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BEST PRACTICE APPROACHES BREAST RADIOLOGY-PATHOLOGY CORRELATION AND MANAGEMENT (J SCHEEL AND MR KILGORE, SECTION EDITORS)

# Radiologic and Pathologic Correlation of Invasive Lobular Carcinoma of the Breast

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## Abstract

**Purpose of Review** The primary goal of this review is to give an update on the radiologic and pathologic features of invasive lobular carcinoma (ILC), with an emphasis on recent studies related to the diagnosis of ILC. We review the imaging features of ILC and also discuss recommendations for avoiding potential pitfalls that can result in a delayed diagnosis. The histologic features of ILC and the role of multidisciplinary radiographic-pathologic correlation in aiding a timely diagnosis of ILC are also discussed.

**Recent Findings** There have been recent technologic advancements in breast imaging, including digital breast tomosynthesis, molecular breast imaging, and contrast-enhanced digital mammography, all of which have been shown to outperform conventional digital mammography in the diagnosis of ILC.

**Summary** The imaging features of ILC can be subtle due to its lack of significant desmoplastic response, thus making it challenging to diagnose. This underscores the importance of careful radiologic-pathologic correlation and appropriate management of suspicious imaging findings and suspicious clinical findings even in the absence of a correlating imaging abnormality.

**Keywords** Invasive lobular carcinoma · Lobular carcinoma in situ · Radiographic-pathologic correlation

## Introduction

Invasive lobular carcinoma of the breast (ILC) is the second most common histological type of breast cancer, following invasive ductal carcinoma not otherwise specified (IDC), accounting for 10–15% of all breast cancers [1]. Different histologic subtypes of ILC have been described. Classic ILC (which will be the focus of this review) makes up about half of all ILC cases. Other histologic subtypes have been described on the basis of their cytonuclear features (apocrine, histiocytoid, pleomorphic, and signet ring) and their architecture (alveolar, solid, and trabecular) [1]. Lobular neoplasia is a term used to describe the lesions that serve as non-obligate precursor lesions for ILC, namely atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS) [2]. There are three variants of LCIS described (i.e., classic, pleomorphic, and florid), which are based on the degree of cytological atypia and the architectural pattern [2].

The clinical presentation and biologic characteristics of ILC make it difficult to detect, both by imaging and on histologic evaluation. Herein, we will review the clinical, radiographic and pathologic features of ILC, and highlight novel imaging technologies and clinical practice recommendations. We will also discuss the ILC diagnostic pitfalls that can result in a delayed diagnosis.

This article is part of the Topical Collection on *Best Practice Approaches Breast Radiology-Pathology Correlation and Management*

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## Clinical Context

There has been an increase in the incidence of ILC cases over the past few decades, particularly in postmenopausal women [3, 4]. ILC is more commonly diagnosed in women at an older age and is often multicentric at presentation [5••]. Compared to IDC, there is a tendency for ILC to present with larger-sized tumors, bilateral breast involvement, and unique metastatic patterns, with a propensity to metastasize to unusual sites, e.g., the peritoneum and gastrointestinal (GI) tract [5••].

ILC cases often demonstrate a favorable prognostic phenotype, with features including a low histologic grade and low mitotic index [2, 5••]. ILCs typically have positive estrogen and progesterone hormone receptor status, while they often lack human epidermal growth factor receptor-2 (HER-2) amplification, p53 overexpression, and basal marker expression [2, 5••]. However, the diagnosis and management of ILC can be challenging, given the difficulty with detection on screening. This increases the likelihood of a later stage at the time of diagnosis, including the risk of multifocality or multicentricity, and diffuse metastatic spread.

The treatment of ILC typically requires multidisciplinary collaboration between breast surgical oncologists, medical oncologists, and radiation oncologists [5••]. The method and details of treatment will depend on the clinical stage of the disease, as well as the pathologic features including hormonal receptor status, histologic grade, and stage.

## Radiology

ILC can be subtle in its clinical and imaging presentation due to its tendency to grow within the stromal tissue surrounding the ducts without causing disturbance of the underlying breast tissue architecture [6••]. Its subtle nature is also due to a lack of significant associated desmoplastic reaction (a stromal response that can occur in the setting of cancer and involves the development of prominent fibrous tissue). Consequently, ILC often presents without a clinically or mammographically evident mass. Of all the breast cancer types, ILC (along with ductal carcinoma in situ (DCIS)) has the highest likelihood of requiring reoperation following breast conserving surgery, which could be related to the ill-defined nature of the imaging abnormality [7].

**Digital Mammography** Due to its relatively low cost and increased accessibility (although this may not be the case in certain international settings), digital mammography is typically the initial breast imaging modality used for breast cancer screening, as well as for the evaluation of patients with concerning breast symptoms, such as palpable lumps, focal pain, and/or nipple discharge [6••]. However, the sensitivity of mammography for detecting ILC is low, approximately 57–79% [8, 9]. A major reason for this low detection rate is that the sensitivity of digital mammography is limited in patients with dense breasts. The masking effect of dense breast tissue can overlap cancer and make it more difficult to detect [6••]. Digital breast tomosynthesis (DBT) is a recent advancement in mammographic technology aimed at lessening the tissue masking effect. It has been shown to be better than conventional digital mammography at detecting the mammographic findings that can be seen with ILC [10, 11]. On mammography, ILC often presents as an irregular mass with spiculated margins (Fig. 1). Other mammographic features that can be seen with ILC includea non-spiculated mass with indistinct margins, architectural distortion (Fig. 2), a focal asymmetry, or an asymmetry seen on only one mammographic view [4].

It is important to note that microcalcification is not a feature of classic ILC [12, 13]. It has been reported that when the detection of mammographic calcifications results in a diagnosis of ILC, the calcifications are typically present in other lesions, e.g., the ductal component of mixed ductal-lobular tumors or associated with DCIS or pleomorphic LCIS (Fig. 3) [12, 13]. ILC is associated with a disproportionately high percentage (up to 30% of cases) of mammographically occult breast cancers and will present with no mammographic abnormality in these cases [4].

**Ultrasound** The role of ultrasound in evaluating ILC has a reported sensitivity of approximately 81–83% [8, 14]. A common sonographic appearance of ILC is an irregular hypoechoic mass with associated posterior acoustic shadowing (Fig. 4).

Sonographically, ILC can also present as a focal area of shadowing without a discrete mass, an irregular hypoechoic mass without posterior acoustic shadowing, or an ill-defined infiltrative hypoechoic area [4, 5••]. It can also show a less suspicious sonographic appearance, such as a round or oval hypoechoic mass with circumscribed margins. ILC has also been reported to occasionally present as a focal hyperechoic mass with associated posterior acoustic shadowing, thus potentially mimicking a focal area of echogenic fat (if the associated shadowing is overlooked) [4]. This underscores the importance of real-time scanning by the radiologist to rule out any suspicious sonographic features, particularly in cases that are unclear or challenging. Ultrasound also plays an important role in evaluating for axillary lymphadenopathy. Another benefit of ultrasound is that it can be useful for assessing findings seen on MRI, particularly masses.

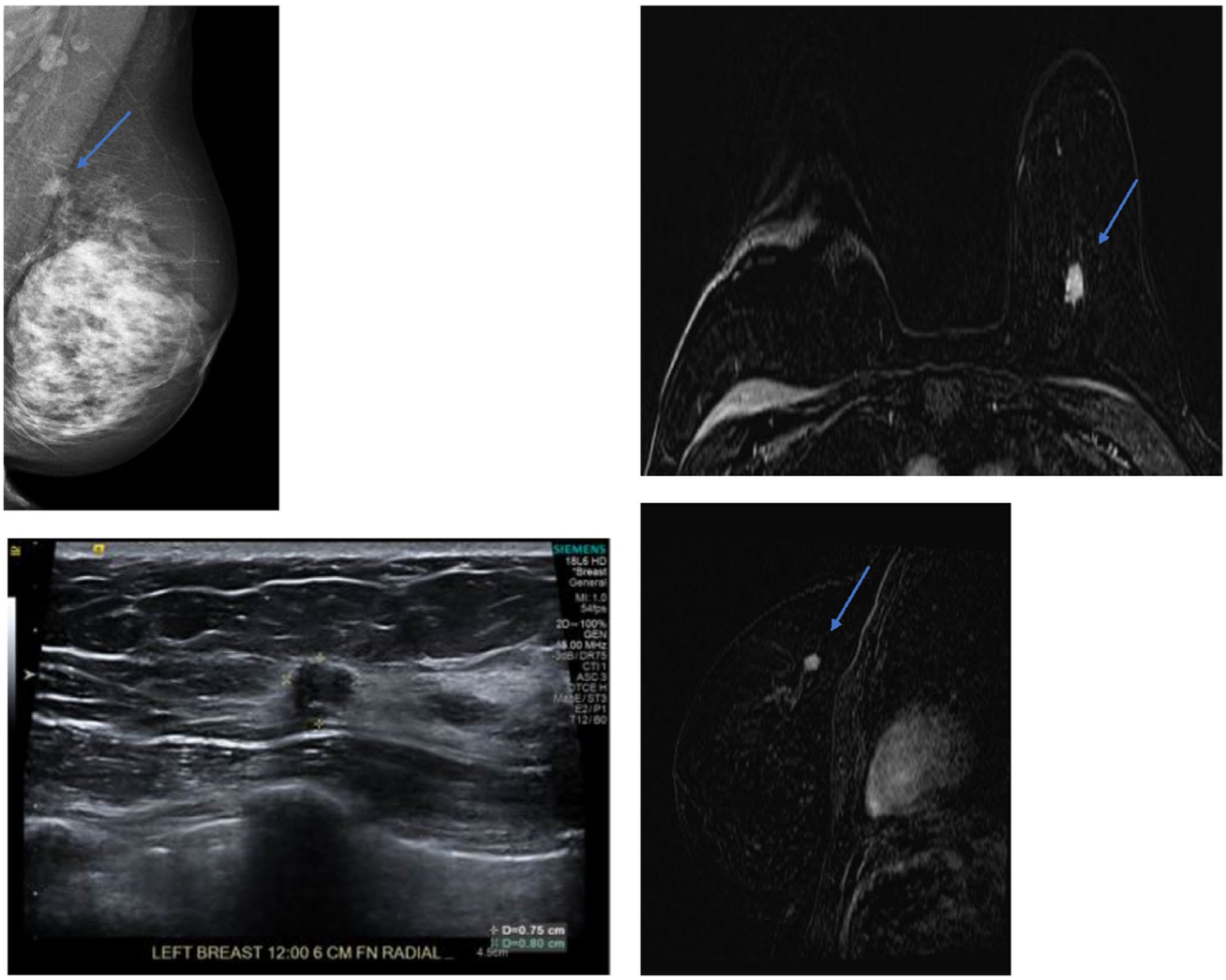



**Fig. 1** Mammographic mass with ILC. A 56-year-old woman found to have a left breast mass on mammography. **A** Left breast mammographic mediolateral oblique view shows an irregular left breast mass with spiculated margins (arrow) on mammography performed at an outside institution. **B** Grayscale sonographic image shows a corresponding irregular hypoechoic mass with indistinct margins at the left breast 12 o'clock position. **C** Axial and **D** sagittal subtracted post-contrast T1-weighted images show a correlating irregular enhancing mass with irregular margins. Ultrasound-guided biopsy revealed ILC

Patients with suspicious enhancing masses on MRI may benefit from targeted ultrasound evaluation of the MRI abnormality to assess for the presence of a correlating sonographic abnormality.

**Magnetic Resonance Imaging** Breast magnetic resonance imaging (MRI) is the most sensitive imaging modality for diagnosing ILC, with a reported sensitivity of 93–96% for the detection of ILC [5••, 15]. MRI plays an important role in the staging of ILC patients, particularly those with dense breast tissue [6••, 16, 17]. It is helpful for evaluating patients with newly diagnosed ILC for multifocal or multicentric disease. Breast MRI has been shown to detect additional lesions in the ipsilateral breast in about 32% of patients and in the contralateral breast in about 7% of patients [8, 15].

The appearance of ILC on MRI includes irregular enhancing masses (Fig. 5) and non-mass enhancement, which can be focal, linear, or segmental in distribution [5••]. In a small subset of cases, ILC can show a less suspicious appearance on MRI, such as circumscribed enhancing masses [6••].

With regard to enhancement kinetics, ILC often demonstrate prolonged time to peak enhancement and overall lower intensity of enhancement, compared to IDC [6••]. Additionally, washout kinetics is less commonly seen with ILC. However, morphologic features on breast MRI take precedence over kinetic features when determining the assessment and management recommendations. Findings with a suspicious morphologic appearance should always be managed appropriately, regardless of the kinetic features. It is also important to note that ILC less commonly shows

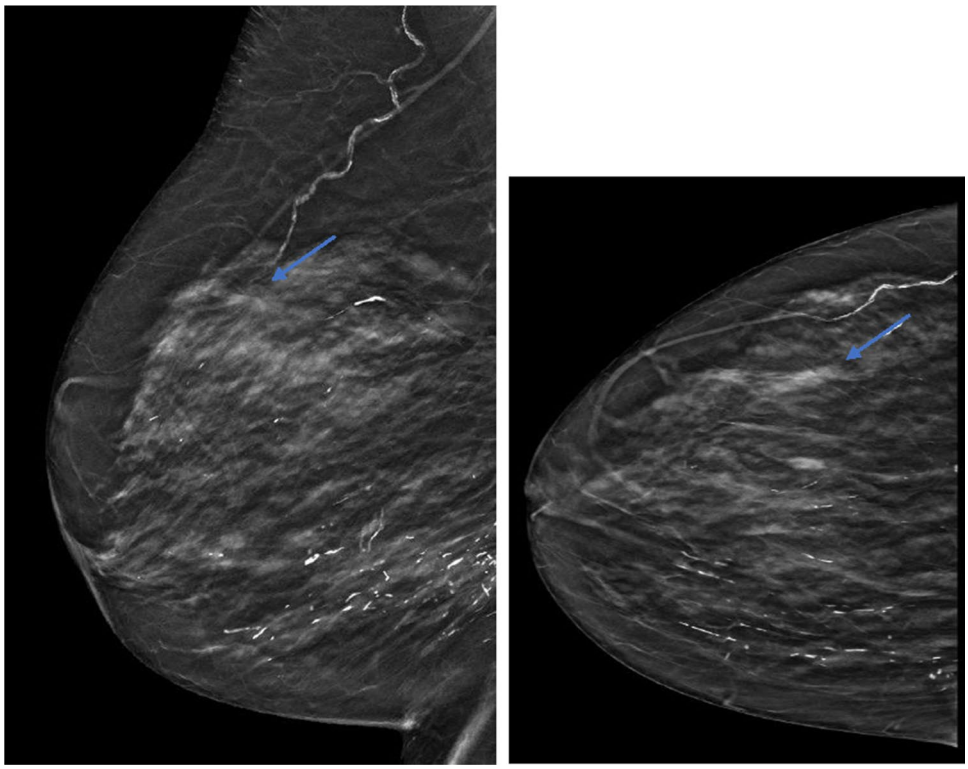
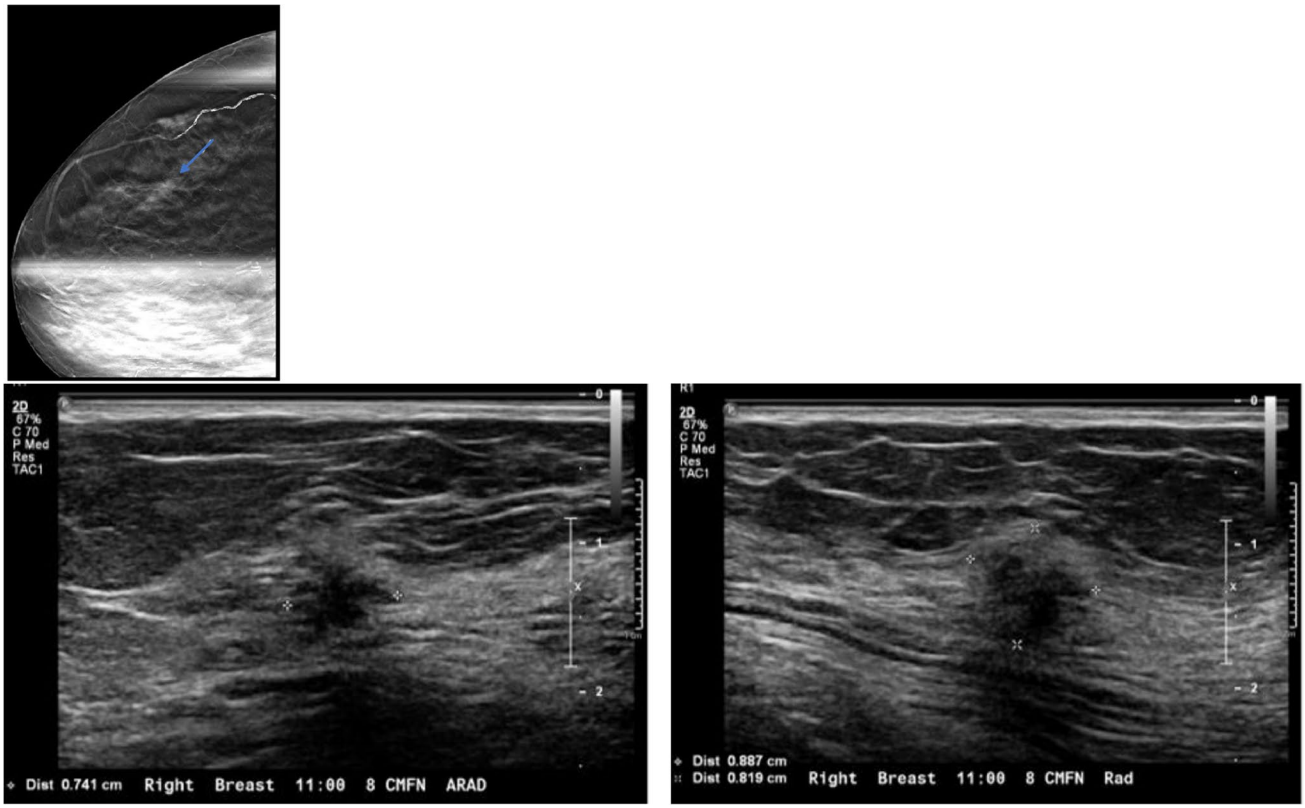


**Fig. 2** Mammographic architectural distortion with ILC. An 87-year-old woman who was called back from screening mammography for right breast architectural distortion. A, B Right breast digital breast tomosynthesis craniocaudal and mediolateral oblique views show an area of architectural distortion (arrow) in the upper outer quadrant of the right breast. C Spot compression digital breast tomosynthesis image shows that the area of architectural distortion persists (arrow). D, E Grayscale sonographic images show a correlating irregular hypoechoic mass with spiculated margins. Ultrasound-guided biopsy was performed, with a diagnosis of ILC

**Fig. 2** (continued)



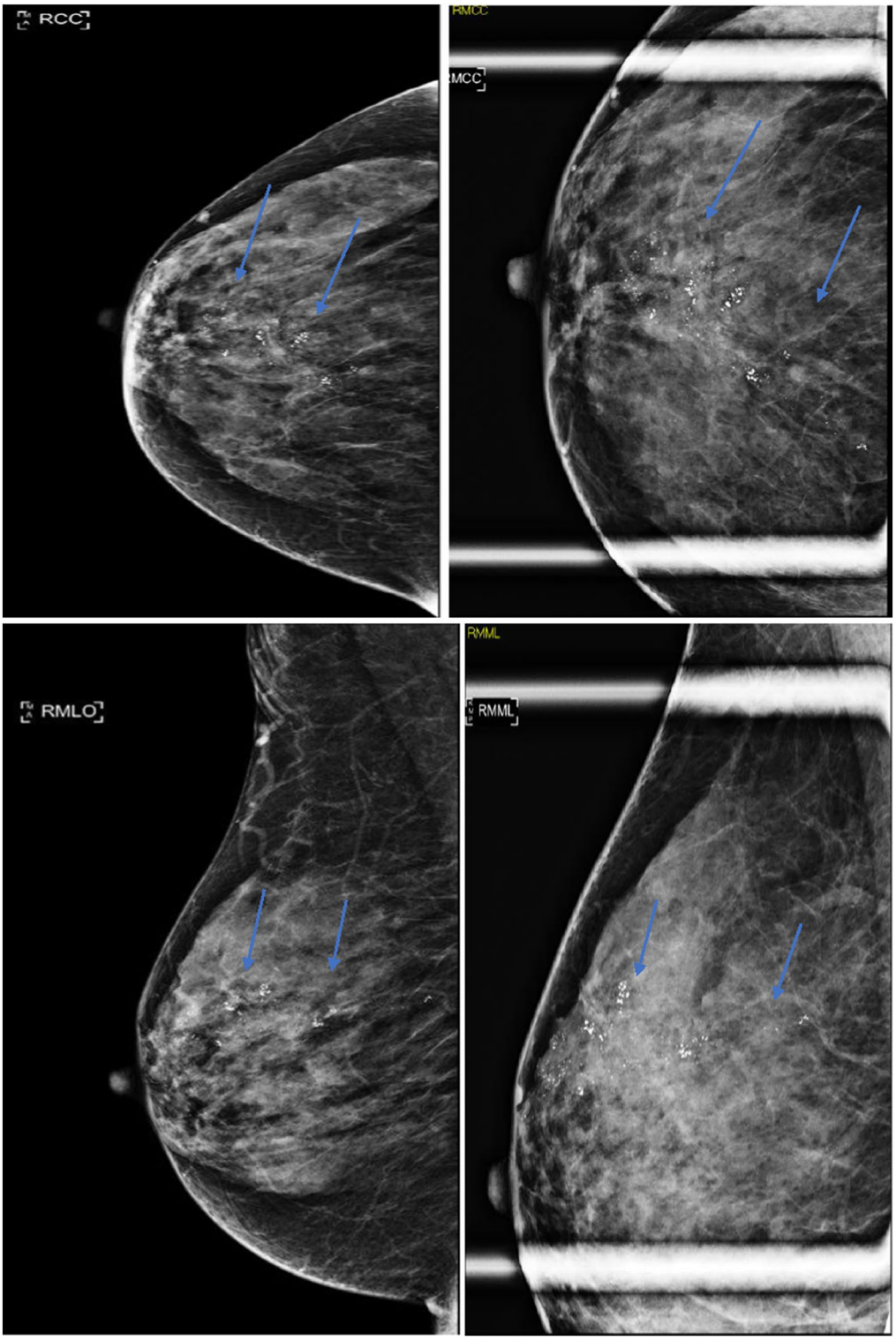



**Fig. 3** Digital mammographic calcifications with ILC. A 59-year-old called back from screening mammography for right breast calcifications. A, B Right breast full-field digital mammographic views and C, D spot magnification craniocaudal and mediolateral views show coarse heterogeneous and fine pleomorphic calcifications in a segmental distribution (arrows) in the upper right breast, overall spanning up to 7 cm in AP dimension. Stereotactic-guided biopsy was performed, with pathology revealing ILC in association with pleomorphic LCIS, which contained microcalcifications

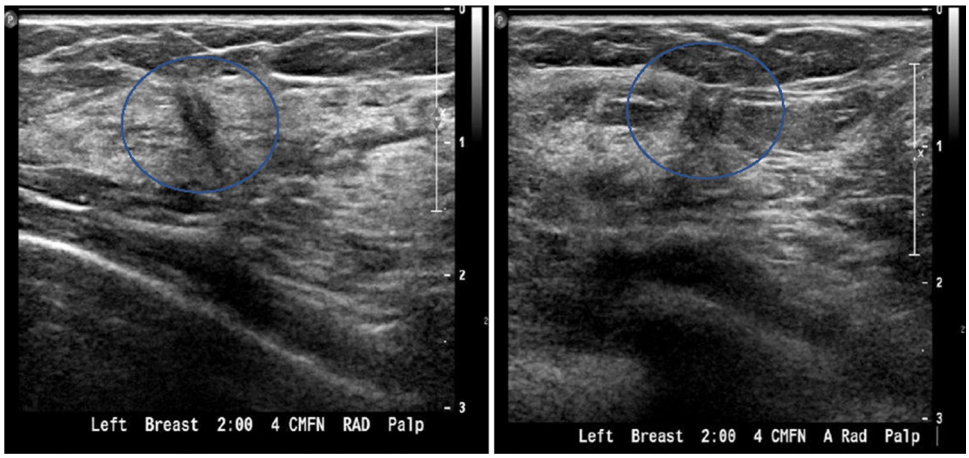



**Fig. 4** Sonographic hypoechoic mass with ILC. An 87-year-old woman with history of left lumpectomy performed 3 years ago for treatment of ILC and DCIS, presented with a palpable near the lumpectomy scar. A, B Grayscale sonographic images demonstrate a 4-mm irregular hypoechoic mass with indistinct margins (blue circle) at the left breast 2 o'clock 20 position, 4 cm from the nipple, which corresponds to the site of palpable concern. The mass was biopsied under ultrasound guidance, with pathology revealing ILC

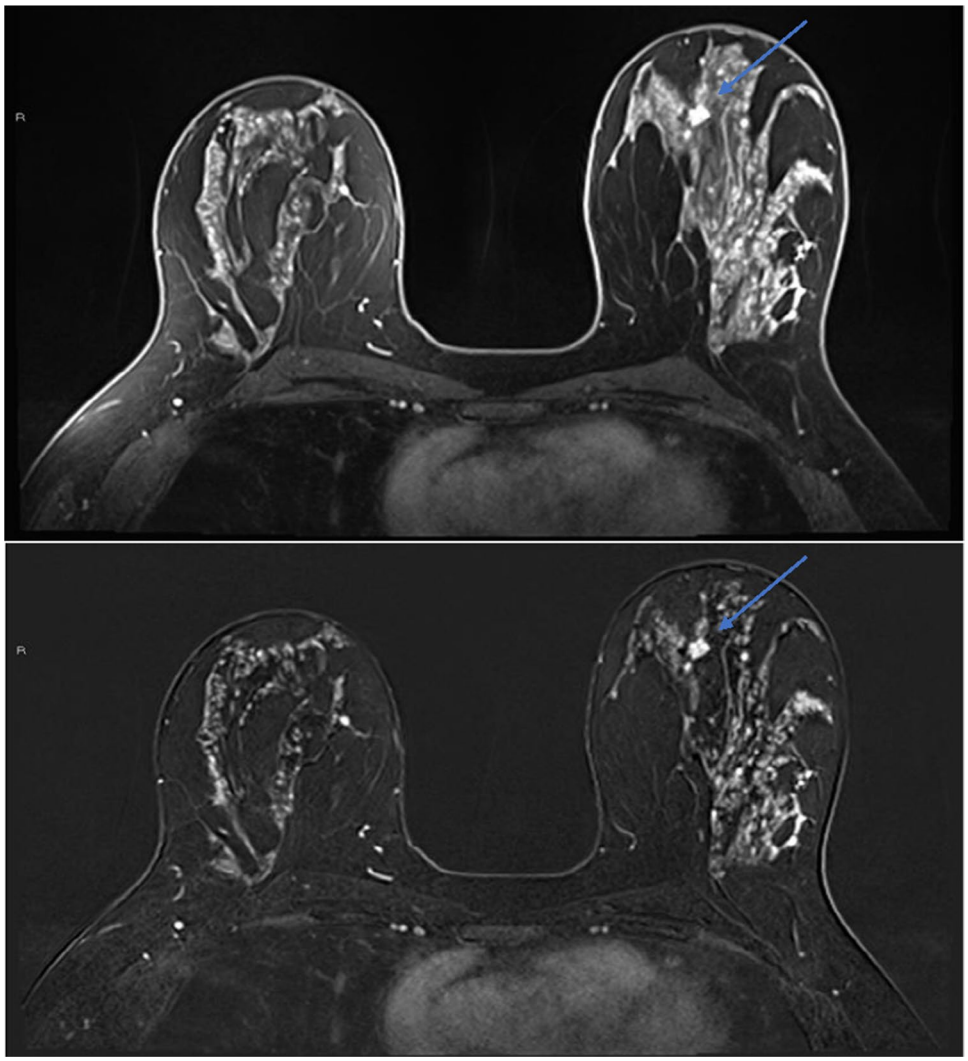


**Fig. 5** MRI enhancing mass with ILC. A 49-year-old woman with recently diagnosed right breast IDC. **A** Axial post-contrast T1-weighted and **B** axial subtracted post-contrast T1-weighted images show an 8-mm irregular enhancing mass with irregular margins (arrow) at the superior aspect of the left breast. No sonographic correlate was found. Therefore, MRI-guided biopsy was performed, which revealed ILC

some of the features that are typically associated with breast malignancy, such as central necrosis or surrounding tissue edema [6••]. Prior research has shown that preoperative breast MRI is helpful for depicting additional malignant foci in ILC patients and reducing the chance of requiring repeat surgery, without increasing the mastectomy rate [18•].

**Emerging Imaging Techniques** There are emerging breast imaging technologies that have shown promise in their ability to diagnose ILC, such as molecular breast imaging and contrast-enhanced digital mammography. Molecular breast imaging (MBI) is a nuclear medicine technology that involves the administration of a radiotracer, Tc-99 m sestamibi, and assesses its uptake in metabolically active breast tissue with the use of a dedicated gamma camera [19]. It has been shown to diagnose mammographically and sonographically occult ILC [19].

Contrast-enhanced digital mammography (CEDM) is a recent breast imaging technology advancement that assesses breast tissue with the use of a high-resolution full-field digital mammographic image and a recombined iodinated contrast-enhanced image to evaluate for tumor neovascularity [20•].

CEDM has been shown to better depict the extent of disease in patients with ILC, compared to standard full-field digital mammography [20•].

**Avoiding Pitfalls in Diagnosis** ILC can have a subtle presentation, which makes it important to highlight potential pitfalls that can result in a delayed diagnosis. ILC can present as a finding that is seen on only one imaging modality. This could be a one-view mammographic asymmetry or architectural distortion seen on only mammography without a sonographic correlate. It underscores the importance of managing all suspicious imaging findings appropriately, even if no suspicious findings are noted on other modalities. Additionally, for patients with concerning clinical findings, such as a new palpable breast lump, negative imaging results should not dissuade the appropriate clinical management of signs and symptoms that are worrisome for breast cancer. For example, consultation with a breast surgeon may be warranted for patients with a clinically suspicious palpable breast lump, even in the absence of suspicious imaging abnormalities.

**Core Biopsy** Tissue diagnosis of ILC can be made via image-guided core-needle biopsy, which may be done using stereotactic, ultrasound, or MRI guidance, depending on the imaging modality with which the finding to be biopsied is best seen. For suspicious findings that are seen well on both ultrasound and MRI, ultrasound-guided biopsy is typically the preferred biopsy modality due to its lower cost and increased patient comfort related to the supine positioning used for the procedure. Similarly, when a finding is seen on both mammography and ultrasound, ultrasound-guided biopsy is the biopsy modality of choice because of the lack of radiation exposure and increased patient comfort during the procedure due to supine positioning.

## Pathology

ILC is difficult to diagnose, not only due to its subtle imaging characteristics, but also its subtle histologic appearances. It is the most common special-type breast carcinoma, with distinct morphologic and genomic changes from IDC and other special-type carcinomas. Attention to increased cellularity within the breast stroma and the use of targeted immunohistochemistry can aid in avoiding misdiagnosis.

**Histologic Features** ILC is characterized by infiltrating discohesive cells arranged in linear rows or present as single cells (Figure 6), and less commonly seen forming solid

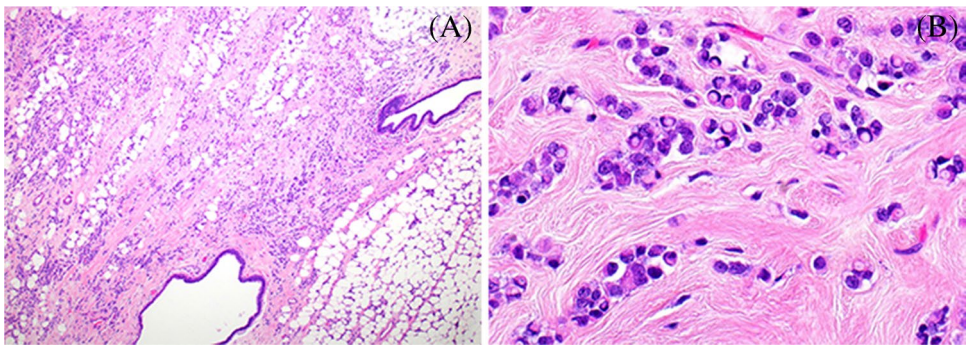



**Fig. 6** Histologic features of classic ILC. **A** Classic ILC appears as small single cells resembling benign lymphocytes, extensively infiltrating the breast parenchyma without eliciting a desmoplastic stromal response (H&E, ×40). **B** On higher magnification, classic ILC consists of loosely cohesive single cells in linear rows or small nests, with minimal cytologic atypia, prominent cytoplasmic signet ring vacuoles, and no stromal desmoplasia (H&E, ×400)

nests or bland tubules [2, 5••, 21, 22]. Classic ILCs are Nottingham histologic grade I–II of III, demonstrating low nuclear grade with smooth nuclear contours and indistinct nucleoli, minimal to moderate amount of cytoplasm, which contains signet ring-like vacuoles, and a low mitotic rate. Low-grade ILC can be particularly challenging to identify histologically, as the neoplastic cells resemble lymphocytes or stromal cells in the benign breast tissue and rarely elicit a desmoplastic stromal response. Pleomorphic ILC (pILC) is a rare subtype of ILC that demonstrates pleomorphic and enlarged nuclei with distinct nucleoli, more abundant cytoplasm, brisk mitotic activity, and is commonly associated with pleomorphic LCIS [23•] (Figure 7). Other uncommon patterns of ILC include histiocytoid and apocrine differentiation [21]. ILC can occur as pure ILC, or in association with atypical lobular hyperplasia (ALH) or lobular carcinoma in situ (LCIS), epithelial atypia, atypical ductal hyperplasia (ADH), or DCIS. Occasionally, ILC can co-occur with other carcinomas, including tubular carcinoma and IDC.

The histologic differential diagnosis for ILC includes other subtypes of breast carcinoma including IDC and solid papillary carcinoma, as well as benign mimickers including lymphocytes, histiocytes, fat necrosis, and sclerosing adenosis. The differential diagnoses can be particularly challenging to resolve on small samples and in cauterized tissue sections. IDC forms glands to varying degrees, elicits stromal desmoplasia, and is often associated with DCIS, which may contain central necrosis and microcalcifications (Figure 8). Like ILC, lymphocytes appear as small, discohesive cells with minimal cytoplasm and absence of a desmoplastic stromal response. The variant of histiocytoid ILC contains abundant, fluffy cytoplasm resembling benign histiocytes.

Close examination will reveal that lymphocytes and histiocytes lack the characteristic cytoplasmic signet ring vacuoles seen in ILC. In sclerosing adenosis, the benign glandular proliferation can be sclerotic with attenuated luminal cells such that it appears as linear rows of cells with a haphazard distribution, resembling ILC. The diagnosis

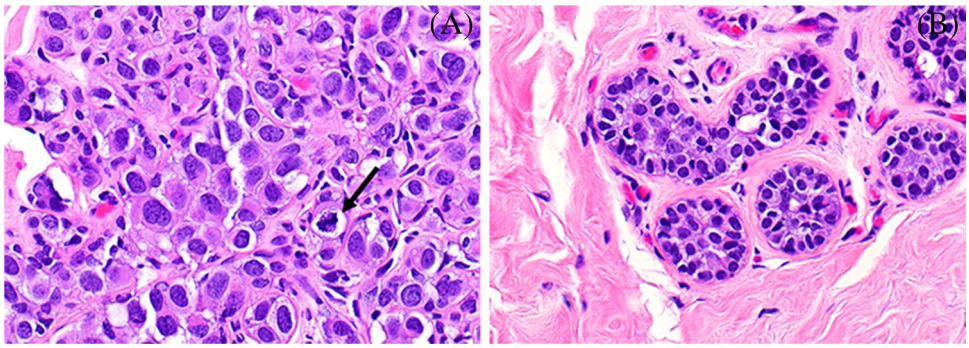



**Fig. 7** Histologic features of pleomorphic LCIS. **A** Pleomorphic LCIS displays large nuclei with irregular nuclear contours, pleomorphism, and mitotic activity (arrow), which are features it shares with its invasive counterpart, pleomorphic invasive lobular carcinoma (H&E, ×400). In contrast, **B** the cells of classic atypical lobular hyperplasia and classic LCIS, shown here at the same magnification, are small and uniform, with minimal cytologic atypia (H&E, ×400)

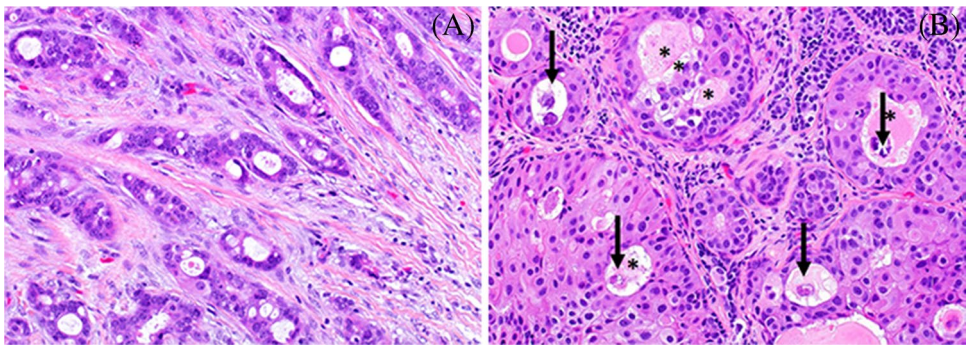



**Fig. 8** Histologic features of IDC and DCIS. In contrast to the features of classic ILC, **A** low-grade IDC displays gland formation and an associated desmoplastic stromal response, evidenced by the blue-gray coloration of the stroma (H&E, ×200). IDC is commonly associated with **B** DCIS, which contains an intraductal proliferation of neoplastic cells with central necrosis (asterisks) and associated microcalcifications (arrows) (H&E, ×200)

is particularly challenging when sclerosing adenosis is involved by lobular neoplasia, as the lobular neoplasia will display the characteristic signet ring vacuoles and appear to be in a linear arrangement. However, low power examination reveals that sclerosing adenosis maintains the lobulated architecture of the underlying terminal duct lobular units, whereas ILC is infiltrative through the parenchyma. Immunohistochemistry may be necessary to resolve these differentials. For instance, immunohistochemistry for p63 and smooth muscle myosin heavy chain (SMMHC) can demonstrate the presence of myoepithelial cells around benign adenosis and the absence of myoepithelial cells around ILC.

**Immunophenotype** A hallmark feature of ILC is aberrant E-cadherin labeling by immunohistochemistry, although it should be noted that this is not universal nor required for the diagnosis of ILC [2, 23•, 24]. Aberrant E-cadherin labeling correlates with the molecular changes underlying ILC, specifically, alterations in the *CDH1* gene encoding E-cadherin protein (see the "Molecular Findings" section). The most common aberrant E-cadherin labeling pattern is loss of membranous E-cadherin labeling (Figure 9); however, diminished membranous labeling and cytoplasmic labeling also occur. Some instances of classic ILC will demonstrate intact membranous E-cadherin labeling, but in these cases, the protein is non-functional and will lead to absent or cytoplasmic immunohistochemical labeling for its partner proteins, p120-catenin, and beta-catenin. Immunohistochemical evaluation of p120-catenin or beta-catenin can be helpful in cases with intact membranous E-cadherin expression, but morphologically suggestive features of ILC. In short, loss of membranous E-cadherin labeling is not required for a diagnosis of classic ILC, which can be made based on the histologic features alone.

Like IDC, the majority of ILC (over 95%) are hormone receptor positive with labeling for both estrogen receptor (ER) (Figure 10) and progesterone receptor (PR) [21, 25]. ILCs are rarely HER-2 amplified or triple negative for ER, PR, and HER-2. These latter uncommon profiles are generally seen in cases of pleomorphic ILC. Immunohistochemistry for Ki67 typically reveals a low proliferation index (<10%), in keeping with the proliferative rate, but it will be elevated in a subset of classic ILC and in pleomorphic ILC.

Additional immunohistochemical stains may be needed to distinguish ILC from its histologic mimickers, specifically inflammatory cells and sclerosing adenosis. ILC is immunoreactive for cytokeratins, including immunohistochemistry for CK7, AE/1AE3, and Cam5.2. In contrast, lymphocytes

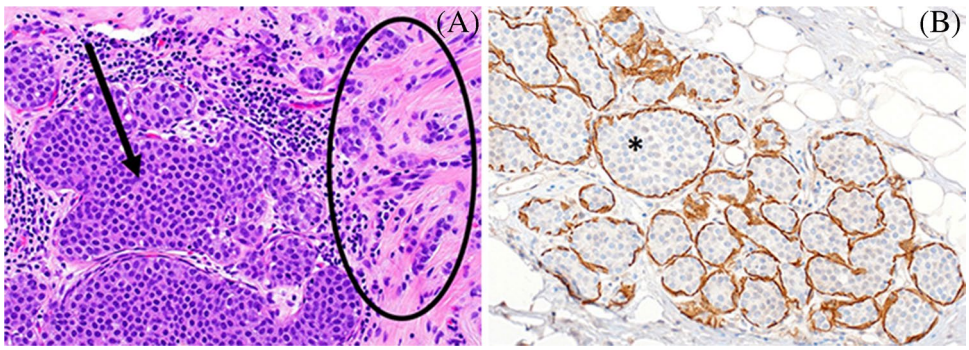



**Fig. 9** E-cadherin labeling in lobular neoplasia. A Classic LCIS (*left*, arrow) consists of uniform, discohesive cells with cytoplasmic vacuoles that distend and distort the lobular unit. An associated classic ILC (*right*, circle) consists of single rows of small, bland cells that percolate into the stroma without a desmoplastic response (H&E, ×200). B An immunostain for E-cadherin demonstrates loss of membranous labeling in the LCIS (asterisk), with intact brown labeling in the myoepithelial cells of the lobules (E-cadherin, ×200). Loss of membranous labeling is also a characteristic feature of ILC (*not shown*)

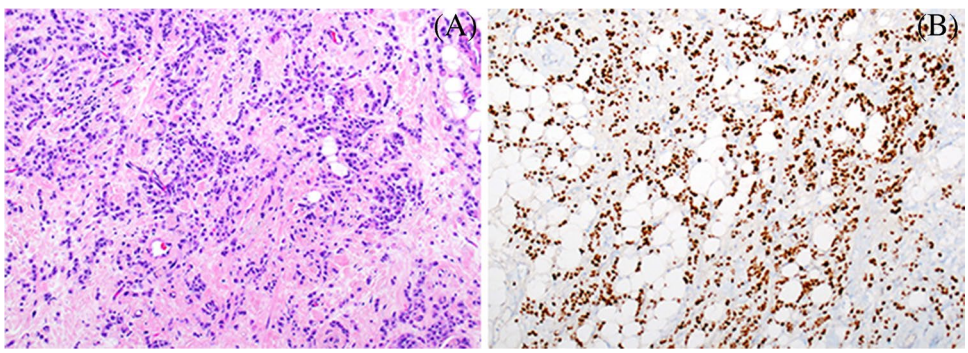



**Fig. 10** Estrogen receptor (ER) labeling in ILC. A Classic ILC consists of small bland cells arranged in linear rows or small nests, with low nuclear grade and minimal mitotic activity (H&E, ×100), and B strong and diffuse labeling for ER (ER, ×100). Although not shown, a photomicrograph for PR IHC would often be similar with strong and diffuse nuclear expression

and histiocytes are cytokeratin negative but label for CD45. Histiocytes can also be highlighted by immunohistochemistry for CD68 and CD163. Of note, similar to ILC, lymphocytes and histiocytes will show absence of membranous E-cadherin labeling. The histologic features and lineage-specific immunohistochemistry (cytokeratin and CD45) are necessary to resolve this differential diagnosis. Immunohistochemistry for p63, smooth muscle myosin heavy chain, calponin, or smooth muscle actin can be used to highlight an intact myoepithelial cell layer throughout benign glandular proliferations such as sclerosing adenosis, whereas ILC will lack a myoepithelial cell layer.

**Molecular Findings** Different molecular pathways underlie the progression of classic ILC and pleomorphic ILC; however, all ILC subtypes are characterized by alterations in *CDH1*, which encodes the E-cadherin protein [2, 21, 22]. The most common molecular alterations are mutations in *CDH1* leading to truncation, coupled with loss of heterozygosity of the wild-type allele, but other alterations such as *CDH1* promoter methylation also occur [2, 21, 22, 23•]. Germline *CDH1* mutations result in the hereditary gastric cancer syndrome, in which patients develop gastric signet ring adenocarcinomas at a young adult age and are also predisposed to developing ILC. Of note, this variant of gastric carcinoma and invasive lobular carcinoma of the breast have similar morphology, which can complicate assessment of primary versus metastatic disease throughout the body.

Classic ILC is part of the low-grade or ER+ neoplastic progression pathway, which also includes flat epithelial atypia, ALH and classic LCIS, ADH and low-grade DCIS, tubular carcinoma, and low-grade IDC. Molecular alterations in this low-grade neoplastic pathway include gains of chromosome 1q and 16p [26]. By molecular phenotyping, classic ILCs are most often classified as luminal A, reflecting their ER/PR positivity and relatively low mitotic rate, but can also be luminal B, and rarely HER2+ or basal-like [1, 21]. Pleomorphic LCIS and pleomorphic ILC are unique among breast in situ and invasive carcinomas (Figure 7), because they display molecular alterations seen in both the low-grade neoplastic pathway and the high-grade or ER-neoplastic pathway including *TP53* mutations [1, 2, 26].

## Radiographic-Pathologic Correlation

ILC rarely elicits a desmoplastic stromal response, but rather percolates insidiously and often extensively through the breast collagen and adipose tissue without any stromal reaction. The lack of desmoplastic response correlates with the low rate of mammographic abnormality for ILC, as it rarely forms a discrete or stellate mass [2, 4]. In addition, ILC is rarely associated with microcalcifications, further hindering its detection on mammogram [13]. Microcalcifications can be seen in other lesions in the vicinity of ILC, including pleomorphic LCIS (Figure 11), DCIS, and other benign lesions such as sclerosing adenosis or hyalinized fibroadenomas. ILC can even be incidentally discovered on core needle biopsy performed for an unrelated mammographic finding, such as microcalcifications that are found to be in association with fibrocystic changes.

As in all areas of breast imaging, the importance of a collaborative relationship between radiologists and pathologists cannot be overstated. Regular radiographic-pathologic concordance conferences and multidisciplinary tumor boards are vital components of patient diagnosis and care.

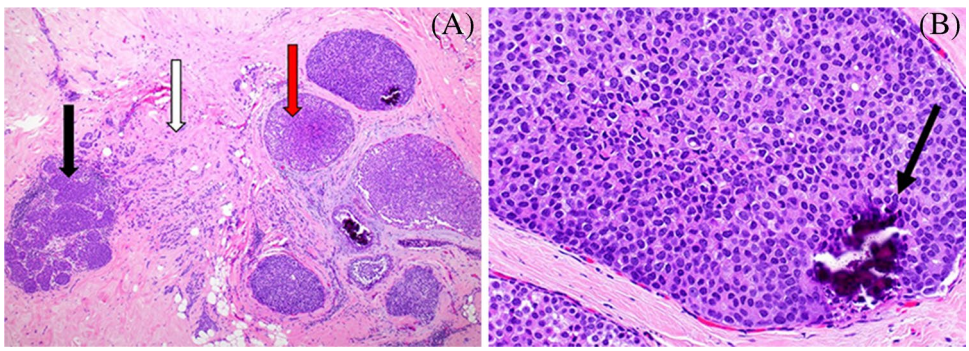



**Fig. 11** ILC with pLCIS and calcifications. **A** Low-grade classic ILC (*center*, white arrow) with adjacent classic LCIS (*left*, black arrow) and pleomorphic LCIS with calcifications (*right*, red arrow) (H&E, ×40). **B** On higher power, the pLCIS displays nuclear pleomorphism and atypia, along with associated microcalcifications as evidenced by purple-stained calcium phosphate (*lower right*, black arrow) (H&E, ×400)

## Conclusion

ILC is the second most common subtype of breast carcinoma with distinct clinical, radiographic, and pathologic characteristics. ILC presents significant diagnostic challenges for radiologists and pathologists. Because ILC rarely elicits a desmoplastic stromal response or contains associated microcalcifications, ILC often lacks significant radiographic abnormalities on screening or diagnostic imaging modalities. The use of imaging modalities with higher sensitivity, a heightened awareness to the subtle histologic characteristics of ILC, and multidisciplinary radiographic-pathologic correlation will enable earlier detection and improved diagnostic accuracy for this challenging disease.

### Declarations

**Conflict of Interest** Eniola Oluyemi, Ani Peshtani, Marissa J. White, and Ashley Cimino-Mathews declare no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance


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