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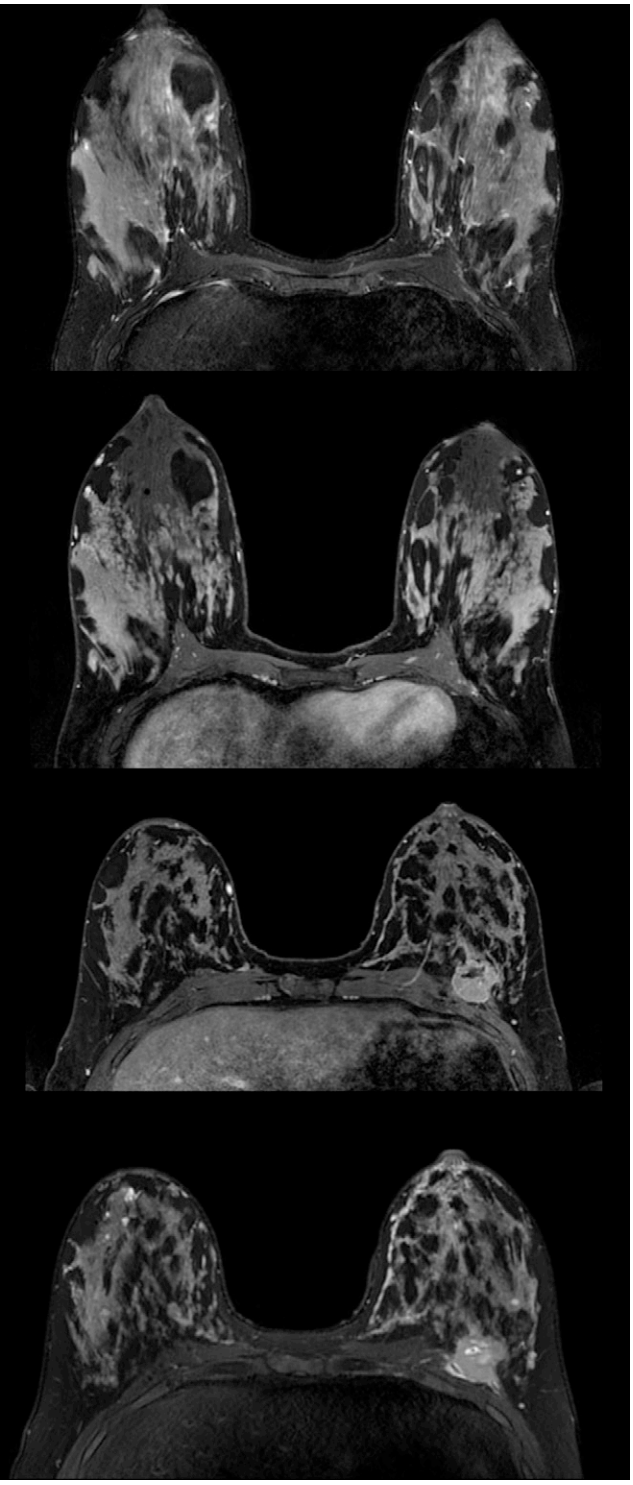
See the invited commentary by Chikarmane in this issue.



The breasts undergo marked physiologic changes during lactation that can make conventional imaging evaluation with mammography and US challenging. MRI can be a valuable diagnostic aid to differentiate physiologic and benign processes from malignancy in patients who are lactating. In addition, MRI may allow more accurate delineation of disease involvement than does conventional imaging and assists in locoregional staging, screening of the contralateral breast, assessment of response to neoadjuvant chemotherapy, and surgical planning. Although the American College of Radiology recommends against patients undergoing contrast-enhanced MRI during pregnancy because of fetal safety concerns, contrast-enhanced MRI is safe during lactation. As more women delay childbearing, the incidence of pregnancy-associated breast cancer (PABC) and breast cancer in lactating women beyond the 1st year after pregnancy is increasing. Thus, MRI is increasingly being performed in lactating women for diagnostic evaluation and screening of patients at high risk. PABC is associated with a worse prognosis than that of non-PABCs, with delays in diagnosis contributing to an increased likelihood of advanced-stage disease at diagnosis. Familiarity with the MRI features of the lactating breast and the appearance of various pathologic conditions is essential to avoid diagnostic pitfalls and prevent delays in cancer diagnosis and treatment. The authors review clinical indications for breast MRI during lactation, describe characteristic features of the lactating breast at MRI, and compare MRI features of a spectrum of benign and malignant breast abnormalities.

Introduction

Marked physiologic changes in the lactating breast can make conventional imaging evaluation with mammography and US challenging. MRI is increasingly recognized as a safe and effective supplemental tool for both screening and diagnostic evaluation of women who are lactating, in the appropriate clinical setting. Familiarity with characteristic MRI features of benign and malignant pathologic conditions that may be encountered during lactation can help to minimize delays in diagnosis and management. This article reviews clinical indications for breast MRI during lactation, describes characteristic features of the lactating breast at MRI, and compares MRI features of a broad spectrum of benign and malignant conditions using case examples and clinical scenarios. Special considerations in the approach to percutaneous biopsy are also discussed.

Clinical Indications for Breast MRI during Lactation

Breast MRI can be performed during lactation for a variety of clinical indications. Supplemental screening MRI can be considered in women at high risk of cancer who are planning to breastfeed for an extended period of time (1). In the diagnostic setting, breast MRI can be performed to evaluate suspicious symptoms that are unexplained at mammography or US; the locoregional extent of disease in patients with newly diagnosed breast cancer; the response to neoadjuvant

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Abbreviations: ACR = American College of Radiology, BI-RADS = Breast Imaging Reporting and Data System, BPE = background parenchymal enhancement, GBCA = gadolinium-based contrast agent, NCCN = National Comprehensive Cancer Network, PABC = pregnancy-associated breast cancer

TEACHING POINTS

- PABC is associated with a worse prognosis compared with that of non-PABCs, which can, in part, be attributed to its more aggressive tumor biology. Another important driver of the poor prognosis is that difficulty in distinguishing PABC from physiologic lactational changes at clinical and imaging evaluation can result in delays in the diagnosis of PABC.
- Expected changes during pregnancy and lactation such as an increase in breast size and nodularity may mask pathologic changes.
- The most common finding of PABC is a mass lesion that enhances more rapidly and intensely than does the normal breast parenchyma and is most conspicuous during the initial postcontrast phase. Delayed washout of contrast material is also commonly observed.
- A distinct feature of PABC is its more marked hypointensity at T2-weighted MRI relative to the surrounding breast parenchyma, which is T2 hyperintense due to lactational change. Therefore, T2-weighted MRI may be helpful for tumor delineation in some cases.
- The MRI appearance of PABC may reflect the breast cancer subtype, as has been described in nonlactating patients.

chemotherapy; and cases of discordant benign results from US, stereotactic, or palpation-guided biopsy (1–3).

MRI Safety

The safety considerations for breast MRI during pregnancy and lactation primarily relate to the effects of gadolinium-based contrast agents (GBCAs) on the fetus or breastfeeding infant. GBCAs are known to cross the placenta and enter the fetal circulation, upon which gadolinium may dissociate from the ligand and be retained as free gadolinium, which can be toxic. The American College of Radiology (ACR) recommends against the routine use of GBCAs in pregnant women (1). Although the ACR acknowledges that there is uncertainty regarding the risk of GBCA administration during pregnancy due to limited evidence, they have chosen to err on the side of caution, citing a retrospective study (4) describing an increased risk of stillbirth and neonatal death as well as rheumatologic, inflammatory, and infiltrative skin conditions after fetal exposure to GBCA. During lactation, GBCA is considered safe to administer because less than 0.04% of the maternal administered dose is excreted into breast milk in the first 24 hours, and subsequently, the amount absorbed by the infant is less than 1% of the permitted dose for neonates (5). The ACR Manual on Contrast Media (6) states that it is safe to continue breastfeeding after administration of GBCA. If a lactating woman remains concerned about potential adverse effects to the infant, she can consider discarding expressed breast milk for 12–24 hours after receiving a GBCA (6).

Physiologic Lactational Changes Demonstrated at MRI

During pregnancy and lactation, the breasts undergo marked physiologic changes that may affect clinical and radiologic evaluation (Fig 1). As early as the first trimester of pregnancy, the ductal system of the breast proliferates in response to increasing estrogen levels. Lobules proliferate and the breast enlarges secondary to an increase in progesterone. As hormone levels increase, the ducts and lobules begin to replace the adipose tissue, resulting in increased breast density at imaging. As patients enter the third trimester, the acini fill with colostrum, which starts to fill and expand the ducts. A few days after birth, the hormone oxytocin results in rapid milk production (7,8).

The physiologic changes in the secretory state directly correlate with MRI findings in the lactating breast. Formation of new ducts and lobular hyperplasia manifest as increased breast size, increased fibroglandular tissue, and decreased adipose tissue at imaging (9). Increased vascularity leads to increased background parenchymal enhancement (BPE), with a fast initial and delayed plateau enhancement curve (9,10). In addition, formation of milk causes diffusely increased T2 signal intensity and decreased T1 signal intensity at MRI, with ductal hyperintensity corresponding to the fat and protein in breast milk. At diffusion-weighted MRI, the apparent diffusion coefficient in lactating breasts has been found to be lower compared with normal values in premenopausal, nonlactating healthy breasts, which is thought to be related to increased viscosity from lipid-rich milk (11,12). The breasts return to their baseline state approximately 3 months after cessation of lactation.

Although lactational changes are typically symmetric, they can be asymmetric due to lactation pattern or treatment changes. For example, breastfeeding exclusively from one side may cause asymmetrically increased size, density, and BPE on that side (13,14). In addition, radiation treatment causes lobular atrophy, vascular changes, and fibrosis, which may result in the appearance of asymmetric lactational changes (Fig 2) that only involve the untreated breast (15). More uncommonly, focal lactational change occurs after mastectomy if there is residual breast tissue that undergoes lactational change (16), a manifestation that can clinically and radiologically mimic recurrent malignancy (Fig 3).

Benign Abnormalities of the Lactating Breast

Galactocele

Galactoceles are the most common benign lesions in lactating women (17). They represent milk retention cysts caused by ductal obstruction and contain variable amounts of fat, protein, lactose, and water. Patients typically present with a painless, slow-growing, palpable mass during the third trimester of pregnancy, during lactation, or after cessation of lactation. At imaging, a galactocele appears as a round or oval circumscribed mass with a homogeneous or heterogeneous appearance, depending on the relative amounts of fluid and solid milk contents (11,18). Although it is not always seen, a fat-fluid level due to separation of milk and water in breast

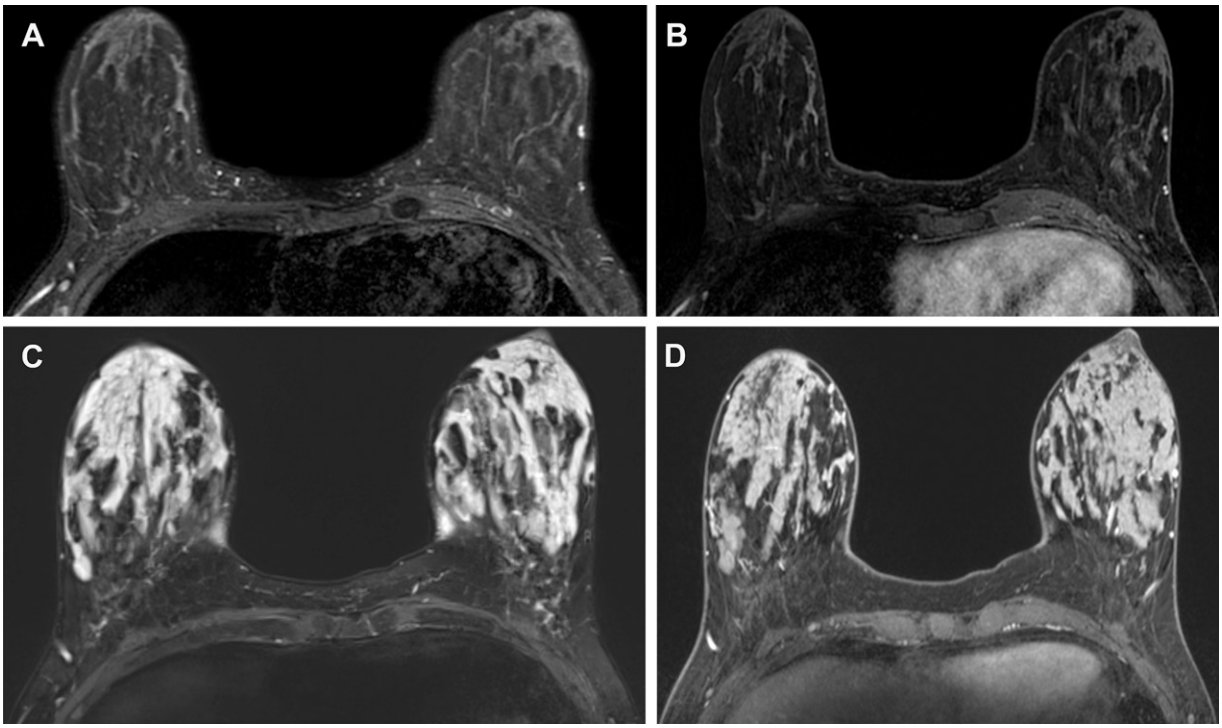


Figure 1. Pregnancy- and lactation-related changes in a 38-year-old woman with a *BRCA1* mutation. **(A, B)** Prepregnancy axial T2-weighted **(A)** and T1-weighted initial postcontrast **(B)** screening MR images show heterogeneous fibroglandular tissue **(A)** and mild BPE **(B)**. **(C, D)** Axial T2-weighted **(C)** and T1-weighted postcontrast **(D)** MR images acquired 1 year later while the patient was lactating show extreme fibroglandular tissue with diffusely increased signal intensity **(C)** and marked BPE **(D)**.

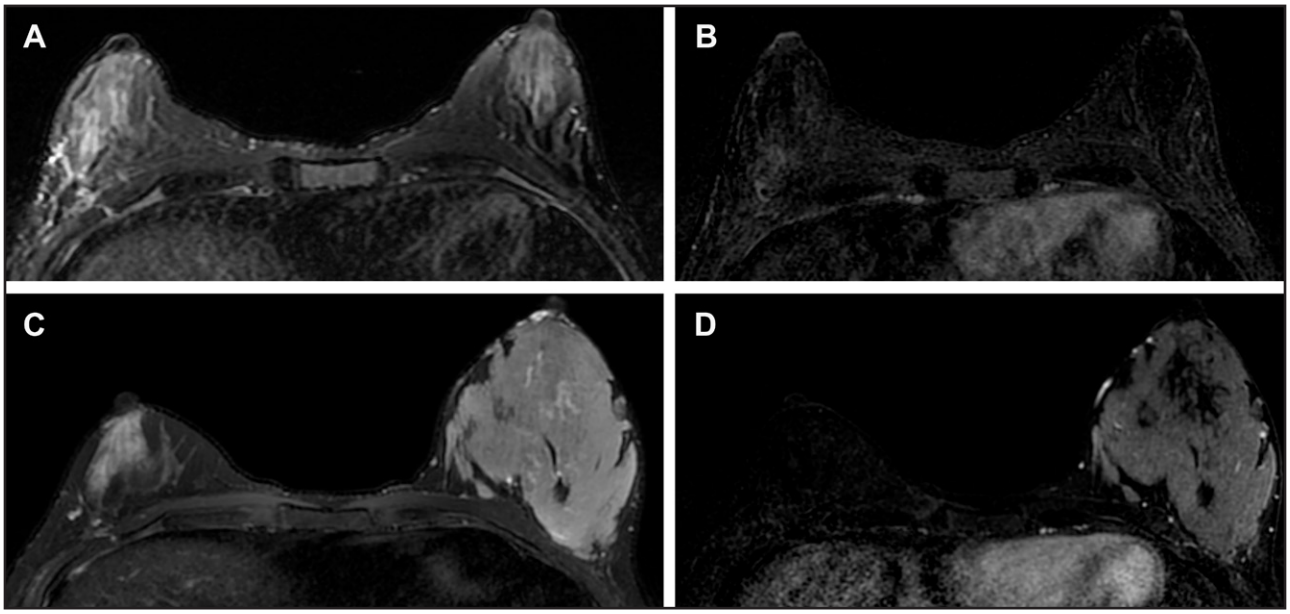


Figure 2. Screening breast MRI in a 31-year-old woman with a history of right-sided breast cancer who underwent lumpectomy and radiation therapy. **(A, B)** Posttreatment baseline axial T2-weighted MR image **(A)** shows heterogeneous fibroglandular tissue, and axial T1-weighted postcontrast subtraction MR image **(B)** shows mild BPE. **(C, D)** Axial T2-weighted **(C)** and axial T1-weighted postcontrast subtracted **(D)** MR images acquired 15 months later while the patient was lactating show the increased size of the left breast with asymmetric extreme fibroglandular tissue **(C)** and marked BPE **(D)**.

milk is highly suggestive of a galactocele (Fig 4). MRI demonstrates varying amounts of T1-hypointense and T2-hyperintense fluid contents and T1- and T2-hyperintense fat contents, which are typically layered along the nondependent aspect of the lesion and are suppressed at fat-saturated MRI. Non–fat-suppressed T1-weighted and fat-suppressed T2-weighted

Figure 3. Diagnostic evaluation of two adjacent palpable breast masses in the left upper outer quadrant in a 39-year-old postpartum woman with a *BRCA1* mutation who underwent prophylactic bilateral mastectomy with free flap reconstruction. **(A)** Left mediolateral oblique and craniocaudal tomosynthesis images show a corresponding focal asymmetry (arrows) in the posterior left upper outer quadrant. **(B, C)** US images show two adjacent oval hypoechoic solid masses with indistinct margins (arrow). Cytologic results from palpation-guided fine-needle aspiration showed benign breast tissue with lactational change. **(D, E)** Axial T1-weighted postcontrast MR images show a conglomerate of enhancing masses in two different sections in the left upper outer reconstructed breast along the posterolateral margin of the flap–native breast interface (arrow), corresponding to the palpable masses in **B** and **C**. Because the patient was at high risk of cancer, subsequent US-guided core biopsy and surgical excision of the palpable masses were performed. Pathologic results confirmed benign breast tissue with lactational change.

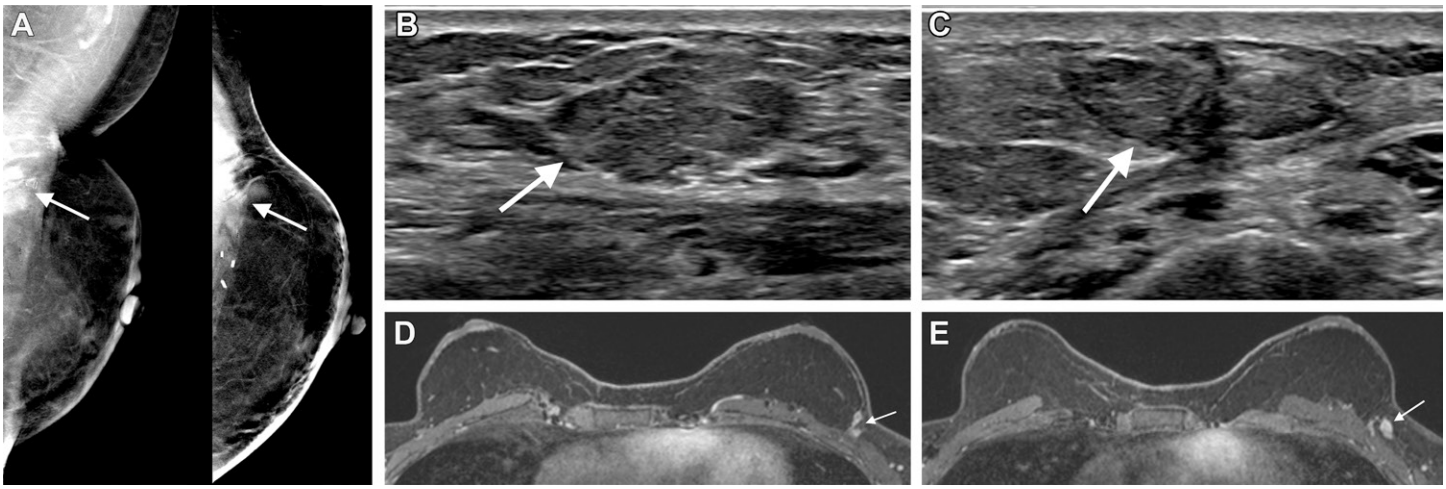
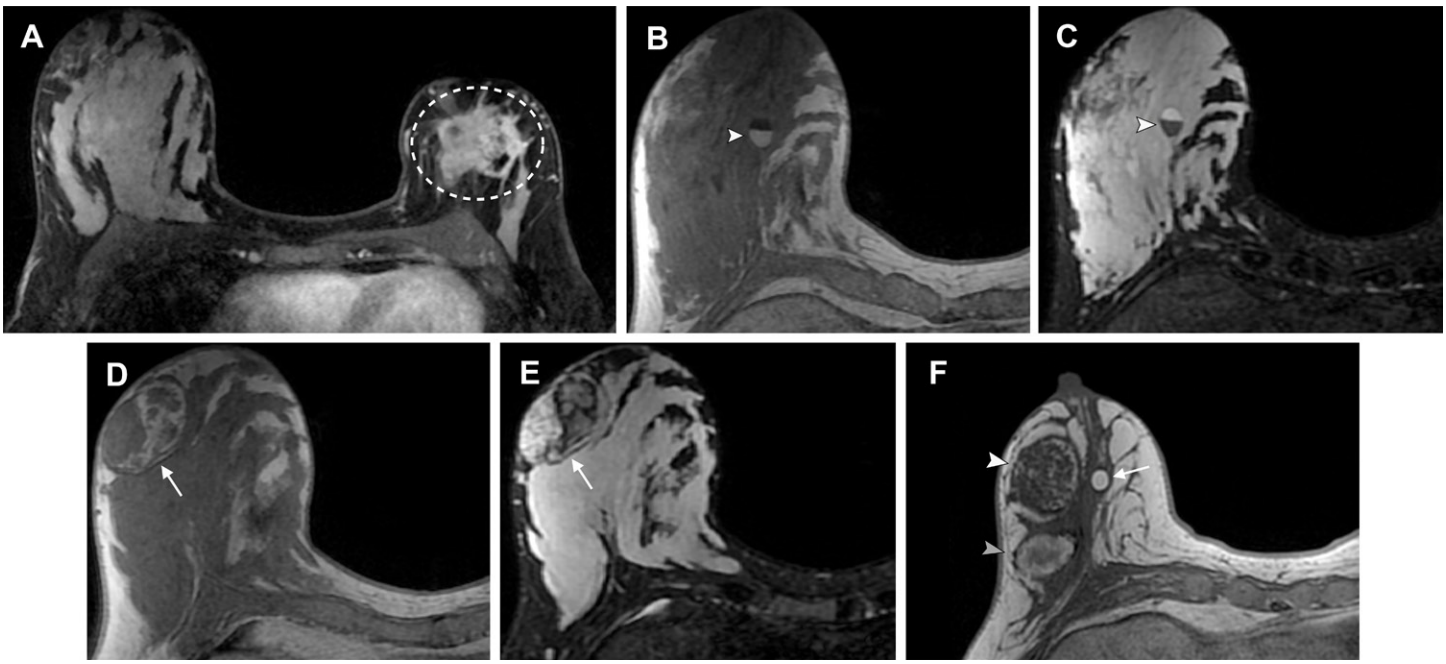


Figure 4. Cancer in the left breast in a 40-year-old lactating woman. **(A)** Axial T1-weighted postcontrast MR image shows a left breast mass (dashed oval) with an irregular shape and margins and heterogeneous internal enhancement, corresponding to the known biopsy-proven estrogen receptor–positive, progesterone receptor–positive, ERBB2 (formerly HER2 or HER2/neu)–negative grade 1 invasive ductal carcinoma and intermediate-grade ductal carcinoma in situ, with associated architectural distortion and nipple retraction. **(B)** Axial T1-weighted precontrast MR image shows an additional small circumscribed oval mass with a fat-fluid level in the right breast, which is consistent with a galactocele, with hyperintense fat contents (arrowhead) along the nondependent aspect (toward the chest wall in the prone position). **(C)** T2-weighted fat-saturated MR image shows suppressed fat signal intensity (arrowhead). **(D)** Axial T1-weighted precontrast MR image shows another circumscribed oval mass in the right breast that is isointense to the surrounding parenchyma, with a hypointense pseudocapsule and internal hyperintense components (arrow). **(E)** Axial fat-saturated T2-weighted MR image shows fat suppression consistent with a hamartoma (arrow). **(F)** Axial T1-weighted precontrast MR image acquired 4 months later after cessation of lactation shows that the galactocele (arrow) is slightly smaller, with no internal fat-fluid level. The adjacent unchanged hamartoma (upper arrowhead) and a hematoma from the recent core biopsy for biomarker assessment (lower arrowhead) are now partially visible. The breast size and amount of fibroglandular tissue have decreased from those at the earlier examination.



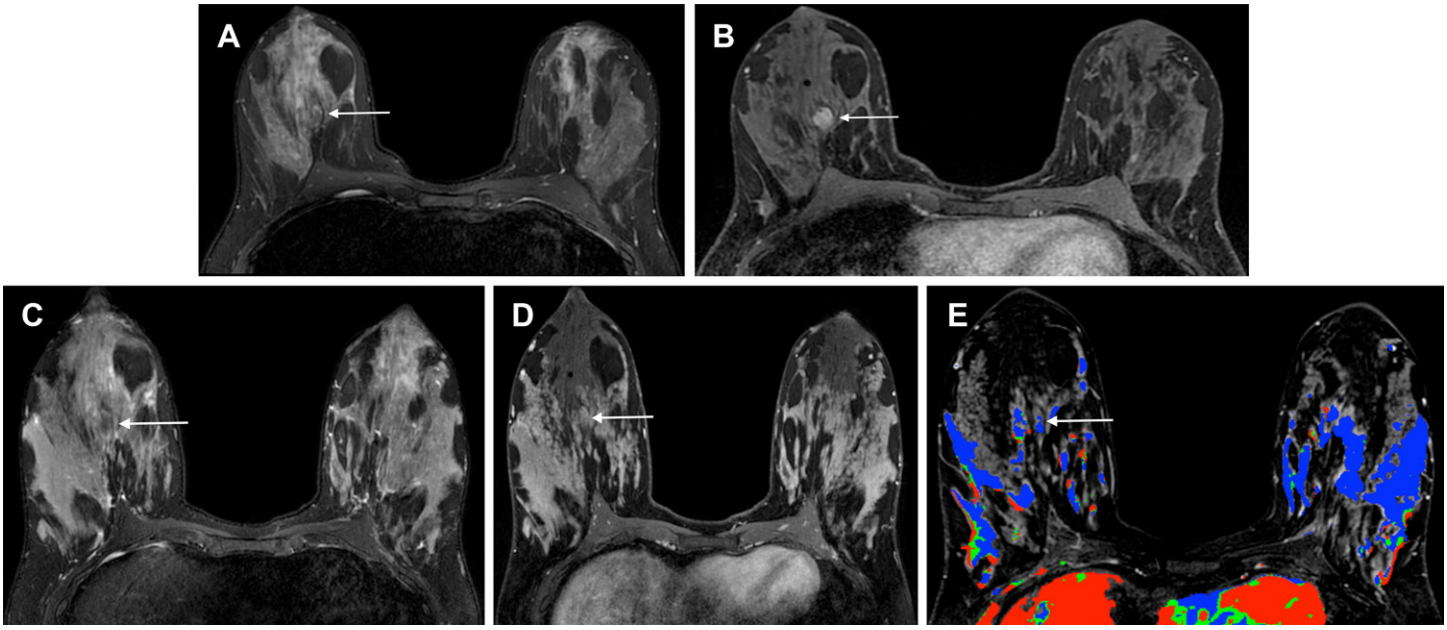


Figure 5. Fibroadenoma in a 31-year-old woman with a *BRCA1* mutation. **(A, B)** Axial T2-weighted **(A)** and axial T1-weighted postcontrast **(B)** MR images show an oval circumscribed mass with T2 intermediate signal intensity (arrow in **A**) and mildly heterogeneous enhancement (arrow in **B**) corresponding to the biopsy-proven fibroadenoma. **(C, D)** Axial T2-weighted **(C)** and T1-weighted postcontrast **(D)** MR images acquired 2 years later when the patient was 5 months postpartum and lactating show the fibroadenoma with similar imaging characteristics as those in **A** and **B,** but it is obscured by diffusely increased surrounding T2 signal intensity (arrow in **C**) and marked BPE (arrow in **D**) due to lactational changes. **(E)** Dynamic contrast-enhanced MR image shows limited visualization of the fibroadenoma (arrow) because of its persistent delayed enhancement, the same enhancement pattern demonstrated by the surrounding normal lactational tissue.

MRI sequences may be helpful for evaluation (11). Although uncomplicated galactoceles do not enhance at postcontrast MRI, superinfection is a potential complication that may be associated with development of rim enhancement at MRI (14). Most galactoceles regress spontaneously; however, when the patient is symptomatic or there is diagnostic uncertainty, aspiration can be both diagnostic and therapeutic (19).

Fibroadenoma

Fibroadenomas are the most common breast masses in women younger than 35 years. They are benign fibroepithelial tumors that can manifest as single or multiple masses. Because they are sensitive to estrogen stimulation, fibroadenomas often enlarge during pregnancy and lactation (18,20). Many are clinically latent before pregnancy and become symptomatic due to rapid growth. Although they most commonly manifest as painless, firm, mobile masses, some fibroadenomas may infarct when their growth outpaces their vascular supply and may manifest as painful palpable masses (17). In the postpartum period, fibroadenomas may involute due to decreased hormonal stimulation.

At MRI, fibroadenomas appear as oval or round circumscribed masses (Fig 5) whose signal intensity characteristics and enhancement patterns depend on their histopathologic features (21,22). Fibroadenomas are composed of epithelial and stromal elements, which tend to vary with patient age. Lesions in younger patients tend to have myxoid stroma that is composed of a T2-hyperintense gelatinous matrix. Epithelial elements also dominate in younger patients, and the increased cellularity correlates with more robust contrast enhancement. In postmenopausal women, the stromal components may hyalinize and/or calcify, resulting in T2 hypointensity, and the decreased cellularity of these involuting fibroadenomas is associated with decreased or absent contrast enhancement (23–25).

Although the internal architecture of fibroadenomas is typically homogeneous, a heterogeneous appearance can also be seen, with degenerative changes and increased size (21,23,26). Nonenhancing low-signal-intensity internal septa corresponding to dense bands of fibrous tissue have been reported in 27%–64% of cases (22,25–27) and are 89%–93% specific for fibroadenoma (27). These septa are best visualized on T2-weighted and nonsubtracted postcontrast T1-weighted images (23). Although previously thought to be pathognomonic for the diagnosis of fibroadenoma, this feature has also been demonstrated in other lesions such as benign and malignant phyllodes tumors and other malignancies (28,29).

Fibroadenomas tend to demonstrate a centrifugal pattern of enhancement over time, starting in the middle and spreading to the periphery, which may result in an irregular appearance on early postcontrast images before enhancement is complete (23). Therefore, lesion morphology is better assessed on delayed postcontrast images (23,30). The most common enhancement kinetic pattern is slow to medium initial enhancement and persistent or plateau delayed enhancement. However, rapid initial enhancement and delayed washout can also be seen, particularly in cellular myxoid fibroadenomas in younger patients, mimicking malignancy (21,30).

Infarction may manifest as T1 intrinsic hyperintensity due to hemorrhage, with heterogeneous T2 hyperintensity due to central necrosis. Rim enhancement can be seen in

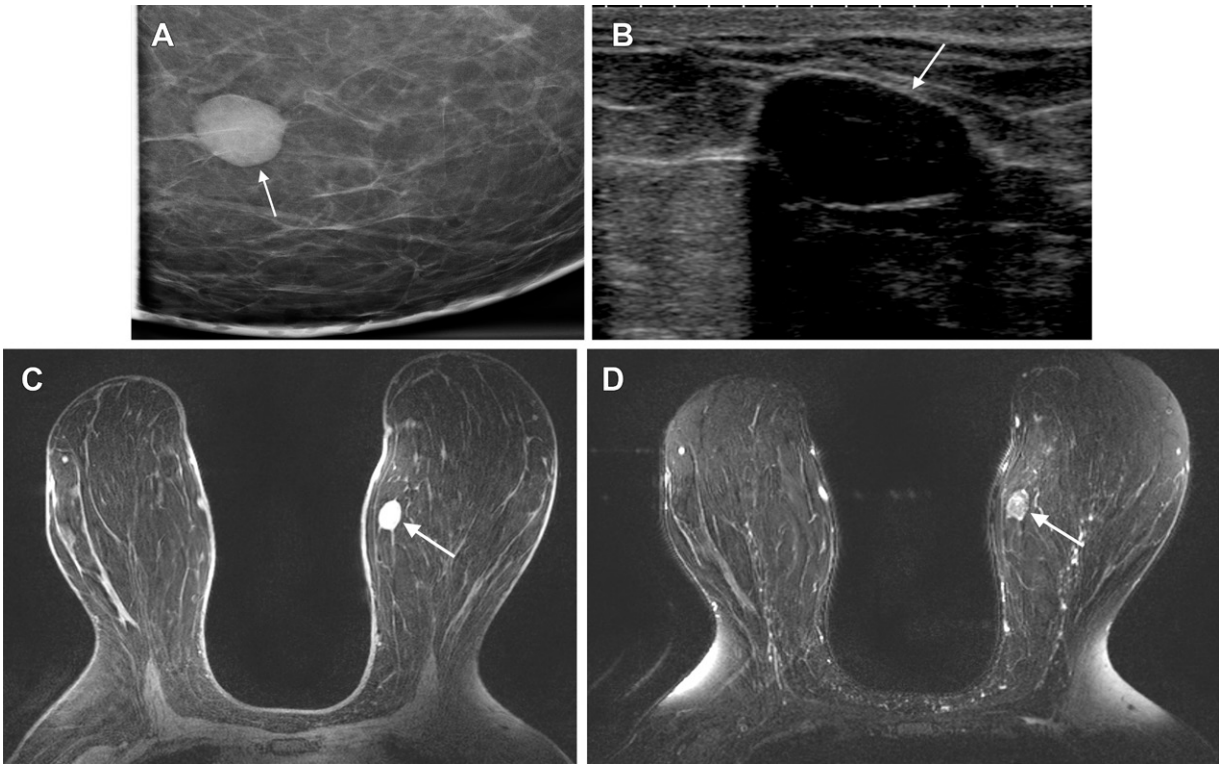


Figure 6. Lactating adenoma in a 36-year-old woman with a strong family history of breast cancer. **(A)** Left spot magnification craniocaudal mammogram acquired at 6 months postpartum after a mass was detected at screening mammography (not shown) shows a corresponding oval circumscribed mass (arrow). **(B)** US image shows a parallel, oval, circumscribed hypoechoic mass (arrow). Subsequent fine-needle aspiration results were consistent with a lactating adenoma. **(C, D)** Axial T1-weighted precontrast **(C)** and T2-weighted **(D)** MR images acquired at 16 months postpartum, when the patient was no longer lactating, show a circumscribed oval mass with intrinsic T1 hyperintensity (arrow in **C**) and intermediate T2 signal intensity (arrow in **D**).

remaining areas of viable tissue (31). During pregnancy and lactation, secretory hyperplasia and lactational changes can lead to internal accumulation of milk, mimicking a galactocele (32).

Lactating Adenoma

Lactating adenomas are benign fibroepithelial tumors similar to fibroadenomas, but with predominantly epithelial elements and a minimal stromal component (18). They most commonly manifest during late pregnancy and the postpartum period as painless soft mobile masses and may grow rapidly during pregnancy and lactation. Similar to fibroadenomas, they can manifest as multiple bilateral masses. They may also infarct if their growth outpaces their vascular supply. A feature of lactating adenomas is that they usually regress after cessation of lactation (18,20,33). Bromocriptine has been reported to decrease lesion size by suppressing the secretion of prolactin and decreasing lactational changes (33). Although lactating adenomas are considered benign, there have been rare reports (34,35) of coexisting carcinoma at histopathologic examination. Imaging was not performed in these reported cases, so it is unknown if the carcinomas would have been visualized at MRI. Also unclear is whether the adenoma transformed to or was infiltrated by an adjacent carcinoma. Regardless, close follow-up is recommended, with consideration of surgical resection in patients with a persistent or growing mass when malignancy cannot be ruled out.

At MRI, lactating adenomas appear as oval or round circumscribed masses (Fig 6), similar to fibroadenomas, usually with T1 hyperintensity or isointensity and variable T2 hyperintensity, depending on the composition of fat and proteinaceous contents (14). In some cases, there may be an associated fat-fluid level due to colostrum in the secretory lobules (36). Similar to fibroadenomas, nonenhancing low-signal-intensity internal septa corresponding to fibrous bands can be visualized in larger lactating adenomas (11,14,36). Cystic areas may also be seen due to lactational secretions (37) or infarction.

Postcontrast imaging can show heterogeneous, homogeneous, or absence of enhancement (11,14,36). Data on the enhancement kinetics of lactating adenomas is limited, but a persistent enhancement pattern has been reported by several authors (11,36).

Hamartoma

Hamartomas, also known as fibroadenolipomas, are benign lesions composed of fibrous, glandular epithelial, and adipose tissue surrounded by a pseudocapsule (38). Although generally slow growing and often asymptomatic, they are hormonally sensitive and may grow more rapidly during pregnancy and lactation. Infarction can occur (39).

Hamartomas classically exhibit a "breast within a breast" appearance, as an encapsulated mass with internal features similar to those of the normal surrounding breast tissue. At MRI, hamartomas appear as oval or round circumscribed masses that exhibit heterogeneous T1 and T2 signal intensity (Fig 4), given varying amounts of fibroglandular and fatty tissue. A T1- and T2-hypointense rim can be seen, corresponding to the pseudocapsule (40). The fibroglandular elements of a hamartoma exhibit a similar degree of contrast enhancement as that of the normal surrounding fibroglandular breast tissue, with a persistent enhancement pattern (14,40,41). The fibroglandular components may also exhibit lactational changes, including T2 hyperintensity and increased enhancement. The fatty elements are intrinsically T1 hyperintense and show suppression on fat-saturated images (14). At diffusion-weighted MRI, associated apparent diffusion coefficients are similar to those of the normal breast parenchyma. MR spectroscopy demonstrates marked water and lipid peaks, without a choline peak, similar to those of normal breast parenchyma (40).

Rare reports of malignancy arising in hamartomas have been published (42–46). Although MRI was not performed in most of these cases, one case report by Choi and Ko (46) describes an irregular spiculated mass seen within a hamartoma at US and MRI, with early enhancement and delayed washout at MRI. A corresponding focal asymmetry within the hamartoma was seen only in retrospect on the mammogram. In the majority of other reported cases, a suspicious mass or suspicious calcifications were seen within the hamartoma at mammography and/or US (45,46). Therefore, although the probability of a coexisting malignancy is low, the presence of suspicious features within a hamartoma should prompt further evaluation.

Pregnancy-associated Breast Cancer

Epidemiology

Pregnancy-associated breast cancer (PABC) is defined as breast cancer that is diagnosed during pregnancy or within the 1st year after birth (47). Breast cancer is one of the most commonly diagnosed cancers during pregnancy, with an estimated incidence of one in 3000 pregnancies. The incidence of PABC is increasing as more women choose to delay childbearing (48–50). A 2020 study (51) of a contemporary cohort of 46 women with PABC also demonstrated an association of PABC with *BRCA* gene mutation carrier status and "non-Caucasian race" (ie, patients who did not identify as White).

Pathology and Prognostic Features

The predominant histologic subtype of PABC is infiltrating ductal carcinoma, accounting for approximately two-thirds of cases, followed by ductal carcinoma in situ and infiltrating lobular carcinoma (51,52). The frequencies of the breast cancer subtypes in PABC are similar to those of age-matched control subjects and are characterized by high rates of triple-negative (up to 70%) and ERBB2-positive (formerly HER2 or HER2/neu–positive) cancers (30%–60%) (53). These findings are consistent with the epidemiologic profile of PABC, including younger age at presentation and higher rates of *BRCA* gene mutation and "non-Caucasian" race (51).The dominant breast cancer subtypes in PABC represent biologically more aggressive disease compared with the estrogen receptor–positive luminal subtypes that predominate in postmenopausal women.

PABC is associated with a worse prognosis compared with that of non-PABCs (54–56), which can, in part, be attributed to its more aggressive tumor biology. Another important driver of the poor prognosis is that difficulty in distinguishing PABC from physiologic lactational changes at clinical and imaging evaluation can result in delays in the diagnosis of PABC (57). Average delays in diagnosis ranging from 1–2 months to more than 6 months from symptom onset have been reported (57). A 1-month delay in treatment increases the risk of axillary nodal metastasis by 1%–2%, and a 3-month delay increases the risk by 5%–10% (58). As a result, pregnant women are two and one-half times more likely to receive a diagnosis of advanced disease than are nonpregnant women, with larger tumor sizes and higher rates of lymph node metastases (53). The literature (54–56) is mixed regarding whether PABC carries a similar or worse prognosis relative to that of non-PABC after controlling for age and cancer stage. Regardless, it is vitally important to minimize delays in diagnosis and treatment.

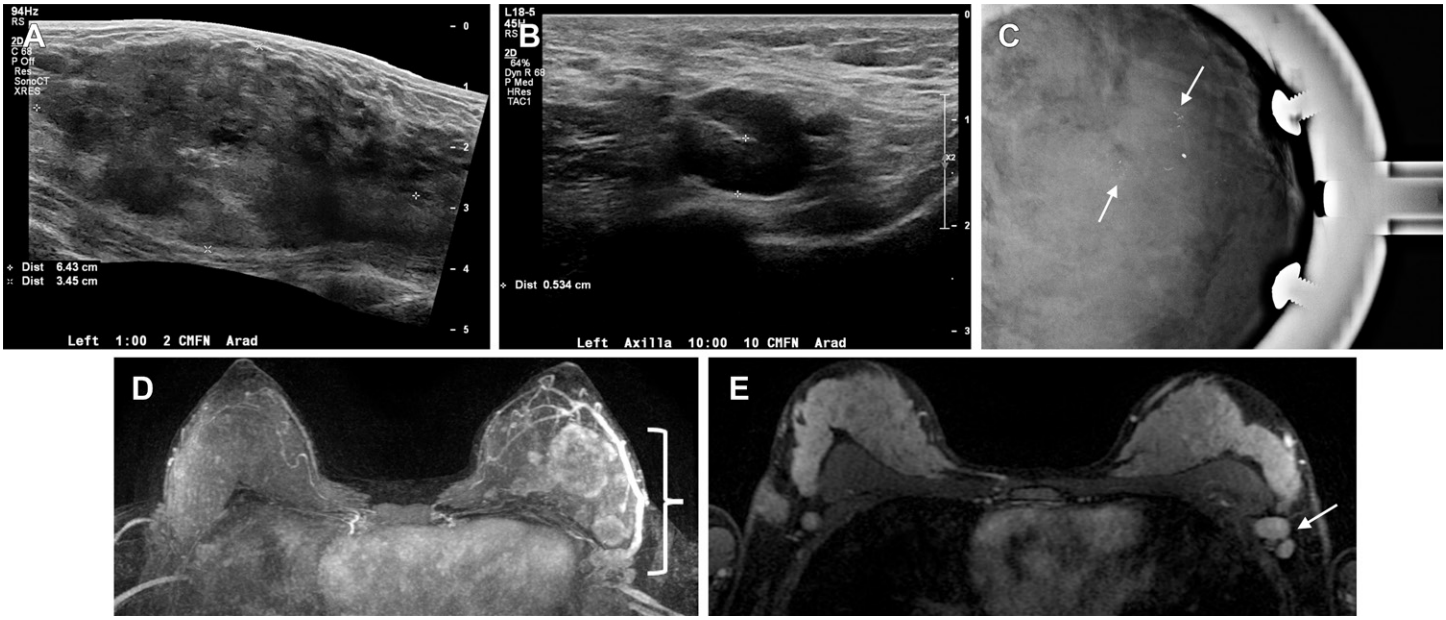
Clinical Presentation

PABC most commonly manifests as a palpable mass. Less common signs at patient presentation include focal pain, bloody nipple discharge, breast enlargement, and skin changes (55,59). There have been anecdotal reports (60,61) of infants refusing to nurse from the breast that is later found to harbor a malignancy, a phenomenon termed the *milk rejection sign*, possibly related to alterations in the taste, odor, or consistency of the milk (60). Many of these signs and symptoms may overlap with those of physiologic or benign processes. For instance, bloody nipple discharge may occur during pregnancy and early lactation due to a physiologic increase in vascularity (18). Expected changes during pregnancy and lactation such as an increase in breast size and nodularity may mask pathologic changes. Despite these diagnostic challenges, a high index of suspicion should be maintained, and prompt imaging evaluation should be performed to prevent delays in diagnosis.

Breast MRI in Diagnostic Imaging

For lactating patients, the general approach to diagnostic breast imaging is the same as that for nonlactating patients (1). Per the ACR Appropriateness Criteria published in 2018 (1) and the National Comprehensive Cancer Network (NCCN) guidelines (3) published in 2023, first-line evaluation of suspicious breast symptoms is performed with US in combination with diagnostic mammography. Because there is no contraindication to MRI or GBCAs during lactation, diagnostic breast MRI can also be performed as clinically indicated in patients with newly diagnosed breast cancers or suspicious symptoms (Fig 7). Lactating patients should breastfeed or pump immediately before breast MRI to reduce ductal secretions and potentially confounding background T2 signal intensity. The NCCN guidelines recommend consideration of diagnostic breast MRI for further

Figure 7. Palpable left breast mass in a 32-year-old *BRCA2* mutation carrier who presented during the third trimester of pregnancy. **(A, B)** Targeted left breast US images show an irregular hypoechoic mass with indistinct margins measuring more than 6 cm, corresponding to the palpable abnormality, and enlarged left axillary lymph nodes with cortical thickening. **(C)** Left mediolateral spot magnification mammogram shows multiple groups of fine pleomorphic microcalcifications (arrows) at the site of the palpable mass, although the mass itself is obscured by extremely dense tissue. Pathologic results showed grade 3 invasive ductal carcinoma, estrogen receptor–negative, progesterone receptor–negative, ERBB2-positive, with axillary lymph node metastasis. **(D)** Axial T1-weighted postcontrast maximum intensity projection MR image shows multiple rim-enhancing masses in the left breast (brackets), with irregular shapes and margins. **(E)** Axial T1-weighted postcontrast MR image shows level 1 axillary lymphadenopathy (arrow) in the left breast. Despite marked BPE due to lactation, the index left breast cancer and additional malignant masses can be visualized because of their more rapid enhancement relative to the normal breast parenchyma.



evaluation of abnormal nipple discharge with Breast Imaging Reporting and Data System (BI-RADS) category 1–3 findings at US and mammography, skin changes with BI-RADS category 4 or 5 findings at US and mammography and benign skin punch biopsy results, and malignant axillary lymph nodes of breast origin without a known breast mass (3).

Because lactating patients tend to demonstrate pronounced BPE at breast MRI due to a physiologic increase in parenchymal vascularity, researchers have postulated that the diagnostic performance of breast MRI may be adversely affected due to the decreased conspicuity of malignancy (10). However, in the general population of women undergoing breast MRI, not limited to lactating patients, studies (62–64) have shown that moderate or marked BPE is not associated with a reduction in sensitivity for cancer detection. Multiple studies (9,65–68) in which the authors evaluated the performance of diagnostic MRI in lactating patients have also shown that sensitivity remains high in this specific group despite increased BPE and additional lactational changes, with enhancement kinetics and morphology assisting in tumor differentiation from physiologic BPE.

Espinosa et al (9) reported in 2005 on a series of five lactating patients who underwent breast MRI for staging of a biopsy-proven palpable breast cancer (9). All tumors were readily identifiable at contrast-enhanced T1-weighted MRI due to their more rapid and avid enhancement relative to that of normal lactating breast parenchyma. The tumors demonstrated delayed washout of contrast material, whereas normal parenchyma displayed a plateau of enhancement. Some tumors demonstrated rim enhancement and mass effect. The tumors were also visible at T2-weighted MRI due to their lower signal intensity relative to the hyperintense surrounding parenchyma.

Taylor et al (65) also reported in 2011 on six women with PABC who underwent breast MRI to assess the extent of disease or establish a baseline before neoadjuvant chemotherapy. Two patients were imaged during the postpartum period, whereas another two patients had stopped breastfeeding for 7 and 20 weeks, respectively. One patient had just terminated her first trimester pregnancy, and another was imaged during the first trimester but terminated her pregnancy immediately after MRI. BPE did not impair lesion detection at MRI in any of these cases. Unsuspected multicentric disease was detected at MRI in one patient, which led to a change in the planned surgical treatment from wide local excision to mastectomy. In one patient who was 8 weeks postpartum and had ceased lactation 4 weeks earlier, the lesion size of a rim-enhancing mass was overestimated at MRI due to a compressed zone of adenosis.

Oh et al (66) reported in 2017 on nine patients who received a diagnosis of PABC during lactation, for which MRI was performed to evaluate the extent of disease. Despite moderate (two cases) or marked (seven cases) BPE, all of the tumors were visible at MRI as round, oval, or irregular masses with irregular margins and heterogeneous or rim enhancement. Imaging for all patients demonstrated rapid initial enhancement and most (five patients) demonstrated delayed washout. In three patients, MRI showed additional sites of cancer other than the index lesion.

In a larger series reported by Myers et al (67) in 2017 of 53 women with PABC who underwent diagnostic breast MRI, the sensitivity of MRI for the primary lesion was 98%. Although it was unknown how many patients in this series were lactating, MRI maintained high sensitivity despite most patients having moderate (32%) or marked (26%) BPE. One lesion was not visualized in the setting of marked BPE. MRI showed a pathologically proven larger tumor size or greater than expected extent of disease compared with that at mammography and breast US in 23% of patients, resulting in a change in surgical treatment in 28% of patients.

Taron et al (68) published another review in 2019 of 19 patients with PABC who underwent breast MRI, one of whom was 19 weeks pregnant, four of whom were breastfeeding, and 14 of whom had recently ceased lactation 2 days to 4 weeks earlier. All tumors were detected at MRI, regardless of the level of BPE. BPE was described as minimal in one patient, mild in three patients, moderate in seven patients, and marked in eight patients. All tumors demonstrated either washout (17 patients) or plateau (two patients) enhancement kinetics. In three patients, MRI showed additional malignant lesions. This study also described the utility of supplemental subtraction images, in which the last postcontrast dynamic series is subtracted from the second early postcontrast dynamic series to improve visualization of areas of washout kinetics typical of malignant lesions while minimizing background plateau enhancement typical of normal lactating tissue. Supplemental subtraction images allowed a 95% (18 of 19) malignancy detection rate, with one lesion not visible because of similar plateau kinetics in the tumor and the normal lactational tissue.

In the general population, elevated BPE is associated with higher abnormal interpretation rates (BI-RADS categories other than BI-RADS 1 or 2) (62,63) and biopsy rates as well as reduced specificity (64). However, data regarding these diagnostic measures in patients who are lactating are lacking. More data are ultimately needed to directly assess the diagnostic performance of breast MRI during lactation. Overall, existing data suggest that breast MRI during lactation demonstrates high sensitivity and may be a helpful adjunct to US and/or mammography for diagnostic evaluation.

During pregnancy, both ACR and NCCN guidelines state that contrast-enhanced MRI is not recommended due to possible toxicity to the fetus through transplacental passage of GBCA (1,3). Per the NCCN guidelines, noncontrast MRI is not recommended during pregnancy due to lack of sensitivity (3). However, patients who receive a diagnosis of PABC during pregnancy may undergo breast MRI after delivery for locoregional staging (1), screening of the contralateral breast, to assess response to NAC, and for surgical planning.

Screening of Asymptomatic Patients

As in nonpregnant patients, asymptomatic screening recommendations during pregnancy and lactation are stratified by breast cancer risk level. High risk is considered lifetime risk of 20% or greater; intermediate risk, 15%–20%; and average risk, less than 15%; as defined by models that are largely dependent on family history (3). During pregnancy, the ACR Appropriateness Criteria and the NCCN guidelines recommend annual screening mammography in all patients aged 40 years and older (1,3). Screening mammography is also recommended by both the ACR and NCCN in patients at high risk for breast cancer with the starting age depending on clinical history, and per the ACR in patients 30–39 years old at intermediate risk. US can be considered a supplemental tool in patients at intermediate or high risk. Screening MRI is not recommended during pregnancy.

During lactation, mammography is recommended as the primary method for annual screening by both the ACR and NCCN (1,3). The ACR specifies that US may be considered as a possible supplemental tool in patients at intermediate or high risk. Per both the ACR and NCCN, supplemental breast MRI with and without contrast material is recommended for patients at high risk. The NCCN specifies that supplemental screening with breast MRI should be considered on an individual basis in patients with intermediate lifetime risk.

The literature on breast cancer screening in lactating patients is limited. In a single-institution study of 117 women with PABC, four cancers were detected in three patients at high risk of cancer who were undergoing screening MRI (52). The specific clinical indication for screening in patients at high risk was not described. Although more clinical data on screening breast MRI are needed, the high sensitivity of breast MRI in diagnostic studies of lactating women with known breast cancers suggests that screening MRI would also likely be of value in lactating women at high risk. The decision to perform screening during lactation depends on the patient's level of risk and the expected duration of lactation. It is generally advised that screening be delayed for at least 3 months after weaning to allow regression of lactational changes and improved sensitivity. However, if the patient is planning to breastfeed for a prolonged period of time, then it is reasonable to proceed to screening without delay (1). In particular, breast MRI screening should not be deferred for patients at high risk.

Breast MRI Features

MRI features of PABC have been described in several studies (9,11,65–68). The most common finding of PABC is a mass lesion that enhances more rapidly and intensely than does the normal breast parenchyma and is most conspicuous during the initial postcontrast phase. Delayed washout of contrast material is also commonly observed. Additional common morphologic features include irregular shape; irregular margins; and heterogeneous, homogeneous, or rim enhancement (9,66,67). A distinct feature of PABC is its more marked hypointensity at T2-weighted MRI relative to the surrounding breast parenchyma, which is T2 hyperintense due to lactational change (9,11). Therefore, T2-weighted MRI may be helpful for tumor delineation in some cases (Fig 8).

The MRI appearance of PABC may reflect the breast cancer subtype, as has been described in nonlactating patients (69). For example, triple-negative breast cancers may exhibit benign morphologic features with an oval shape and relatively circumscribed margins (Fig S1). Some triple-negative breast cancers appear partially cystic at US and MRI due to areas of central necrosis (Figs 9, S1) (70). ERBB2-enriched cancers have high rates of multifocal disease, associated ductal carcinoma in situ, and axillary adenopathy at presentation (69).

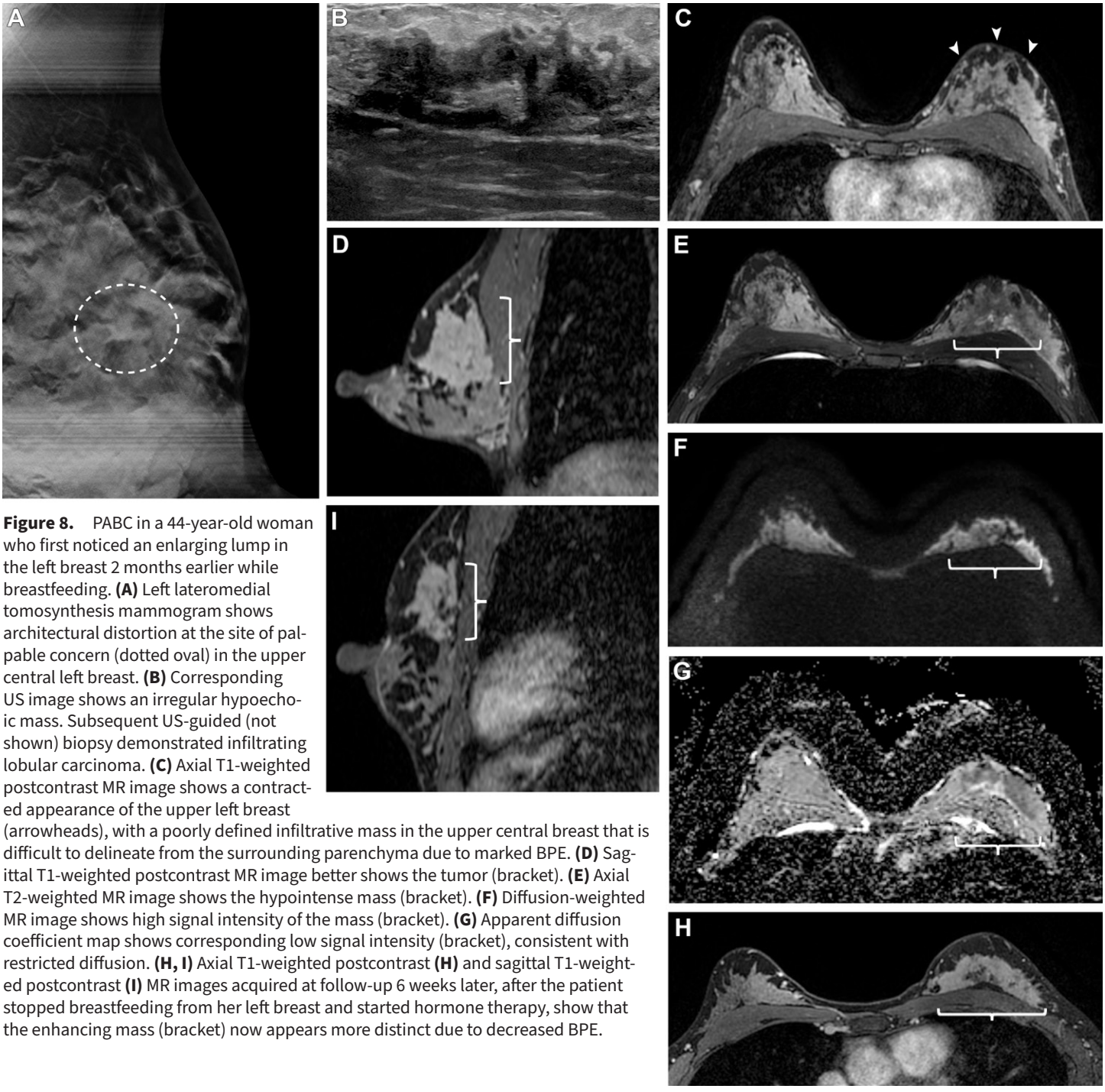


Figure 8. PABC in a 44-year-old woman who first noticed an enlarging lump in the left breast 2 months earlier while breastfeeding. **(A)** Left lateromedial tomosynthesis mammogram shows architectural distortion at the site of palpable concern (dotted oval) in the upper central left breast. **(B)** Corresponding US image shows an irregular hypoechoic mass. Subsequent US-guided (not shown) biopsy demonstrated infiltrating lobular carcinoma. **(C)** Axial T1-weighted postcontrast MR image shows a contracted appearance of the upper left breast (arrowheads), with a poorly defined infiltrative mass in the upper central breast that is difficult to delineate from the surrounding parenchyma due to marked BPE. **(D)** Sagittal T1-weighted postcontrast MR image better shows the tumor (bracket). **(E)** Axial T2-weighted MR image shows the hypointense mass (bracket). **(F)** Diffusion-weighted MR image shows high signal intensity of the mass (bracket). **(G)** Apparent diffusion coefficient map shows corresponding low signal intensity (bracket), consistent with restricted diffusion. **(H, I)** Axial T1-weighted postcontrast **(H)** and sagittal T1-weighted postcontrast **(I)** MR images acquired at follow-up 6 weeks later, after the patient stopped breastfeeding from her left breast and started hormone therapy, show that the enhancing mass (bracket) now appears more distinct due to decreased BPE.

Pregnancy-associated infiltrating lobular carcinomas may present a diagnostic challenge. Infiltrating lobular carcinoma is more likely to appear as a nonmass lesion (2,28) and tends to have less rapid enhancement than infiltrating ductal carcinoma, and therefore may be difficult to distinguish from the avidly enhancing normal breast parenchyma (Fig 8). Secondary signs such as architectural distortion and low signal intensity at T2-weighted MRI and restricted diffusion at diffusion-weighted MRI may help to delineate the tumor (71).

Future Directions

Given the limitations of contrast-enhanced MRI during lactation and its contraindication during pregnancy, there is clinical interest in developing robust noncontrast breast MRI techniques. Diffusion-weighted MRI is a noncontrast technique that relies on differences in the brownian motion of water molecules to provide tissue contrast. Because lesions with high cellular density such as breast malignancies tend to show restricted diffusion and are therefore detectable at diffusion-weighted MRI, this technique has the potential to serve as a screening and diagnostic tool. Diffusion-tensor MRI is an extension of conventional diffusion-weighted MRI that provides additional information regarding the directionality of diffusion and reflects tissue microstructural features, which may help to distinguish between benign and malignant lesions (12). In a pilot study of 10 patients with PABC, Nissan

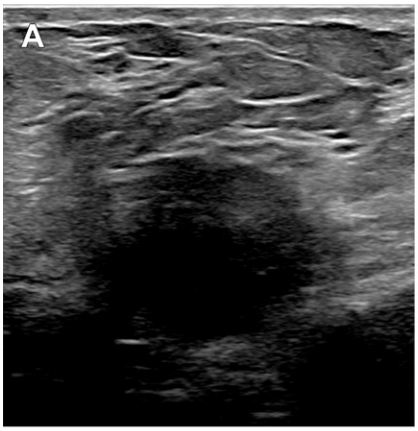
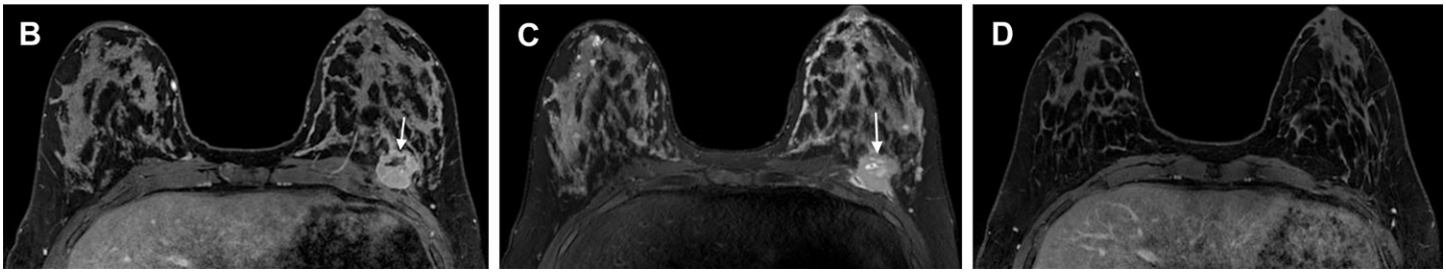


Figure 9. PABC in the lower outer quadrant of the left breast in a 36-year-old woman who presented with a palpable mass during pregnancy at 37 weeks gestation. **(A)** US image shows a corresponding irregular complex cystic and solid mass with angular margins. Core biopsy showed triple-negative invasive ductal carcinoma with necrosis. Labor was induced at 38 weeks, given the new cancer diagnosis. **(B)** Axial T1-weighted postcontrast MR image acquired 1 week after birth shows an irregular mass (arrow) corresponding to the biopsy-proven carcinoma, with rim enhancement and areas of central nonenhancement. **(C)** Axial T2-weighted MR image shows areas of T2 hyperintensity consistent with necrosis (arrow). The mass abuts the pectoralis muscle without evidence of underlying muscle enhancement to suggest chest wall invasion. The patient underwent neoadjuvant chemotherapy. **(D)** Axial T1-weighted postcontrast MR image shows complete imaging resolution of the mass 3 months later, which allowed prediction of pathologic complete response at subsequent surgery.



et al (72) reported that diffusion-tensor MRI allowed identification of nine of 11 malignancies. Further studies are needed to establish the clinical utility of diffusion-based techniques, particularly if they are to be considered as stand-alone studies in lieu of contrast-enhanced MRI.

Procedural Considerations

Percutaneous biopsy of suspicious findings in the lactating breast should be performed whenever there is a clinical indication for biopsy. The National Comprehensive Cancer Network (NCCN) and Academy of Breastfeeding Medicine recommend core biopsy rather than fine-needle aspiration to establish a specific diagnosis regardless of lactation status, because fine-needle aspiration can lead to false-negative (Fig 10) and false-positive diagnoses due to overlapping features of lactational changes with malignancy (3,55,73).

Core biopsy can be safely performed under US, mammographic, or MRI guidance in lactating patients; however, there are certain procedural nuances to consider. There is an increased risk of biopsy-associated bleeding and infection related to increased vascularity of the breast (17), which can be mitigated with careful postprocedural hemostasis and aseptic technique. Although it is a rare complication, a milk fistula can develop between the biopsy tract and a milk duct, leading to chronic milk leakage (74). To minimize this risk, patients should continue to breastfeed or pump before and after the biopsy, which encourages milk to flow toward the nipple rather than out through the biopsy tract (75). Decreasing needle movement during sampling and using an entry site as far from the nipple as possible may decrease the risk, but these options must be balanced with the risk of inadequate sampling. Despite the small risk of milk fistula, core biopsy of suspicious findings is the standard of care to facilitate prompt and accurate diagnosis.

Conclusion

MRI is a sensitive and safe method to evaluate the lactating breast. Recognition of physiologic and classic benign entities can help to avert unnecessary biopsies, while ensuring recognition of concerning findings. MRI is a valuable diagnostic aid in patients with a known breast malignancy or clinically suspicious findings and may depict more extensive disease than conventional imaging shows, leading to changes in clinical management. MRI may also be of value for screening in lactating patients who are at high risk of developing breast cancer. Careful correlation of radiologic, pathologic, and clinical findings is essential to avoid delays and errors in cancer diagnosis.

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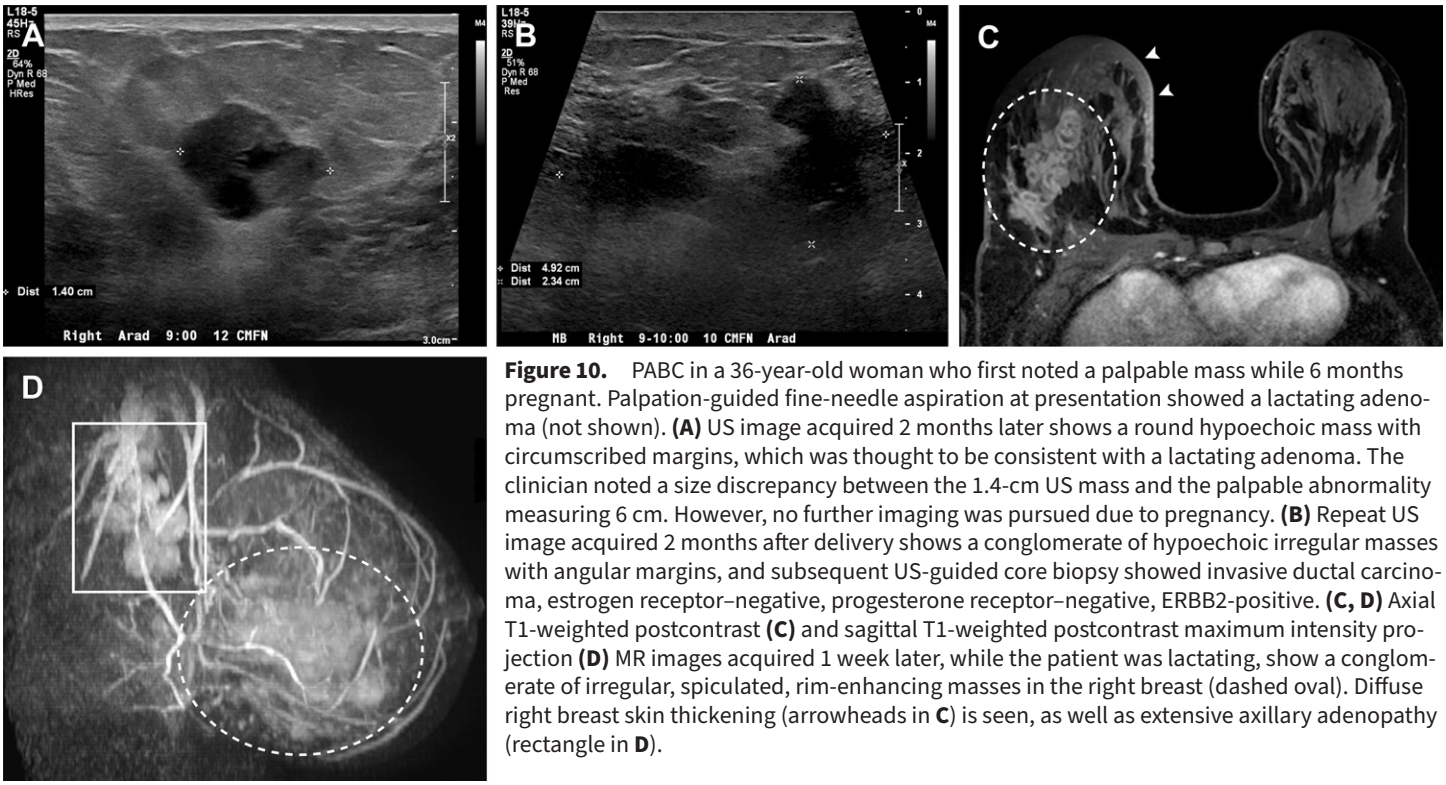

Figure 10. PABC in a 36-year-old woman who first noted a palpable mass while 6 months pregnant. Palpation-guided fine-needle aspiration at presentation showed a lactating adenoma (not shown). **(A)** US image acquired 2 months later shows a round hypoechoic mass with circumscribed margins, which was thought to be consistent with a lactating adenoma. The clinician noted a size discrepancy between the 1.4-cm US mass and the palpable abnormality measuring 6 cm. However, no further imaging was pursued due to pregnancy. **(B)** Repeat US image acquired 2 months after delivery shows a conglomerate of hypoechoic irregular masses with angular margins, and subsequent US-guided core biopsy showed invasive ductal carcinoma, estrogen receptor–negative, progesterone receptor–negative, ERBB2-positive. **(C, D)** Axial T1-weighted postcontrast **(C)** and sagittal T1-weighted postcontrast maximum intensity projection **(D)** MR images acquired 1 week later, while the patient was lactating, show a conglomerate of irregular, spiculated, rim-enhancing masses in the right breast (dashed oval). Diffuse right breast skin thickening (arrowheads in **C**) is seen, as well as extensive axillary adenopathy (rectangle in **D**).

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