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Breast magnetic resonance imaging as a problem-solving modality in mammographic BI-RADS 3 lesions

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Abstract

The probability of a mammographic Breast Imaging Reporting and Data System (BI-RADS) 3 lesion being cancer is considered to be less than 2%. Therefore, the work-up of a mammographic BI-RADS 3 lesion should be biopsy or follow-up mammography after 6 months. However, most patients referred for biopsy have benign disease. Although the negative predictive value (NPV) of magnetic resonance imaging (MRI) is highest of all imaging techniques, it is not yet common practice to use breast MRI as a problem-solving modality to exclude patients for further diagnostic work-up. Therefore, in this meta-analysis the usefulness of breast MRI as a problem-solving modality in mammographic BI-RADS 3 lesions is investigated. After a systematic search only 5 out of 61 studies met the inclusion criteria. The NPV in 2 of those studies was reported to be 100%. It was concluded that MRI can be used as an adjunctive tool to mammographic BI-RADS 3 findings to exclude patients for further diagnostic work-up. The other 3 studies assessed the accuracy of MRI in mammographic BI-RADS 3 microcalcifications. These studies reported an NPV of MRI between 76% and 97%. Therefore, MRI cannot be implemented as a diagnostic tool to evaluate mammographic microcalcifications at this time. The first solid data indicate that breast MRI might be useful as a problem-solving modality to exclude patients with non-calcified mammographic BI-RADS 3 lesions for further diagnostic work-up. However, further research is needed to verify these results.

Keywords: *MRI; mammography; probably benign lesions; BI-RADS; microcalcifications.*

Introduction

Mammography is the primary imaging modality for the early detection of breast cancer. Despite advances in mammographic techniques (digital), mammography still has its limitations with regard to both sensitivity (65.6–85.5%) and specificity (87.7–94.3%)[1,2]. Mammograms are coded using the ordered categories of the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) lexicon: category 1, negative; 2, benign finding; 3, probably benign; 4, suspicious finding; 5, highly suggestive of malignancy[3]. The diagnostic work-up of breast lesions depends on the BI-RADS classification of the breast lesions. The guideline for non-invasive diagnostic tests for breast abnormalities of the Agency for Health Care Research and Quality in the United States (AHRQ) states that breast lesions classified as BI-RADS 1 and 2 require no further work-up or follow-up other than routinely called for[4]. The chance of a BI-RADS 4 lesion being malignant varies from 2% to 95%, whereas this chance is over 95% for a BI-RADS 5 lesion[4]. Therefore, the work-up for these categories demand a biopsy procedure. This biopsy procedure cannot be replaced by breast magnetic resonance imaging (MRI), because histology is obligatory in these cases[4]. The most difficult mammographic lesions are the lesions that are classified as BI-RADS 3. The probability of a BI-RADS 3 lesion being cancer is considered to be less than 2%. For the work-up of a BI-RADS 3 lesion, biopsy or follow-up mammography after 6 months is advised[4]. In practice, the decision on the work-up of BI-RADS 3 lesions depends on the possibilities for biopsy procedures, the wishes of the patient and the preference of the radiologist. Most patients who are referred for a biopsy have benign disease because of the low predictive value of both physical examination and mammography[5,6]. The value of breast MRI in BI-RADS

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3 lesions is not yet clear[4]. Breast MRI is emerging as a clinically useful additional diagnostic tool[4,7] and has an excellent sensitivity and negative predictive value (NPV), which usually exceeds 90%[8–10]. However, the overall specificity of breast MRI varies between 67% and 72%[8–10]. The diagnostic accuracy of breast MRI varies with the expertise of the radiologist and the particular patient population studied. It is important that breast MRI is used for those groups of patients for whom there is evidence of acceptable diagnostic accuracy. Breast MRI as a first-line imaging modality is performed by screening women at increased risk for breast cancer[7,11–14]. As a second-line modality, breast MRI can be used for the following indications: inconclusive findings in conventional imaging, preoperative staging, axillary node malignancy and unknown site of primary tumor, the evaluation of therapy response in the neoadjuvant chemotherapy setting[7,11–14], imaging of the breast after conservative therapy, prosthesis imaging[7,13], nipple discharge[7,14] and MR-guided biopsy and lesion localization[13]. Although the NPV of MRI in breast cancer is the highest of all imaging techniques[8,15,16] and in most cases a negative breast MRI excludes malignancy[17–19], it is not yet common practice to use breast MRI as a problem-solving modality in excluding patients for further diagnostic work-up.

Therefore, in this meta-analysis, the usefulness of breast MRI as a problem-solving modality in patients with mammographic BI-RADS 3 lesions is investigated.

Materials and methods

Search strategy

A computerized search was performed to identify relevant studies in Medline and Embase up to 2010. The following strategy was followed in Medline: "Magnetic Resonance Imaging" [Mesh term] OR "Magnetic Resonance Imaging" [Text Word] OR "MRI" [Text Word] OR "MR imaging" [Text Word] AND "probably benign lesions" [Text Word] OR "microcalcifications" [Text Word] OR "inconclusive findings" [Text Word] AND mammography [Mesh term] OR mammography [Text Word] AND "Sensitivity and Specificity" [Mesh term] OR "specificity OR sensitivity" [Text Word]. In Embase the same strategy was used. All languages were considered.

Eligibility criteria and study selection

Medline and Embase were searched for studies that used breast MRI as a problem-solving modality in mammographic BI-RADS 3 lesions. Studies were included if the following inclusion criteria were met: (1) all patients underwent a mammography and breast MRI; (2) the study population had mammographic BI-RADS 3 lesions or mammographic BI-RADS 3 microcalcifications; (3) accuracy, sensitivity, specificity, positive predictive value (PPV) and/or NPV was/were measured; (4) studies with original data that were published in peer-reviewed journals. The selected relevant studies were based on title, abstract and full paper. All selected studies were published in the English language.

The complete search yielded 61 studies, of which 9 were duplicates. Forty-one out of the 52 studies were excluded based on the title. From the 11 remaining studies the abstract or full paper was reviewed. Four studies were excluded because no BI-RADS classification was used and 2 studies were reviews. Only 5 studies[20–24] met the inclusion criteria.

Results

In the 5 selected studies, 376 breast lesions were reported, of which 213 were microcalcifications, 110 were asymmetric mammographic findings, 36 were non-calcified regular-shaped lesions, 12 were architectural distortion and 5 were scar lesions. In 2 studies[22,23], mammographic BI-RADS 3 lesions were included; one[22] only included category 3 lesions, the other[23] also included BI-RADS 0 and 4 lesions. In the other 3 studies[21,24], mammographic BI-RADS 3 microcalcifications were included but microcalcifications that were classified as BI-RADS 4 and 5 were also included (Table 1).

Mammographic BI-RADS 3 lesions

In one study[22], the role of MRI in the evaluation of mammographic BI-RADS 3 lesions was investigated. MRI was performed on 56 lesions described as BI-RADS 3 by mammography in 43 patients. The 56 mammographic BI-RADS 3 lesions were distributed into non-calcified regular-shaped lesions (64.3%), focal asymmetric densities (21.4%), generalized microcalcifications (12.6%) and a cluster of tiny calcifications (1.7%). The sensitivity, specificity, accuracy, PPV and NPV of MRI in the determination of malignancy in these mammographic BI-RADS 3 lesions were calculated as 100%, 96.4%, 96.4%, 33.3% and 100%, respectively. Gokalp *et al.*[22] concluded that MRI may be helpful in the evaluation of focal asymmetric densities as MRI confirmed that 9 of the 12 mammographic focal asymmetric densities were breast tissue and the other 3 were masses.

Another study[23] evaluated the usefulness of breast MRI in cases of inconclusive mammographic or sonographic findings. In this study, not only mammographic BI-RADS 3 lesions ($n = 15$) were included but also BI-RADS 4 lesions ($n = 22$) and mammographic BI-RADS 0 lesions ($n = 78$). In total, 115 breast MRI scans were used as an adjunctive tool and the findings were correlated with pathology. The equivocal mammographic findings for which MRI was performed were asymmetry without associated microcalcifications (85.2%), architectural distortion (10.4%) and change in the appearance of

Table 1 Study characteristics

	Study (first author, year of publication)				
	Moy 2009[23]	Gokalp 2006[22]	Akita 2009[20]	Cilotti 2007[21]	Uetmatsu 2007[24]
No. of patients	115	43	53	55	96
Study design	R, c	P, c	NR	NR	P, c
No. of lesions	115	56	50	55	100
Mammographic findings					
Asymmetry	98	12			
Architectural distortion	12				
Scar lesion	5				
Non-calcified regular-shaped lesions		36			
Generalized calcifications		7			
A cluster of tiny calcifications		1			
Microcalcifications			50	55	100
Mammographic BI-RADS					
0	78				
1					
2					
3	15	56	9	23	55
4	22		41	25	27
5				7	18
Gold standard	Pathology	Pathology, follow-up 6 months	Pathology	Pathology	Pathology
Mammography[a]					
Sensitivity (%)	NR	NR	100	77	NR
Specificity (%)	80.7	NR	24	59	NR
PPV (%)	8.7	NR	NR	63	67
NPV (%)	NR	NR	NR	74	93
Accuracy (%)	78.3	NR	44	67.2	NR
MRI[a]					
Sensitivity (%)	100	100	85[b]	73	NR
Specificity (%)	91.7	96.4	100[b]	76	NR
PPV (%)	40	33.3	NR	73	86
NPV (%)	100	100	NR	76	97
Accuracy (%)	92.2	96.4	96[b]	74.5	NR

c, consecutive; NR, not reported; P, prospective; R, retrospective.
[a]In the analysis of Moy *et al.*[23], Cilotti *et al.*[21] and Uematsu *et al.*[24] BI-RADS 3 lesions were considered as benign and BI-RADS 4 and 5 as malignant.
[b]MG+MRI.

the site of a previous benign biopsy finding (4.3%). MRI had a sensitivity of 100%, NPV of 100% and compared with mammography had significantly higher specificity (91.7% versus 80.7%, $p = 0.029$), PPV (40% vs 8.7%, $p = 0.032$), and overall accuracy (92.2% vs 78.3%, $p = 0.00052$). Moy *et al.*[23] concluded that breast MRI can be a useful adjunctive tool when equivocal findings at conventional mammography are asymmetry or architectural distortion.

Mammographic BI-RADS 3 microcalcifications

Three published studies[20,21,24] evaluated the role of MRI in patients with mammographic BI-RADS 3 microcalcifications. Akita *et al.*[20] also included mammographic BI-RADS 4 microcalcifications and Cilotti *et al.*[21] and Uetmatsu *et al.*[24] included mammographic BI-RADS 4 and 5 microcalcifications.

In the study of Akita *et al.*[20] the clinical value of additional breast MRI in patients with microcalcifications on mammography and negative ultrasound findings was evaluated. Fifty patients with mammographic microcalcifications (9 BI-RADS category 3 and 41 BI-RADS category 4) were included. These patients underwent MRI before stereotactic vacuum-assisted biopsy. Mammography had a sensitivity of 100%, a specificity of 24% and an accuracy of 44%, whereas mammography plus MRI had a sensitivity of 85%, a specificity of 100% and an accuracy of 96%. They concluded that breast MRI significantly improved the rate of diagnosis of malignancy in breast lesions that were detected as mammographic BI-RADS 3 or 4 microcalcifications compared with mammography alone[20].

In the study of Uematsu *et al.*[24], breast MRI was performed in 100 microcalcifications detected at screening mammography in 96 patients. These patients also underwent a stereotactic vacuum-assisted biopsy as gold standard. PPVs and NPVs were calculated on the basis of a BI-RADS category and the absence or presence of contrast uptake in the area of microcalcifications. NPV of

BI-RADS mammography 3 was 93% versus 97% NPV of MRI ($p = 0.167$). The PPV of contrast uptake of MRI was 86%, which is significantly higher than the 67% PPV of BI-RADS mammography 4 and 5 ($p = 0.033$). Uematsu *et al.*[24] concluded that the imperfect PPVs and NPVs of MRI in the evaluation of microcalcifications detected at screening cannot replace stereotactic vacuum-assisted biopsy.

Cilotti *et al.*[21] concluded that the PPV and NPV of MRI in the characterization of microcalcifications are not high. In their study, 55 patients with mammographic calcifications classified as BI-RADS categories 3, 4 or 5 underwent MRI and stereotactic vacuum-assisted biopsy. The sensitivity, specificity, PPV, NPV and diagnostic accuracy were 73%, 76%, 73%, 76% and 74.5%, respectively. Their conclusion is that MRI cannot be considered a diagnostic tool for evaluating microcalcifications[21] .

Discussion

The AHRQ guideline states that the work-up for mammographic BI-RADS 3 lesions should be biopsy or follow-up imaging after 6 months. There is not yet a role for breast MRI, because ultrasonography- or mammography-guided core or vacuum biopsy can obtain histological proof of a BI-RADS 3 lesion. A variety of minimally invasive procedures are widely available, relatively safe, inexpensive and provide a diagnosis without surgical intervention. Furthermore, breast MRI has its limitations, which include higher costs, longer examination time, and lower availability compared with mammography and ultrasound[7,11]. If breast MRI is to be an effective addition to the work-up of a mammographic BI-RADS 3 lesion, the NPV of breast MRI must be sufficiently high to definitively rule out further work-up with biopsy. Although there were only 5 studies that investigated the usefulness of MRI as a problem-solving modality in mammographic BI-RADS 3 lesions, the NPV was 100% in non-calcified mammographic BI-RADS 3 lesions and 76–97% in mammographic BI-RADS 3 microcalcifications. On the other hand, Kuhl[7] indicated that the evidence for the effectiveness of breast MRI is relatively weak in helping to solve mammographic problems, because in a multicenter trial of Bluemke *et al.*[8] the NPV was not high enough to exclude malignancy with sufficient confidence in the case of an equivocal or suspicious lesion seen at conventional imaging. The diagnostic accuracy of MRI was studied in 821 patients with a suspicious mammographic BI-RADS 4 or 5 lesion (85%) or a suspicious clinical finding with a negative or benign conventional work-up (15%) before biopsy[8]. MRI had an NPV of 85% with cancer missed in 48 of 329 negative MRI examinations. This NPV is not sufficiently high to avoid biopsy in suspicious mammographic BI-RADS 4 or 5 lesions[8]. This widely referenced multicenter study was performed in 14 hospitals from 1998 to 2001 and therefore used now outdated MR equipment. Furthermore, the study of Bluemke *et al.*[8] included patients with microcalcifications of the breast, which have a negative influence on the NPV. In this meta-analysis, 3 studies[20,21,24] assessed the role of MRI in mammographic BI-RADS 3 microcalcifications. These studies also included BI-RADS 4 and 5 microcalcifications. An NPV between 76% and 97% was reported[21,24] in concordance with Bluemke's results[8]. Therefore, MRI cannot be implemented as a problem-solving modality in mammographic microcalcifications at this time. Mammography and stereotactic biopsy remain the only techniques for characterizing microcalcifications[21,24].

According to Kuhl *et al.*[7] MRI can be useful as an additional tool in patients with calcifications; it can be helpful in demonstrating or excluding underlying invasive cancer, because MRI has a high NPV for invasive cancer. An important application of MRI in patients with associated with suspicious microcalcifications could be to evaluate disease extension[7].

However, the studies that comply with the inclusion criteria of the meta-analysis, i.e. non-calcified mammographic BI-RADS 3 lesions[22,23], reported an NPV of 100% and concluded that MRI can be a useful tool in mammographic BI-RADS 3 lesions, especially when mammographic findings are asymmetry or architectural distortion[22,23].

Although there are sparse data, the first solid data indicate that breast MRI might be useful as a problem-solving modality to exclude patients with non-calcified mammographic BI-RADS 3 lesions from further diagnostic work-up. However, further research is needed to verify these results.

References

[1] Barlow WE, Lehman CD, Zheng Y, *et al.* Performance of diagnostic mammography for women with signs or symptoms of breast cancer. J Natl Cancer Inst 2002; 94: 1151–9.

[2] Carney PA, Miglioretti DL, Yankaskas BC, *et al.* Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. Ann Intern Med 2003; 138: 168–75.

[3] American College of Radiology (ACR). Illustrated Breast Imaging Reporting and Data System (BI-RADS), 1998.

[4] Agency for Health Care Research and Quality. Effectiveness of non-invasive diagnostic test for breast abnormalities. AHRQ publication no. 06-EHC005-EF, 2006, 2009.

[5] Kerlikowske K, Grady D, Barclay J, Sickles EA, Ernster V. Likelihood ratios for modern screening mammography. Risk of breast cancer based on age and mammographic interpretation. JAMA 1996; 276: 39–43. doi:10.1001/jama.276.1.39. PMid:8667537.

[6] Meyer JE, Eberlein TJ, Stomper PC, Sonnenfeld MR. Biopsy of occult breast lesions. Analysis of 1261 abnormalities. JAMA 1990; 263: 2341–3. doi:10.1001/jama.263.17.2341. PMid: 2157903.

[7] Kuhl CK. Current status of breast MR imaging. Part 2. Clinical applications. Radiology 2007; 244: 672–91. doi:10.1148/radiol.2443051661. PMid:17709824.

[8] Bluemke DA, Gatsonis CA, Chen MH, *et al.* Magnetic resonance imaging of the breast prior to biopsy. JAMA 2004; 292: 2735–42. doi:10.1001/jama.292.22.2735. PMid:15585733.

[9] Hrung JM, Sonnad SS, Schwartz JS, Langlotz CP. Accuracy of MR imaging in the work-up of suspicious breast lesions: a diagnostic meta-analysis. Acad Radiol 1999; 6: 387–97. doi:10.1016/S1076-6332(99)80189-5.

[10] Peters NH, Borel Rinkes IH, Zuithoff NP, Mali WP, Moons KG, Peeters PH. Meta-analysis of MR imaging in the diagnosis of breast lesions. Radiology 2008; 246: 116–24. doi:10.1148/radiol.2461061298. PMid:18024435.

[11] DeMartini W, Lehman C. A review of current evidence-based clinical applications for breast magnetic resonance imaging. Top Magn Reson Imaging 2008; 19: 143–50. doi:10.1097/RMR.0b013e31818a40a5. PMid:18941394.

[12] DeMartini W, Lehman C, Partridge S. Breast MRI for cancer detection and characterization: a review of evidence-based clinical applications. Acad Radiol 2008; 15: 408–16. doi:10.1016/j.acra.2007.11.006. PMid:18342764.

[13] Mann RM, Kuhl CK, Kinkel K, Boetes C. Breast MRI: guidelines from the European Society of Breast Imaging. Eur Radiol 2008; 18: 1307–18. doi:10.1007/s00330-008-0863-7. PMid:18389253.

[14] Orel S. Who should have breast magnetic resonance imaging evaluation? J Clin Oncol 2008; 26: 703–11. doi:10.1200/JCO.2007.14.3594. PMid:18258977.

[15] Berg WA, Gutierrez L, NessAiver MS, *et al.* Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004; 233: 830–49. doi:10.1148/radiol.2333031484. PMid:15486214.

[16] Heywang-Kobrunner SH, Bick U, Bradley Jr WG, *et al.* International investigation of breast MRI: results of a multicentre study (11 sites) concerning diagnostic parameters for contrast-enhanced MRI based on 519 histopathologically correlated lesions. Eur Radiol 2001; 11: 531–46. doi:10.1007/s003300000745.

[17] Vassiou K, Kanavou T, Vlychou M, *et al.* Characterization of breast lesions with CE-MR multimodal morphological and kinetic analysis: comparison with conventional mammography and high-resolution ultrasound. Eur J Radiol 2009; 70: 69–76. doi:10.1016/j.ejrad.2008.01.012. PMid:18295425.

[18] Fischer U, Kopka L, Grabbe E. Breast carcinoma: effect of preoperative contrast-enhanced MR imaging on the therapeutic approach. Radiology 1999; 213: 881–8.

[19] Kuhl CK, Schmutzler RK, Leutner CC, *et al.* Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. Radiology 2000; 215: 267–79.

[20] Akita A, Tanimoto A, Jinno H, Kameyama K, Kuribayashi S. The clinical value of bilateral breast MR imaging: is it worth performing on patients showing suspicious microcalcifications on mammography? Eur Radiol 2009; 19: 2089–96. doi:10.1007/s00330-009-1396-4. PMid:19350244.

[21] Cilotti A, Iacconi C, Marini C, *et al.* Contrast-enhanced MR imaging in patients with BI-RADS 3–5 microcalcifications. Radiol Med 2007; 112: 272–86. doi:10.1007/s11547-007-0141-9. PMid:17361370.

[22] Gokalp G, Topal U. MR imaging in probably benign lesions (BI-RADS category 3) of the breast. Eur J Radiol 2006; 57: 436–44. doi:10.1016/j.ejrad.2005.10.004. PMid:16316732.

[23] Moy L, Elias K, Patel V, *et al.* Is breast MRI helpful in the evaluation of inconclusive mammographic findings? AJR Am J Roentgenol 2009; 193: 986–93. doi:10.2214/AJR.08.1229. PMid:19770320.

[24] Uematsu T, Yuen S, Kasami M, Uchida Y. Dynamic contrast-enhanced MR imaging in screening detected microcalcification lesions of the breast: is there any value? Breast Cancer Res Treat 2007; 103: 269–81. doi:10.1007/s10549-006-9373-y. PMid:17063274.