

# Imaging Appearance and Clinical Impact of Preoperative Breast MRI in Pregnancy-Associated Breast Cancer

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**OBJECTIVE.** The purpose of this study is to describe the imaging features of pregnancy-associated breast cancer (PABC) on breast MRI and to consider the impact of preoperative MRI on patient management.

**MATERIALS AND METHODS.** A retrospective review of medical records from January 1994 to May 2014 identified 183 women who presented with a new diagnosis of breast cancer during pregnancy or within 1 year postpartum. MR images were available for 53 of these patients, all of whom were included in the study. Clinical history and available breast images were reviewed. The clinical impact of preoperative breast MRI was also recorded.

**RESULTS.** Of the 53 women, nine (17%) presented during pregnancy and 44 (83%) presented during the first year postpartum. The sensitivity of MRI was 98% (52/53). Among the 53 patients, the most common findings of PABC on MRI included a solitary mass (29 patients [55%]), nonmass enhancement (12 patients [23%]), and multiple masses (eight patients [15%]). For 12 patients (23%), MRI showed a pathologically proven larger tumor size or greater extent of disease than did mammography or ultrasound, with an additional eight patients (15%) having findings suspicious for greater extent of disease but having unavailable pathologic data. Breast MRI changed surgical management for 15 patients (28%), with four patients (8%) requiring a larger lumpectomy, seven (13%) no longer being considered candidates for lumpectomy, two (4%) having contralateral disease, and two (4%) having unsuspected metastasis.

**CONCLUSION.** Breast MRI had a high sensitivity for PABC in our study population. MRI may play an important role in PABC because it changed the surgical management of 28% of patients.

**P**regnancy-associated breast cancer (PABC), defined as breast cancer occurring during pregnancy or within 1 year of delivery, fortunately is rare, occurring in one in 3000–10,000 pregnancies [1–3]. However, when PABC does occur, it is often associated with an increased rate of recurrence and death, compared with age- and stage-matched cancers [4, 5].

Women with PABC usually are seen with a palpable breast mass at presentation, at which time breast imaging helps to differentiate potential cancers from other benign processes [6]. The mammographic and sonographic appearance of PABC has been described elsewhere [7–11], with palpable masses the most common finding observed on both mammography and ultrasound. The reported sensitivity of mammography for these cancers ranges from 78% to 100%, with most studies reporting a sensitivity of ultrasound of 100%.

It is commonly believed that breast MRI would be of limited clinical usefulness in the evaluation of PABC because of the hormonal changes in this patient population and because of associated pronounced background parenchymal enhancement [12]. However, to our knowledge, only one small study ( $n = 5$ ) has investigated the use of breast MRI in this population, showing that MRI successfully detected cancer in all five patients [13]. To our knowledge, no study to date has investigated the role of preoperative MRI in this population, although preoperative MRI is reported to affect the clinical management of 10–34% of breast cancers that are not pregnancy-associated [14–18]. Because pregnancy-associated cancers are often aggressive, it may be especially important to accurately define the extent of disease in this population at presentation [4, 5].

The aim of this study is to describe the appearance of PABC on breast MRI and to

**TABLE 1: Risk Factors for Breast Cancer in 53 Women**

Risk Factor for Breast Cancer	Value
Family history, no. (%) of patients	12 (23)
First-degree premenopausal woman	6
First-degree postmenopausal woman	6
First-degree man	0
Genetic risk, no. (%) of patients <sup>a</sup>	12 (32)
<i>BRCA1</i> -positive status	7
Known before cancer diagnosis	1
Found after cancer diagnosis	6
<i>BRCA2</i> -positive status	4
Known before cancer diagnosis	1
Found after cancer diagnosis	3
Mutation in <i>BRCA2</i> gene of uncertain significance	1
Known before cancer diagnosis	0
Found after cancer diagnosis	1
Negative for <i>BRCA1</i> and <i>BRCA2</i>	26
Known before cancer diagnosis	5
Found after cancer diagnosis	21
History of mantle radiation	0
History of high risk breast lesion	0

Note—Except where otherwise indicated, data are the number of patients.

<sup>a</sup>Genetic data were available for only 38 of 53 patients.

**TABLE 2: Presentation of 53 Patients With Pregnancy-Associated Breast Cancer and Available Pretreatment Breast MR Images**

Characteristic	No. (%) of Patients
Timing of presentation	
During pregnancy	9 (17)
First trimester	5 (9)
Second trimester	0 (0)
Third trimester	4 (8)
Within 1 year postpartum	44 (83)
Lactating	24 (45)
Not lactating	12 (23)
Unknown whether lactating	8 (15)
Presenting sign or symptom <sup>a</sup>	
Palpable abnormality	45 (84)
Redness and swelling	1 (2)
Incidental finding during workup of another finding	1 (2)
Pain	2 (3)
Induration	1 (2)
Finding on routine screening mammography	1 (2)
Patient “felt different”	1 (2)
Nipple discharge	1 (2)
Finding on routine screening MRI	1 (2)

<sup>a</sup>Please note that percentages do not total 100% because of rounding.

consider the impact of preoperative MRI on patient management.

## Materials and Methods

This HIPAA-compliant study was approved by the institutional review board at the Memorial Sloan-Kettering Cancer Center. The need for informed consent was waived. A retrospective review of medical records from January 1994 to May 2014 identified 187 PABCs in 183 women at Memorial Sloan-Kettering Cancer Center. PABC was defined as breast cancer occurring during pregnancy or within 1 year of delivery. Fifty-three of the women who were identified had available MR images and were included in the study. The breast MRI technique and imaging protocol used were variable because many patients were referred to our institution after undergoing MRI at another facility. All studies included at least three contrast-enhanced series. Additional specifics regarding imaging technique, such as in-plane resolution and slice thickness, were largely unavailable.

Clinical history was recorded, including information on risk factors for breast cancer, tumor type, receptor status, stage, treatment, and disease status at clinical follow-up. Data regarding tumor type and size were extracted from the surgical pathology reports. Breast imaging was reviewed by a single reader who was blinded to the outcomes. The reader recorded imaging descriptors in accordance with the BI-RADS lexicon. If preoperative breast MRI was performed, the clinical impact of MRI on the basis of the original interpretation was also recorded. All patients who received neoadjuvant chemotherapy underwent MRI before treatment. Descriptive statistics were calculated.

## Results

### Clinical Information

The study population consisted of 53 women with PABC who had breast MR images available for review. The mean ( $\pm$  SD) patient age at presentation was  $36 \pm 3.5$  years (range, 29–43 years). Most patients had no known risk factors for breast cancer (Table 1). Most women (45/53 [85%]) presented with a palpable abnormality during their first year postpartum (Table 2). Although nine patients were pregnant at the time of diagnosis, all nine underwent a postpartum MRI examination before receiving treatment (four patients presented late in the third trimester and had delivery induced before undergoing MRI, and five patients received a diagnosis in the first trimester and terminated the pregnancy before undergoing MRI).

Most cancers (52/53; 98%) were invasive ductal carcinoma, and their receptor status is

## Pregnancy-Associated Breast Cancer on Preoperative Breast MRI

**TABLE 3: Surgical Pathologic Finding and Clinical Stage of 53 Patients With Pregnancy-Associated Breast Cancer and Available Pretreatment Breast MR Images**

Pathologic Finding	No. (%) of Patients
Tumor type ( <i>n</i> = 53)	
Invasive ductal carcinoma	52 (98)
Invasive lobular carcinoma	1 (2)
Histologic grade ( <i>n</i> = 50) <sup>a</sup>	
Grade 2	5 (10)
Grade 3	45 (90)
Receptor status ( <i>n</i> = 51) <sup>b</sup>	
Luminal A	25 (49)
Luminal B	8 (16)
Positive ErbB-2 (also known as HER2/neu) status	6 (12)
Basallike (triple negative)	12 (23)
Clinical stage ( <i>n</i> = 52) <sup>c</sup>	
IA	8 (15)
IB	1 (2)
IIA	17 (33)
IIB	10 (19)
IIIA	8 (15)
IIIB	2 (4)
IIIC	3 (6)
IV	3 (6)

<sup>a</sup>Histologic grade data were unavailable for three of 53 cancers.

<sup>b</sup>Receptor status data were unavailable for two of 53 cancers.

<sup>c</sup>Clinical stage data were unavailable for one of 53 patients.

presented in Table 3. Of the 52 patients for whom the clinical PABC stage was known, nine (17%) had stage I PABC, 27 (52%) had stage II, 13 (25%) had stage III, and three (6%) had stage IV. For the 13 patients (25%) who received neoadjuvant chemotherapy, only the pretreatment images were reviewed. The mean follow-up was 2.9 years (range, 3 months to 12.8 years). At follow-up, 45 of 53 patients (85%) were without evidence of disease, seven (13%) were alive with disease, and one (2%) was deceased.

### MRI Appearance of Pregnancy-Associated Breast Cancer

MR images were available for 53 patients. The sensitivity of MRI in the study population was 98% (52 of 53 patients), with one cancer not visualized in a patient for whom MRI showed marked background enhancement. For the 52 patients with cancer identified on MRI, the mean size of abnormal enhancement was 5.5 ± 3.0 cm (range, 1.0–13.0 cm). Most patients (49/53 [92%]) had heterogeneous or extreme fibroglandular tissue, al-

though background parenchymal enhancement was more evenly distributed between minimal (8/53 [15%]), mild (14/53 [26%]), moderate (17/53 [32%]), and marked (14/53 [26%]) enhancement (Table 4). At the time MRI was performed, all patients had already delivered or undergone elective abortion, but it is unknown how many patients were lactat-

ing at the time of the examination. The most common MRI appearance of PABC in the study population was a mass (29/53 [55%]), with 18 of 29 masses (62%) having an irregular shape and 19 (66%) having irregular margins (Table 4).

Images obtained using three modalities (mammogram, ultrasound, and MRI) were available for 33 patients. Within this group, the sensitivity of mammography, ultrasound, and MRI for detection of the index lesion was 91% (30/33), 100% (33/33), and 97% (32/33), respectively. For these 33 patients, mammography most often showed unicentric disease, whereas MRI often showed multicentric disease not seen on mammography or ultrasound (Fig. 1).

### Impact of Breast MRI

**Overview**—Preoperative breast MR images were available for 53 patients. For 29 of these patients (55%), MRI showed findings suspicious of a larger tumor size or greater extent of disease than seen that seen on mammography or ultrasound. Core biopsy or surgical pathologic findings were available for 21 of the 29 patients (72%) with suspicious MRI findings. Specifically, of the 29 patients with additional suspicious findings on MRI, 10 had such findings were confirmed by MRI-guided biopsy, four by ultrasound-guided biopsy, and seven by surgical excision. Therefore, of the 53 patients who underwent breast MRI, 12 (23%) were found to have a pathologically proven greater extent of disease, eight (15%) had MRI findings suspicious for greater extent of disease but had no direct pathologic findings available, nine (17%) had MRI findings that were suspicious for disease but were found to be benign on pathologic analysis,

**TABLE 4: MRI Appearance of Pregnancy-Associated Breast Cancer (PABC)**

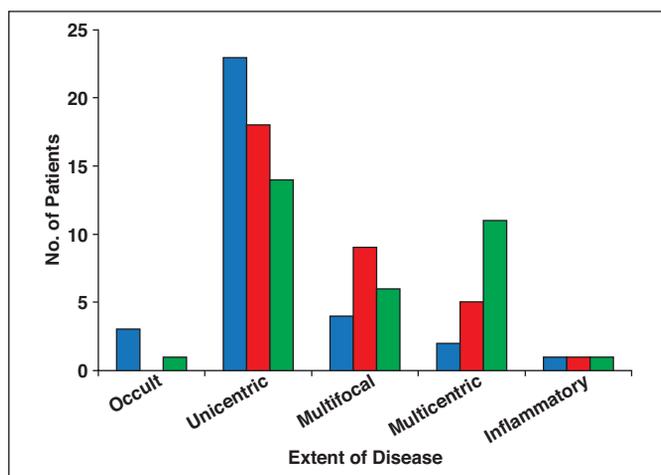
MRI Characteristic	No. (%) of Patients
Amount of fibroglandular tissue ( <i>n</i> = 53)	
Predominantly fatty	0 (0)
Scattered fibroglandular tissue	4 (8)
Heterogeneous fibroglandular tissue	17 (32)
Extreme fibroglandular tissue	32 (60)
Background parenchymal enhancement ( <i>n</i> = 53)	
Minimal	8 (15)
Mild	14 (26)
Moderate	17 (32)
Marked	14 (26)

(Table 4 continues on next page)

**TABLE 4: MRI Appearance of Pregnancy-Associated Breast Cancer (PABC) (continued)**

MRI Characteristic	No. (%) of Patients
Dominant finding of PABC ( <i>n</i> = 53)	
Mass	29 (55)
Nonmass enhancement	12 (23)
Mass with nonmass enhancement	3 (6)
Multiple masses	8 (15)
Occult	1 (2)
Mass characteristics on MRI ( <i>n</i> = 37)	
Shape	
Oval	6 (16)
Round	9 (25)
Irregular	22 (59)
Margin	
Circumscribed	2 (5)
Irregular	25 (68)
Spiculated	10 (27)
Enhancement pattern	
Homogeneous	11 (30)
Heterogeneous	18 (49)
Rim enhancing	8 (21)
Nonmass enhancement characteristics on MRI ( <i>n</i> = 15)	
Distribution	
Focal	2 (13)
Linear	1 (7)
Segmental	4 (26)
Regional	7 (47)
Diffuse	1 (7)
Enhancement pattern	
Homogeneous	6 (40)
Heterogeneous	2 (13)
Clumped	5 (34)
Clustered ring enhancement	2 (13)

Note—MR images were available for 53 patients.



**Fig. 1**—Extent of disease as detected by imaging modality. Bar graph shows that, for 33 patients for whom mammography (blue bars), ultrasound (red bars), and MR (green bars) images were all available for review, mammography was more likely to show unifocal disease, whereas MRI often revealed suspicion for multicentric disease.

and 24 (45%) had MRI show an extent of disease similar to that shown by mammography and ultrasound.

*Extent of disease shown by MRI*—For 11 of 53 patients (21%), breast MRI showed findings suspicious of tumor size at least 1 cm larger than was expected on the basis of mammography and ultrasound findings. This suspicion of a larger tumor size was pathologically proven for five of 11 patients (45%) and was shown by pathologic analysis to be a false-positive finding in two of 11 patients (18%). Pathologic analysis was not available for four of 11 patients (36%) who received neoadjuvant chemotherapy.

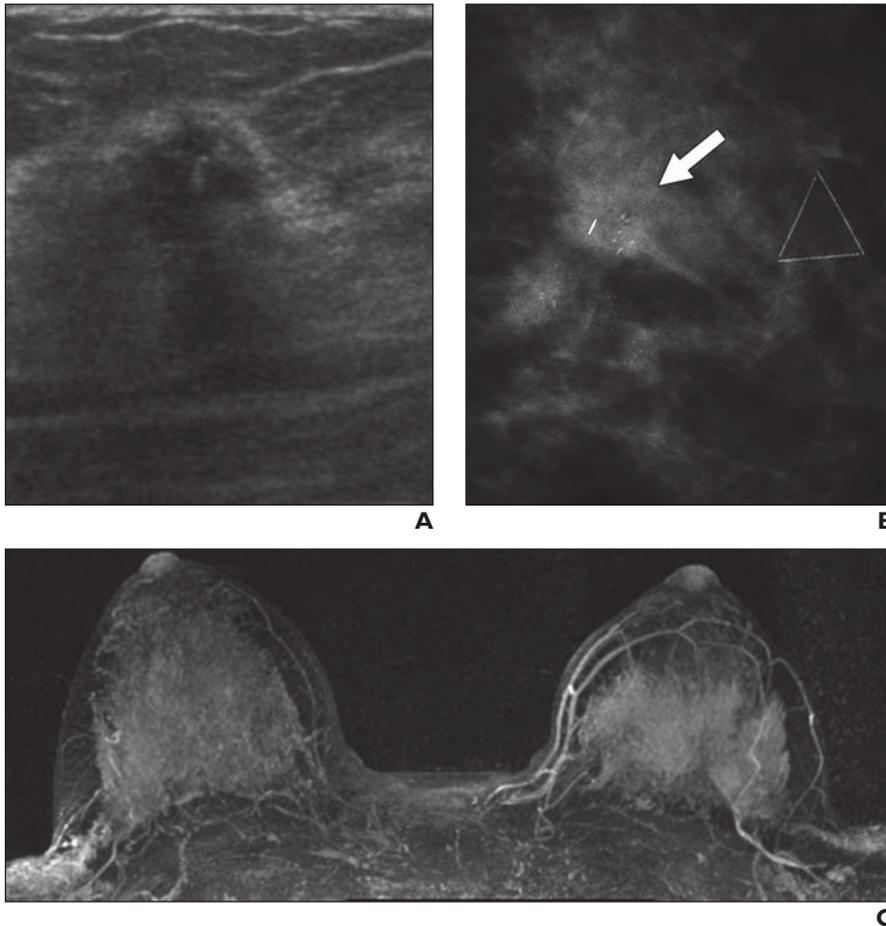
MRI revealed findings suspicious for new multicentric disease in nine of 53 patients (17%) (Fig. 2), although direct pathologic analysis of the MRI finding was available for only five of these nine patients (56%).

Overall, of the 53 patients, three (6%) were found to have unsuspected pathologically proven multicentric disease, four (8%) had MRI findings suspicious for multicentric disease but did not have available pathologic data for correlation, and two (4%) had MRI findings suspicious for multicentric disease but with pathologic results indicating that disease was benign. Direct pathologic analysis was not available for four patients: pathology reports described additional ductal carcinoma in situ without a specified location in three of four patients (75%), which limited comparison with MRI findings, and one of four patients (25%) was found to have distant metastatic disease after breast MRI examination and did not undergo further biopsy or receive local therapy.

MRI findings suspicious for unsuspected contralateral disease were seen in seven of 53 patients (13%). Core biopsy was performed for all seven patients, with a result indicating malignancy noted for two patients (29%). Therefore, among the 53 patients who underwent preoperative breast MRI, unsuspected contralateral disease was diagnosed in two (4%) (Fig. 3). In two patients (4%), breast MRI findings prompted additional workup that resulted in the diagnosis of unsuspected distant metastasis.

*Additional interventions resulting from MRI*—Of the 53 patients who underwent preoperative breast MRI, 12 (23%) underwent additional core biopsy, with five of the 12 patients (42%) undergoing core biopsy of the breast ipsilateral to the known cancer and with seven (58%) undergoing core biopsy in the contralateral breast. Biopsy findings were positive for malignancy in two of five specimens (40%) from the ipsilateral breast and in two of seven specimens (29%) from the contralateral breast, for an

## Pregnancy-Associated Breast Cancer on Preoperative Breast MRI



**Fig. 2**—33-year-old woman with new diagnosis of left breast cancer who presented with palpable abnormality in left breast during first trimester of pregnancy.

**A**, Ultrasound image shows palpable mass. Ultrasound-guided biopsy yielded diagnosis of invasive ductal carcinoma.

**B**, Mammogram shows asymmetry and pleomorphic calcifications (*triangle* denotes palpable skin marker, which is included in FOV spanning 2.7 cm (*arrow*)).

**C**, Maximum-intensity-projection image from breast MRI performed 2 weeks after patient chose to terminate her pregnancy shows extensive nonmass enhancement involving most of upper left breast. Patient underwent mastectomy, which yielded multicentric disease.

overall positive predictive value 3 (i.e., the percentage of all known biopsies done as a result of positive diagnostic examinations [BI-RADS categories 4 and 5] that resulted in a tissue diagnosis of cancer within 1 year) of 33% (4/12). MRI-guided biopsy was recommended for one additional patient but was cancelled on the day of biopsy because of nonvisualization. This patient underwent prophylactic contralateral mastectomy with benign surgical pathologic findings. Overall, breast MRI changed the surgical management of 15 of 53 patients (28%) (Fig. 4). Of the 53 patients, four (8%) required a larger lumpectomy, seven (13%) were no longer considered candidates for lumpectomy, two (4%) had contralateral disease, and two (4%) had unsuspected metastasis.

### Discussion

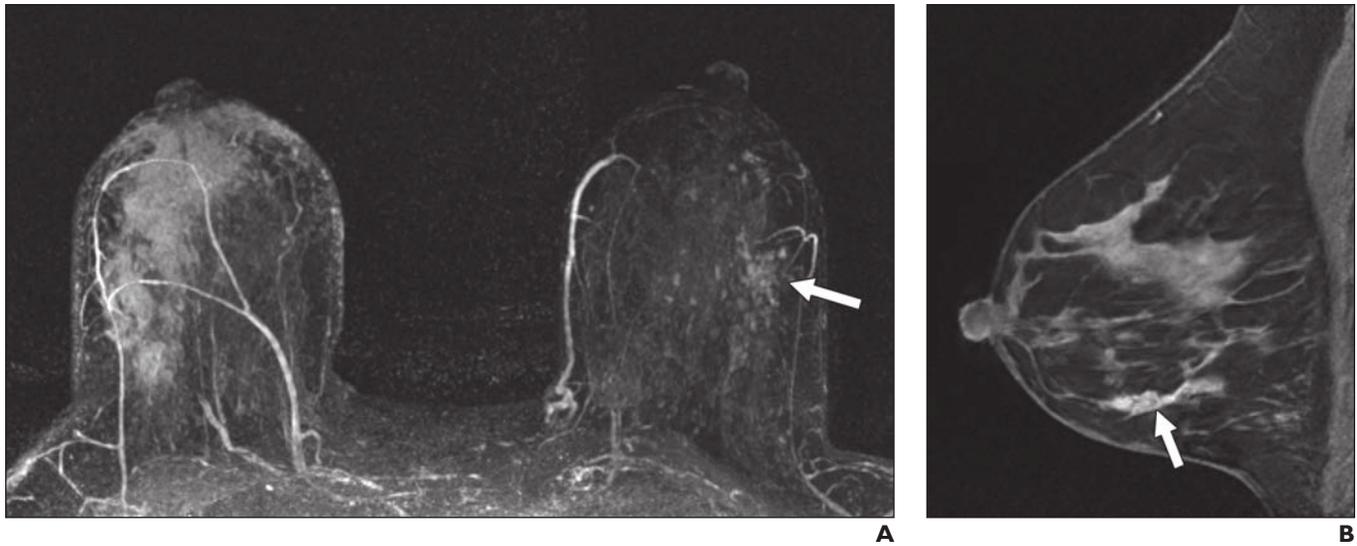
PABC fortunately is rare, although when it does occur it is often aggressive, with some studies suggesting poorer outcomes than those noted for age- and stage-matched control subjects [4, 5, 19, 20]. In our study population, most women had no known risk factors at the time of diagnosis, with only 23% having a family history of breast cancer in a first-degree relative and with only two patients (4%) known to be carriers of the *BRCA* mutation. These findings may emphasize the role of imaging in the workup of a palpable abnormality in a pregnant or postpartum patient, because clinical history may not reliably indicate the risk of breast cancer in this population.

In our study population of 53 women, most patients presented with a palpable ab-

normality, confirming the findings of previous reports [8, 9, 19]. The most common abnormality was invasive ductal carcinoma, with more than half of the cancers showing a positive hormone receptor status, which is also similar to the findings of previous studies [5, 8, 19, 20]. A recent meta-analysis of PABC reported that invasive lobular carcinoma is the tumor type in 2.4–7% of all PABCs [3]. In our study, although only one of 53 tumors (1.9%) was found to be invasive lobular carcinoma, this finding was just below the reported range, with the small number of invasive lobular carcinomas possibly resulting from the relatively small sample size.

To our knowledge, only one small study to date has reported the appearance of PABC on MRI, and that study reported findings for only five patients [13]. The present study of 53 patients with pregnancy-associated breast cancer who underwent breast MRI therefore is, to our knowledge, the largest such study to date. Despite most patients having moderate (32%) or marked (26%) background parenchymal enhancement, breast MRI had a very high sensitivity of 98%. Although the one cancer that was identified by MRI as occult disease indeed occurred in a patient with marked background parenchymal enhancement, the overall high sensitivity noted in our study challenges the common assumption that background parenchymal enhancement would limit the utility of breast MRI in this population. Similar to findings observed on mammography and ultrasound, the most common finding seen on breast MRI was a solitary mass (55%), although a significant number of cancers (23%) presented as non-mass enhancement on MRI.

Preoperative breast MRI had a large impact on clinical management in our study population. Twenty-three percent of patients were found to have a pathologically proven greater extent of disease, and an additional 15% of patients had MRI findings suspicious for a greater extent of disease but had no direct pathologic data available. Specifically, findings suspicious for new multicentric disease were confirmed pathologically in three of 53 patients (5.7%) and were suspected but not confirmed in an additional four patients (8%). New contralateral disease was found in two of 53 patients (4%). These findings are similar to those noted in previous studies of patients with non-pregnancy-associated cancers [21], which suggests that a pregnancy-associated state does not significantly affect the ability of breast MRI to detect additional unsuspected disease. Fur-



**Fig. 3**—40-year-old woman with new diagnosis of right breast cancer who presented with right breast redness and swelling 5 months postpartum while lactating. Mammography and ultrasound detected inflammatory right breast cancer (not shown).

**A and B**, Maximum-intensity-projection image (**A**) and left breast sagittal contrast-enhanced T1-weighted MR image (**B**) show known multicentric inflammatory right breast cancer (*arrow, A*) and left breast nonmass enhancement (*arrow, B*) in linear distribution. MRI-guided biopsy of left breast yielded diagnosis of ductal carcinoma in situ.

thermore, the positive predictive value 3 in our study was high (33%), implying an acceptable false-positive rate even in the setting of potentially increased background parenchymal enhancement in this population.

Overall, surgical management was changed for 28% of patients. For non-PBAC, previous studies have reported MRI to change surgical management for 10–34% of patients [14–17], and therefore MRI may have at least as great an impact for PABC as it does for non-PBAC. Our findings challenge the common assumption that background parenchymal enhancement in patients with PABC would limit the utility of preoperative breast MRI.

Unique safety concerns exist regarding MRI and administration of IV gadolinium during pregnancy and lactation. Although, in general, unenhanced MRI examinations may

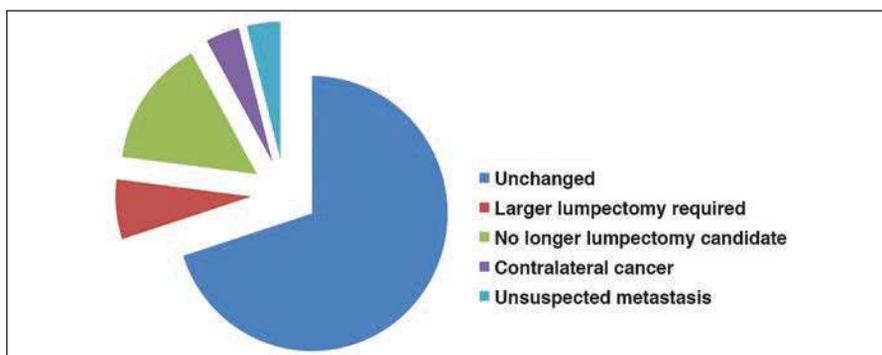
be considered for pregnant patients if the benefits outweigh the risks [22], breast MRI for the evaluation of breast cancers requires administration of IV gadolinium-based contrast medium, which is not recommended during pregnancy because of insufficient safety data [22, 23]. Breast MRI performed with an IV gadolinium-based contrast medium is safe during lactation, however. Less than 0.04% of the administered gadolinium will be excreted into the breast milk, and less than 1% of this will be absorbed by the gastrointestinal tract of the infant [24–26]. It is therefore acceptable for a lactating patient to continue breastfeeding after receiving IV gadolinium. Nonetheless, if a patient is concerned about her infant's exposure to this very small amount of gadolinium, the milk may be discarded for up to 24 hours.

The present study markedly expands on the current literature regarding breast MRI for patients with PABC, with only five patients previously reported in the literature. Although, to our knowledge, the present study is the largest series of breast MRI examinations performed in the setting of PABC, our sample size is still small, including only 53 patients. Other limitations include a lack of data regarding the timing of the breast MRI in relation to the cessation of lactation, which could potentially impact the sensitivity of MRI. Pathologic confirmation of MRI findings was not always available, because some patients received neoadjuvant chemotherapy, underwent mastectomy, or both, therefore foregoing additional tissue sampling.

Preoperative planning is especially important for patients with PABC because of the often aggressive nature of these cancers. In contrast to the previous assumption that breast MRI would be of limited utility in this population, we found that it showed a pathologically proven larger tumor size or greater extent of disease in 23% of patients (with suspicious findings noted but pathologic findings unavailable for an additional 15% of patients). In addition, MRI changed the surgical management of 28% of postpartum patients with PABC. Breast MRI may play an important role the management of PBAC.

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**Fig. 4**—Pie chart shows change in surgical management resulting from breast MRI findings. Of 53 patients who underwent preoperative breast MRI examination, surgical management changed for 28%.

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