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BREAST IMAGING

ORIGINAL ARTICLE

Is biopsy necessary? Role of DCE-MRI in BIRADS-3 lesions

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PURPOSE
We aimed to evaluate BIRADS-3 breast lesions with dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and compare with histopathology, and to investigate the effectiveness of breast MRI for follow-up and management.

METHODS
A total of 84 BIRADS-3 lesions reported by US or mammography and evaluated by DCE-MRI between September 2014 and October 2015 were included in this study. All patients underwent percutaneous or surgical biopsy for histopathologic diagnosis. Morphologic and kinematic features on MRI were compared with histopathologic results.

RESULTS
Of the 84 BIRADS-3 breast lesions, 9 (10.7%) had malignant features on DCE-MRI and all were verified with histopathologic results. DCE-MRI had 96.7% sensitivity, 72% specificity, 92% positive predictive value, and 82.5% negative predictive value. MRI and histopathology results were correlated for the diagnosis of malignant lesions. The sensitivity and negative predictive value of MRI for diagnosis of malignant lesions were both 100%.

CONCLUSION
Differentiation of benign versus malignant lesions was accomplished with 100% accuracy with DCE-MRI. We suggest that DCE-MRI should be an additional diagnostic tool and problem-solving modality for BIRADS-3 lesions, particularly in patients with relative risk factors.

Breast carcinoma is the most common solid organ malignancy in women living in developed countries. It is the second most common cause of cancer-related mortality in women, after lung cancer (1).

With the introduction of breast cancer screening, malignant lesions are easily identified at much earlier stages. In dense breasts, ultrasonography (US) increases the sensitivity for malignant lesion detection (2). Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a helpful tool that has been used widely in clinical practice in addition to standard diagnostic methods of physical examination, mammography (MMG), and US. For the detection of breast lesions, the sensitivity of DCE-MRI is reported as 94%–100% and the specificity as 37%–97% in the literature (1, 3).

Negative predictive value (NPV) of DCE-MRI is over 90% and is higher than any imaging modality. A negative breast MRI rules out the malignancy (4).

BIRADS classification is a reporting system in order to better describe the breast lesions and ease the communication with the clinician, thus, improving the management of the patient. BIRADS-3 category defines most probably benign lesions with malignancy risk less than 2% and includes ovoid lesions with smooth margins that are located parallel to the skin (5). Since the malignancy risk is low, short-term follow-up imaging is advised for these patients. However, due to many risk factors such as advanced age and family history of breast cancer, palpable mass BIRADS-3 lesions may undergo biopsy, which can increase the false negative results and patient stress. Although the place of DCE-MRI in the management of BIRADS-3 lesions is not clearly defined, it may be used as an additional assessment tool in these cases (6, 7).

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In this study we aimed to evaluate BI-RADS-3 lesions with DCE-MRI and compare the results with histopathologic findings. The effectiveness and necessity of breast MRI follow-up in these patients will also be evaluated as a secondary outcome.

Methods

Patient selection

A total of 84 BIRADS-3 lesions reported by US or MMG and evaluated by DCE-MRI between September 2014 and October 2015 were retrospectively analyzed. All patients underwent percutaneous or surgical biopsy for histopathologic diagnosis. None of the patients had family history of breast cancer. Sonographic and MRI characteristics of the lesions, histopathologic type, tumor size, tumor grade and lymph node positivity on the pathologic specimen were recorded.

Ethical approval was obtained for this study (approval number: 2016/23).

Imaging technique and radiologic analysis

All patients underwent DCE-MRI with 1.5 T MRI (GE Medical systems, Signa HDxt) with a standard breast coil. The protocol involved axial T2-weighted short tau inversion recovery (TR, 5000–5300 ms; TE, 70–82 ms; TI, 110 –140 ms), axial T1-weighted turbo spin-echo (TR, 540–620 ms; TE, 7–10 ms), axial dynamic contrast enhanced fat suppressed gradient-echo (TR, 3.6–4.4 ms, TE, 1.4–2 ms; TI, 15 ms; flip angle, 12–34) sequences. For dynamic imaging, after intravenous administration of 0.1–0.2 mmol/kg contrast agent with an automatic injector, first axial image was obtained 30 ms later and the same procedure was repeated 5 more times. By a specific program, pre-contrast images were subtracted from post-contrast images on a separate workstation and enhancement curves were obtained. Morphologic features of the lesions were identified on conventional MRI sequences.

Statistical analysis

SPSS v. 22 statistical package program was used for statistical analysis (IBM Corp.). Descriptive statistics were given as mean± standard deviation for continuous variables and n (%) for categorical variables.

Results

Mean age of the patients was 43±9.4 years, with a range of 15–76 years. The patients underwent advanced imaging due to new onset or worsened pain in the ipsilateral breast (n=42) and advanced age (n=17). Eighteen patients had deep concerns about the presence of a lesion and they were willing to undergo surgery; therefore, further pre-procedural investigations were performed. For 21 patients both the clinician and radiologist were not sure if they would attend the follow-up visits. Lastly, in 13 cases the biopsy request was done by the clinicians' own concern but the MRI was added by the radiology department prior to the biopsy.

In total, 20 lesions were categorized as BIRADS-2 and 37 lesions as BIRADS-3 on MMG. For 15 patients MMG was inconclusive due to dense breast tissue or technical inadequacy; 12 patients had no MMG due to young age. Of MMGs, 30 were diagnostic and 42 were screening MMGs. On US, 12 lesions were reported as BIRADS-2 and 70 lesions as BIRADS 3; whereas in two patients no sonographic abnormality was detected in correlation with the MMG.

Pre-diagnoses of these 84 lesions on US and/or MMG are given in Table 1.

On DCE-MRI, 35 lesions (41.6%) were reported as fibroadenomas (Fig. 1), 6 (7.1%) as simple cysts, 10 (11.9%) as fibrocystic foci, two as complicated cysts, two as phylloides tumors, one as fat necrosis, one as periductal mastitis, and one as ductal ectasia. DCE-MRI of 17 patients were reported as normal. Nine lesions had malignant features on DCE-MRI (10.9%). Of these malignat lesions: Three lesions had irregular mass enhance-

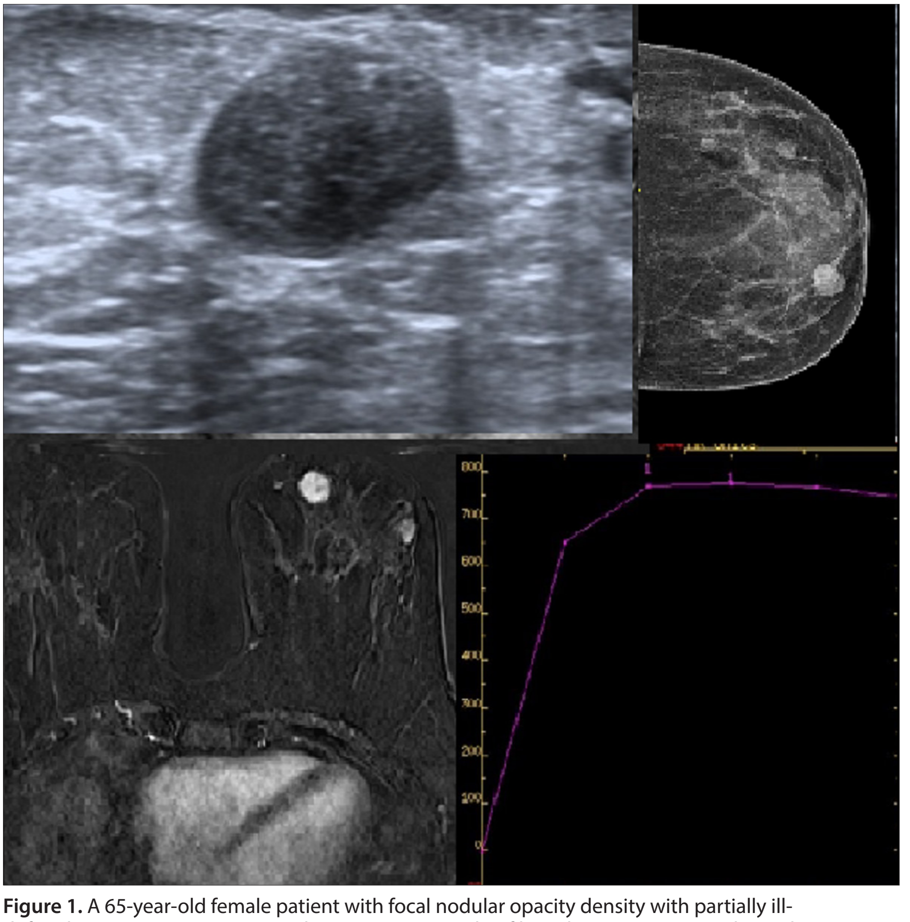

Figure 1. A 65-year-old female patient with focal nodular opacity density with partially ill-defined contours on mammography. US was reported as fibroadenoma. DCE-MRI showed type 2 enhancement curve. Histopathologic analysis revealed a fibroadenoma.

Main points

- BIRADS-3 lesions are most probably benign lesions that are mostly followed up by US or mammography without histopathologic examination.
- Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a helpful tool that enables further analysis of breast lesions by using the enhancement pattern.
- Particularly for patients with relative risk factors such as family history, advanced age and palpable lesions, histopathologic examination may be mandatory. In these patients, DCE-MRI may be used for malignancy detection in order to avoid biopsies.

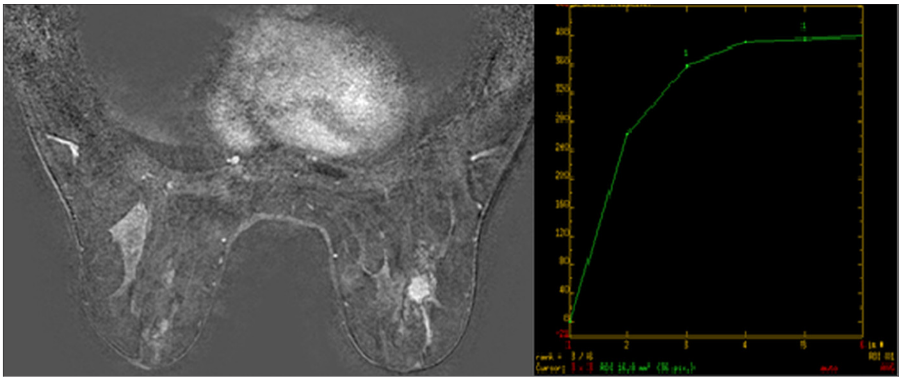

Figure 2. A 40-year-old female patient with mastodynia. US showed a complicated cyst in the left breast. On DCE-MRI, the lesion displayed a type 3 enhancement. Biopsy revealed invasive ductal carcinoma.

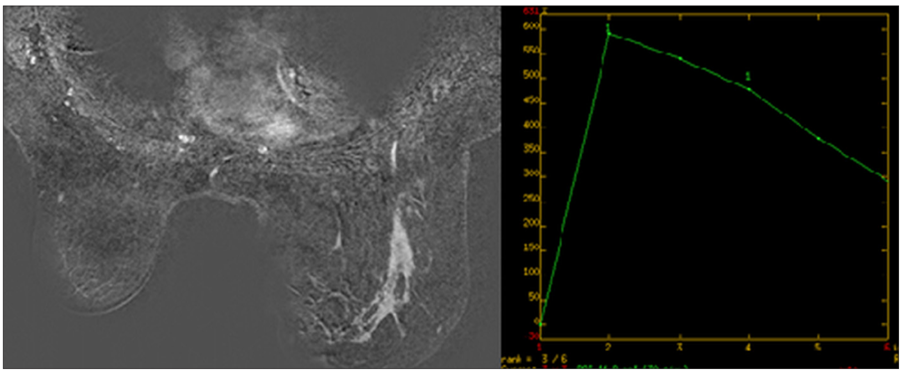

Figure 3. A 50-year-old female patient clinically and sonographically diagnosed as mastitis. On DCE-MRI, non-mass linear segmental enhancement with type 3 enhancement curve was depicted. The lesion was proven to be infiltrative ductal carcinoma by biopsy.

Table 1. Pre-diagnoses of the lesions on US and/or mammography

Pre-diagnosis	n (%)
Fibroadenoma	46 (54.7)
Complicated cyst	24 (28.5)
Microcysts	9 (10.8)
Mastitis[a]	2 (2.4)
Focal asymmetry[b]	1 (1.2)
Punctate microcalcification cluster[b]	1 (1.2)
Intraductal papilloma[c]	1 (1.2)
Total	84 (100.0)

[a]Both patients had asymmetric densities on mammography and on US examination lesions were suggestive for mastitis. Clinical findings were not consistent and both patients underwent advanced imaging.
[b]Both patients were referred for US, but no focal lesion was identified.
[c]Mammography showed asymmetrical retroareolar opacity. On US, intraductal lobulated iso- or hyperechogenic lobulated structure was noted, suspicious for an intraductal papilloma. MRI was recommended by the radiologist.

ment, five lesions had mass enhancement with spiculated borders (Fig 2). One patient had non-mass segmental linear contrast enhancement (Fig 3). Sonographic and histopathologic features of lesions with malignant features on MRI are given in Table 2.

Of 46 lesions which were reported as fibroadenoma on US, 30 were reported as fibroadenoma, two as complicated cysts, two as fibrocystic foci, two as benign phylloides tumor, one as fat necrosis and one as periductal mastitis. Four of these patients had normal MRI findings and four had malignant features. These four lesions were also proven to be malignant on histopathologic specimens.

None of the patients with benign features or normal findings on MRI had malignant features in histopathologic examination. The sensitivity of DCE-MRI was 96.7%, the specificity was 72%, positive predictive value (PPV) was 92%, and negative predictive value (NPV) was 82.5%. Smallest diameter of the malignant lesions was 14 mm, the largest diameter was 50 mm, with a mean diameter of 24±8.6 mm.

Discussion

Breast cancer is among the leading causes of death in women. The mortality rates have declined due to early diagnosis and effective treatment methods (8). Although MMG is the major screening tool for breast cancer, its sensitivity and specificity changes according to the age and breast density of the patient. The sensitivity of MMG may be as low as 30% in young patients with dense breasts, for which US plays an important role as an additional diagnostic tool. However, operator-dependent nature, inability to show the microcalcifications and high false-negative rates are the disadvantages of US.

DCE-MRI has become a radiologic tool that is being increasingly used in clinical practice besides MMG and US for identification, characterization and response evaluation in primary and recurrent breast cancer. In their study of 164 patients, Pediconi et al. (9) identified 226 lesions on DCE-MRI. Of these, 175 lesions were detected on MMG and US. However, 51 lesions were only spotted on MRI. In this study sensitivity and accuracy of DCE-MRI for detection of malignancy was reported as 100% and 93.4%, respectively. NPV of DCE-MRI is higher than any other imaging modality in breast imaging and in most cases a negative DCE-MRI excludes possible malignancy (4). In order to end the conflicts of malignant/benign lesion discrimination on reports, BIRADS system was developed by ACR. BIRADS-3 lesions are classified as most probably benign lesions with a malignancy risk less than 2%. The group includes solitary grouped punctate calcifications, fibroadenomas, microcyst clusters, and isolated complicated cysts. ACR advises short-term follow-up imaging for BIRADS-3 lesions; but tissue diagnosis could be performed instead of imaging follow-up due to concern on patient's or referring clinician's part (6, 10). In clinical practice the biopsy is preferred in case of certain relative risk factors such as advanced age, palpable mass, and family history of breast cancer. At this point, DCE-MRI may be helpful as an additional diagnos-

Table 2. Sonographic pre-diagnosis and histopathologic diagnoses of the lesions with malignant features on DCE-MRI

DCE-MRI	Enhancement curve	US	Histopathology
Mass enhancement with spiculated borders	Type 3	Microcysts	IDC
	Type 2	Complicated cyst	IDC
	Type 3	Mastitis	ILC
	Type 3	Punctate microcalcifications	IDC
	Type 3	Fibroadenoma	IDC
	Type 2	Fibroadenoma	IDC
Irregular mass enhancement	Type 2	Fibroadenoma	Mucinous carcinoma
	Type 2	Fibroadenoma	Malignant epithelial tumor
Non-mass segmental linear contrast enhancement	Type 3	Mastitis	IDC

DCE-MRI, dynamic contrast-enhanced magnetic resonance imaging; US, ultrasonography; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

tic tool; however, there is not enough data in the literature on the use of MRI in BIRADS-3 lesions (6).

In this study, DCE-MRI findings and histopathologic results of 84 lesions which were identified as BIRADS-3 by MMG and/or US were compared. Nine of these lesions were malignant (10.9%). The sensitivity of DCE-MRI was 96.7%, the specificity was 72%, PPV was 92%, and NPV was 82.5%. Our results corroborated with the literature, except that our NPV was slightly lower than that reported in the literature. We attributed this to some of the lesions being less than 10 mm in diameter and not well depicted on MRI. Our results showed that malignant/benign differentiation could accurately be done by MRI.

In the literature there are few studies on MRI for BIRADS-3 lesions. Dorrius et al. (11) has reported malignancy in 13 of 76 BIRADS-3 lesions (17%). Similar to our study, this number was higher than AHRQ and NABON guidelines, and sensitivity of MRI for malignant lesions was 100%. The authors attributed the high rate of malignancy to difficulty of categorization and compatibility problems among observers. The compatibility problems were also mentioned by Ciatto et al. (12). In their study, authors advised histopathologic evaluation for BIRADS-3 lesions in case of relative risk factors such as family history for breast carcinoma, palpable lesions, and advanced age.

On the other hand, Oswald et al. (13) reported less than 2% malignancy in their series consisting of 147 BIRADS-3 lesions. The authors concluded that since the malignancy rate was very low, follow-up would be adequate.

Multiple radiologists taking part in breast imaging and lack of breast-specified radiologists causes problems in accurate categorization of breast lesions, particularly in BIRADS-2, -3, and -4A categories. In addition, increased imaging requests result in increased workload and therefore aggravate this miscategorization. We believe our high malignancy rates can be attributed to this problem, as well as still-remaining grey areas, and subjectivity in the BIRADS classification. In their study on BIRADS reproducibility on US, Abdullah et al. (14) found fair interobserver agreement on margin evaluation, particularly for microlobulated and indistinct margins (k= 0.33 and 0.39, respectively). This discordance was noted to be more prominent in small lesions (14). Considering that this study was conducted by radiologists with at least 4 years of experience in breast imaging, higher disagreements can be expected when US is performed by general radiologists. Accordingly, some BIRADS-4 lesions may have been miscategorized as BIRADS-3, which may also explain our increased malignancy rates compared to the literature.

Our study has some limitations. First of all, this is a retrospective study, therefore extensive data review and detailed history was not possible. Second, our small sample size limits the statistical analysis and decreases the power of our results. Third, since US examinations were done by different radiologists that were not specialized in breast imaging, the subjective interpretation of lesions on US and MMG according to BIRADS categorization may lead to confusing results, which may require further investigation such as MRI or biopsy.

In conclusion, this study shows that the high sensitivity and accuracy of DCE-MRI may help the clinician in the management of BIRADS-3 lesions and eliminate unnecessary biopsies, particularly in patients with relative risk factors such as family history of breast cancer, advanced age, and palpable mass.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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