Prediction of Residual Malignancy After Excisional Biopsy for Breast Cancer With Suspicious Microcalcifications: Comparison of Mammography and Magnetic Resonance Imaging

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Abstract

The ability of mammography and magnetic resonance imaging (MRI) to predict residual malignancy after excisional biopsy for microcalcifications and whether background parenchymal enhancement (BPE) on MRI influences diagnostic performance was assessed in 51 patients. MRI was more accurate than mammography; however, BPE decreased the diagnostic performance of MRI. Patients with breast cancer with moderate or marked BPE require careful assessment.

Background: Whether surgery should be performed after excisional biopsy based on mammography or magnetic resonance imaging (MRI) findings has not been evaluated for breast cancer with suspicious microcalcifications on mammography. This study investigated the ability of mammography and MRI to predict residual malignancy after excisional biopsy for suspicious microcalcifications and whether background parenchymal enhancement (BPE) influences the diagnostic performance of MRI. **Patients and Methods:** Fifty-one patients with breast cancer who underwent excisional biopsy for suspicious microcalcifications between January 2009 and February 2019 were enrolled in this single-center retrospective study. Two expert readers independently evaluated the ability of mammography and MRI to predict residual malignancy at the surgical site. The diagnostic value of mammography and MRI was evaluated using histopathology as the standard. **Results:** Thirty-two patients had residual malignancy. The average overall sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and area under the curve for residual malignancy were 78.1%, 42.1%, 69.4%, 42.1%, 62.7%, and 0.601 for mammography and 81.2%, 57.8%, 76.4%, 57.8%, 73.5%, and 0.696 for MRI; the respective values for residual malignancy were 88.8%, 57.1%, 72.7%, 57.4%, 76.5%, and 0.73 in the low BPE group and 71.4%, 60%, 83.3%, 57.4%, 65.7%, and 0.657 in the high BPE group. **Conclusions:** MRI is more accurate than mammography for prediction of residual malignancy after excisional biopsy for breast cancer with suspicious microcalcifications. However, the BPE of MRI influences diagnostic performance, so careful assessment is needed in patients with moderate or marked BPE.

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Introduction

The detection rate for microcalcifications has increased since the advent of screening mammography.[1,2] Suspicious microcalcifications visible on mammography are often considered to be an early sign of breast cancer. Approximately 70% of ductal carcinoma in situ (DCIS) lesions are accompanied only with suspicious microcalcifications on mammography.[3,4] Most suspicious microcalcifications are assessed by histopathologic examination of an

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excisional biopsy and assisted by mammography.[5] If a diagnosis of breast cancer is made, it is important to be able to identify residual malignancy for complete removal of all tumor tissue. Positive resection or a close margin has been associated with an increased risk of local recurrence.[6]

Magnetic resonance imaging (MRI) is considered a useful imaging technique for identification of residual breast cancer and for guiding treatment after excisional biopsy.[7-11] However, the role of MRI in determining the surgical area is unclear if residual suspicious calcifications are present on mammography after excisional biopsy. Furthermore, the value of routine mammography after excisional biopsy is debatable. Mammography may be able to establish a baseline for radiologic follow-up but whether it helps to determine the adequacy of tumor excision is controversial.[12-16]

Diagnostic assessment of the postoperative breast is often challenging because inflammatory changes may be vague or mimic malignancy.[14,17,18] However, to perform a complete excision, it is important to accurately predict residual malignancy after excisional biopsy if suspicious microcalcifications are present. This study compared mammography and MRI for their ability to predict residual malignancy after excisional biopsy for suspicious microcalcifications. We also investigated whether background parenchymal enhancement (BPE) influences the ability of MRI to predict residual malignancy.

Patients and Methods

Study Population

This single-center retrospective study was approved by the institutional review board of Ulsan University Hospital. Review of the radiology department database identified 88 patients with a diagnosis of breast cancer who underwent excisional biopsy for suspicious microcalcifications at Ulsan University Hospital between January 2009 and February 2019. Seventeen patients were excluded because they did not have post-excision mammography, 15 because they did not have MRI prior to definitive surgery, and 2 because they did not have either. Another patient was excluded because she received definitive surgery at another hospital, and a further patient was excluded because of MRI artifact caused by a remnant hook wire.

The remaining 51 patients were included in the study. The patients ranged in age from 35 to 68 years. The final histologic diagnosis was DCIS in 38 cases, invasive ductal carcinoma in 12, and invasive lobular carcinoma in one. All patients underwent definitive surgery within 30 days of the excisional biopsy.

Image Interpretation

The mammographies and MRI scans were read independently by 2 board-certified radiologists (B.M. and B.K.) with 6 and 10 years of experience in breast imaging. Both readers were blinded to all clinical and histopathologic information.

The presence of remnant suspicious microcalcifications adjacent to the excision site on the post-excision mammography was considered positive residual disease and their absence as negative residual disease.

The MRI scans were inspected visually for enhancement on the contrast-enhanced subtraction images. Irregular or nodular enhancement at the surgical cavity and extensive focal non-mass enhancement around the excision site were interpreted as the presence of residual disease at the excision site. The presence of a regular thin enhancing rim around the surgical cavity or no enhancement of the surgical cavity was interpreted as negative residual disease at the excision site. BPE was graded in accordance with the Breast Imaging Reporting and Data System (BI-RADS)[19] as minimal, mild, moderate, or marked. When there was a discrepancy regarding categorization of BPE between the 2 readers, the final categorization was made by consensus.

Pathologic Evaluation

Pathology served as a reference for definitive surgery in all patients. At the time of surgery, a positive margin was defined as the presence of breast cancer at the surgical margin. The histologic diagnosis was made by a pathologist with more than 10 years of experience in breast histology.

Image Acquisition

Standard 2-view diagnostic mammography was performed in all patients. Three different mammography machines were used during the study period (Senograph DS, GE Healthcare, Milwaukee, WI; Brestige, Medifuture, Seongnam-si, South Korea; Selenia Dimensions, Hologic, Bedford, MA). Standard breast MRI was performed using either of 2 3-T scanners (Achieva, Phillips, Best, The Netherlands; Magnetom Skyra, Siemens Healthcare, Erlangen, Germany) equipped with bilateral 8-channel or 16-channel breast array coils. The MRI protocol included the following pulse sequences: an axial T2-weighted sequence; an unenhanced and contrast-enhanced fat suppressed axial T1-weighted sequence; and an axial delayed contrast-enhanced fat suppressed T1-weighted sequence for evaluation of the supraclavicular and axillary lymph nodes. Six dynamic sequences were performed before and after intravenous injection of the contrast medium (0.1 mmol kg^{-1} gadoterate dimeglumine [Dotarem, Guerbet, Villepinte, France]). Post-processing manipulation included production of standard subtraction, reverse subtraction, multiplanar reconstruction, and maximum intensity projection images. Mammography was performed at 0 to 23 days and MRI at 0 to 28 days after the excisional biopsy.

Statistical Analysis

We calculated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of both mammography and MRI for prediction of residual malignancy. A receiver-operating characteristic curve was constructed to assess the ability of mammography and MRI to predict residual malignancy; the area under the curve (AUC) was based on the Hanley and McNeil method. The inter-observer variability was expressed as the κ value. The statistical analyses were performed using SPSS software (version 21.0; IBM Corp, Armonk, NY). A P-value $\leq .05$ was considered statistically significant.

Results

Thirty-two of the 51 patients who underwent mammography or dynamic contrast-enhanced MRI were diagnosed with residual

Table 1 Comparison of Mammography and MRI for Prediction of Residual Malignancy

	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
Mammography						
Reader 1	78.1%	31.5%	65.7%	31.5%	60.7%	0.549
Reader 2	75%	47.3%	70.5%	47.3%	64.7%	0.612
Average	78.1%	42.1%	69.4%	42.1%	62.7%	0.601
MRI						
Reader 1	84.3%	57.8%	77.1%	57.8%	74.5%	0.711[a]
Reader 2	81.2%	52.6%	74.2%	52.6%	72.5%	0.667[a]
Average	81.2%	57.8%	76.4%	57.8%	73.5%	0.696[a]

Abbreviations: AUC = area under the receiver-operating characteristic curve; MRI = magnetic resonance imaging; NPV = negative predictive value; PPV = positive predictive value.
[a]Statistically significant.

malignancy at the surgical site, and 19 had no residual malignancy on histopathologic examination after definitive surgery.

Comparison Between Mammography and MRI

The sensitivity, specificity, PPV, NPV, and accuracy of mammography and MRI are summarized for each reader in Table 1. The average sensitivity, specificity, PPV, NPV, and accuracy of MRI were higher than the respective values for mammography (81.2%, 57.8%, 76.4%, 57.8%, and 73.5% vs. 78.1%, 42.1%, 69.4%, 42.1%, and 62.7%). Using the pathologic results as the criterion standard, the average AUC was 0.601 (P = .231) for mammography and 0.696 (P = .02) for MRI for prediction of residual malignancy after excisional biopsy (Table 1). The inter-observer agreement for diagnostic performance was almost perfect for both mammography (κ = 0.813) and MRI (κ = 0.909).

Diagnostic Performance According to BPE

BPE was low (minimal or mild) in 62.7% of cases and high (moderate or marked) in 37.3%. The sensitivity, specificity, PPV, NPV, and accuracy of MRI according to BPE are summarized in Table 2. The sensitivity and accuracy values were higher in the low BPE group than in the high BPE group (88.8% and 76.5% vs. 71.4% and 65.7%, respectively); however, the PPV was lower in the low BPE group (72.7% vs. 83.3%) (Table 2). Using the pathologic results as the criterion standard, the average AUC for the ability of MRI to predict residual malignancy after excision was 0.73 (P = .028) in the low BPE group and 0.657 (P = .308) in the high BPE group (Table 2).

Discussion

To our knowledge, there have been no studies comparing the ability of mammography and MRI to detect residual breast cancer lesions presenting as suspicious microcalcifications after excisional biopsy. Given that multiple modalities are used in the preoperative evaluation of patients with breast cancer, there is concern in clinical practice regarding the criteria that should be used to evaluate these patients. The present study demonstrated that MRI was more accurate than mammography for prediction of residual malignancy after excisional biopsy in patients with suspicious microcalcifications (Figures 1 and 2). Furthermore, BPE influenced the diagnostic performance of MRI.

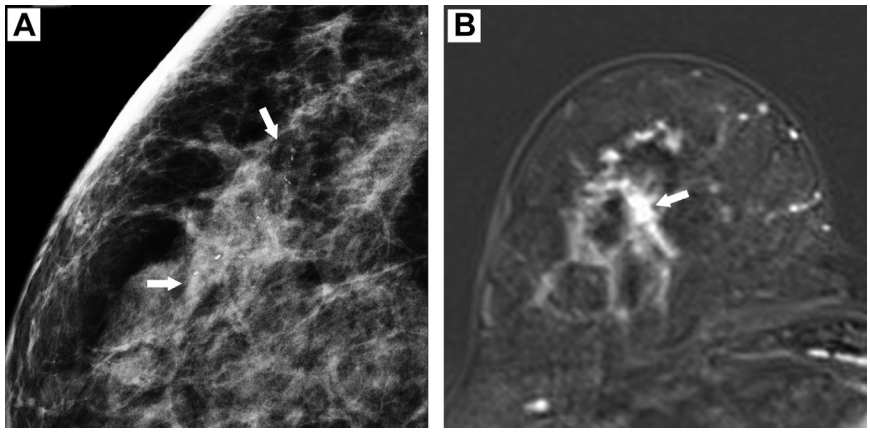
There are no guidelines for or against routine post-excision mammography in patients with calcifications who undergo excision. Aref et al[20] and Gluck et al[14] reported that post-excision mammography is useful for predicting residual disease and the adequacy of tumor excision. However, in other studies, if the margin was subjected to careful pathologic assessment, post-excision mammography led to a change in surgical management in only 2% to 7% of patients, and an additional 1.8% to 4% residual malignancy rate was found on re-excision after positive post-excision mammography with a negative margin.[13,21] Whaley et al found no difference in the 10-year local recurrence-free survival rate between patients who did and not receive post-excision mammography.[21] The results of those studies differ from ours in that the patients in the other studies underwent pathologic assessment of margin status at the time of the initial surgery, and those with

Table 2 Diagnostic Performance Value According to Background Parenchymal Enhancement

	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
Low BPE						
Reader 1	94.4%	57.1%	73.9%	57.1%	78.1%	0.758[a]
Reader 2	88.8%	57.1%	72.7%	57.1%	75%	0.73[a]
Average	88.8%	57.1%	72.7%	57.4%	76.5%	0.73[a]
High BPE						
Reader 1	71.4%	60%	83.3%	60%	68.4%	0.657
Reader 2	71.4%	40%	76.9%	40%	63.1%	0.557
Average	71.4%	60%	83.3%	60%	65.7%	0.657

Abbreviations: AUC = area under the receiver-operating characteristic curve; BPE = background parenchymal enhancement; NPV = negative predictive value; PPV = positive predictive value.
[a]Statistically significant.

Figure 1 Imaging for a 49-year-old Woman Who Underwent Excisional Biopsy. A, Both Readers Suspected Her Mammography to Indicate Residual Amorphous Microcalcification (Arrows) Adjacent to the Surgical Site. B, Both Readers Interpreted the Magnetic Resonance Imaging Scans to Indicate Suspected Residual Malignancy in that the 2-Minute Subtraction T1-Weighted Images Demonstrated Nodular enhancement(arrow) at the Surgical Site. The Patient Underwent Definitive Surgery for Residual Invasive Ductal Carcinoma



negative post-excision mammography or a negative margin did not undergo definitive surgery. However, our receiver-operating characteristic curve analysis also found that mammography did not have a statistically significant predictive ability, and therefore is not an appropriate test for predicting residual disease after excisional biopsy for suspicious microcalcifications.

Despite the fact that the definition of residual cancer on post-excision mammography is whether or not residual calcification exists, the readers in our study had different rates of detection of residual calcifications on mammography (38/52 for reader 1 and 34/52 for reader 2). Mammography basically provides 2-dimensional images and the findings may differ according to the reader if fine or amorphous microcalcifications are present because they can be obscured by postoperative changes, such as inflammation and seroma. In our study, the pathologic results could not be analyzed when residual microcalcifications were detected on mammography but in the absence of residual malignancy (13/38 for reader 1, 10/38 for reader 2) (Figure 3). Because this was a retrospective study, there were many cases that had not been investigated further if there was no residual cancer at the time of definitive surgery. Gluck et al investigated patients in whom residual microcalcifications were present and reported that the pathologic findings were of sclerosing

Figure 2 Imaging for a 37-year-old Woman Who Underwent Excisional Biopsy for Ductal Carcinoma in Situ. A, Both Readers Interpreted Her Mammography as Negative Residual Malignancy because There was No Residual Microcalcification at Surgical Site (Arrow). B, However, the 2-Minute Subtraction T1-Weighted Images Showed Nodular Enhancement (Arrows) at the Surgical Site, which was Interpreted by Both Readers as Suspicious for Residual Malignancy. The Patient Underwent Definitive Surgery for Residual Ductal Carcinoma in Situ

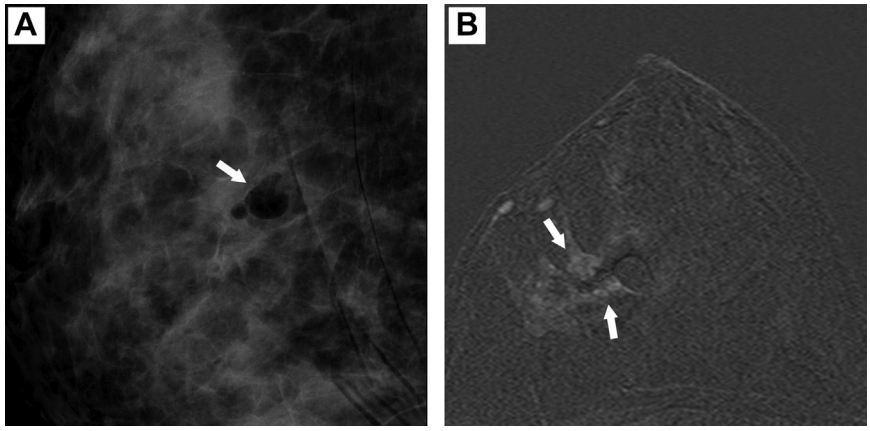
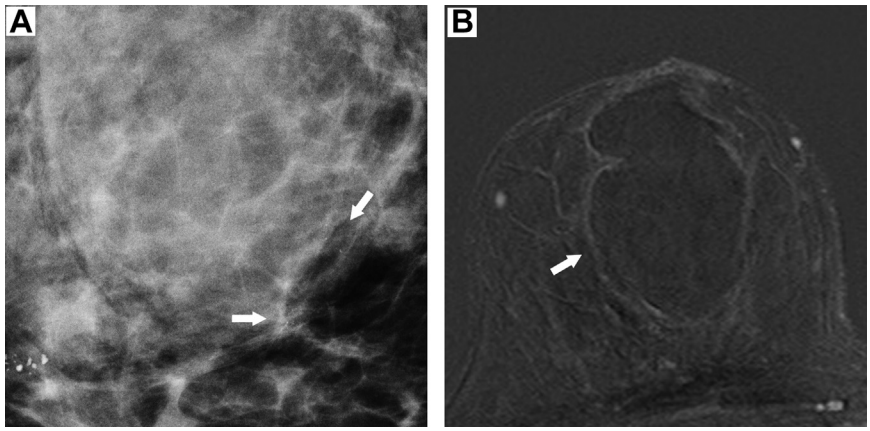


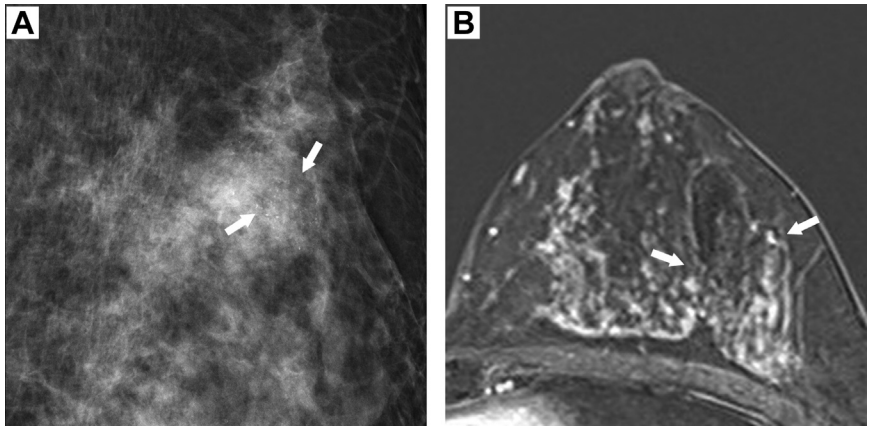
Figure 3 Imaging for a 45-year-old Woman Who Underwent Excisional Biopsy for Invasive Ductal Carcinoma. A, Both Readers Interpreted Her Mammography as Suspicious for Residual Malignancy because of the Presence of Residual Suspicious Microcalcifications (Arrows) Adjacent to the Surgical Site. B, However, Magnetic Resonance Imaging Showed Thin Regular Rim Enhancement (Arrow) at the Surgical Cavity, which Both Readers Interpreted as Negative Residual Malignancy. The Patient Underwent Definitive Surgery With No Residual Malignancy



adenosis, fat necrosis, or a foreign body reaction but not carcinoma.[14] As in their study, residual microcalcifications in our present study were thought to be benign entities that occurred adjacent to the cancer.

There are a few reports on the accuracy of MRI for assessment of residual disease after excision in patients with breast cancer.[7-10] The sensitivity of MRI for detection of residual disease ranged from 61.2% to 79.9% and the PPV from 75% to 91% in previous studies. Our present results are within these ranges, even for breast cancer presenting only as microcalcifications. The majority of cancers presenting only with microcalcifications on mammography are DCIS.[4] The sensitivity of MRI for detection of DCIS was reported to be lower than that for invasive ductal carcinoma, and its sensitivity for calcifications alone was lower than that for calcifications associated with a mass regardless of the type of cancer.[20] Even though the incidence of DCIS in our study population (75%; 39/52) was higher than the range of 18.3% to 47.8% in earlier reports,[7-9] the ability of MRI to detect residual disease after excisional biopsy of breast cancer presenting with suspicious microcalcifications proved to be useful. Improved MRI techniques over time may have contributed to our results.

Figure 4 Imaging for a 38-year-old Woman Who Underwent Excisional Biopsy and Definitive Surgery for Residual Invasive Ductal Carcinoma. A, Both Readers Interpreted Her Mammography to Indicate Suspected Residual Malignancy because of the Finding of Amorphous Microcalcifications (Arrows) Adjacent to the Surgical Site. B, However, Both Readers Interpreted Her Magnetic Resonance Imaging Scans as Negative for Residual Malignancy because Moderate Background Parenchymal Enhancement was Obscuring Residual Nodular Enhancement at the Surgical Cavity (Arrows)



BPE on breast MRI is the normal enhancement of the patient's fibroglandular tissue seen on the first post-contrast image.[19] Most studies have reported diagnostic difficulties when the BPE is high. Increased BPE on breast MRI is associated with an increased abnormal interpretation rate and decreased specificity in patients with breast cancer.[21,22] Furthermore, evaluation of the extent of disease is likely to be inaccurate in patients with high BPE, leading to underestimation or overestimation of the extent of disease.[23] In a report by Preibsch et al,[24] BPE had no statistically significant effect on detection of DCIS. However, MRI could not detect 2 of 295 cases of DCIS, one of which involved moderate BPE and the other involved marked BPE. We found that BPE influenced the diagnostic performance of MRI such that it was not an appropriate test in the high BPE group. High BPE may obscure or mimic residual malignancy, and a small remnant of residual disease was harder to detect in the high BPE group (Figure 4).

This study has several limitations. First, it had a retrospective single-center design, which may have caused a degree of selection bias. Moreover, the sample size was small, especially in the group with high BPE. Therefore, multicenter studies in larger populations are needed to verify our findings. Second, the rates of residual suspicious calcifications on post-excision mammography and residual malignancy in our study was higher than those previously reported.[12,25,26] However, excisions were performed in our study for pathologic confirmation and not for complete tumor removal.

Conclusions

Our findings suggest that MRI is a more accurate predictor of residual malignancy than mammography after excisional biopsy for breast cancer presenting only as suspicious microcalcifications. However, BPE influences the diagnostic performance of MRI; therefore, careful assessment is needed in patients with breast cancer if there is moderate or marked background BPE.

Clinical Practice Points

- MRI is more accurate than mammography for prediction of residual malignancy after excisional biopsy for suspicious microcalcifications in patients with breast cancer.
- However, BPE influences the diagnostic performance of MRI as a predictor of residual disease.
- Careful assessment is needed in patients with breast cancer if there is moderate or marked BPE.

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Disclosure

The authors have stated that they have no conflicts of interest.

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