Educational Review

Breast Imaging During Pregnancy and Lactation

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Abstract

Breast imaging during pregnancy and lactation is important in order to avoid delays in the diagnosis and treatment of pregnancy-associated breast cancers. Radiologists have an opportunity to improve breast cancer detection by becoming familiar with appropriate breast imaging and providing recommendations to women and their referring physicians. Importantly, during pregnancy and lactation, both screening and diagnostic breast imaging can be safely performed. Here we describe when and how to screen, how to work up palpable masses, and evaluate bloody nipple discharge. The imaging features of common findings in the breasts of pregnant and lactating women are also reviewed. Finally, we address breast cancer staging and provide a brief primer on treatment options for pregnancy-associated breast cancers.

Key words: pregnancy; lactation; PABC, pregnancy-associated breast cancer; ACR Appropriateness Criteria.
Key Messages
- Breast cancer screening with mammogram and ultrasound can be performed throughout pregnancy.
- Breast cancer screening during lactation can include mammography, ultrasound, and magnetic resonance imaging. Nursing or pumping before imaging may help decrease breast density and increase patient comfort.
- Diagnostic imaging during pregnancy should begin with ultrasound, with mammogram to follow as needed.
- In pregnant women, breast cancers can be treated with surgical and chemotherapeutic options like those available to nonpregnant women.

Introduction
How, when, and even whether to perform breast imaging during pregnancy and lactation has been a nebulous topic, with some women and physicians preferring to delay imaging until after both pregnancy and lactation because of concerns about imaging safety, sensitivity, and specificity. However, pregnancy does not preclude breast cancer, and deferring breast imaging in any setting puts a patient at risk for a delayed breast cancer diagnosis. A delay may be especially harmful in pregnant and lactating patients, who have higher rates of death and lower rates of disease-free survival than do nonpregnant age-matched peers (1). The risk of delayed diagnosis has been recognized by the American College of Radiology (ACR), which published Appropriateness Criteria for breast imaging in women who are pregnant or lactating in November 2018 (2). In this article, we review imaging guidelines and highlight them in the context of clinical presentations and in entities common during pregnancy and lactation, and we provide an overview of treatments for breast cancer detected during pregnancy.

Imaging by modality
Mammography
The ACR Appropriateness Criteria emphasize foremost that breast imaging is safe as both a screening and diagnostic tool during pregnancy and lactation. Mammography is not contraindicated during pregnancy or lactation, and the dose to the fetus has been described by the ACR as negligible (2). Specifically, the fetal radiation dose from a four-view mammogram is less than 0.03 mGy (3), which is less than 1/10000th of 50 mGy, under which level no teratogenic effects have been shown (4). The National Comprehensive Cancer Network guidelines also state that mammography with shielding can be done safely in pregnant women (5). The ACR further comments that digital breast tomosynthesis (DBT) may be of particular use in this setting, which includes younger women with increased breast density (2).

Ultrasound
Ultrasound is safe during pregnancy, and lactation and may be used both in the diagnostic setting and as an adjunct to screening mammography. Although no studies have addressed screening ultrasound in this setting, screening ultrasound has been shown to increase cancer detection in women with dense breasts (6, 7), a common finding in pregnant and lactating women. Screening ultrasound may yield increased false positive exams (2), as has been shown in nonpregnant and nonlactating women (6, 7).

Magnetic Resonance Imaging
Magnetic resonance imaging (MRI) is not safe during pregnancy (8) but can be performed during lactation. Gadolinium administration in pregnant women has been associated with an increased risk of rheumatological, inflammatory, and infiltrative skin conditions and with an increased risk of stillbirth or neonatal death (8). However, during lactation, the amount of gadolinium excreted into the breast milk has been characterized as exceedingly low (9, 10). Although the ACR Manual on Contrast Media notes that breastfeeding after the IV administration of gadolinium is safe (10), a mother can always choose to pump and discard milk for 24 hours following gadolinium administration.

Imaging by clinical scenario
Screening
For breast cancer screening, DBT or mammography is appropriate in both pregnant and lactating women. In women at high risk, screening can begin under age 30 years; in women at intermediate risk, screening can begin between ages 30 and 39 years; and in normal risk women, screening is recommended beginning at age 40 years (2). In women with dense breasts, screening ultrasound may be useful as a supplement to DBT or mammography, and, in lactating women only, MRI can be performed in high-risk women.

Diagnostic Imaging
For pregnant women who present with a palpable mass or bloody nipple discharge, ultrasound is indicated as initial imaging, with mammogram to be performed if the ultrasound exam does not explain the clinical presentation or when ultrasound findings are suspicious (2).

Staging a Known Breast Cancer
The ACR states that both mammogram and ipsilateral axillary ultrasound are indicated for staging pregnancy associated breast cancer (PABC) (2). Although the ACR did not recommend bilateral whole-breast ultrasound for staging, they did cite several studies that showed increased cancer detection in nonpregnant patients when ultrasound was performed for staging (11–13). These studies suggest that a whole-breast ultrasound may provide additional staging information and could be considered. Breast cancer staging in lactating women should be performed just as would be performed in nonpregnant, nonlactating women.

Imaging findings
Lactational Changes
Pregnancy and lactation increase the size and density of breasts. Lactational changes begin early in and continue throughout pregnancy, as rising estrogen levels allow for increased secondary and tertiary ductal branching, which increases available ductal arbors for the progesterone- and prolactin-dependent generation of new alveoli, which become milk-secreting lobules (14–17) (Figure 1). By midpregnancy, there is marked increased vascularization, with capillaries surrounding the new alveoli (18). As lobular proliferation continues, lobules replace much of the fibro-fatty stroma, and breast density begins to increase. By late pregnancy, secretory activity can be seen. After parturition, estrogen and progesterone levels decrease, and prolactin then causes full milk production after birth and through breast feeding (14, 15), at which time breast density further...
increases (Figure 2). Notably, lactational changes are not uniform throughout the breasts, and nonuniform lactational changes can result in palpable and even radiologically detectable masses known as lactating adenomas (19).

Mammographic screening throughout lactational changes is safe and should be encouraged. Although there are no studies addressing screening mammography in pregnant women, in one study of 134 lesions that included four breast cancer lesions, mammogram detected all four cancers for a sensitivity of 100% (20). In other studies of PABC, patients with known breast cancers had clinically occult breast cancers detected mammographically (21, 22).

Mammography may be more sensitive and likely more comfortable following nursing or pumping, as pumping may decrease breast density, which has been shown to decrease mammographic sensitivity (23–25). In this setting, digital mammography (DM) should be preferred over screen-film mammography (26), and DBT may be preferred over DM, to decrease the masking effect of dense breast tissue (2). Further, as lactational changes are less complete during pregnancy than during lactation, breast density is also likely to be lower during pregnancy than during lactation.

Ultrasound may be used as an adjunct to screening mammography, just as in nonpregnant, nonlactating women. Expected ultrasound findings include diffusely increased breast tissue and, during lactation, increased echogenicity because of the high fat content of milk (Figure 3). MRI may be used as a screening tool in high-risk women who are lactating, but it should not be performed during pregnancy. Expected findings during lactation include increased glandular tissue, diffusely increased background parenchymal enhancement, T2 hyper-echogenicity, and vascularity (Figure 4) (27).

**Pregnancy-Associated Masses**

All new palpable areas of concern presenting during pregnancy and lactation must undergo diagnostic imaging. In addition, focal pain, diffuse unilateral breast enlargement, nipple discharge,
and, uncommonly, milk rejection can be presenting symptoms of PABC and, therefore, warrant immediate imaging evaluation (28, 29). Ultrasound has demonstrated 100% sensitivity for PABC in many studies (2, 20, 29) and is the first-line imaging modality. Mammogram should follow if 1) ultrasound shows no imaging correlate or 2) ultrasound demonstrates a suspicious imaging correlate, in which case mammogram is performed to assess for additional findings such as associated microcalcifications (2).

If ultrasound demonstrates a solid mass, ultrasound-guided core biopsy should be strongly considered (2, 27), even if the mass meets Breast Imaging Reporting and Data System (BI-RADS) 3–probably benign criteria of oval shape, circumscribed margins, and parallel orientation (30). This recommendation takes into account both the sometimes confoundingly benign appearance of PABC (21, 31) and the potential for the hormonal milieu that facilitates pregnancy and lactation to also potentiate rapid cancer growth. Consent for biopsy should include the possibilities of increased bleeding, owing to the hypervascular state of pregnancy, and milk fistula (2).

In the special case of a pre-existing benign mass that has increased in size (eg, a biopsy-proven fibroadenoma or possibly a solid mass with benign features that has shown at least 24 months of stability) an allowance of 20% increase in dimension at 6 months, which is allowed in nonpregnant patients (32), may be acceptable (28).

**Bloody Nipple Discharge**

During pregnancy, the breasts undergo proliferative changes and increased vascularity along with lobular distension, which may lead to unilateral or bilateral bloody nipple discharge in up to 20% of patients (2). This physiologic bloody nipple discharge usually occurs during the second or third trimester, is spontaneous, involves multiple ducts, and resolves within 2 months (33). Persistent bloody nipple discharge may be related to persistent infection, papillary lesions, or breast cancer, and, therefore, imaging work-up first with ultrasound and then with diagnostic mammogram with retroareolar magnification views is recommended (2).

**Benign masses**

**Fibroadenoma**

Fibroadenomas are benign tumors that arise from the epithelium and stroma of the terminal duct-lobular unit (34). They are hormone dependent (35, 36) and may grow in response to pregnancy, presenting as either new or enlarging masses. Rapid growth may lead to infarction and, therefore, tenderness, which is not typical of noninfarcted fibroadenomas (37).

Fibroadenomas are very common in young women overall and are the most commonly detected solid mass during pregnancy. Sonographically, fibroadenomas typically appear as circumscribed, homogeneously hypoechoic, oval (or round) masses, oriented parallel to the skin, sometimes with a few gentle macrolobulations (38). They may be single or multiple and are often bilateral. Their appearance is similar in pregnant and lactating women, although infarcted fibroadenomas may demonstrate cystic spaces and borders that are less regular (27, 39).

**Lactating Adenoma**

Lactating adenomas are histologically distinct from fibroadenomas in that they are composed of compact aggregates of lobules with secretory hyperplasia and, clinically, occur most often in the third trimester of pregnancy (33). Ultrasound may show diffuse increased echogenicity, which may be more prominent on retroareolar magnified views (27, 39). The response to MRI depends on the stage of lactation and the degree of vascularization (27, 29, 33).

**Figure 3.** Ultrasound in a lactating patient with color flow (A) demonstrates diffusely increased vascularity (short arrows) (long arrow points to the nipple). Gray-scale ultrasound images in the same woman (B) show diffusely increased tissue echogenicity (arrow) and (C) prominent retroareolar ducts (arrow).

**Figure 4.** A: Postcontrast T1-weighted fat-subtracted MRI image shows fibroglandular tissue in a nonlactating woman. B: The same woman underwent breast MRI during lactation, and a postcontrast T1-weighted fat-subtracted MRI image shows an asymmetric, heterogeneous increase in glandular tissue (arrows) and increased enhancement related to diffuse hypervascularity. C: T2-weighted image shows diffusely increased T2 signal (arrow) thought to be related to the fluid content of milk.
trimester or postpartum during lactation (34, 39), although they have been documented in the first and second trimesters (15, 38). These masses are similar in presentation to fibroadenomas, and, typically, manifest as smooth, painless, palpable masses. Sonographically, lactating adenomas frequently demonstrate circumscribed margins, an oval shape, parallel orientation, and posterior acoustic enhancement, which may be pronounced because of milk secretions. Interestingly, these masses may also demonstrate microlobulated margins, perhaps related to distended acini (Figure 5) (30). As with fibroadenomas, infarction may occur and may lead to pain and suspicious imaging findings including irregular margins and posterior acoustic shadowing (27, 30). After the cessation of lactation, these masses often involute in parallel with the breast (39).

**Galactocele**

Galactoceles are milk-filled distended terminal ducts and are the result of duct obstruction in a lactating patient, commonly because of inspissated milk. These masses are benign and are the most common breast masses in patients who are breastfeeding and in patients who have recently stopped or decreased breast feeding, as the body titrates down milk production, although they can also be seen in the third trimester of pregnancy (38, 40).

On imaging, galactoceles usually appear as circumscribed round or oval masses, sometimes with a fat-fluid level that can be seen on mammogram and ultrasound (41) (Figures 6 and 7). Internal echoes are often seen; these echoes should not demonstrate internal vascularity (38) and may change with positioning. Depending on their fat content, galactoceles may be anechoic, hypoechoic, or hyperechoic (35). They may be single or multiple, unilateral or bilateral, and typically measure 2 cm in diameter, but can measure upward of 5 cm (41). The inspissated milk can calcify. Galactoceles often resolve spontaneously, and aspiration is indicated for symptomatic relief or when the imaging appearance is equivocal. Aspiration will yield milky fluid, is diagnostic, and does not need to be sent to cytology.

**Figure 5.** Lactating adenomas. A: Gray-scale ultrasound image in a 34-year-old lactating woman who presented with a palpable mass shows a hyperechoic mass with lobulated margins (arrow) and parallel orientation. B: Color-flow image in the same patient shows internal flow and increased through transmission (arrow). Ultrasound-guided core biopsy confirmed a lactational adenoma. C: Gray-scale ultrasound image in a 36-year-old lactating woman who presented with a palpable area of concern demonstrates an iso- to hypoechoic mass with lobulated margins (long arrow) and cystic spaces (short arrow). D: Color-flow image of the same mass shows internal vascularity and a mixed posterior acoustic pattern (arrow). Ultrasound-guided core biopsy confirmed a lactational adenoma.

**Figure 6.** Galactocele. A: Gray-scale ultrasound image demonstrates a mixed-echogenicity oval mass with smooth margins (long arrow), cystic spaces, and posterior acoustic enhancement (short arrow) in a 36-year-old lactating woman. B: Color-flow image shows only peripheral vascularity. Aspiration yielded milky fluid consistent with galactocele.
Galactoceles can become infected and can then present with symptoms of an abscess, and imaging findings including indistinct and microlobulated margins (Figure 8).

**Mastitis and Abscess**

Mastitis most often occurs within 6 weeks of delivery. The combination of *staphylococcus aureus* from the baby’s skin or mouth and the accumulation of milk in the ducts and lobules is thought to potentiate a retrograde infection (34). Although mastitis itself does not need an imaging work-up, ultrasound to check for abscess can be done when the patient is not responding well to antibiotics or when there is associated focal hardness.

An abscess will appear as a hypoechoic or anechoic mass with microlobulated margins (arrow) that was associated with fevers. Aspiration yielded thick pus and milky fluid, consistent with an infected galactocele.

**Pregnancy-associated breast cancer**

PABC includes breast cancer diagnosed in pregnancy, up to 12 months postpartum, and during lactation. PABC is the most common invasive cancer diagnosed during pregnancy, with an incidence of 1 in 3000 to 1 in 10 000 (44, 45). Cancers in pregnant and lactating patients are more likely to be diagnosed at a later stage than cancers in nonpregnant patients (46–50). Prompt diagnosis is important because treatment is available.

PABC typically presents as a painless mass but may also present as unilateral breast enlargement, skin thickening, bloody nipple discharge, axillary adenopathy, or milk rejection (28, 29). The most common immunohistochemical profile of a PABC is a high-grade invasive ductal carcinoma that is both estrogen and progesterone receptor negative (46). Although these cancers demonstrate similar rates of estrogen- and progesterone receptor negativity, similar human epidermal growth factor receptor HER2/neu status, and similar rates of p53 mutations to cancers in age-matched nonpregnant patients, PABCs are more likely to be larger in size and to show lymphovascular invasion than cancers in nonpregnant age-matched women (46–50).

The advanced stage of PABC may be related to delays in diagnosis, which have been reported at between 2.5 months and greater than the duration of pregnancy (28, 51). Historically, PABC has been associated with a poor prognosis, though when compared with age- and stage-matched controls, prognosis may be similar (52).

Overall, the imaging findings of PABC compared to nonpregnant patients of the same age have been shown to be similar, and the most common finding on ultrasound is of a solid mass, though it may be more likely to show posterior acoustic enhancement, have circumscribed margins, and contain cystic components (Figures 9 and 10) (53, 54).

**Staging during pregnancy and lactation**

Local-regional breast cancer staging is important for treatment planning. Once a breast cancer is diagnosed, the ACR recommends mammography to look for the presence of suspicious calcifications and to assess for multifocal and multicentric disease and ipsilateral axillary ultrasound for staging the axilla (2). Additionally, several studies demonstrate increased cancer detection in up to...
25% of nonpregnant patients who undergo staging with whole-breast ultrasound (11, 12, 53). This increased detection may be especially important in pregnant women with dense breasts, as mammographic sensitivity in dense breasts was shown to be low (45%) for staging (12). Breast MRI with gadolinium is contraindicated during pregnancy (8).

In lactating patients, staging can be performed just as it would be in nonlactating patients. In this setting, breast MRI may be safely performed to evaluate for extent of disease; the patient is advised to breast feed or pump immediately before the exam. Patients do not have to discontinue breast feeding after the MRI, according to the ACR guidelines, given the small amount of gadolinium that is...
excreted into breast milk (10), although pumping for 24 hours could be recommended.

**Treatment**

PABC is treatable with chemotherapeutic and surgical options like those available in nonpregnant patients. Surgery is the local definitive treatment for PABC, and surgical options should generally not differ from those offered to nonpregnant patient, although radiation therapy (RT) cannot be administered. Breast and axillary lymph node surgery during any trimester of pregnancy seems to be associated with minimal fetal risk. However, most surgeons and patients will choose to wait until after 12 weeks of gestation, in order to reduce the risk of spontaneous abortion (55). Many published studies looking at the risk of anasthesia during pregnancy have failed to show an increase in fetal abnormalities (56, 57). A recent review suggested that the optimal timing for surgery during pregnancy is the window between 16 and 20 weeks of gestation (58).

Choice of surgical treatment should be made according to the usual criteria considered for nonpregnant patients. The therapeutic equivalence of mastectomy and breast conserving surgery (lumpectomy followed by radiation) has been demonstrated in nonpregnant women, and this should also apply to the pregnant patient. Breast conserving surgery (BCS) can be used effectively, if RT can be delayed—in some cases, after the administration of adjuvant or neoadjuvant chemotherapy. BCS is a reasonable option and is reported to have no adverse effect on locoregional recurrence rates or complication rates (59–61). As evidenced by multiple breast conservation studies, however, RT is an essential part of BCS in order to achieve optimal local control, and therapeutic RT is contraindicated until after delivery because of the risks associated with fetal exposure to radiation. If RT cannot be delayed, such as in cases where the diagnosis is made early on during the pregnancy and systemic therapy is not necessary, mastectomy can be considered. If breast resection is desired, delaying until after delivery may be preferred in order to minimize intraoperative time.

Axillary staging is an essential component of breast cancer surgery, and the same should be applied to PABC. Assessment of nodal status both preoperatively and intraoperatively provides prognostic information useful when determining need for systemic therapy, and axillary lymph node dissection provides local control when indicated. The use of sentinel lymph node biopsy (SLNB) remains controversial because it has not been systematically evaluated in this setting, and its use should be carefully discussed with the patient. Case series, however, have demonstrated increasing evidence of safety and efficacy of the procedure in PABC (62, 63). Isosulfan blue dye is not recommended because of the risk of anaphylaxis (64). SLNB with radioisotopes is associated with low radiation exposure to the fetus, with some authors suggesting that use of low-dose, double-filtered technetium sulfur colloid should be safe (65). In addition to possible safety issues, it is not clear whether lymphatic pathways in the breasts of patients with PABC are altered, which could make identification of the sentinel node more challenging. Should SLNB be offered, the limited data should be discussed with the patient. Of note, patients presenting with clinically positive ipsilateral axillary lymph node metastases or with inflammatory breast cancer undergoing a surgery-first approach would require complete axillary lymph node dissection (66).

Rojas et al provide an excellent review of breast cancer treatment in pregnant patients (67). Systemic treatment in the adjuvant or neoadjuvant setting should be as close to regimens in nonpregnant patients as possible because delaying systemic treatment in PABC patients may worsen prognosis (68, 69). Moreover, avoidance of pre-term delivery appears to have a positive effect on birth outcomes (69). Chemotherapy should, however, be deferred until after 14 weeks (the first trimester) because organogenesis is considered complete at 10 weeks (69). Congenital malformations have been shown to be higher in patients who receive chemotherapy during the first trimester and to be like that in the general population with chemotherapy administered during the second or third trimesters (70). Specific chemotherapeutic agents including doxorubicin, cyclophosphamide, and combined 5-fluorouracil, doxorubicin, and cyclophosphamide have been studied and not been shown to have significant adverse effects (71–73). Taxanes and platinum derivatives are less studied (74, 75).

**Conclusions**

Breast imaging is safe during pregnancy and lactation, and it should not be delayed. Although most pregnancy-associated masses are benign, newly discovered solid masses should undergo ultrasound-guided core biopsy, with consent for milk fistula and an increased risk of bleeding. PABCs can be treated both locally and systemically during the second and third trimesters similarly to breast cancers not associated with pregnancy—with the exception of RT.

**Conflict of interest statement**

None declared.

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**References**


