Linear & grouped	4C	Segmental & clumped	5	Invasive carcinoma
4	Fine pleomorphic & grouped	4B	Segmental & clumped	5	Invasive carcinoma
5	Amorphous & grouped	4B	Irregular, circumscribed mass & heterogeneous	4	Invasive carcinoma
6	Amorphous & regional	4B	Focal & clustered ring	4	DCIS (intermediate-grade)
7	Amorphous & grouped	4B	Segmental & heterogeneous	4	DCIS (low-grade)
8	Linear & regional	4C	Irregular mass & rim	5	Invasive carcinoma
9	Fine pleomorphic & regional	4B	Segmental & clumped	5	Invasive carcinoma
10	Fine pleomorphic & grouped	4B	Segmental & clustered ring	5	DCIS (high-grade, with comedo change)
11	Amorphous & grouped	4B	Irregular, circumscribed mass & heterogeneous	4	Invasive carcinoma
12	Amorphous & grouped	4B	Segmental & clustered ring	5	DCIS (intermediate-grade)
13	Coarse heterogeneous & grouped	4B	Linear	4	DCIS (high-grade)
14	Fine pleomorphic & grouped	4B	Irregular mass & heterogeneous	5	Invasive carcinoma
15	Linear & regional	4C	Segmental & clustered ring	5	DCIS (low-grade)
16	Fine pleomorphic & grouped	4B	Linear	4	DCIS (high-grade, with comedo change)
17	Amorphous & grouped	4B	Linear	4	DCIS (low-grade)

Table 4: MRI diagnosis for MG-BI-RADS 4 microcalcifications

	Total(n=108)	Benign(n=91)	Malignant(n=17)
MRI BI-RADS category			
1	37	37	0
2	2	2	0
3	33	33	0
4	27	18	9
5	9	1	8
MRI Enhancement			
Negative	46	46	0
Positive	62	45	17

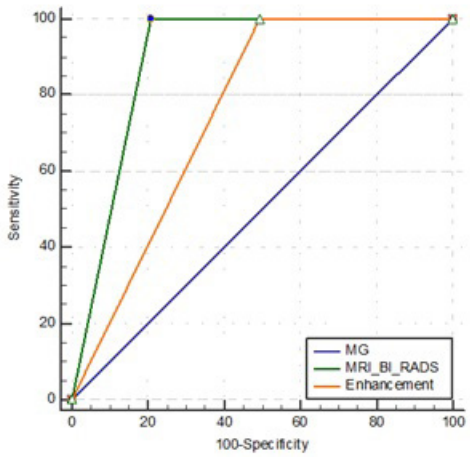
Table 5: Breakdown of mammography and MRI diagnosis of 108 MG-BI-RADS 4 lesions

	MG-BI-RADS		Total
	4B (n=92)	4C (n=16)	
MRI-BI-RADS			
Positive	13/29	7-Apr	17/36
Negative	0/63	0/9	0/72
Enhancement			
Positive	13/50	12-Apr	17/62
Negative	0/42	0/4	0/46
Total	13/92	16-Apr	17/108

Note: numbers behind slash are number of total lesions in the category, and numbers before slash are number of malignant lesions. In MRI-BI-RADS criterion, category 4 and 5 are considered positive.

4.3. Diagnostic Validity of Imaging Criteria

The detailed comparison between mammography only and combined with each MR imaging criteria were exhibited in Table 6 and Figure 2. The AUC of mammography alone was only 0.500 (95% CI, 0.402-0.598). Additional MR imaging led to a significant improvement for both MRI criteria in AUC. It increased to 0.896 (95% CI, 0.822-0.946, P<0.0001) for MR-BI-RADS criteria and to 0.753 (95% CI, 0.660-0.831, P<0.0001) for enhancement criteria. MRI-BI-RADS criteria had higher AUC (P<0.0001), specificity (79.12 vs. 50.55, P=0.0001) and positive likelihood ratio (4.79 vs. 2.02) than enhancement criteria.



MG: mammography. The AUC is 0.500, 0.896 and 0.753, respectively (P <0.0001).

Figure 2: ROC curve for diagnosis of mammography alone and combined with each MR imaging criterion.

Table 6: Comparison of MG and MRI in determining microcalcifications.

	AUC (95% CI)	P	Sensitivity (95% CI)	P	Specificity (95% CI)	P	Positive LR (95% CI)
MG	0.500 (0.402, 0.598)	<0.0001	100.00 (80.5, 100.0)	1	0.00 (0.0, 4.0)	<0.0001	1.00 (1.0, 1.0)
MRI-BI-RADS	0.896 (0.822, 0.946)		100.00 (80.5, 100.0)		79.12 (69.3, 86.9)		4.79 (3.2, 7.1)
Enhancement	0.753 (0.660, 0.831)		100.00 (80.5, 100.0)		50.55 (39.9, 61.2)		2.02 (1.6, 2.5)

5. Discussion

Our study provides insights into the validity of breast MR imaging for distinguishing benign from malignant microcalcifications which are mammographically suspicious. In the present study, 108 MG-BI-RADS 4 pure microcalcification lesions were delicately investigated by preoperative breast MR imaging. We found that by adopting the 5th BI-RADS criteria, AUC was increased from 0.500 for mammography to 0.896 for MRI-BI-RADS assessment (P<0.0001) with no compromise on sensitivity and none false-negative diagnosis. Hence, breast MRI significantly improved the work-up for mammographically suspicious microcalcifications, especially in avoiding unnecessary biopsy.

Microcalcification is the most frequently encountered abnormality on mammography, accounting for 39.4% suspicious findings [10]. Due to the lack of sound alternatives, mammographic calcifications are mostly followed by biopsy procedures, the majority of which turned out to be benign in pathology. A meta-analysis showed that about 60% of women underwent biopsy for a benign finding [11]. But unlike other mammography detected abnormalities, MR imaging has traditionally not been used in the evaluation of microcalcifications. Several studies [12, 13] have shown that MRI has insufficient sensitivity in the diagnosis of malignant microcalcifications. In a study of MRI in the assessment and management of BI-RADS category 4 lesions, MRI had a 12% false-negative rate for malignancy for microcalcifications, all of which represented low-grade ductal carcinoma in situ [10]. MRI in the evaluation of microcalcifications remains an area of debate. But in our research, all malignancy, including 3 low-grade DCIS were correctly categorized by MR imaging, with none false-negative diagnosis. Our superior results might be a consequence of different patient cohort, but also has a solid biologic basis: a) neoangiogenesis is considered one of the hallmarks of cancer [14] and contrast media used in breast MR imaging highlight tissue vascularization [15]. b) ductal enhancement observed in patients with DCIS is intraductal cancer directly [16], and a high-grade DCIS lesion without enhancement is rare (about 2% of cases), absence of enhancement is observed in about 20% of low-grade DCIS lesions [17].

Another possible reason for our favored results could be the imaging protocol introduced in the present study. We conducted all MR imaging at 3.0T scanners with high-resolution dynamic sequences, on the contrary, prior studies either were performed at 1.5T scanners [10, 18, 19] or used inadequate thickness [20]. We did observe delicate thin linear enhancement on MR imaging at the indicated location in 2 cases which were both categorized as MR-BI-RADS 4 and proved to be DCIS (Figure 3). Thus, we suppose that thorough investigation on MR imaging is a necessity because the pretest prevalence is as high as 15.7% (17/108) for mammographic microcacifications.

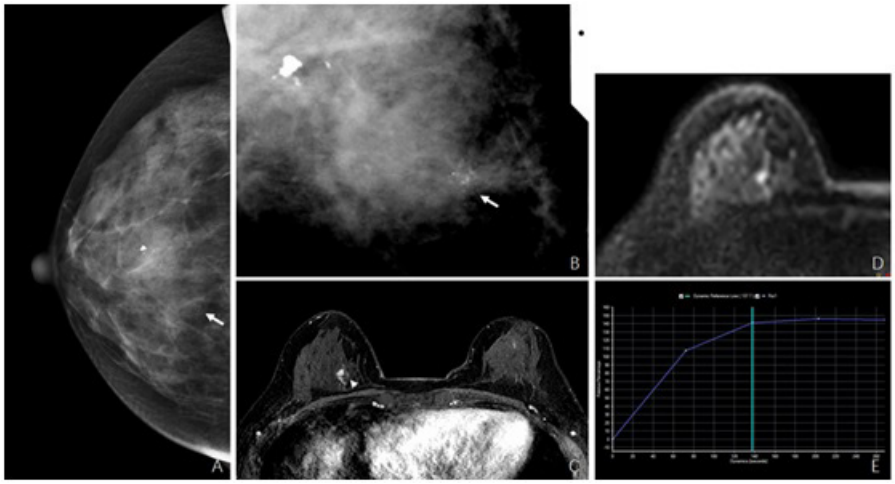


Figure 3: A 59-year-old female underwent screening mammography was detected with grouped amorphous calcification in the inner-upper quadrant of the right breast (A. craniocaudal projection and B. additional spot compression image, arrow) which was categorized as MG-BI-RADS 4B. Breast MRI showed vivid linear enhancement at the indexed region (C. arrow head) which was hyperintense on DWI (D) with an ADC value of 1.26×10-3mm2/s and had plateau enhancement pattern (E). The lesion was categorized as MRI-BI-RADS 4. Hook-wire localization and open-surgical biopsy confirmed low-grade DCIS.

At the same time, one of the strengths of our study comes from that we strictly stuck to the new edition of BI-RADS atlas, which has clear guidance on a specific categorization of calcifications and enhancement based on morphology and distribution, compared with the prior version (BI-RADS 2003). Presence of enhancement was applied as the sole diagnostic criterion in some earlier publications, and was considered better in comparison with BI-RADS criteria in sensitivity [18, 21]. However, our results revealed that both criteria had the same high sensitivity (100%) and MRI-BI-RADS criterion was significantly better in AUC, specificity, and positive LR. Especially, all 26 enhancing lesions considered negative by MRI-BI-RADS criterion were proved benign. We suppose that with delicate imaging protocol, MR imaging is adequate in depicting lesions in an informative way to make a proper diagnosis. Thus MRI-BI-RADS is the preferable tool in evaluation mammographic suspicious microcalcifications. Lastly but not the least, we focused on BI-RADS 4 mammographically suspicious microcalcifications. According to a meta-analysis [11], only patients with BI-RADS 4 microcalcifications would have benefited from MR imaging to rule out malignancy. But most prior publications recruited BI-RADS 3-5 or 4-5 microcalcifications and all were categorized according to the prior version (BI-RADS 2003), to which major alteration had been made. Therefore, our results should provide insight on a targeted issue with progress with the times.

There are several limitations in our study. Firstly, only lesions with a pathologic diagnosis were included in this study, which may lead to selection bias. Secondly, hook-wire localization & open surgical biopsy is not the standard procedure worldwide for mammographically suspicious microcalcifications. In fact, it's more common a decade ago and currently has mostly been replaced by SVAB. But SVAB is not covered by most insurance in our district, thus most patients are reluctant to pay the full bill, ~5000 yuan, which is almost as expensive as an open surgery. On the other hand, a hook-wire localization procedure cost only ~800 yuan, and the following open surgical biopsy is supported by insurance for most patients, as well as mastectomy or breast-conserving surgery if needed. However, inconsistency in biopsy method should not influence the golden standard we used in the present study.

In conclusion, breast MR imaging is useful in the evaluation of BI-RADS 4 mammographic microcalcifications by avoiding 79.12% unnecessary biopsies with none false-negative diagnosis, thus should be considered in the diagnostic workup for this patient subgroup.

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