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Dynamic Contrast Enhancement Magnetic Resonance Imaging Evaluation of Breast Lesions: a Morphological and Quantitative Analysis

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ABSTRACT

Objective: *To correlate the qualitative and quantitative characteristics of breast lesions on magnetic resonance imaging with histopathology.*

Methods: *Diagnostic dynamic contrast-enhanced magnetic resonance imaging of the breast was performed with a double breast coil at 1.5 T for 43 lesions. The diagnostic images were evaluated on a workstation. Lesion morphology (size, shape, margin type, enhancement pattern), signal intensity parameters (time to peak enhancement, maximum slope of enhancement curve, washout), and scores analogous to the Breast Imaging Reporting and Data System categories were correlated with the histology.*

Results: *The sensitivity of breast magnetic resonance imaging for carcinoma was 85.7%. The relatively low specificity of magnetic resonance imaging for benign lesions (82.8%) was due to overlapping features between benign and malignant pathology, including granulomatous mastitis, fibroadenoma with atypical ductal hyperplasia, fibrocystic changes, sclerosing adenosis, and normal breast parenchyma. Irregular margins of a focal mass and rim-like enhancement were morphologic criteria that correlated with malignancy, with positive predictive values of 75.0% and 83.3%, respectively. Malignant and benign lesions did not differ significantly in any of the quantitatively evaluated signal intensity parameters. Carcinomas showed a tendency toward faster and stronger enhancement and stronger washout than the benign lesions. Nevertheless, there was a considerable overlap of both parameters.*

Conclusions: *Benign breast pathology may mimic malignancy on magnetic resonance imaging. A combination of morphologic and perfusion parameters helps the classification of breast lesions by magnetic resonance imaging. Due to the overlap in enhancement characteristics between benign and malignant lesions, quantitative signal intensity data alone is not sufficient. An awareness of the problematic factors of breast magnetic resonance imaging will improve diagnostic accuracy and enable understanding of the limitations of this modality.*

Key Words: *Breast tumors; Magnetic resonance imaging; Pathology*

INTRODUCTION

Contrast-enhanced magnetic resonance imaging (MRI) of the breast is a technique that offers morphological and functional information on lesion features such as tissue perfusion and enhancement kinetics. Since the late 1980s, several problems were identified that hampered the transfer of the modality into clinical practice, including lack of standardisation of image acquisition and interpretation guidelines, lack of MRI-compatible interventional materials, and lack of evidence regarding the diagnostic accuracy.

The sensitivity of MRI for the detection of breast cancer is high, with 90% being reported in most studies.[1] Invasive breast cancers that grow larger than a few millimetres have a high metabolic demand for oxygen and nutrients, which exceeds the supply brought about by diffusion through the normal vessels of fibroglandular tissue. The gap between demand and supply increases

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with increasing tumour size, and causes hypoxic stress on the tumour cells. This stimulates the release of peptide hormones (growth factors, particularly vascular endothelial growth factor) that promote the formation of new vessels and/or the sprouting of existing capillaries in the peritumoural stroma. This process is referred to as angiogenesis or neoangiogenesis.[2] The angiogenic activity of cancers yields a dedicated vasculature that supports the tumour and helps to maintain its metabolic homeostasis. Angiogenesis is closely correlated with invasive cancers, thus this angiogenic activity constitutes the basis for breast cancer detection and differential diagnosis with breast MRI.

In T1-weighted MRI, the signal intensity increases after contrast injection, but it does not depend linearly on the amount of contrast agent, local perfusion, or intravascular spaces.[3] Enhancement is attributed to contrast agent concentration, T1 contrast pulse sequence, baseline T1 relaxation time of different tissues, efficacy in shortening T1 relaxation time with contrast agents, and diffusion rates. As it is not only vessel density that determines enhancement, it is not surprising that enhancement is not pathognomonic for cancer, but can be associated with a variety of benign changes and normal breast parenchyma in the presence of hormonal stimulation.[4] In addition, angiogenic activity is found not only in malignant tissues but also in other conditions such as inflammatory changes or wound healing.

A specificity of 37% to 100% has been reported for breast MRI,[1] resulting in a number of unnecessary biopsies being performed. The relatively low specificity of breast MRI is a disadvantage, and rigorous criteria have been proposed for the interpretation of breast scans. The breast imaging lexicon — Breast Imaging Reporting and Data System (BI-RADS) — published by the American College of Radiology enables a standardised and consistent description of the morphologic and kinetic characteristics of breast lesions.[5] However, many challenges are still present when interpreting breast enhancement patterns and kinetics.

To decrease the number of unnecessary biopsies, a more precise way to differentiate between false-positive enhancing lesions and true-positive malignancies is needed. Additionally, optimisation of subjective breast MRI interpretation by standardising the interpretation and scoring in a more objective manner is required. Therefore, the purpose of this study was to correlate qualitative and quantitative characteristics of MRI lesions with the histology results. Benign lesions that shared malignant MRI features and both common and atypical appearances of malignancy were identified.

METHODS

Patients

Prospective dynamic-contrast enhancement MRI study was performed for 41 patients, aged from 21 to 72 years (mean, 47.1 years), with breast lesions detected at mammogram or ultrasound study and clinically palpable lesions. Two patients had 2 lesions, so 43 lesions were assessed radiologically and histologically investigated for malignancy. The patients were from the 3 major ethnic groups in Malaysia — Malay, Chinese and Indian.

The study was approved by the hospital Institutional Review Board, and all patients provided informed consent before undergoing MRI. All patients underwent MRI before undergoing breast biopsy. Those patients who were premenopausal were imaged during the second or third week of the menstrual cycle. The time-signal intensity curve was not evaluated for 5 lesions for technical reasons.

A questionnaire was completed by each of the patients to document their medical history and to assess their suitability to undergo MRI before the procedure. Those patients who were medically unfit, claustrophobic, or could not tolerate the lengthy examination time were excluded from the study.

Imaging

Diagnostic MRI was performed using a 1.5 T MR scanner (Siemens Magnetom Vision, Erlangen, Germany) with a homogeneity of 5 ppm over a 50-cm sphere, and a field stability of <0.1 ppm/hour using a double breast coil with the patient in the prone position. Each breast was centred within the double breast coils. Both breasts were imaged simultaneously and breast motion was prevented with cushioning material. In all patients, a bolus of contrast medium (gadopentetate dimeglumine) was administered intravenously at a dose of 0.1 mmol/kg body weight, followed by 1.0% saline solution 10 mm. The MRI protocol was standardised for all patients. Scans were obtained at a slice thickness of 3 mm with no intersection gap. The field of view used 16+ with a matrix of 512 x 256. The MRI sequences were:

- dynamic post-contrast scans — 3D fast low-angle shot (FLASH) sequence (axial plane, repeated x 8)
- T1 pregadolinium 3D FLASH sequence (axial plane)
- T1 fat-suppressed inversion recovery sequence (axial/

sagittal plane was included to aid localisation of the lesions).

Post-processing included subtraction of the enhanced images from the unenhanced images for studying contrast enhancement. A semiquantitative analysis of the signal intensity–to-time was performed with the region of interest (ROI) technique (3- x 3-mm pixels). The time for the standardised MRI protocol was 45 minutes. Most of the lesions were larger than 10 mm and they were noticeable on a mammogram or ultrasound scan and were palpable. For most patients, the axilla and axillary lymph nodes were not included due to the limited field of view.

Qualitative Lesion Characteristics

The following morphological (qualitative) characteristics of the lesions were prospectively analysed on the first and last contrast-enhanced series:

- size — small (≤10 mm) or large (>10 mm)
- shape — characterised as regular (oval, round, or polygonal) or as irregular (linear, branching, or stellate)
- margins — well defined or ill defined
- homogeneity of contrast enhancement — homogenous, heterogeneous, or rim.

The positive predictive values (PPV) for malignancy with regard to lesion size, lesion shape, margin type, and homogeneity of contrast medium enhancement were determined.

Quantitative Lesion Characteristics

The diagnostic dynamic time-intensity curve (quantitative) characteristic analysis was independently assessed for each lesion. An ROI focusing on the area of strongest early contrast enhancement within the lesion was chosen to measure the signal intensity values in T1-weighted unenhanced (SI1) and contrast-enhanced (SI2-SI7 or SI2-SI8) series. With this information, the following MRI parameters were analysed.

The time in minutes from the administration of the contrast medium to the maximum signal intensity within the first 3 minutes after contrast medium injection, which was referred to as the time to peak enhancement (T_p), was recorded. The maximum slope of the enhancement curve (S_{max}) was determined. This value was calculated as the relative lesion enhancement (related to maximum lesion enhancement) per minute. In all patients, the maximum slope was reached either between the unenhanced and first contrast-enhanced series or between the first and second contrast-enhanced series. The highest value (either SI_2-SI_1 or SI_3-SI_2) was chosen for the calculation of the maximum slope.

The percentage of washout was analysed according to the change of the relative lesion enhancement (related to the maximum lesion enhancement) from the maximum initial enhancement to the last contrast-enhanced series. Subtracting the initial enhancement from the enhancement of the last study yielded the percentage of washout. If the enhancement decreased during the dynamic study, then the resulting value was negative.

The curves were classified into:

- continuous (type 1) — a pattern of progressive enhancement, with continuous increase in signal intensity
- plateau (type 2) — initial increase in signal intensity followed by a flattening
- washout (type 3) — an initial increase and subsequent decrease in signal intensity.

Lesion Categorisation

In accordance with the BI-RADS system,[5] which was developed to categorise mammographically detected findings, all MRI-detected lesions were prospectively divided into different groups. Depending on various parameters (shape, margin type, enhancement pattern, and kinetics), each lesion was assigned a score analogous to one of the following BI-RADS categories: probably benign finding (category 3), suspicious abnormality (category 4), and highly suggestive of malignancy (category 5).

To establish an objective and reproducible scoring system, the system described by Fischer et al[6] was modified (Table 1). This modified scale was used to categorise 3 morphologic and 2 enhancement dynamics, with a total score ranging from 0 to 8 points. Lesion scores of 3, 4, and 5-8 points were analogous to BI-RADS categories 3, 4, and 5, respectively. The BI-RADS categories 3, 4, and 5 corresponded with the Fischer scores of 3, 4 and 5-8, respectively. The PPV for malignancy according to the analogous BI-RADS category was evaluated.

Two reviewers interpreted the MRI examination by integrating the morphological and dynamic data into the 0 to 8 point score proposed by Fischer et al.[6] The lesions detected on MRI were recorded and evaluated based on the morphological appearances, enhancement, and time-intensity curve. The lesions were then correlated with the histology results.

Table 1. Scoring system for magnetic resonance imaging–detected breast lesions.

Lesion characteristic	Score*
Qualitative lesion characteristics	
Shape	
Regular (round, oval, or polygonal)	0
Irregular (linear, branching, or stellate)	1
Margin type	
Well-defined	0
Ill-defined	1
Enhancement pattern	
Homogeneous	0
Heterogeneous (rim)	1 (2)
Quantitative lesion characteristics	
Initial peak signal intensity (within 3 minutes)	
<50%	0
50-100%	1
>100%	2
Signal intensity at 3 to 8 minutes after contrast injection	
Continuous enhancement	0
Plateau	1
Washout	2
Range of total possible scores	0-8

* Modified from Fischer et al.[6] Breast Imaging Reporting and Data System categories 3, 4, and 5 correspond to scores of 3, 4, and 5-8, respectively.

Histopathologic Correlation

Histopathologic correlation of the lesions was determined based on surgical pathology specimens and/or tissue from ultrasound-guided core biopsy. For lumpectomies, lesions were localised with guide wires under either ultrasonographic or mammographic guidance. The position of all localising wires was confirmed on craniocaudal and mediolateral mammographic projections before surgery. Specimen radiographs were reviewed to ensure that the targeted lesion was resected.

One patient underwent bilateral mastectomy, 2 patients had unilateral mastectomy, and the remaining patients had lumpectomy. Tumour size, histologic subtype, and the presence of invasion were documented. Pathologic-imaging correlation was performed in conjunction with the pathologists and the breast imagers with regard to lesion location and size to ensure that the imaged lesion was evaluated histologically. The MRI results were correlated with the proven histological reports.

Statistical Analysis

The histological findings were reviewed and correlated with the MRI interpretations using a quantitative approach to kinetic evaluation or enhancement pattern and a qualitative method for evaluation of overall shape of the enhancement curve when attempting to distinguish benign from malignant lesions. Data were entered and tabulated into a computerised spread sheet (Excel; Microsoft, Redmond, USA). Statistical analysis was performed using the Statistical Package for the Social Sciences, version 13.0, and chi-squared and Fisher's exact tests were used for independent variables to assess the lesion qualities and the analogous BI-RADS category to determine whether any of the lesion qualities showed a significant correlation with the histological results. Benign and malignant lesions were evaluated for significant differences in enhancement kinetics and washout pattern using Student *t* test for independent samples. After reviewing the results and discussing with the physicist, the sensitivity, specificity, PPV, and negative predictive value (NPV) were calculated for morphology, enhancement, and time-intensity curve.

RESULTS

Histology

Histology showed that 14 of 43 lesions (32.6%) were malignant. The 14 malignant lesions were invasive ductal carcinoma (n = 10), ductal carcinoma in situ (DCIS; n = 1), mixed lobular and ductal invasive carcinoma (n = 1), medullary carcinoma (n = 1), and mucinous carcinoma (n = 1). The 29 benign lesions included fibroadenoma (n = 13), benign proliferative changes (n = 5), non-proliferative fibrocystic disease (n = 5), sclerosing adenosis (n = 2), inflammatory mastitis (n = 2), and papilloma (n = 1); 2 specimens were normal lymph node (n = 1) and normal glandular tissue (n = 1). Atypical hyperplasia was seen in 1 patient with proliferative fibrocystic disease and 2 patients with fibroadenoma.

Qualitative Lesion Characteristics

As shown in Table 2, the overall PPV of MRI-detectable malignant lesions was 68.7%. The diameters of these lesions ranged from 3 to 30 mm (mean, 12 mm). The PPV of small (≤10 mm) and of large (>10 mm) lesions were 6.0% and 50.0%, respectively. The descriptions of the margin, shape, and heterogeneous/rim contrast enhancement of a focal mass were significantly associated with malignant histology ($p < 0.05$) [Table 1]. Lesions with ill-defined margins had a higher PPV for malignancy (75.0%) than those with well-defined margins (7.4%). Of the round, oval, or polygonal lesions, 11.1% were malignant, and 37.1% of irregularly shaped lesions were malignant.

Of the lesions with homogeneous late enhancement, 20.0% were malignant and 50.0% of the lesions with heterogeneous late enhancement were malignant. Early homogeneous lesion enhancement was more frequently

associated with malignancy (42.9%) than heterogeneous early enhancement (32.4%). Rim-like enhancement highly correlated with a diagnosis of cancer (PPV, 83.3%) [Table 2]. Of the lesions that showed homogeneous enhancement, 8.0% were malignant, compared with more than half of the lesions with heterogeneous enhancement (58.3%).

A typical benign feature was a smooth margin (NPV, 92.6%) and shape (NPV, 88.9%) [Table 3]. Lack of enhancement has a high NPV for malignancy (92.0%). There was a 14.3% false-negative rate for 2 non-enhancing tumours: 1 DCIS and 1 mucinous carcinoma.

Dynamic Magnetic Resonance Imaging Enhancement Pattern

As shown in Table 4, malignant lesions had a higher maximum slope of the enhancement curve, reached mean signal intensity peak earlier, and had a stronger loss of enhancement (washout) from the initial signal intensity peak to the last contrast-enhanced measurement. Nevertheless, there was a considerable overlap of these parameters: 9 of 12 lesions (75.0%) diagnosed as carcinoma by MRI showed >100% enhancement; 6 of 26 lesions (23.0%) diagnosed as benign by MRI also showed >100% enhancement, showing this parameter to be a poor predictor for malignancy. Using either the plateau or washout curve as an indicator of malignancy yielded a sensitivity of 58.3% and a specificity of 65.4%. Although, the washout curve had a PPV of 62.5%, a similar pattern was also seen in 3 benign lesions: fibroadenoma with atypical ductal hyperplasia, mastitis, and benign proliferative nodule.

Lesion Categorisation

The PPV for malignancy for MRI-detectable lesions increases as the BI-RADS category increases: from 9.0% (2/22) for category ≤3 lesions to 40.0% (2/5) for category 4 lesions and 88.9% (8/9) for category 5 findings. Although the p value was <0.05 (p = 0.001), the chi-squared test was not valid because more than 20% of the squares showed expected values of <5.

Table 2. Positive predictive values and p values for detecting malignancy in magnetic resonance imaging–detectable breast lesions.

Variable	Positive predictive value Number (%)	p Value
Size (mm)		0.06
≤10	1/17 (5.9)	
>10	13/26 (50.0)	
Margin type		0.00
Well defined	2/27 (7.4)	
Ill defined	12/16 (75.0)	
Shape		0.00
Regular (round, oval, or polygonal)	3/27 (11.1)	
Irregular (linear, branching, or stellate)	11/16 (68.8)	
Enhancement pattern		0.01
Homogenous	2/25 (8.0)	
Heterogenous	7/12 (58.3)	
Rim enhancing	5/6 (83.3)	
Initial peak signal intensity (within 3 minutes)		0.06
<50%	1/17 (5.8)	
50-100%	2/6 (33.3)	
>100%	9/15 (60.0)	
Signal intensity 3 to 8 minutes after contrast injection		0.28
Continuous	5/21 (23.8)	
Plateau	2/9 (22.2)	
10% washout	5/8 (62.5)	

Table 3. Characteristics of the malignant lesions.

Characteristics	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Ill-defined margin	85.7	86.2	75.0	92.6
Irregular shape	78.6	82.8	68.8	88.9
Heterogenous/rim enhancement	85.7	79.3	66.7	92.0
Initial enhancement >100% within 3 minutes	75.0	76.9	60.0	87.0
Signal intensity curve, plateau and washout pattern	58.3	65.4	43.8	77.3
Overall	85.7	82.8	70.6	92.3

Table 4. Comparison of signal intensity parameters for benign versus malignant breast lesions using Student *t* test for 38 lesions.

Parameter	Benign (n = 26) Mean (SD)	Malignant (n = 12) Mean (SD)	p Value
Time to peak enhancement (minutes)	2.21 (0.41)	1.93 (0.53)	0.09
Maximum slope of lesion enhancement curve (% per minute)	63.30 (15.40)	72.40 (13.10)	0.26
Washout*	-2.83 (0.23)	-5.30 (0.19)	0.08

* Change in enhancement from initial maximum enhancement (first 3 minutes after administration of contrast medium) to last enhancement measurement obtained after contrast medium administration.

Sensitivity and Specificity

Of the 14 lesions with carcinoma, MRI identified 12 as malignant, resulting in a sensitivity (Fischer score) for carcinoma of 85.7% (Figure 1). Of 29 lesions without cancer, MRI was negative for malignancy for 24 lesions, resulting in a specificity of 82.8%. Of 17 lesions with a positive MRI for malignancy, 12 patients had cancer, resulting in a PPV of 70.6% (Figure 2). Of the 26 lesions with a negative MRI for malignancy, 24 patients had no evidence of cancer, resulting in a high NPV of 92.3%. The false-negative lesions included DCIS and mucinous carcinoma (Figure 3).

DISCUSSION

Although breast MRI has shown great potential for characterising suspicious breast lesions, its use is still largely limited to university or research centres. One reason preventing broader acceptance and more widespread clinical use of breast MRI is the lack of interpretation guidelines for lesion characterisation. Most published diagnostic criteria use site-specific software programmes or unique MRI sequences that have shown precision.[7-24] Nevertheless, decreasing the number of false-positive findings at breast biopsy by differentiating benign from malignant lesions by MRI is desirable.

This study attempted to optimise subjective breast MRI interpretation by standardising the interpretations and scoring in a more objective manner. This could be considered for a consensus statement regarding lesion features that are thought to be diagnostically relevant, and should be evaluated for the purpose of differential diagnosis and management. This system provides a sound basis for the reporting of a breast MRI study and incorporates both morphologic and kinetic criteria. Although the PPV or NPV of the many different findings are not yet fully clarified, this will be a step toward not only standardised reporting but also standardised interpretation of breast MRI studies. To establish an objective and reproducible scoring system, the system described by Fischer et al[6] was modified to be analogous to the BI-RADS scoring system.[5] A more precise way of differentiating false-positive enhancing lesions and true-positive malignancies was sought, so the qualitative and

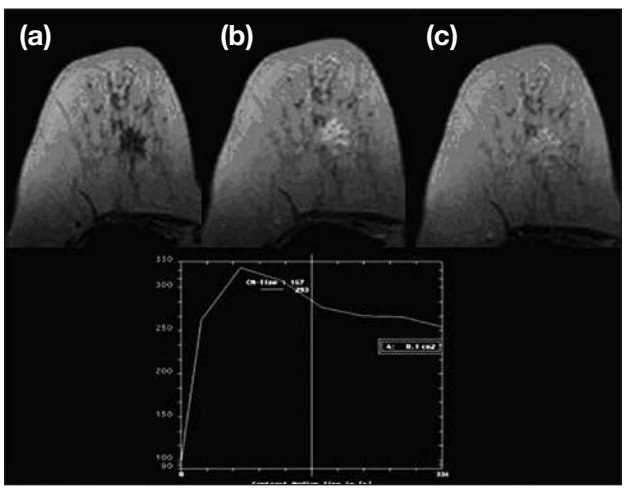

Figure 1. Positive magnetic resonance images. (a) Precontrast image with marker at the region of interest; (b) contrast-enhanced T1-weighted gradient-recalled echo subtraction image showing an ill-defined margin and irregular lesion; and (c) early enhancement postcontrast and early washout on enhancement. The curve indicates early enhancement with early washout in the lesion — a type III curve. Histopathology confirmed infiltrating ductal carcinoma.

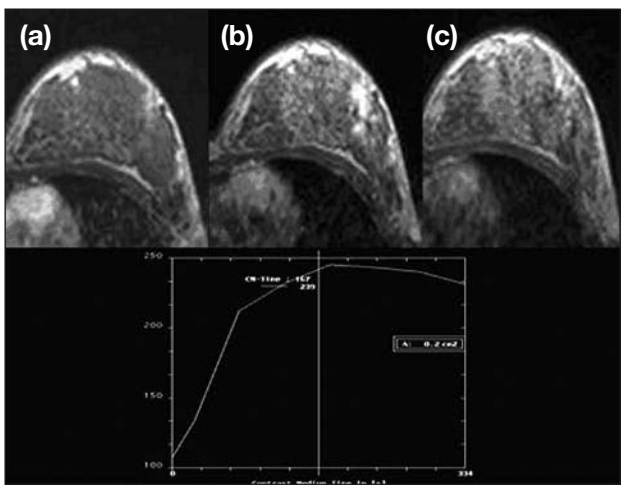

Figure 2. False-positive magnetic resonance images. (a) Precontrast; (b) early contrast-enhanced; and (c) delayed contrast-enhanced T1-weighted 3-dimensional fast low-angle shot demonstrating an irregular ill-defined lesion suggestive of carcinoma. The enhancement curve is type III, with an early peak and delayed phase washout. Fischer's score was 7 (analogous to the Breast Imaging Reporting and Data System category 5). Histology confirmed chronic granulomatous mastitis.

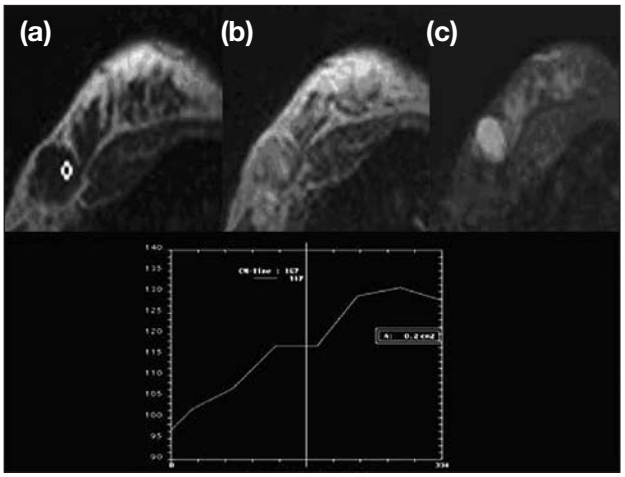

Figure 3. False-negative magnetic resonance images. (a) Pre-contrast; (b) early contrast-enhanced; and (c) delayed contrast-enhanced T1-weighted 3-dimensional fast low-angle shot demonstrating a well-defined oval lesion with smooth margin — features typical of a benign lesion. The enhancement curve is type I with gradual but progressive contrast enhancement. Histology confirmed mucinuos carcinoma.

quantitative MRI characteristics of these lesions were correlated with the histology results.

This study provides optimised diagnostic criteria for lesion characterisation. Among the 4 morphologic and 2 dynamic enhancement imaging parameters, margin, shape, and enhancement pattern were the optimal discriminators for breast lesion characterisation. The combination of both morphologic and dynamic information represented by the BI-RADS system (Fischer's score) achieved an optimised specificity and NPV of 82.8%, while maintaining a sensitivity of 85.7%.[25-27] The sensitivity of breast MRI for the detection of breast cancer is high, with 90% to 100% being the reported value in most studies.[1] The reported false-negative results were due to the presence of DCIS or an invasive ductal or lobular malignancy. Previous investigators estimated the sensitivity of MRI for the detection of DCIS to be approximately 70%.[28] In this study, MRI was negative for 1 invasive ductal carcinoma (minimum enhancement, based on the Fischer's score). The difference in sensitivity was expected on the basis of pronounced neo-angiogenesis in these tumours.

The lesions that had a false-negative result by enhanced MRI were visualised by ultrasonography. The intraductal carcinoma showed 1 or more malignant features on ultrasound imaging (angulated/spiculated margins, posterior acoustic shadowing), which would have warranted a biopsy. The other lesion, which was a mucinous tumour, demonstrated continuous enhancement on MRI (false-negative). However, benign morphology was seen on both ultrasound and MRI, meaning that the diagnosis could have been missed by both imaging methods. The imperfect sensitivity of MRI (87%) is a crucial point that prevents clinical use of MRI for the diagnosis of mammographically or ultrasonographically detected lesions. These results are similar to those of Teifke et al, who described a false-negative rate of 12% for breast cancer detection using enhanced MRI.[29] However, there are some differences in the methodologies between Teifke et al's study[29] and this study. The false-negative lesion described by Teifke et al included malignancies that were not detected for technical reasons and lesions that were not visualised due to the anatomical features of the tumour and/or the surrounding tissues.[29] However, lesions that were not detected due to technical factors were excluded from this study, and only breast malignancies that were visible on MRI were included.

While the reported sensitivity of breast MRI is high, the reported specificity of MRI for detection of abnormalities is variable, ranging from 37% to 97%. The specificity was 80% in this study. While tumours have been shown to be enhanced after intravenous administration of gadopentetate dimeglumine, several benign lesions, including fibroadenomas, lymph nodes, non-proliferative and proliferative fibrocystic changes, and lesions associated with an increased risk for breast cancer such as atypical hyperplasia have also been shown to be enhanced. This overlap has resulted in low reported specificity of MRI for detection of malignant lesions.

Smooth well-defined masses (NPV for malignancy, 93%), lobulated and rounded masses (NPV for malignancy, 89%), and masses that displayed minimal or homogenous contrast enhancement (NPV for malignancy, 92%) remained highly predictive of benign findings. Malignancies that masqueraded as these lesion types tended to be rare but predictable diseases. Smooth masses in this study were shown to be colloid cancer and medullary cancer. Unfortunately, no architectural features could be identified that routinely distinguished these cancers from the benign entities they mimicked.

For a better understanding of the high PPV of well-defined margins, MRI resolution should be considered. Stomper et al stated that analysis of the margins of focal enhancing areas is of less value than analysis of the margins in mammograms because MRI does not have as high a resolution as film-screen mammograms.[30] The shape of small lesions is difficult to judge for the

same reason. This study deferred the above concept, as most of the enhancing lesions measured >10 mm. In this study, heterogeneous and rim enhancing lesions (more than 6 minutes after gadopentetate dimeglumine injection) correlated significantly with malignancy. This correlation can be explained by the washout phenomenon of malignant lesions, which show an irregular enhancement pattern within the lesion that subsequently becomes heterogeneous. No enhancement or minimal enhancement was not suggestive of benign abnormalities. This was seen in 1 patient with a previous scar in whom DCIS was missed. It was hypothesised that absent or minimal enhancement would be benign subcategories for irregular masses due to previous scar. Lack of enhancement of such masses may still reliably lead to prediction of benign abnormalities, but sample sizes adequate to prove this were not achieved in this study.

The quantitative features most indicative of cancer have been reported to be the maximum enhancement rate (percentage of enhancement per second) and the percentage of enhancement at 1 minute,[31] with rapid enhancement being characteristic of malignancy. Thorough analysis of lesion signal intensity data in correlation with histology seemed promising for the differentiation of benign from malignant breast lesions. In this study, malignant lesions had faster and stronger enhancement with a stronger washout than benign lesions; malignant and benign lesions did not differ significantly in any of the quantitatively evaluated signal intensity parameters. Similar results have been reported by Siegmann et al[32] and Stomper et al,[30] who evaluated MRI of the breast in patients with known palpable or mammographically detected lesions. Although enhancement and washout tended to be more rapid for malignant lesions, these researchers found considerable overlap in signal intensity and enhancement characteristics of malignant and benign lesions. However, Kaiser and Zeitler[33] and Gribbestad et al[34] reported that all malignant lesions could be differentiated from benign lesions by early signal enhancement among 25 and 18 dynamic contrast-enhanced breast MRI examinations, respectively. The difference between the results of this study and those of Kaiser and Zeitler[33] and Gribbestad et al[34] may be explained by the frequent occurrence of proliferative changes and young fibroadenomas among the benign samples in this study. An increase in signal intensity correlates with vascularisation, which reflects proliferative activity and does not necessarily imply malignancy.

Although the amplitude of signal intensity does not lead to more precise identification of breast carcinomas, Kuhl et al found that the shape of the time–signal intensity curve is important for differentiating benign from malignant lesions.[15] These authors distinguished 3 different curves of continuous enhancement, plateau, and washout. Fifty seven percent of all carcinomas in Kuhl et al's study showed a washout.[15] In this study, 62.5% of the lesions with a washout pattern were carcinomas. Nevertheless, there were 37.5% benign lesions that also had a loss of enhancement that was > 10% from the initial signal intensity.

Neo-angiogenesis is not the same for all malignant breast lesions, being more pronounced in invasive ductal carcinoma and not always present in DCIS and lobular carcinomas, in which cells present a growing model 'in single file' and the pre-existing capillaries are unable to support all the tumour cells. It is well known that absence of a visible lesion on contrast-enhanced MRI that corresponds to a palpable or mammographically visible abnormality is highly predictive of a benign finding. However, the absence of observed enhancement at breast MRI does not exclude in situ or invasive cancer, as for the patients in this study. Many invasive cancers that show no enhancement are small or have a small invasive component.[27] Lack of enhancement has a high NPV for malignancy (94%). This study also found that MRI depicted additional multifocal or multicentric tumours in 3 patients with cancer. Inevitably, the management was changed from lumpectomy to quadrantectomy or mastectomy.

Assigning a score to lesions as a synopsis of all lesion features and using the score to determine the analogous BI-RADS category seems to be helpful for assessing the likelihood of malignancy in mammographically or ultrasonographically detectable lesions. The score used in this study was described by Fischer et al,[6] and helped to achieve an objective categorisation of these lesions.

These results emphasise that MRI of the breast can reveal lesions that are occult at mammography and ultrasound. Approximately one-third of the lesions detected exclusively by MRI were malignant. For these lesions, signal intensity data alone was not helpful for defining malignant and benign abnormalities. However, classifying lesions into BI-RADS categories according to a published scoring system is helpful for identifying the lesions for which intervention is required. Both parameters are reproducible and easy to learn. For patients

with suspicious breast lesions, the following diagnostic MRI criteria are proposed for lesion characterisation:

- lesions with spiculated margins and lesions with washout and non-smooth margins are classified as malignant
- lesions without washout or spiculated margins and lesions with washout and smooth margins are classified as benign.

While acknowledging that this study is limited by the relatively small sample size, these results show that breast malignancies with suspicious features on ultrasound may not be detected by MRI due to non-enhancement of the lesions. While the clinical indications for breast MRI have yet to be precisely defined and universally accepted, radiologists must be aware of the limitations of these techniques. Furthermore, as the availability and clinical demand for breast MRI increases, the ability of MRI to differentiate between benign and malignant lesions of the breast should not be overestimated. Therefore, these authors suggest that breast lesions that appear to be of concern for malignancy by ultrasound due to their morphologic features should be evaluated by tissue sampling in the correct clinical setting, despite a lack of enhancement on MRI.

The morphologic characteristics of the margins and an enhancement pattern of washout emerged as the most useful MRI parameters for the characterisation of suspicious breast lesions using a 3-timepoint method of acquisition. Both parameters are reproducible and easy to learn. The specificity of breast MRI is improved when both morphologic and kinetic features are considered in the interpretation. Due to the overlap in enhancement characteristics between benign and malignant lesions, reliance on a kinetics assessment alone is not recommended. The exclusion of cancer on the basis of persistent enhancement alone would lead to false-negative results.

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