



Nonpalpable Mammographically Occult Invasive Breast Cancers Detected by MRI

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OBJECTIVE. The purpose of this study was to determine the MRI findings and histology of clinically and mammographically occult invasive breast cancers detected by MRI.

MATERIALS AND METHODS. A retrospective review was undertaken of 1,336 breast MRI examinations performed during a 2-year period. Among these, 68 nonpalpable mammographically occult invasive cancers were identified in 57 women with a median age of 50 years (range, 30–72 years). MRI findings were classified according to the breast MRI lexicon. Medical records were reviewed to determine the histology.

RESULTS. Indications for performing MRI were extent of disease assessment in 72% (41/57), high-risk screening in 25% (14/57), and problem solving in 3% (2/57). MRI lesion types in these 68 invasive cancers were nonmass in 57% (39/68) and mass in 43% (29/68). Kinetics were plateau in 59% (40/68), washout in 38% (26/68), and persistent in 3% (2/68). Histology was invasive ductal cancer in 65% (44/68), mixed invasive ductal and lobular cancer in 19% (13/68), and invasive lobular cancer in 16% (11/68). The cancer stage was I in 61% (34/56), II in 32% (18/56), and more advanced in 7% (4/56). Sixty-three percent (43/68) of lesions were minimal cancers, defined as invasive cancers measuring under 1 cm.

CONCLUSION. In this study of mammographically and clinically occult cancers detected by MRI, 57% (39/68) of invasive breast cancers were evident as nonmass enhancement, and 63% were minimal breast cancers.

Breast MRI has a high sensitivity for breast cancer detection, reported as high as 94–100%, but with a lower reported specificity of 37–97% [1, 2]. MRI can detect invasive breast cancers that are mammographically and clinically occult [3]. Until recently, one of the limiting factors in the utility of breast MRI has been the lack of standardized criteria for interpretation and reporting of breast MRI [1, 4]. The American College of Radiology recently published a lexicon for breast MRI [5]. The purpose of our study was to analyze the features of mammographically and clinically occult MRI-detected invasive cancers according to the American College of Radiology's Breast MRI Lexicon.

high risk for breast cancer with a positive family history (Fig. 2), prior lobular carcinoma in situ, treated breast cancer, or current contralateral breast cancer (Fig. 3); and problem solving such as an unknown primary (Fig. 4) and equivocal mammogram. For MRI-detected lesions warranting biopsy, correlative sonography was performed at the discretion of the radiologist interpreting the MRI study; if a sonographic correlate was identified, biopsy or localization was usually performed under sonographic guidance. For MRI-detected lesions warranting biopsy that had neither mammographic nor sonographic correlates, MRI-guided localization and surgical excision were performed unless patient management had been otherwise planned to include surgical excision of the area in question.

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Materials and Methods

Indications for Breast MRI and MRI-Guided Needle Localization

The indications for breast MRI at our institution are assessment of disease extent in the ipsilateral breast in women with known biopsy-proven breast cancer (Fig. 1); screening of women who are at

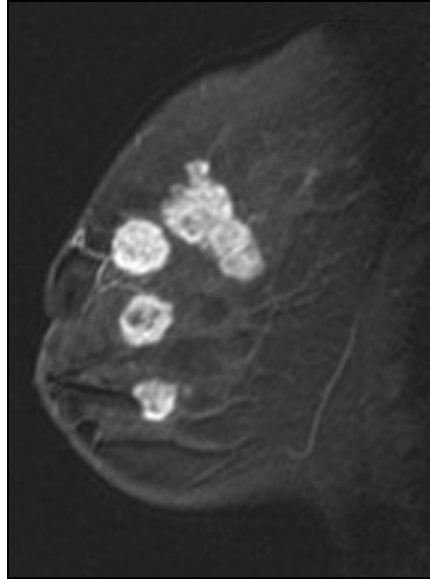
Patient Selection, Lesion and Breast Characteristics, Lesion Sampling

A retrospective review was performed of 1,336 breast MRI examinations performed over a 2-year period (January 2000–December 2001). Medical records were reviewed to identify patients with invasive breast cancer found on MRI that was clinically and mammographically occult. The histology

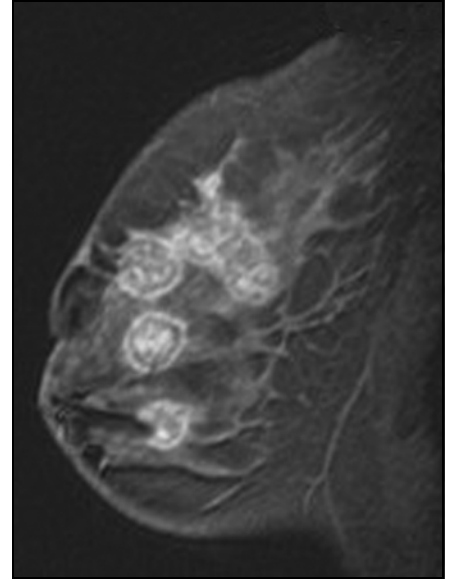
Fig. 1—31-year-old woman with palpable, biopsy-proven left breast invasive ductal cancer in upper outer quadrant. Corresponding to palpable mass, sonography showed focal mass and mammogram showed pleomorphic calcifications.

A, Sagittal T1-weighted MRI of left breast immediately after injection of IV gadolinium shows multiple heterogeneously and rim-enhancing masses.

B, Sagittal T1-weighted contrast-enhanced, delayed MRI of left breast shows masses have washout kinetics. Histologic analysis showed multicentric invasive ductal cancer. Patient had left mastectomy.



A



B

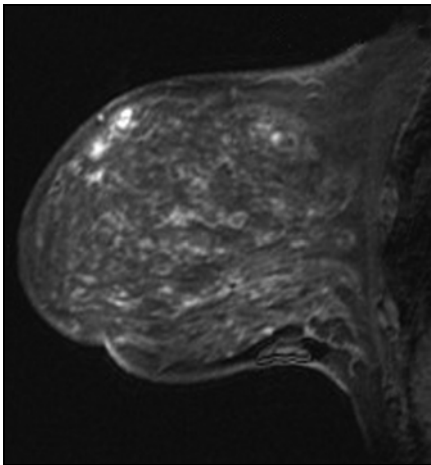


Fig. 2—49-year-old woman at high risk for breast cancer had screening breast MRI examination. Sagittal T1-weighted contrast-enhanced MRI of right breast shows focal clumped enhancement superiorly. MRI-guided needle localization and surgical excision yielded invasive lobular cancer (0.7 cm).

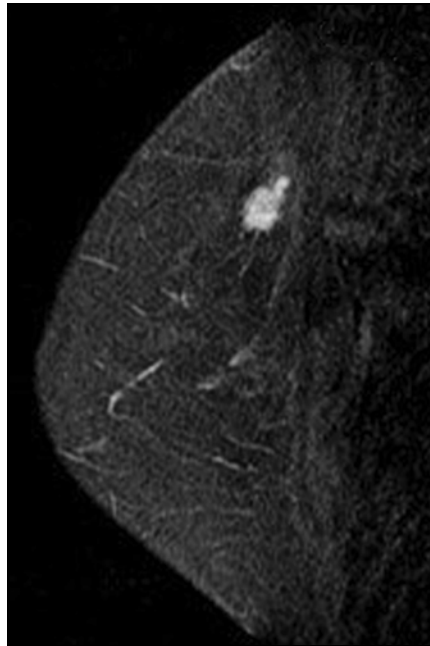


Fig. 3—60-year-old woman with palpable left breast mass that yielded invasive lobular cancer. Sagittal contrast-enhanced T1-weighted image of opposite (right) breast showed mammographically occult, nonpalpable heterogeneously enhancing mass. Biopsy yielded invasive mammary cancer with mixed ductal and lobular features.

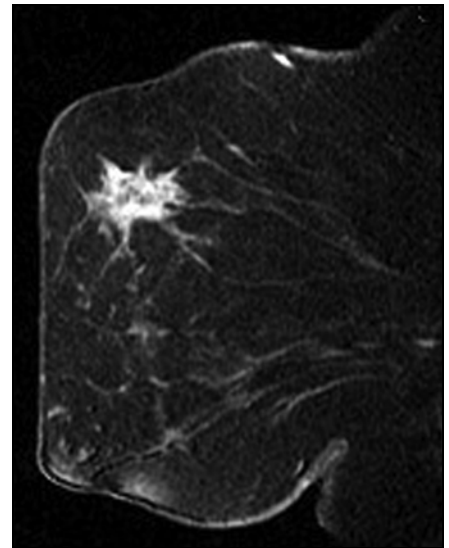


Fig. 4—69-year-old woman who presented with palpable left axillary nodes positive for metastatic mammary cancer with no primary cancer identified on mammography or physical examination. Sagittal T1-weighted contrast-enhanced MRI of left breast shows spiculated, irregular, heterogeneously enhancing mass. Biopsy yielded invasive ductal cancer.

of the invasive cancer was noted. In all cases, breast MRI was performed at our facility before biopsy.

Sixty-eight nonpalpable mammographically occult invasive breast cancers were identified in 57

women. The median age was 50 years (range, 30–72 years). The indication for breast MRI was assessment of disease extent in women with known biopsy-proven ipsilateral breast cancer in 72%

(41/57), screening of high-risk women in 25% (14/57), and problem solving in 3% (2/57). In the 41 women with biopsy-proven cancer, the primary known breast cancer was not examined in this

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study. The protocol for this review was approved by our institutional review board.

Directed sonography using the Acuson Sequoia 512 and an 8–15 MHz probe was performed in 24 patients, and a sonographic correlate was identified in five. In the remaining 33 women, directed sonography was not performed at the discretion of the interpreting radiologist and treating clinician. The mammographic parenchymal density [5] was class 4 (dense) in 15 patients, class 3 (heterogeneously dense) in 32, class 2 (scattered fibroglandular densities) in nine, and class 1 (fatty) in one. The average interval between the mammography and breast MRI was 6 weeks (range, 0–24 weeks).

Histologic sampling of these lesions was performed using MRI-guided needle localization and surgical excision in 46% (26/57) of patients, mastectomy in 26% (15/57), lumpectomy or reexcision in 23% (13/57), and sonogram-guided biopsy in 5% (3/57).

Breast MRI Technique and Interpretation

Diagnostic breast MRI examinations were performed with the patient prone in a 1.5-T commercially available system (Signa, Lightning, or Excite; GE Healthcare) using a dedicated surface breast coil. Our imaging protocol includes a localizing sequence followed by a sagittal fat-suppressed T2-weighted sequence (TR/TE, 4,000/85). A T1-weighted 3D fat-suppressed fast spoiled gradient-echo sequence (17/2.4; flip angle, 35°; bandwidth, 31.25 MHz) was then performed before and three times after a rapid bolus injection of 0.1 mmol/L of gadopentetate dimeglumine (Magnevist, Berlex Laboratories) per kilogram of body weight and delivered through an indwelling IV catheter.

Image acquisition started after injection of contrast material and saline bolus. Images were obtained sagittally for an acquisition time per volumetric acquisition of less than 3 min each. Total imaging time per breast, including three contrast-enhanced acquisitions, was approximately 20 min. Section thickness was between 2 and 3 mm without a gap using a matrix of 256 × 192 and a field of view of 18–22 cm. Frequency was in the anteroposterior direction. After the examination, the unenhanced images were subtracted from the first contrast-enhanced images on a pixel-by-pixel basis.

Breast MRI examinations were interpreted by breast imaging specialists in conjunction with clinical history and other breast imaging studies, including mammograms and sonograms when available.

Data Collection and Analysis

The institution at which the study was performed is an academic center where more than 600 breast MRI examinations, 16,000 mammograms, and 1,000 new breast cancer cases were evaluated annually dur-

ing the study period. Mammograms were reviewed by one of nine attendings specializing in breast radiology. Diagnostic breast MRI for 68 consecutive, mammographically occult nonpalpable invasive breast cancers were reviewed by one radiologist with 4 years of experience as a breast imaging specialist.

T2-weighted, T1-weighted unenhanced, and T1-weighted images obtained within the first 2 min after IV contrast injection in all cases were reviewed on the PACS™ workstation (Centricity PACS, GE Healthcare) for review by the radiologist. The radiologist could page back and forth through sequential slices and adjust the window and level settings at the workstation.

Data recorded included lesion size, signal intensity on T2-weighted images (hyperintense vs not hyperintense), morphologic features, and final assessment categories according to the Breast BI-RADS MRI Lexicon [5]. Visual analyses of the time course of enhancement in these three enhanced sequences were performed and categorized as “persistent” (increasing signal intensity throughout the dynamic period), “plateau” (stabilized enhancement without change in signal intensity between the initial and subsequent enhanced images), or “washout” (abrupt decline in signal intensity after the initial enhanced images) [6–9].

After these data were recorded, histologic findings were reviewed and correlated with MRI interpretations. Medical records were reviewed to determine breast cancer stage and treatment. Minimally invasive breast cancers were defined as invasive breast cancers smaller than 1 cm [10]. Data were entered into a computerized spreadsheet (Excel, Microsoft).

Results

Lesion Histology and MRI Characteristics

Histologic analysis of these 68 invasive breast cancers showed invasive ductal carcinoma in 65% (44/68), invasive mammary (mixed ductal and lobular) in 19% (13/68), and invasive lobular carcinoma in 16% (11/68). Associated ductal carcinoma in situ (DCIS) was found in 66% (45/68). Forty-four percent (20/45) of lesions associated with DCIS were mass lesions and 56% (25/45) were nonmass lesions. The median MRI size of the lesions was 1.7 cm (range, 0.4–10 cm). Data regarding the histology size were available for 62 of 68 lesions. The median histologic size was 0.7 cm (range, 0.05–9.7 cm). Sixty-three percent (43/68) were minimal breast cancers (< 1 cm in size). Histologically, multifocal disease was identified in 47% (32/68) of specimens. MRI lesion characteristics in these 68 invasive cancers are shown in Table 1.

Masses

MRI features of invasive cancer in 29 masses are shown in Table 2. The most common MRI features of invasive breast cancers evident as masses were irregular margins in

TABLE 1: MRI Features of 68 Invasive Cancers

Feature	No. (%) of Cancers
Morphology	
Masses	29 (43)
Nonmasses	39 (57)
T2 signal	
High	16 (24)
Intermediate	8 (11)
None	44 (65)
T1 signal	
High	0 (0)
Intermediate	9 (13)
None	59 (87)
Visual kinetics	
Washout	26 (38)
Plateau	40 (59)
Persistent	2 (3) (Fig. 7)

TABLE 2: MRI Features in 29 Mass Lesions

Feature	No. (%) of Lesions
Margins	
Irregular	19 (66)
Spiculated	7 (24)
Smooth	3 (10)
Enhancement	
Heterogeneous	17 (59)
Homogeneous	7 (24)
Rim enhancing	4 (14)
Dark septations	1 (3)
Visual kinetics	
Washout	14 (48)
Plateau	14 (48)
Persistent	1 (3)
T2 signal	
High	19 (66)
Intermediate	8 (28)
None	2 (7)
T1 signal	
High	0 (0)
Intermediate	2 (7)
None	27 (93)

Note—All percentages do not add up to 100% due to rounding.

66% (19/29), heterogeneous enhancement in 59% (17/29), visual kinetics that were wash-out in 48% (14/29), plateau in 48% (14/29), no T2 signal in 67% (19/29), and no T1 signal in 93% (27/29).

Nonmass Enhancement

MRI features of invasive cancer in 39 nonmass lesions are shown in Table 3. The most common MRI features of these lesions were focal clumped enhancement in 35% (14/39), plateau kinetics in 67% (26/39), no T2 signal in 65% (25/39), and no T1 signal in 82% (32/39).

Sonographic Correlation

Sonographic correlates were found in only five of 24 lesions that were scanned. In this small group, there were two invasive ductal carcinomas, two invasive lobular carcinomas, and one invasive mammary cancer. Four lesions were masses and one was a non-mass lesion on MRI. MRI lesions ranged in size from 1.2–2.9 cm. Histologic lesion size, known in three of the five lesions, ranged from 0.7–2.5 cm.

Histology Subtypes and MRI Characteristics

MRI lesion features as a function of invasive cancer histology are shown in Table 4. Fifty-seven percent (25/44) of invasive ductal and 73% (8/11) of invasive lobular carcinomas were evident as nonmass lesions; 54% (7/13) of invasive carcinomas with mixed ductal and lobular features were evident as masses. No T2 signal was present in 61% (27/44) of invasive ductal carcinomas, 73% (8/11) of invasive lobular carcinomas, and 69% (9/13) of mixed invasive ductal and lobular cancer. Forty-five of 68 invasive cancers had associated DCIS. Of these, 44% (20/45) were masses and 56% (25/45) were nonmass lesions. Twenty-two percent (10/45) had a high T2 signal, 13% (6/45) had an intermediate T2 signal, and 65% (29/45) had no associated T2 signal.

The MRI lesion features did not differ as a function of the indication for the initial MRI scan.

Staging

Staging information was available for 56 of 57 patients. Thirty-four (61%) women had stage I disease and 18 (32%) had stage II disease. Four (7%) patients had more advanced disease; one had bone metastases and three had metastatic skin nodules at the time of diagnosis. Eighty-two percent (47/57) of

TABLE 3: MRI Features in 39 Nonmass Lesions

Feature	No. (%) of Lesions
Morphology	
Focal clumped	14 (35)
Regional	11 (28)
Segmental	4 (10)
Linear	4 (10)
Ductal	3 (8)
Multiple regions	3 (8)
Visual kinetics	
Washout	12 (30)
Plateau	26 (67)
Persistent	1 (3)
T2 signal	
High	8 (21)
Intermediate	6 (15)
None	25 (65)
T1 signal	
High	0 (0)
Intermediate	7 (18)
None	32 (82)

TABLE 4: MRI Features as a Function of Invasive Cancer Histology

Feature	No. (%) of Lesions
Invasive ductal carcinoma (n = 44)	
Mass	19 (43)
Nonmass	25 (57)
High T2 signal	10 (23)
Intermediate T2 signal	7 (16)
No T2 signal	27 (61)
Invasive lobular carcinoma (n = 11)	
Mass	3 (27)
Nonmass	8 (73)
High T2 signal	3 (27)
Intermediate T2 signal	0 (0)
No T2 signal	8 (73)
Invasive mammary carcinoma (n = 13)	
Mass	7 (54)
Nonmass	6 (46)
High T2 signal	3 (23)
Intermediate T2 signal	1 (8)
No T2 signal	9 (69)

the women had a known biopsy-proven breast cancer at the time of the MRI-detected

disease. In 11% (6/57), the known cancer was in the contralateral breast. In 47% (32/68) of the lesions, pathology yielded multifocal invasive malignancy.

Discussion

Previous reports have described the MRI patterns associated with breast cancer. Liberman et al. [11] reported that the features with highest likelihood for malignancy include spiculated margin, rim enhancement and irregular shape for masses, and segmental or clumped ductal enhancement for nonmass lesions. Kuhl et al. [7] concluded that a washout (type 3) time–signal intensity curve is a strong independent predictor of malignancy. However, analysis of previous studies is limited by different terminology used to describe MRI patterns. This study was undertaken to describe MRI patterns associated with invasive breast cancer using the BI-RADS lexicon and to quantitate the likelihood of invasive carcinoma associated with the BI-RADS descriptions. This would facilitate communication and comparison of results from different institutions.

Most invasive cancers in our study were evident on MRI as nonmass (57%) rather than mass (43%) lesions and had plateau (59%) versus washout (38%) kinetics (Fig. 5). Among masses, the most common enhancement pattern was heterogeneous (59%) rather than rim (14%) enhancement. A substantial percentage (24%) of these invasive cancers had high T2 signal (Fig. 6), contrary to the findings of Kuhl et al. [12], who reported that high T2 signal is a sign of benign disease; an additional 12% had an intermediate signal on T2 imaging. It is important to know that invasive cancers may have high or intermediate T2 signal, so as not to dismiss such lesions as benign.

Another interesting finding was the total absence of high signal in fat-suppressed un-enhanced T1-weighted images in any of the lesions. Most lesions had no T1 signal at all. To our knowledge, this finding has not been reported in the literature. High signal on un-enhanced T1-weighted images has been observed with hemorrhagic cysts or cysts and ducts with proteinaceous debris. Metastases from melanoma have been reported to have a high signal on T1-weighted images [13].

Our findings show that a high percentage of invasive lobular cancers (73%) manifested as nonmass rather than mass lesions; this finding is concordant with a previous report from Nunes et al. [14]. Otherwise, the results from this study do not show a definite corre-

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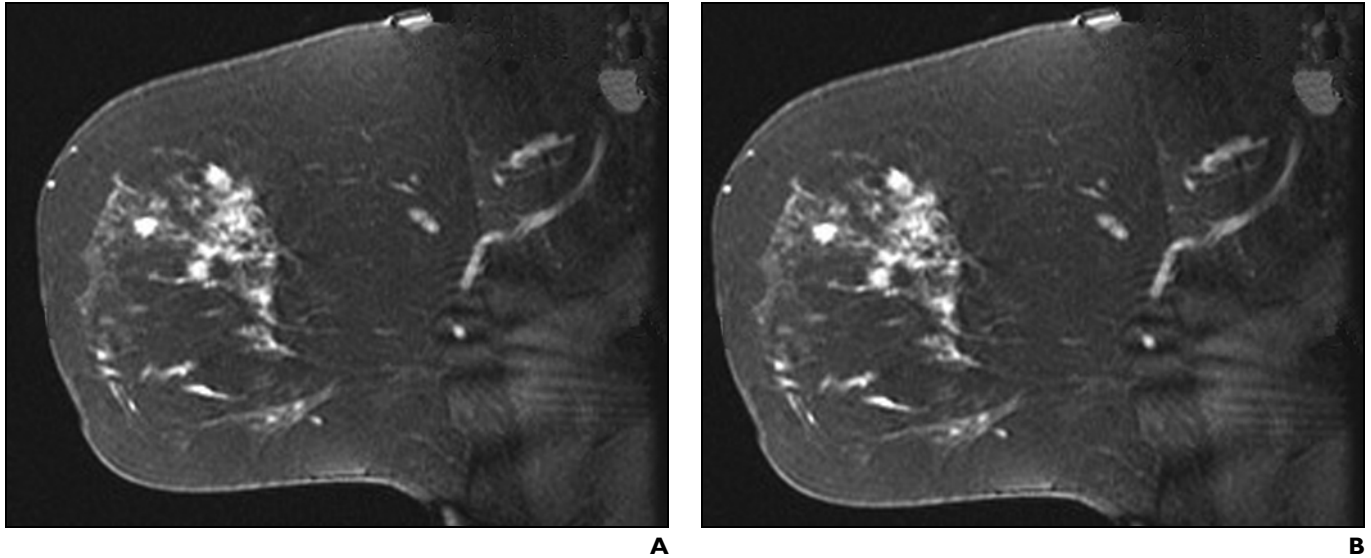


Fig. 5—65-year-old woman presented with palpable right breast cancer.
A, Sagittal T1-weighted MRI of right breast immediately after contrast injection shows suspicious regional clumped enhancement in separate quadrant.
B, Delayed postcontrast image from sagittal T1-weighted MRI of right breast shows plateau kinetics in regional clumped enhancement. Histologic analysis yielded invasive lobular cancer. Patient had right mastectomy.

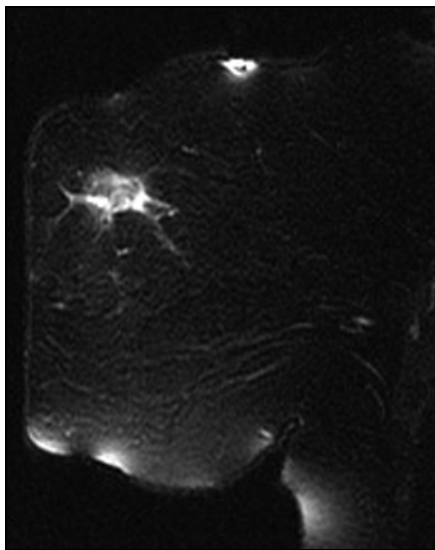


Fig. 6—69-year-old woman with mammographically occult, nonpalpable breast cancer evident as spiculated mass with washout kinetics on MRI T1-weighted images (not shown). Sagittal T2-weighted unenhanced image shows high signal in mass.

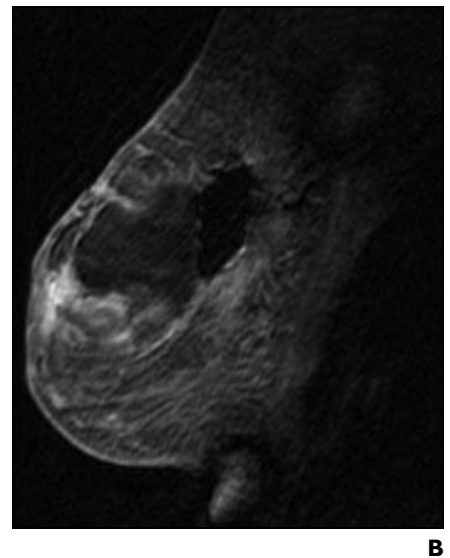
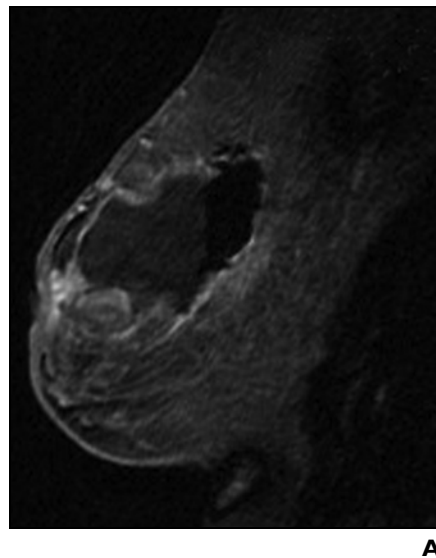


Fig. 7—64-year-old woman 12 days after left lumpectomy for invasive ductal carcinoma with positive surgical margins.
A, Sagittal T1-weighted image from postoperative MRI of left breast immediately after contrast injection shows focal clumped enhancement at anterior aspect of seroma cavity.
B, Delayed contrast-enhanced T1-weighted image from left breast MRI shows clumped enhancement has persistent kinetics. Surgery revealed residual invasive ductal cancer at site.

lation of the MRI characteristics of invasive breast cancers with the histology subtypes, although the number of lesions in specific subgroups is relatively small. Further work with larger numbers of invasive cancers with various histologies is needed for detailed subgroup analysis.

The relative lack of sonographic correlates for these invasive cancers is an important finding. Only 21% of the lesions scanned in our series had a sonographic correlate. Few published data address the frequency of sonographic correlates specifically for invasive breast cancers. In previous reports, the fre-

quency of sonographic correlates for MRI-detected lesions warranting biopsy has ranged from 23–100% [15–17]. LaTrenta et al. [17] found that in the cancers with a sonographic correlate, 78% were invasive and 22% were DCIS; in the cancers without a sonographic correlate, 50% were invasive and 50% were

DCIS. The absence of a sonographic correlate for MRI-detected invasive breast cancers in our series stresses the need for facilities performing breast MRI to have the capacity for MRI-guided localization and biopsy.

Our study has several limitations. This is a retrospective study. Eighty-two percent of the patients had a concurrent biopsy-proven cancer and had undergone breast MRI for extent of disease assessment. These MRI-detected cancers were nonpalpable and mammographically occult, but 83% of the women had dense or heterogeneously dense breasts on mammography (classes 3 and 4). Because the study included only invasive cancers, the data address the prevalence of specific MRI features in invasive cancers but do not address the positive predictive value of different features. Issues of cost effectiveness, interobserver variability, and long-term outcome are not addressed.

In conclusion, among our patients, most mammographically occult, nonpalpable invasive breast cancers identified on MRI were nonmass lesions (57%) and were minimal breast cancers (63%). A high T2 signal, lack of a sonographic correlate, lack of T1 precontrast signal, and heterogeneous, plateau enhancement are features that should not be dismissed when encountered. Use of BI-RADS lexicon descriptors should facilitate comparison of our results with future studies. Further work is necessary to evaluate the positive predictive value of MRI features, to determine if MRI features are predictive of cancer type or histology, and

to assess the long-term outcome in women with breast cancers detected by MRI.

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