

Anna I. Holbrook<sup>1</sup>

Keywords: breast cancer, breast pain, malignancy, mastalgia

doi.org/10.2214/AJR.19.21923

Received June 26, 2019; accepted after revision September 13, 2019.

<sup>1</sup>Department of Radiology and Imaging Sciences, Emory University, 1701 Uppergate Dr, Ste C1104, Atlanta, GA 30322. Address correspondence to A. I. Holbrook (aiholbr@emory.edu).

AJR 2020; 214:259-264

0361-803X/20/2142-259

© American Roentgen Ray Society

# Breast Pain, A Common Grievance: Guidance to Radiologists

**OBJECTIVE.** Breast pain is a common complaint among women and a frequent reason they seek health care, including imaging. However, breast pain is infrequently associated with breast cancer. This article reports and synthesizes the evidence about the risk of malignancy with breast pain, the use of imaging to evaluate breast pain, the detection of treatable symptomatic lesions by imaging, and the ability of negative examination findings to reassure patients. Evidence-based guidance for the imaging evaluation of breast pain is presented, and areas that warrant further research are described.

**CONCLUSION.** The studies evaluating the role of imaging in breast pain are limited and conflicting. The clinician and patient should discuss the drawbacks and benefits of imaging to decide whether it is worth pursuing. If imaging is performed, ultrasound, mammography, or both should be done depending on the age of the patient. Areas worthy of further research include larger studies using modern techniques to evaluate the utility of imaging in patients with breast pain, the best way to assist clinicians in avoiding unnecessarily imaging patients with breast pain, and the utility of imaging results to reassure patients with breast pain.



reast pain is a common complaint among women and a frequent reason they seek health care, including imaging.

# **Clinical Vignette**

A 48-year-old woman presents with 2 months of constant focal pain in the left breast at the 2-o'clock position. Clinical examination findings are normal. The referring provider ordered diagnostic mammography and ultrasound. Mammography (Figs. 1A–1C) shows heterogeneously dense breast tissue with no abnormality. Ultrasound (Fig. 1D) reveals no abnormality at the site of pain.

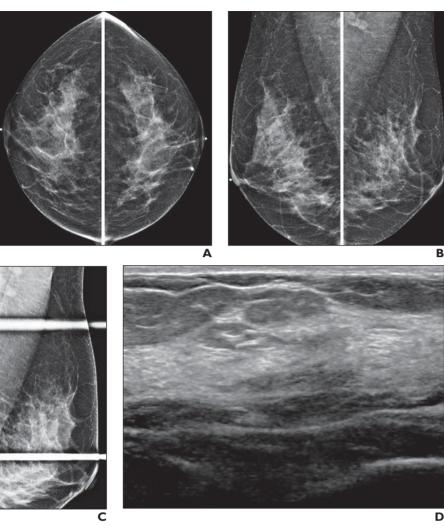
# **The Imaging Question**

Breast pain without other suspicious symptoms is rarely, if ever, associated with cancer [1–6]. Despite this, breast pain is an exceedingly common reason for women to undergo a diagnostic imaging workup [6], typically including ultrasound with or without preceding mammography depending on the patient's age [7]. Why perform imaging of patients with pain if the likelihood of cancer is so low? The answer lies in exactly how low that likelihood is. If it is greater than the background rate of cancer detected by screening, diagnostic imaging should be considered. If it is not more than the background rate of cancer, diagnostic imaging could be considered a waste of health care resources; however, some argue that even with a very low probability of detecting breast cancer, imaging in the setting of breast pain is important to exclude treatable causes of pain and to reassure the patient that she does not have breast cancer [3, 8, 9].

Many questions are raised regarding how we currently manage breast pain. How appropriate is imaging in the workup of breast pain? How likely is it that malignancy will be found on imaging? How well do the various imaging modalities perform in the evaluation of breast pain? How effective is imaging in detecting treatable causes of pain? Finally, is a normal result helpful in reassuring patients?

## Background

Breast pain is a very common complaint and frequently leads to health care utilization. A study of 2400 women enrolled in an HMO found that breast pain was the most common breast symptom experienced, accounting for almost half of all primary care encounters for a breast-related complaint [10]. Scurr et al.



**Fig. 1**—48-year-old woman who presented with 2 months of constant focal pain in left breast at 2-o'clock position and normal findings at clinical examination.

A and B, Bilateral diagnostic mammograms including craniocaudal (A) and mediolateral oblique (B) views show heterogeneously dense breast tissue with no abnormality.

**C**, Mediolateral oblique spot mammogram of left breast also shows heterogeneously dense breast tissue with no abnormality.

D, Ultrasound image obtained at 2-o'clock position reveals no abnormality at site of pain.

[11] found that more than half of the women they surveyed experienced breast pain. Another study found that up to 69% of women reported regular premenstrual breast pain and that 36% of these women had consulted a health care provider about the pain. Women younger than 36 years old with pain were almost 5 times more likely to have undergone mammography than women in the same age group without pain [12].

# Synopsis and Synthesis of Evidence

Risk of Malignancy in Patients With Breast Pain

The risk of malignancy in patients presenting with pain depends on the type of pain experienced. Cyclic pain, or that associated with the menstrual cycle, and diffuse pain are not known to correlate with the presence of breast cancer. Many studies show the benign nature of cyclic pain and diffuse pain [1, 2].

Noncyclic focal pain has been found to have a low, yet extant, association with malignancy in some studies. In one of the classic studies describing the association of breast pain with malignancy, Preece et al. [13] determined in 1982 that of 240 patients presenting with operable breast cancer, 17 (7%) had pain as the sole presenting symptom, with the pain being described as "well localized and persistent." This study's applicability to current times is likely limited because it was performed when screening mammography was much less prevalent than it is today and more patients presented with other additional symptoms. In a more recent study, Leddy et al. [8] found three cancers in 257 (1.2%) women with focal breast pain (Table 1).

On the other hand, many studies have found that there is no association of even noncyclic and focal pain with malignancy. In a study of 200 women younger than 30 years old presenting with both cyclic pain (38% of patients) and noncyclic pain (62% of patients) and normal breast examination findings, no cancers were found on ultrasound [1]. Similarly, Leung et al. [9] found no cancers in 110 ultrasound examinations for focal pain.

In other studies, investigators report a nonzero malignancy rate at the site of focal pain; however, they found that the malignancy rate was not higher than that found in women without pain or in areas that were not painful (i.e., similar to background incidence). Duijm et al. [3] followed 987 women with isolated breast pain referred for diagnostic workup and 987 women with no breast symptoms who underwent screening mammography. Four (0.4%) malignancies were found in the group with pain, and seven (0.7%) cancers were found in the control group [3]. Noroozian et al. [14] found three (0.5%) cancers in the painful breast of 617 women within 12 months of presentation (95% CI, 0-1.0%). They reported that the Surveillance, Epidemiology, and End Results Program data of a similar age group showed a 0.3% incidence of malignancy, which falls within the 95% CI of the study group [14]. Tumyan and colleagues [15] found that in 86 women with isolated focal pain, there were two (2.3%) cancers at the site of pain and two (2.3%) cancers at sites unrelated to the pain. Owen et al. [5] had similar results, with a cancer incidence of 0.3% (3/944) at the site of focal breast pain in women with no other symptoms and an incidence of 0.4% (4/944) remote from the site of pain. In a study of 799 patients with breast pain and no other symptoms, Kushwaha and colleagues [6] found one cancer (0.1%) in the contralateral asymptomatic breast, which is lower than the concurrent cancer detection rate in their screening population (5.5/1000, 0.6%). Cho et al. [16] found no cancers in 413 cases of breast pain at initial workup but found one (0.2%) cancer within 1 year of follow-up. Chetlen and colleagues [2] reviewed the data of 236 women with isolated breast pain and found one cancer (0.4%). Although the Cho

First Author [Reference No.] (Year of Publication)	No. of Patients	Mean (Range) Age (y)	Pain Type	Imaging Technique	No. (%) of Cancers at Site of Pain	No. (%) of Benign Imaging Findings at Site of Pain	No. (%) of Biopsies Recommended at Site of Pain With Benign Result	False-Positive Findings (%)
Chetlen [2] (2017)	236	Cyclic pain, 36.8 (19–48); noncyclic focal pain, 44.9 (19–80); noncyclic nonfocal pain, 49.8 (25–83)	Isolated, focal and nonfocal, cyclic and noncyclic	Mammography, ultrasound, or both	1 (0.4)	6 (2.5)	NN	NR
Cho [16] (2017)	369 <sup>a</sup>	53 (23–86)	Isolated, focal	Mammography and ultrasound	0 (0) at presentation; 1 (0.2) within 12 mo of presentation	NR	24	5.8
Duijm [3] (1998)	987	50 (10–86)	Isolated, focal and nonfocal	Mammography, ultrasound, or both	4 (0.4)	85 (8.6)	20	2.0
Kushwaha [6] (2018)	799	46 (13–92)	Isolated, focal and nonfocal	Mammography, ultrasound, MRI, or a combination of these techniques	0 (0)	39 (4.9)	R	NR
Leddy [8] (2013)	257	48.7 (12–85)	Isolated, focal	Ultrasound alone or ultrasound and mammography	3(1.2)	73 (28)	19	7.4
Leung [9] (2002)	d 66	41 (23–77)	Isolated, focal	Ultrasound alone or ultrasound and mammography	0 (0)	22 (20)	m	2.7
Mema [17] (2019)	559	46 (27–97)	Focal and nonfocal; cyclic and noncyclic; isolated and associated with other symptoms	Ultrasound (after negative mammogram)	2 (0.4) when other symptoms present; 0 (0) when isolated pain	NR	24	4.3
Noroozian [14] (2015)	617	49 (23–88)	Isolated, focal and nonfocal	Mammography, ultrasound, or both	2 (0.3) at presentation; 9 (1.5) after presentation	52 (8.4) at presentation; 11 (1.8) after presentation	27	4.4
Ölçücüoğlu [1] (2013)	200	24.6 (18–30)	Isolated, cyclic and noncyclic	Ultrasound	0) (0)	102 (51)	NR	NR
Owen [5] (2019)	944	47 (18–90)	Isolated, focal	Mammography, ultrasound, or both	3 (0.3)	94 (10)	9	0.6
Tumyan [15] (2005)	86	54 (26–88)	Isolated, focal	Mammography and ultrasound	2 (2.3)	R	7	8.1
Note—NR = not reported. <sup>a</sup> 413 cases. <sup>b</sup> 110 examinations.								

and Chetlen studies did not compare the malignancy rates of the group with pain and the control group, the malignancy rates in those studies are similar to those of other studies reporting malignancy rates of women with breast pain to be equal to malignancy rates in women without pain or in areas that are not painful [2, 16].

## Performance of Imaging Modalities in Evaluating Breast Pain

Mammography and ultrasound have been found to perform well in excluding cancer in women with breast pain. One study found a negative predictive value (NPV) of mammography with or without ultrasound in women with isolated breast pain to be 99.8% [14]. Tumyan and colleagues [15] found an NPV for mammography and ultrasound of 100% in patients with focal breast pain in the absence of a palpable mass. In a study evaluating women presenting with focal breast pain in the absence of a palpable lump, Leddy et al. [8] calculated the specificity of mammography alone to be 87.8%, ultrasound alone to be 92.5%, and mammography combined with ultrasound to be 83.7%. The sensitivity as well as the NPV of mammography, ultrasound, and the two modalities combined were all 100%. Owen et al. [5] found similar results in a study of women with isolated focal breast pain, with combined mammography and ultrasound having a sensitivity of 100%, NPV of 100%, and specificity of 98.9%.

However, given the low incidence of cancer and the effectiveness of the modalities in showing benign as well as malignant lesions, the positive predictive value (PPV) of the modalities was also low. In the study by Leddy et al. [8], mammography alone detected three cancers with 25 false-positives for a PPV of 10.7%; ultrasound alone found three cancers with 19 false-positives for a PPV of 13.6%; and combined mammography and ultrasound found three cancers with 33 false-positives for a PPV of 8.3%. Owen et al. [5] reported that combined mammography and ultrasound detected three malignancies and six false-positives for a PPV of 33.3%. In another study, 46 of 987 women (4.7%) underwent biopsies of the painful area that ultimately turned out to be benign [3]. In the study of Noroozian et al. [14], 63 of 617 (10.2%) women had a benign lesion detected, and almost half of those women (28/63, 44.4%) underwent biopsy. In the series of 413 cases of breast pain evaluated by Cho et

## Holbrook

al. [16], there were 76 cases of an imaging finding (all benign), and 24 (31%) underwent biopsy. They also found that ultrasound detected incidental findings unrelated to pain in 7% (27/413) of cases.

Several studies question whether ultrasound can be avoided in cases in which mammography findings are negative. A retrospective study of 375 women with isolated breast pain and a negative mammogram had no malignancies detected on ultrasound regardless of breast density [17]. Leddy et al. [8] found that in 206 patients who underwent ultrasound in addition to mammography, there were a resulting eight additional biopsies and 14 additional 6-month followup examinations without the detection of any additional cancers. In a study by Owen et al. [5], all cancers detected in women with focal breast pain were seen on mammography. but none were detected only by ultrasound. However, Cho and colleagues [16] found that with regard to lesion detection (all benign), negative mammography findings did not suffice, especially in women with dense breasts. In women with dense breasts, ultrasound was able to detect a lesion that mammography missed in 40 of 56 cases (71%). In women with nondense breasts, ultrasound found lesions that were not detected on mammography in six of 20 (30%) cases [16].

#### Detection of Treatable Lesions

Studies have shown that if a cyst is detected in cases of isolated focal breast pain, then the cyst is generally small and rarely undergoes aspiration for symptomatic relief. In a study of 200 women younger than 30 years old who presented with pain and underwent ultrasound, a simple cyst (mean diameter, 7.8 mm) was detected in 45 patients (22.5%) [1]. In another study, of the 85 of 987 (8.6%) women with isolated pain in whom benign findings were detected, most benign findings were small cysts [3]. The authors raised doubts about whether small nonpalpable cysts can cause pain [3]. Tumyan et al. [15] found cysts in the area of pain in 24 of 86 patients, but only two underwent aspiration. Leung and colleagues [9] found 15 cysts, ranging in size from 3 to 30 mm, in 110 (13.6%) ultrasound examinations for focal pain. None were aspirated for symptomatic relief because either the patient declined or the referring physician declined [9]. In another study of 617 patients, intervention for symptomatic relief was performed for only four (0.6%) women for findings of painful cysts (n = 2),

granulomatous mastitis (n = 1), and a schwannoma (n = 1) [14]. In a study of 799 patients, Kushwaha et al. [6] found that 39 (5%) had an imaging correlate at the site of pain, including simple cysts, benign circumscribed masses, edema and skin thickening, and fluid collections; however, none underwent intervention for relief of symptoms [6].

#### Role of Reassurance by Negative Examination Findings

Many studies state that imaging should be performed to provide reassurance in women with pain [3, 8, 9]; however, proof that negative examination findings actually reassure patients is lacking [18]. One small study of 51 patients with breast pain found that the patients experienced a reduction in pain and anxiety immediately after receiving negative ultrasound examination findings; however, the median anxiety score after ultrasound was still in the moderate to low range, suggesting only partial reduction in anxiety [19]. Also, because no longer-term testing was done, it is not known if the decrease in anxiety was maintained over time. A study of women who presented to a specialty breast clinic with pain found that a benign diagnosis did not reassure 41.5% of patients independent of the type of diagnostic test performed [20]. Furthermore, several studies have suggested that a negative test result may have no effect on patient anxiety and may actually increase anxiety [21, 22]. In fact, Howard et al. [23] reported that women with breast pain who were imaged at the time of their initial provider visit had an increased chance of further clinical services utilization such as more imaging tests, biopsies, or clinical visits to breast specialists compared with those who did not receive imaging. Even when imaging findings were normal, the women who underwent imaging were more likely to undergo further clinical services utilization than women who did not undergo imaging by an odds ratio of 18 (95% CI, 9.4-59.0) [23].

#### **Evidence-Based Guidance**

The studies evaluating the role of imaging in breast pain are limited. They are small, few in number, retrospective, and contradictory. A review article that included several of these studies found the quality of evidence to be very low [24]. The authors stated that there was not enough evidence to recommend imaging in the setting of pain and made a weak recommendation for shared decision making in the clinical setting [24]. Patients should be in-

#### **Breast Pain**

formed of the low risk of malignancy associated with breast pain, and clinicians should keep in mind that negative imaging examination findings are unlikely to reassure the patient.

If the decision is made to image, the American College of Radiology Appropriateness Criteria expert panel has developed recommendations for the initial evaluation of patients presenting with breast pain that can be followed [7]. Recommendations vary depending on the age of the patient and whether the pain is considered clinically significant or insignificant. Pain is categorized as clinically significant if it is focal and noncyclic. Clinically insignificant pain is nonfocal (defined as greater than one quadrant), diffuse, or cyclic. In women younger than 30 years old with clinically significant pain, ultrasound is recommended. Women 30-39 years old with clinically significant pain can be evaluated with mammography or ultrasound as the initial study. In women 40 years old or older, both mammography and ultrasound should be performed, although some argue that if mammography is done, ultrasound should be performed only if the area of pain is dense enough to potentially obscure a malignancy [5]. Mammography may be omitted if the patient has undergone mammography within the previous 3-6 months [7]. Imaging other than that prescribed by screening guidelines is not recommended in women with clinically insignificant pain. There is no role for MRI in evaluating breast pain. Patients presenting with pain plus another symptom, such as a lump, nipple retraction, or nipple discharge, should be evaluated for that symptom.

# Outstanding Issues That Warrant Research

The literature regarding the association of breast pain with malignancy is limited. The few studies that have been performed are retrospective and small. Although they report similar low rates of malignancy (0-2.3%), interpretations of these results vary [1-3, 5, 6, 8, 9, 14-16]. Some studies compare the small numbers of cancer found at the site of pain with the number of cancers found either at a nonpainful site or in women without pain. These studies conclude that there is no need for diagnostic imaging [3, 6]. Other studies conclude that the existence of any cancers justifies diagnostic imaging without taking into account the background rate of cancers that would have been found by screening [2, 8, 14]. It should also be noted that the definition of "site of pain" in many of these studies may be vague, perhaps focused on a quadrant of the breast. Even when the cancer is reported to have been found "at the site of pain," it is not possible to undoubtedly conclude that the cancer and pain truly coincide because pain is subjective.

Although there is ongoing disagreement, patients with breast pain as the only symptom continue to be imaged and to use health care resources. Kushwaha and colleagues [6] estimated the cost of working up breast pain with imaging and found a mean cost per patient of \$328. Given that approximately 6% of their almost 14,000 patients were referred for diagnostic evaluation of breast pain during the 1-year-long study period, this strategy resulted in a total estimated cost of \$261,816 and no malignancies were found at the site of pain [6].

What is needed is more research with a large number of patients using modern techniques, such as tomosynthesis. Imaging patients with breast pain is a significant part of the day-to-day practice of most breast imagers, and it would be of great benefit to our specialty to see conclusively if there is truly an association between pain and malignancy that is greater than that found by screening or if imaging may not be necessary beyond that recommended by screening guidelines. Long-term studies evaluating the incidence of cancer in the painful breast over time would also be of interest.

Another issue is that raised by the patients who are referred to imaging for cyclic or diffuse pain—the types of pain definitively not associated with malignancy. It is not known what percentage of patients seen by clinicians for benign pain are referred for imaging, but certainly some still are. More work needs to be done about the best ways to communicate with and educate clinicians about the low risk of malignancy in patients with breast pain, particularly cyclic or diffuse pain, and support them as they reassure the patient in the clinic without sending them for imaging. Reassurance by clinicians has been found to decrease breast pain [25].

Finally, another unsolved issue is that of how much reassurance can be offered by imaging. Many authors declare patient anxiety as a reason to image patients with breast pain [3, 8, 9], but only one study shows a benefit and that benefit was only partial reduction in anxiety [19]. Several other studies raise doubts about whether negative imaging findings are actually reassuring [18, 20– 23]. There is also certainly variability in the interaction between breast imagers or clinicians and their patients, which may impact the effectiveness of reassurance.

More work could be done in this area, with large studies evaluating the anxiety levels of patients before and after imaging, including at long-term follow-up, as well as communication techniques that may increase patient reassurance.

#### Summary

The recent literature regarding the association of breast pain and malignancy suggests limited or no association. Several studies recommend decreased use of imaging resources for this common and usually benign complaint. The clinician and patient should discuss the drawbacks and benefits of imaging and decide whether it is worth pursuing. If imaging is done, ultrasound, mammography, or both should be done depending on the age of the patient.

Large trials using modern techniques are needed to conclusively prove or disprove any benefit of diagnostic imaging in patients with isolated breast pain. Additionally, more work should be done to assist clinicians in avoiding unnecessarily imaging patients with breast pain. Finally, it would be helpful to perform studies that prove or disprove the utility of imaging for the reassurance of patients with breast pain.

## References

- Ölçücüoğlu E, Yılmaz G. Mastodynia: is imaging necessary in young patients? Ulus Cerrahi Derg 2013; 29:17–19
- Chetlen AL, Kapoor MM, Watts MR. Mastalgia: imaging work-up appropriateness. *Acad Radiol* 2017; 24:345–349
- Duijm LE, Guit GL, Hendriks JH, Zaat JO, Mali WP. Value of breast imaging in women with painful breasts: observational follow up study. *BMJ* 1998; 317:1492–1495
- Khan SA, Apkarian AV. Mastalgia and breast cancer: a protective association? *Cancer Detect Prev* 2002; 26:192–196
- Owen WA, Brazeal HA, Shaw HL, Lee MV, Appleton CM, Holley SO. Focal breast pain: imaging evaluation and outcomes. *Clin Imaging* 2019; 55:148–155
- Kushwaha AC, Shin K, Kalambo M, et al. Overutilization of health care resources for breast pain. *AJR* 2018; 211:217–223
- Expert Panel on Breast Imaging; Holbrook AI, Moy L, Akin EA, et al. ACR Appropriateness Criteria breast pain. J Am Coll Radiol 2018; 15(suppl 11):S276–S282

- Leddy R, Irshad A, Zerwas E, et al. Role of breast ultrasound and mammography in evaluating patients presenting with focal breast pain in the absence of a palpable lump. *Breast J* 2013; 19:582–589
- Leung JW, Kornguth PJ, Gotway MB. Utility of targeted sonography in the evaluation of focal breast pain. J Ultrasound Med 2002; 21:521–526; quiz, 528–529
- Barton MB, Elmore JG, Fletcher SW. Breast symptoms among women enrolled in a health maintenance organization: frequency, evaluation, and outcome. *Ann Intern Med* 1999; 130:651–657
- Scurr J, Hedger W, Morris P, Brown N. The prevalence, severity, and impact of breast pain in the general population. *Breast J* 2014; 20:508–513
- Ader DN, Browne MW. Prevalence and impact of cyclic mastalgia in a United States clinic-based sample. Am J Obstet Gynecol 1997; 177:126–132
- Preece PE, Baum M, Mansel RE, et al. Importance of mastalgia in operable breast cancer. Br Med J (Clin Res Ed) 1982; 284:1299–1300

## Holbrook

- 14. Noroozian M, Stein LF, Gaetke-Udager K, Helvie MA. Long-term clinical outcomes in women with breast pain in the absence of additional clinical findings: mammography remains indicated. *Breast Cancer Res Treat* 2015; 149:417–424
- Tumyan L, Hoyt AC, Bassett LW. Negative predictive value of sonography and mammography in patients with focal breast pain. *Breast J* 2005; 11:333–337
- Cho MW, Grimm LJ, Johnson KS. Focal breast pain: does breast density affect the need for ultrasound? Acad Radiol 2017; 24:53–59
- Mema E, Cho E, Ryu YK, et al. In the setting of negative mammogram, is additional breast ultrasound necessary for evaluation of breast pain? *Curr Probl Diagn Radiol* 2019; 48:117–120
- Neal RD, Morley S. Value of breast imaging in women with painful breasts: negative results are not reassuring. *BMJ* 1999; 318:1009
- Zarei F, Pishdad P, Hatami M, Zeinali-Rafsanjani
  B. Can breast ultrasound reduce patient's level of

anxiety and pain? Ultrasound 2017; 25:92-97

- Meechan GT, Collins JP, Moss-Morris RE, Petrie KJ. Who is not reassured following benign diagnosis of breast symptoms? *Psychooncology* 2005; 14:239–246
- McDonald IG, Daly J, Jelinek VM, Panetta F, Gutman JM. Opening Pandora's box: the unpredictability of reassurance by a normal test result. *BMJ* 1996; 313:329–332
- Fitzpatrick R. Telling patients there is nothing wrong. BMJ 1996; 313:311–312
- Howard MB, Battaglia T, Prout M, Freund K. The effect of imaging on the clinical management of breast pain. J Gen Intern Med 2012; 27:817–824
- 24. Martín-Díaz M, Maes-Carballo M, Khan KS, Bueno-Cavanillas A. To image or not in noncyclic breast pain? A systematic review. *Curr Opin Obstet Gynecol* 2017; 29:404–412
- Barros AC, Mottola J, Ruiz CA, Borges MN, Pinotti JA. Reassurance in the treatment of mastalgia. *Breast J* 1999; 5:162–165