
Management of Benign Breast Disease

Heather R. Macdonald

Abstract

The purpose of identifying and treating benign breast disease is twofold: to identify underlying breast cancer or exclude its presence and treat symptoms. The most common breast complaints are breast masses, breast pain, nipple discharge, and breast infections. A palpable breast mass should be evaluated by the triad of clinical breast exam (CBE), imaging (ultrasound in all patients with the addition of mammogram in patients over 30), and biopsy. Mastalgia is the most common breast complaint. A thorough evaluation should be performed to exclude malignancy. Nipple discharge may be physiologic, especially if bilateral, multiple ducts, seen only with expression and clear, green, or black. Medications, especially centrally acting or psychotropic drugs, and nipple stimulation are potential causes of non-pathologic discharge. Nipple discharge that is spontaneous, unilateral, single duct, clear or bloody, or associated with a palpable mass is especially concerning for underlying malignancy. Mastitis is a common occurrence even in non-lactating women. Inflammatory cancer must be ruled out, especially in an inflammation not responding to antibiotics

and supportive measures. Lactating women with a breast infection must drain the breast regularly to prevent milk stasis that encourages bacterial growth. Antibiotic therapy should be guided by what is safe for the nursing infant. Skin flora is the most common pathogen. Referral for specialty services should be provided to patients with atypical biopsies, discordant biopsies, breast cancer, biopsy findings that require excision, nonhealing abscesses, and hereditary breast and ovarian cancer syndromes.

Keywords

Clinical breast exam • Breast mass • Fibroadenoma • Mastalgia • Nipple discharge • Mastitis • Galactorrhea

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H.R. Macdonald (✉)
Keck School of Medicine, University of Southern
California, Los Angeles, CA, USA
e-mail: hmacdona@medmail.usc.edu;
hmacdona@med.usc.edu

1 Introduction

The purpose of identifying and treating benign breast disease is twofold: to identify underlying breast cancer or exclude its presence and treat symptoms. Breast complaints are common in gynecologic practice, and benign breast conditions are within the scope of practice of a general ob-gyn. Referral for specialty services should be provided to patients with atypical biopsies, discordant biopsies, breast cancer, biopsy findings that require excision, nonhealing abscesses, and hereditary breast and ovarian cancer syndromes. Elsewhere in this book, breast cancer screening in the asymptomatic woman is described. This chapter will focus on the evaluation and treatment of the symptomatic patient. Focus will be on the most common breast complaints: breast masses, breast pain, nipple discharge, and breast infections. Table 1 lists conditions for which specialty care is required, and the patient should be referred.

1.1 Clinical Breast Exam

Clinical breast exam (CBE) should be part of a well woman health evaluation. The American College of Obstetricians and Gynecologists recommends women undergo CBE every 1–3 years between ages 20 and 39 and every year after age 40. If the patient is still menstrual, the ideal time to perform the exam is immediately after menses when breast tissue is most quiescent.

The clinical breast exam should encompass all breast tissue from the clavicles to the inframammary folds and from the midaxillary lines to the sternal borders. Axillary and

supraclavicular lymph nodes should be included in the field of examination. On clinical breast exam, dominant masses should be described by size, position on the clockface (with the nipple at the center, 12 o'clock superior, 6 o'clock inferior, etc.), and distance from the nipple (e.g., 2 cm mass at 4:00 3 cm from the nipple). The mobility of the lesion or lack thereof should be described as well as any overlying skin changes. The presence or absence of lymphadenopathy in the axillary or supraclavicular beds should be noted. Findings on clinical breast exam concerning for malignancy include tethering to the skin or underlying muscle, relative immobility of the mass, irregular or indistinct borders of a dominant mass, the presence of a mass with single duct bloody nipple discharge, overlying skin changes including erythema or induration, and the presence of axillary or supraclavicular adenopathy.

1.2 Palpable Mass

A palpable mass is a three-dimensional finding distinct from the surrounding breast tissue and is a common breast complaint. When a patient presents with suspicions of a palpable mass, she should be asked to describe when and how it was first discovered, how long it has been present, and if it is still palpable, does it change with her menstrual cycle, has she appreciated it before (i.e., does it come and go), is it painful, are there skin changes or nipple discharge, and has she had a breast mass previously in either breast. Masses that wax and wane with menstrual cycles are consistent with fibrocystic changes and are rarely pathologic. History of a previous breast cyst or fibroadenoma may be informative as patients are at risk for additional lesions. Alternatively a palpable mass in conjunction with bloody nipple discharge is highly concerning for carcinoma. Overlying skin changes indicate an inflammatory process but can also be concerning for inflammatory carcinoma.

Table 2 describes what should be documented when examination reveals a mass distinct from the surrounding breast tissue. A palpable breast mass should be evaluated by the triad of clinical breast

Table 1 Indications for referral to a breast specialist

Indications for referral to a breast specialist
Atypical breast biopsy
Malignancy
Histologic findings on biopsy that require excision
Nonhealing breast abscess or inflammation
Familial breast cancer syndromes
Discordant breast biopsy results

Table 2 Pertinent findings when documenting a breast mass

Pertinent findings when documenting a breast mass
Laterality
Location expressed as clockface position and distance from the nipple
Size
Associated skin changes (edema, erythema, retraction)
Fixation
Texture (smooth, lobulated)
Tenderness
Presence or absence of axillary or supraclavicular lymphadenopathy

exam (CBE), imaging (ultrasound in all patients with the addition of mammogram in patients over 30), and biopsy. Even in recent series, between 9% and 22% of palpable breast cancers were not apparent on breast imaging (Morrow 2000). In young patients with a benign clinical breast exam and benign appearing imaging (BIRADS 2), tissue sampling may be omitted, but as breast carcinoma or cancerous lesions metastasizing to the breast (lymphoma, sarcoma) can present in teenaged patients, careful consideration should be given to securing a definitive diagnosis of any dominant mass with tissue sampling. Tissue sampling should be accomplished with a needle wherever possible (Silverstein et al. 2009). Surgical excision of a previously unsampled breast mass should be rare. The majority of lesions will be benign and unlikely to need excision. The uncommon malignant lesion will not be completely treated by simple excision (if breast cancer) or may not be treated surgically at all (if lymphoma or metastatic sarcoma). A concordant diagnostic triad of benign CBE, benign imaging, and benign biopsy carries a false-negative rate (or the chance that an underlying cancer may be missed) of less than 1% (Ariqa et al. 2002). Concordance of all three elements of the diagnostic triad is key. Any discordance between the clinical exam, imaging impression, and biopsy results should trigger a second biopsy or surgical excision.

Management of the lesion is guided by the biopsy results. Asymptomatic benign masses less than 3 cm in size can be followed with ultrasounds to demonstrate stability every 6 months for

2 years. Any patient who is bothered by the sensation or presence of a mass should be offered excision. Surgical excision should be considered for lesions larger than 5 cm due to sampling concerns as breast lesions can be heterogeneous. Additionally, larger lesions can be cosmetically destructive even if benign and are better excised before they require more extensive if not reconstructive surgery. If atypia is identified within any lesion, surgical excision is warranted for definitive diagnosis and cancer risk reduction. Table 3 summarizes benign breast histology by risk of breast cancer as well as treatment considerations. Not all lesions listed will present as a palpable mass. For example, radial scar is most often identified by stereotactic core biopsy after a mammographic finding. However they are including Table 3 as a reference for interpreting breast biopsy results.

Table 4 includes benign causes of palpable breast abnormalities and recommendations for management. Common benign causes of palpable breast masses include simple cysts and fibroadenomas. Cysts appear as empty black circles on ultrasound as cyst fluid allows free passage of ultrasound waves without reverberating back to the transducer. They often grow suddenly and are painful at first detection. They may be symptomatic with menses. They may be aspirated to alleviate tenderness. Cyst fluid should only be sent for cytology only if it is frankly bloody, as analysis of cyst aspirate has not been shown to be sensitive or specific for malignancy (Ciatto et al. 1987). Green, black, dark brown, yellow, and clear fluid may be discarded. After cyst aspiration if any mass remains, it should be biopsied to avoid missing the solid component of a complex cyst. Cysts should only be surgically excised if they recur after multiple aspirations.

Fibroadenomas are the most common solid benign mass, occurring in up to 25% of asymptomatic patients (El-Wakeel and Umpleby 2003). Fibroadenomas are biphasic lesions with both epithelial and stromal components. They belong to a family of lesions that include benign phyllodes tumors and cystosarcoma phyllodes. They frequently are nontender, firm, and very mobile and do not change with menses. Lesions less than

Table 3 Breast histology stratified by risk of breast cancer

Breast histology	Lifetime risk of breast cancer	Therapeutic considerations
Carcinoma in situ (DCIS, LCIS)	High risk 30–50%	Breast oncologic care
Proliferative lesions with atypia	Intermediate risk	Surgical excision
Atypical ductal hyperplasia	15–30%	Consider chemoprevention
Atypical lobular		
Proliferative lesions without atypia	Low risk	Annual mammography may consider surgical excision; excise if symptomatic, biopsy discordant, or diagnosis in doubt
Fibroadenoma	<15%	
Moderate/florid ductal hyperplasia of the usual type		
Radial scar/complex sclerosing lesion		
Papilloma		
Papillomatosis		
Sclerosing adenosis		
Flat epithelial atypia		
Nonproliferative lesions (cysts)	Minimal to no increase risk	No intervention indicated
Duct ectasia		May aspirate or excise if symptomatic
Papillary apocrine changes		Note: excise lipoma if >5 cm
Non-sclerosing adenosis		
Periductal fibrosis		
Mild epithelial hyperplasia of the usual type		
Lipoma		

3 cm may be followed expectantly or excised based on patient preference. Many patients with fibroadenoma will form more than one lesion and may not desire multiple excisions. Fibroadenomas larger than 5 cm raise the suspicion of a phyllodes

Table 4 Common causes of palpable breast masses and management

Histology	Management
Breast cyst	Observation; aspiration if painful
Fibroadenoma	Observation if asymptomatic <3 cm Excision if atypical, symptomatic or >3 cm
Fibrocystic change	Observation
Proliferative fibroepithelial lesion	Repeat sampling with needle biopsy or excision to rule out phyllodes tumor

tumor. Larger lesions may be undersampled by needle biopsy and should be excised. Preoperative needle biopsy remains important however because a known phyllodes tumor is excised with a 1 cm margin to minimize recurrence, whereas a known fibroadenoma is not. In fact the compressed pseudocapsule of breast tissue that surrounds a fibroadenoma is carefully preserved at excision as it will decompress, often by the time the skin is closed, to fill in the defect left by the excised lesion. Phyllodes tumors even if benign are always excised as they are locally aggressive and cosmetically destructive.

The management of breast cancers, carcinomas or sarcomas, is beyond this chapter.

1.2.1 Breast Pain

Mastalgia is the most common breast complaint (Morrow 2000). It is more common among premenopausal patients than postmenopausal. Association with an underlying cancer is unusual but not impossible: in one series 16% of 240 patients with breast cancer presented with pain alone as an initial symptom (Preece et al. 1982). Concern for an underlying cancer may be what prompts the patient to seek medical attention, and a thorough evaluation should be performed to exclude malignancy.

Cyclic mastalgia is generally described as a dull heaviness, worsened with pressure and movement and poorly localized. It may radiate to the axilla or shoulder. It may be alleviated with anti-inflammatory medications. Noncyclic mastalgia is unrelated to timing of the menstrual cycle and is more common in the 40s and 50s. It may also be

poorly localized and may not respond to over-the-counter medications. The underlying cause of breast pain is unknown. Premenstrual mastalgia suggests a hormonal cause, but no fluctuations or abnormalities of serum estrogen or progesterone levels have been shown to be associated with breast pain. Overuse of caffeine has also been postulated, but three studies looking at caffeine exposure and restriction in response to breast pain, including randomized control trials, have not demonstrated an association (Allen and Froberg 1987).

In eliciting a history from a patient with breast pain, the duration and character of the pain should be characterized, as well as its location and relationship to the menstrual cycle. Any patient with recently missed menses should be evaluated for pregnancy as breast pain can be an initial symptom of a recently pregnant patient. The evaluation of mastalgia includes a clinical breast exam and a screening mammogram if the patient is over 35. Younger women may be appropriately evaluated with clinical breast exam alone without imaging if the exam is normal. Any palpable abnormality should be evaluated with ultrasound and possibly biopsy. Focal areas of tenderness may be ultrasounded to detect an underlying cyst too deep to appreciate on exam. Mastalgia is often self-limiting, resolving spontaneously in 3–6 months up to 80% of cases (Orr and Kelley 2016). Patients for whom the pain is severe enough to interfere with daily life and for whom it has persisted beyond the 3–6-month window expected for spontaneous resolution are candidates for intervention. Table 5 outlines treatment options for mastalgia. The only FDA-approved medication for breast pain is danazol, an antigonadotropin. Response rates in clinical trials approached 75% for both cyclic and noncyclic breast pain at doses of 100–400 mg/day, with a slightly better rate seen in noncyclic pain patients (Mansel et al. 1982). Side effects include virilizing symptoms including deepening voice, weight gain, acne, and male-pattern hair loss and hair growth and limit its acceptability to patients. Tamoxifen a mixed estrogen receptor agonist/antagonist can be tried in an off-label manner for 3–6 months. It blocks estrogen stimulation of the breast. Small studies of 10–20 mg daily have demonstrated pain relief

Table 5 Treatments for breast pain

Agent	Comments and side effects
NSAIDs	Short-term efficacy
Evening primrose oil	Equivalent to placebo in randomized control trials
Danazol	Only FDA-approved medication for mastalgia Side effects: acne, androgenic (male-pattern weight gain and hair growth and loss, deepening voice)
Bromocriptine	Off-label use Decrease prolactin and stimulation of the breast Side effects: dizziness, potential for seizure if stopped suddenly
Tamoxifen	Off-label use Estrogen antagonist at the breast Off-label use Side effects: menopausal symptoms, irregular vaginal bleeding due to endometrial stimulation; rare (VTE, cataracts, uterine cancers)

(Fentiman et al. 1986; Messinis and Lolis 1988). Side effects include vaginal discharge, irregular uterine bleeding, and hot flushes. Long-term use has been associated with increased thromboembolic events, endometrial stimulation including hyperplasia and cancer, and cataracts.

For patients wanting to try a herbal approach, evening primrose oil has been studied to treat breast pain with mixed results that mimic placebo effect; however, side effects were rare (Morrow 2000). Studies investigating caffeine restriction and vitamin E supplementation showed no benefit. Surgery has no role in the treatment of breast pain outside the excision of a tender mass.

1.2.2 Nipple Discharge

Nipple discharge can be divided into physiologic discharge, potentially pathologic discharge, and discharge due to an underlying endocrine disorder or medication use. Single duct spontaneous clear or bloody nipple discharge is concerning for underlying breast pathology and should be worked up rigorously. The most common cause of spontaneous bloody nipple discharge is a benign intraductal papilloma, but an underlying ductal carcinoma must be ruled out.

Table 6 Characteristics of nipple discharge

Likely physiologic discharge	Likely breast pathology	Consider endocrinopathy or medication cause
Bilateral	Unilateral	Unilateral or bilateral
Multi-duct	Single duct	Multi-duct
Seen with expression only	Spontaneous	Spontaneous
Clear, green, brown, black	Clear or bloody	Milky
History of nipple stimulation	No history of nipple stimulation	No history of nipple stimulation
	Presence of a palpable mass	Menstrual irregularities

Key questions to ask when taking the history of a patient complaining of nipple discharge include the color of the discharge, with bloody or clear being most concerning and black or green being most likely physiologic. The patient should be asked to describe whether it is spontaneous or seen only with expression or manipulation of the nipple. If the patient has seen the discharge as it exists the nipple, she should be asked if it extrudes from one duct or several, with physiologic discharge seen at multiple points on the nipple. Single duct spontaneous discharge is most concerning. Table 6 describes pertinent characteristics that discern physiologic discharge from pathologic.

On clinical breast exam, the examiner should perform the exam as usual but then sweep all four breast quadrants with an eye on the nipple to note where pressure on the breast elicits the discharge. If discharge is expressed, the area of the breast being examined when the discharge was seen should be noted, as well as the color and how many ducts it involves. In the past, discharge has been sent for cytology. Studies have shown low sensitivity and specificity of cytologic studies of nipple discharge, so the test should no longer be ordered. Nipple discharge most concerning for underlying malignancy is single duct spontaneous clear or sanguineous discharge associated with a palpable mass. Workup includes diagnostic mammography, retroareolar ultrasound on

the affected side, and biopsy of any identified lesions. If exam, mammogram, and ultrasound fail to identify a source, a ductogram may be considered. By injecting a radiopaque dye into the affected ductal system, a filling defect on subsequent mammogram may identify an intraductal mass. The ductogram is limited in its ability to localize and biopsy a lesion however. In the past decade, ductogram has largely been replaced by breast MRI with and without contrast, as lesions can be localized and biopsied with MRI guidance.

Physiologic nipple discharge is common with repeated nipple stimulation, for example, with rigorous routine self breast exam, sexual activity, or nipple piercing or accessories. Once discharge is seen, some patients may feel a sensation of fullness behind the nipple that is alleviated by expressing the discharge, and others may feel compelled to express discharge in an effort to keep the area clean. By repeatedly expressing or checking for discharge, they are reinforcing its production and increasing its occurrence. The color is often black, brown, green, creamy, or clear and usually is elicited from more than one duct in the nipple. Retroareolar ultrasound may identify dilated ducts or duct ectasia. Green or black multi-duct nipple discharge that is seen only with expression from the nipple is not pathogenic but may be unnerving for the patient. Careful explanation of the mechanism of nipple stimulation to increase fluid production from the nipple and breast is important for patient reassurance, and treatment is cessation of nipple stimulation to diminish fluid production.

Galactorrhea, or bilateral milky or creamy nipple discharge, usually identified in the absence of breast stimulation and coming from multiple ducts in both breasts is suggestive of an underlying endocrine disorder. Both prolactin-secreting tumors and hypothyroid disorders can present with galactorrhea. Please see the chapter entitled “► [Hyperprolactinemia, Galactorrhea, and Pituitary Adenomas](#)” for a more detailed discussion of galactorrhea. History and physical should focus on symptoms and signs of endocrinopathy

including infrequent or absent menses, headaches, bitemporal vision loss, changes in appetite and weight, dryness of the hair and skin, and depressed energy and mood. Lab studies should include TSH and prolactin. If prolactin is elevated, a brain MRI focused on the sella turcica for pituitary lesions should be obtained and the patient referred for specialty care. Treatment may involve resection or medical therapy with anti-prolactin medication like bromocriptine.

Nipple discharge may also be related to medication use, particularly psychotropic medications. A careful medication history should be taken with attention paid to medications started or stopped in coincidence with onset of discharge.

1.3 Mastitis

Mastitis or inflammation of the breast can be due to several underlying causes: an acute peripheral abscess, a subareolar or periareolar abscess or fistula, granulomatous mastitis most commonly idiopathic in this country, or inflammatory breast cancer. Each has distinct presentation, treatment, recurrence risks, and workup.

Mastitis is most commonly due to a bacterial infection. The most common pathogen is *Staphylococcus aureus* or skin flora. Antibiotic treatment is often initiated after a presumptive diagnosis of bacterial infection is made, but careful follow-up within 1 week is warranted to exclude a missed diagnosis of breast cancer. Risk factors for breast infections and abscesses in non-lactating women include diabetes, smoking, and obesity. Common presenting symptoms are pain, redness, warmth, and fever. On physical exam, the affected breast is warm to touch, erythematous, and tender. An associated mass suggests an underlying abscess, and a breast ultrasound should be ordered for further evaluation. Abscesses smaller than 5 cm are often amenable to needle drainage; larger abscesses may require surgical incision and drainage. Antibiotic coverage should vary by local sensitivities, but Table 7 lists suggested targeted therapies to common pathogens. Patients should

Table 7 First-line antibiotic therapy for mastitis

Condition	Therapy
Mastitis	Dicloxacillin, cephalexin
If penicillin allergic	Clindamycin, erythromycin
If MRSA is suspected or confirmed	Trimethoprim-sulfamethoxazole double strength, clindamycin

be followed closely for several weeks to ensure response to treatment. A clinical diagnosis of mastitis that does not respond to appropriate antibiotic treatment should be reevaluated for underlying malignancy. Ultrasound may be used to identify an underlying mass or lymph node for needle biopsy. If pus is encountered, it should be cultured for pathogen and sensitivities as antibiotic resistance is a growing problem.

Bacterial infections of the breast are common in 10–20% of patients who are postpartum or nursing but may occur in otherwise healthy non-lactating women. Risk factors include milk stasis, blocked ducts, ineffectual infant feeding due to latch issues or poor suck, stress, tight-fitting clothes or bras, or skin irritation and breakdown. Clinical presentation is similar to breast infections in non-lactating women. Treatment includes antibiotics, warm compresses to encourage milk expression, and aggressive massage and nursing (or pumping) to alleviate milk stasis. Antibiotic therapy should include aerobic and anaerobic coverage and should be with an agent safe for breastfeeding (see Table 7). Continuation of breastfeeding should be encouraged as prevention of milk stasis is of paramount importance to clear the infection. Infants are more effective at draining the breast than pumps. Mothers can be reassured the breast infection does not pose a risk to her infant due to mother's immunity present in the milk, antibiotic present in the milk, and an infant's gastrointestinal immune defenses. If the mother chooses to stop breastfeeding, often due to discomfort, she should be educated she needs to continue to drain the breast with hand expression or a pump until the infection resolves. If an abscess is present, it should be treated similarly to that in a non-lactating patient. She should be

counseled regarding the rare risk of milk fistula formation but be reassured most spontaneously resolve with cessation of breastfeeding.

Peri- or subareolar abscesses are a distinct entity from peripheral breast abscesses. Patients will present with a painful subareolar infection that commonly fistulizes with drainage of pus from a defect at the periareolar border. They are frequently recurrent. Smoking is an important risk factor (Orr and Kelley 2016). The pathogenesis is thought to be squamous metaplasia of the terminal ductal epithelium with intussusception of secretions leading to infection and abscess formation. Acute abscesses should be treated with drainage if not draining already and antibiotics. When the inflammation has subsided, a duct excision via a radial incision is indicated to remove the occluded duct and excise the fistulous tract to prevent or treat a chronic fistula.

Every nonhealing abscess should be evaluated with biopsy of the abscess wall to rule out inflammatory breast cancer. If no breast mass is identifiable by exam or imaging, the leading edge of skin erythema should be sampled with a punch biopsy. Inflammatory breast cancer can be readily identified by tumor cells in the dermal lymphatic system, creating the classic peau d'orange skin appearance of thickened erythematous skin with dimpled appearance. Inflammatory breast cancer is a poorly differentiated aggressive breast cancer that is systemic at its inception and carries a poor prognosis. The patient should be referred immediately to oncology for chemotherapy.

Rarely biopsy may reveal granulomatous mastitis, caused by either fungal or tuberculosis infections in the developing world but more commonly idiopathic granulomatous mastitis (IGM) in the USA. IGM describes an even more rare condition that presents with acute inflammatory changes and abscesses in the absence of infection or malignancy. It is a diagnosis of exclusion with granulomas seen on biopsy but no TB or fungal infections identified on special staining. The natural history is that of spontaneously occurring and resolving breast abscesses. Effective treatment is unknown although short courses of steroids are often used to diminish inflammation.

2 Conclusion

Breast complaints are common and distressing to patients, both due to their symptomatology and an underlying cancer-related anxiety. The evaluation of a breast complaint should be thorough to detect or rule out breast cancer and if appropriate reassuring to the patient. We have discussed the most common causes of benign breast disease. Patient education regarding normal breast health and abnormal breast findings is important.

References

- Allen SS, Froberg DG. The effect of decreased caffeine consumption on benign proliferative breast disease: a randomized clinical trial. *Surgery*. 1987; 101:720–30.
- Ariqa A, Bloom K, Reddy VB, Kluskens L, Francescatti D, Dowlat K, Szipikou P, Gattuso P. Fine-needle aspiration of clinically suspicious palpable breast masses with histopathologic correlation. *Am J Surg*. 2002; 184(5):410–3.
- Ciatto S, Cariaggi P, Bulgaresi P. The value of routine cytologic examination of breast cyst fluids. *Acta Cytol*. 1987;32:301–4.
- El-Wakeel H, Umpleby HC. Systematic review of fibroadenoma as a risk factor for breast cancer. *Breast*. 2003;12:302–7.
- Fentiman IS, Brame K, Caleffi M, Chaudary MA, Hayward JL. Double blind controlled trial of tamoxifen therapy for mastalgia. *Lancet*. 1986;1:287–8.
- Mansel RE, Wisbey JR, Hughes LE. Controlled trial of the antigonadotropin danazol in painful nodular benign breast disease. *Lancet*. 1982;1:928–30.
- Messinis IE, Lolis D. Treatment of premenstrual mastalgia with tamoxifen. *Acta Obstet Gynecol Scand*. 1988; 67:307–9.
- Morrow M. The evaluation of common breast problems. *Am Fam Physician*. 2000;61(8):2371–8.
- Orr B, Kelley JL. Benign breast diseases: evaluation and management. *Clin Obstet Gynaecol*. 2016;59(4): 710–26.
- Preece PR, Baum M, Mansel RE, Webster DJ, Fortt RW, Gravelle IH. Importance of mastalgia in operable breast cancer. *Br Med J*. 1982;284:1299–300.
- Silverstein MJ, REcht A, Lagios MD, Bleiweiss IJ, Blumencranz PW, Gizienski T, Harms SE, Harness J, Jackman RJ, Klimberg VS, Kuske R, Levine GM, Linver MN, Rafferty EA, Rugo H, Schilling K, Tripathy D, Whitworth PW, Willey S. Image-detected breast cancer: state-of-the-art diagnosis and treatment. *J Am Coll Surg*. 2009;209(4):504–20.