



APPROACH TO PAPILLARY LESIONS

Zahra Mahboubi Fooladi, MD-MPH
SBMU

- Nipple discharge is common with a prevalence of 4.8% to 7.4%.
- Nipple discharge is the third most common breast complaint after pain and a lump.
- Nipple discharge can be characterized as physiologic or pathologic.
- Physiologic discharge is often provoked, originates from multiple duct orifices, and is bilateral and white, green, or yellow in color.
 - **no further radiologic investigation is needed**

Pathologic nipple discharge,

At least one of the following:

Unilateral

Spontaneous

Single duct
orifice

Clear or
Blood-
stained

Causes

papilloma

Duct ectasia

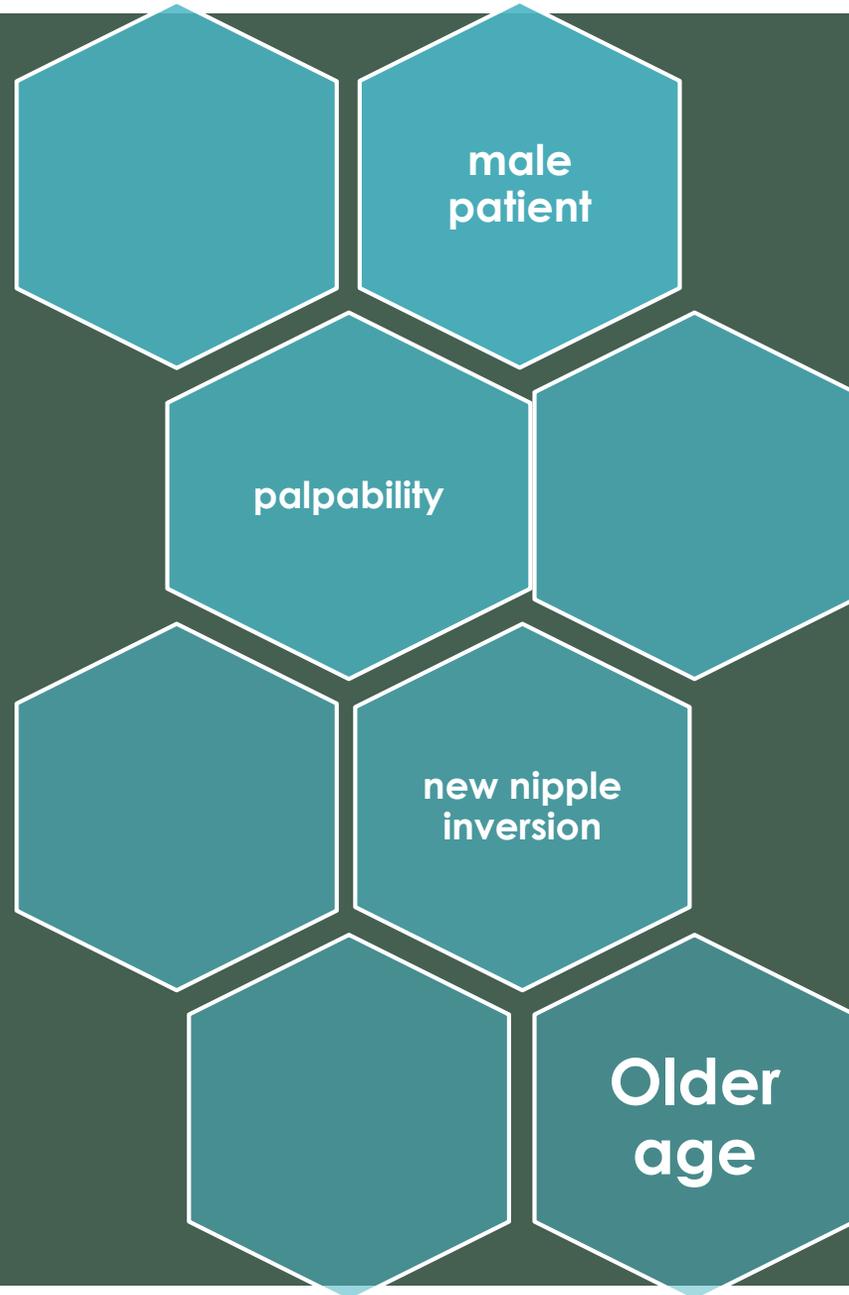
DCIS

Patients may also note bloody nipple discharge after a needle **biopsy** of the retro areolar region.

- Imaging features of non physiologic duct ectasia that may indicate malignancy include **irregularity of the duct margin, a peripherally dilated duct, focal wall thickening, and adjacent hypoechoic tissue** that may represent a mass.
- **Cancer is found in 5–15% of patients with pathologic nipple discharge, the most common type being DCIS.**

- The standard evaluation for nipple discharge includes a detailed clinical history and physical examination that directs the need for any type of breast imaging.

More attention!



- Historically, major duct excision has been the reference standard for defining the causative lesion of the nipple discharge and eliminating symptoms. However, this approach may not be optimal for all, because the lesion may not be identifiable on pathology, the procedure may impair a patient's ability to breastfeed, and peripheral breast lesions may not be amenable to excision.
- If a target is identified by imaging, excision by diagnostic vacuum-assisted percutaneous core needle biopsy (CNB) may offer an alternative to surgery.

Initial step?

Breast US is usually appropriate as the initial imaging of pathologic discharge in adult female patients younger than 30 years of age

Adult male or female
40 years of age or
older

- Mammography
Diagnostic or DBT

adult male or female
patients 30 to 39
years of age

- Mammography
Diagnostic or DBT

adult male or female
patients younger
than 30 years of age

- DBT or diagnostic
mammography

Adult male or female 40 years of age or older

- Although 3% to 29% of pathologic nipple discharge is due to underlying breast cancer, full-field mammography often does not demonstrate these lesions because they may be very small, contain no calcifications, or are completely intraductal.
- To better evaluate the subareolar breast in patients with an asymmetry/focal asymmetry or suspicious microcalcifications, additional mammographic views with spot compression and magnification may be needed.

- Imaging findings of **papilloma** include asymmetrically dilated ducts, a circumscribed benign-appearing subareolar mass, or grouped microcalcifications.
- **DCIS** is usually detected mammographically as fine, linear, discontinuous, and branching microcalcifications in linear, ductal, or segmental distribution and less often as a mass, symmetry/focal asymmetry, or architectural distortion on mammography.
- The mammographic features of **invasive carcinomas** are well known, including a mass of various margin characteristics with or without microcalcifications or an asymmetry, focal asymmetry, or architectural distortion

US:

- In patients with pathologic nipple discharge, US identifies lesions not visible on mammography 63% to 69% of the time.
- US adds specificity for some lesions when compared with mammography if it identifies the mammographic finding as a simple cyst or duct ectasia.
- Although more sensitive than mammography, US suffers from lower specificity in differentiating benign versus malignant lesions.

- False-positive US results may be due to volume averaging with the ductal wall in a tortuous duct, intraductal and periductal fibrosis, adherent blood clots, or inspissated debris.
- In male and female patients, US is useful in identifying and assessing lesions and for biopsy guidance.

Ductography

A negative ductogram does not exclude malignancy or a high-risk lesion and a positive ductogram cannot reliably distinguish between a benign and malignant abnormality.

- Ductography is performed with a 30-gauge blunt-tipped straight or angled cannula. First, the nipple is gently cleansed using an alcohol swab. A warming pad may be used to relax the tissues and facilitate cannulation. A small amount of discharge is elicited by squeezing the nipple or applying pressure at the trigger point. Once the discharging pore is identified, the tip of the cannula is placed on the orifice, where it should pass easily into the duct. Then, 1–3 mL of nonionic iodinated contrast medium is slowly administered, and two orthogonal views are obtained, with additional views obtained as indicated.

- The resulting ductograms are classified as normal or showing ductal ectasia (*i.e.* duct diameter over 2 mm), filling interruption, filling stops, and ductal distortions
- Findings on ductography suggestive of malignant or papillary lesions include **intraductal filling defect, partial or complete obstruction of a duct, duct expansion or distortion, and duct wall irregularity.**
- In the setting of negative findings with conventional imaging, ductography can localize 76% of otherwise occult high-risk and malignant lesions.

- Ductography may demonstrate small lesions and localize the duct responsible for the nipple discharge.
- Ductography is minimally invasive, may be uncomfortable, and can be time-consuming.
- Ductography is not recommended in lactating women or patients with active mastitis. Known hypersensitivity to iodinated contrast agents is a relative contraindication.

- Ductography is more sensitive than mammography and US but has lower specificity than both modalities.
- As such, the primary value of ductography is to localize intraductal lesions and assist in surgery.

- As reported by Indeed, it is an invasive technique and may cause discomfort and pain. Galactography can also be performed only when the duct discharge is demonstrated at the time of the study.
- Therefore it can be technically impossible, especially in patients with intermittent discharge or nipple retraction. Duct rupture can happen if too much contrast material or pressure is used during injection. The incomplete or failed galactography rate has been reported as high as 15%.

Breast MRI

- Conventional mammography and US findings may be negative in up to half of patients with pathologic nipple discharge.
- High NPV
- MRI also allows visualization of lesions in the peripheral ducts that are not clearly visualized on US, help to better identify lesions located in the deepest areas of breast, at a significant distance from the nipple as it is difficult to visualize them with other techniques as ductoscopy or galactography.

In a meta-analysis comparing the diagnostic accuracy of MRI and ductography in women with PND: **sensitivity and specificity of MRI to be significantly higher than ductography.**

Compared to galactography in which only one duct can be cannulated, MRI **allows evaluating at the same time all the ductal system.**

NIPPLE DISCHARGE CYTOLOGY

Cytologic assessment of the discharge is not recommended because it is neither sensitive nor specific and adds to the cost of the evaluation.

In conclusion:

- The first step in the management of nipple discharge depends on the characteristics of the discharge and assessing whether the discharge is physiologic or pathologic.

Physiologic discharge

- does not require imaging evaluation other than routine screening mammography

Pathologic discharge

- requires evaluation with diagnostic mammography and US of the retro areole

- If the initial steps are negative, additional management is based on clinical suspicion.
- The incidence of malignancy is low even in patients with pathologic nipple discharge.
- Scheurlen et al in a systematic review: *“Galactography can no longer be considered as a mandatory standard in modern multimodal imaging of the breast”*.





PAPILLOMA

Central (Solitary) Papilloma

- Arise from the large major lactiferous ducts, beneath the areola.
- Most are small (<5 mm in diameter), and they can be occult mammographically, especially when located in the retroareolar region.

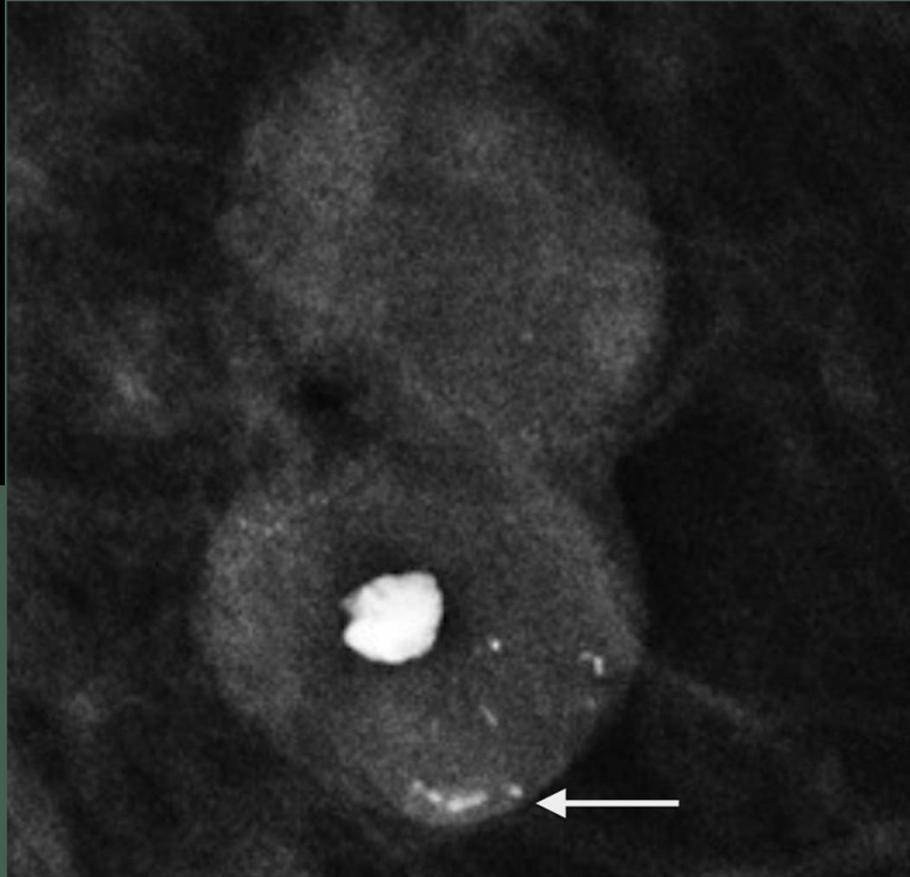
Intraductal papilloma usually appears as a hypoechoic nodule with a central vascular pedicle on color Doppler. Doppler ultrasound is helpful in differentiating intraductal viscous secretion *versus* intraductal nodule with vascular sign.



(a)



(b)



On mammogram

- a distended retroareolar duct with coarse intraductal calcifications.
- a bilobed mass with associated coarse and amorphous calcifications, some of which appear to layer (upgraded to DCIS at surgical excision)

Ultrasound

- In reporting an intraductal mass:

- ✓ *size*

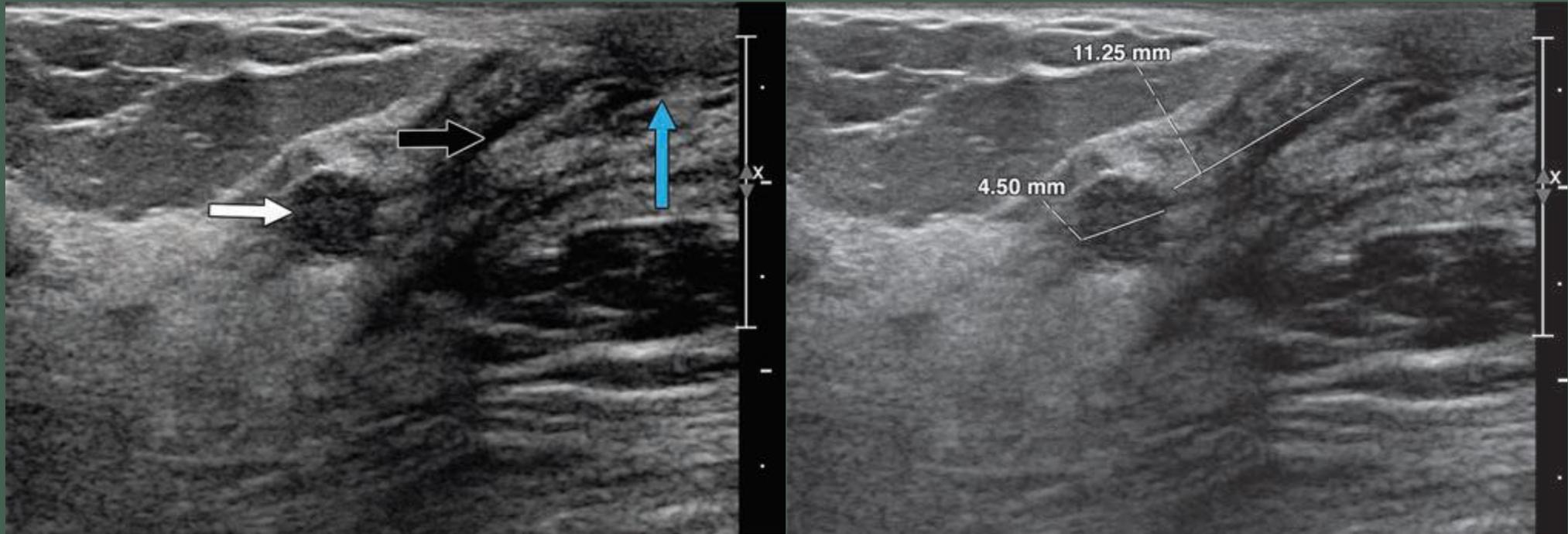
- ✓ *clock-face position*

- ✓ *distance from the nipple*

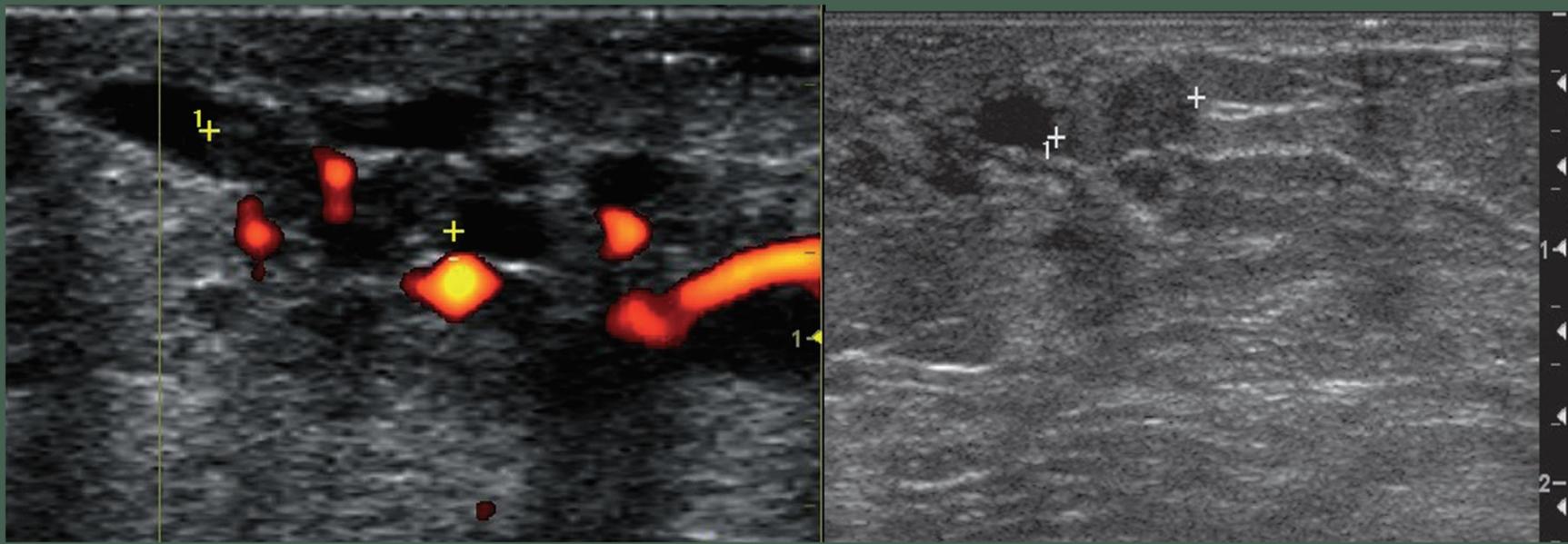
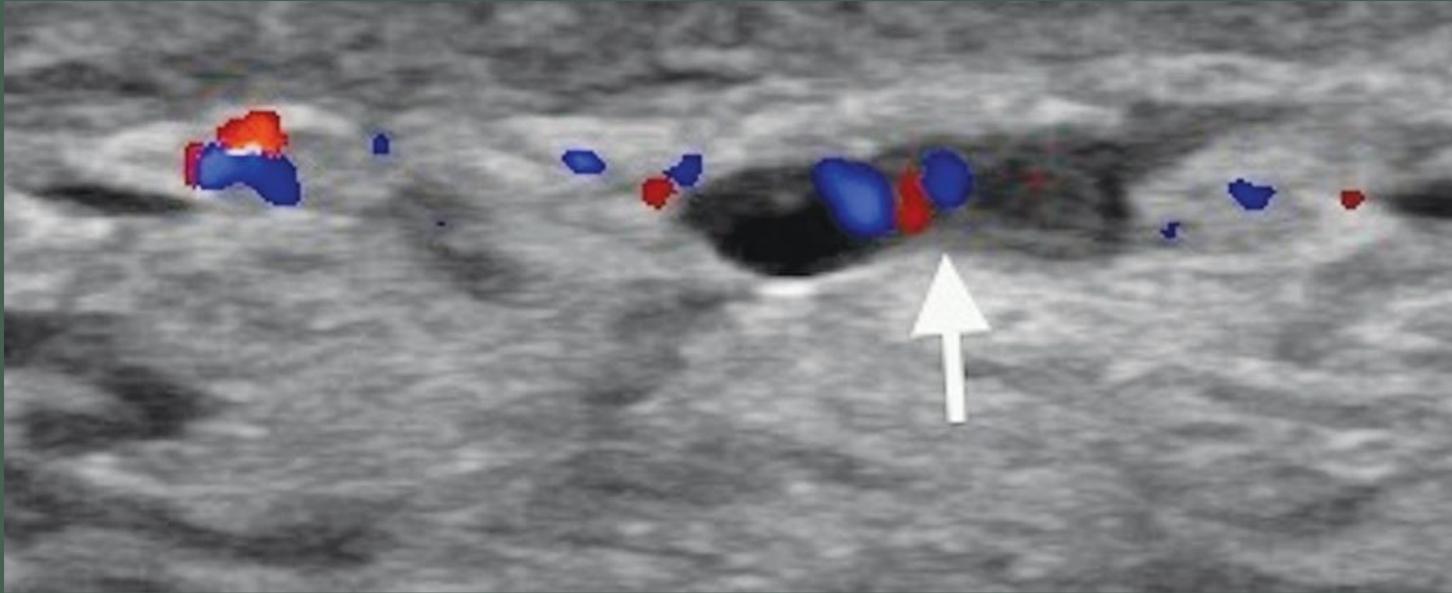
- ✓ *length of duct from nipple base to mass*

Ductal ectasia, defined by a duct caliber greater than 3 mm, is one of the most common findings well seen on ultrasound.

A dilated duct should be imaged as peripherally as possible to assess the extent of involvement.

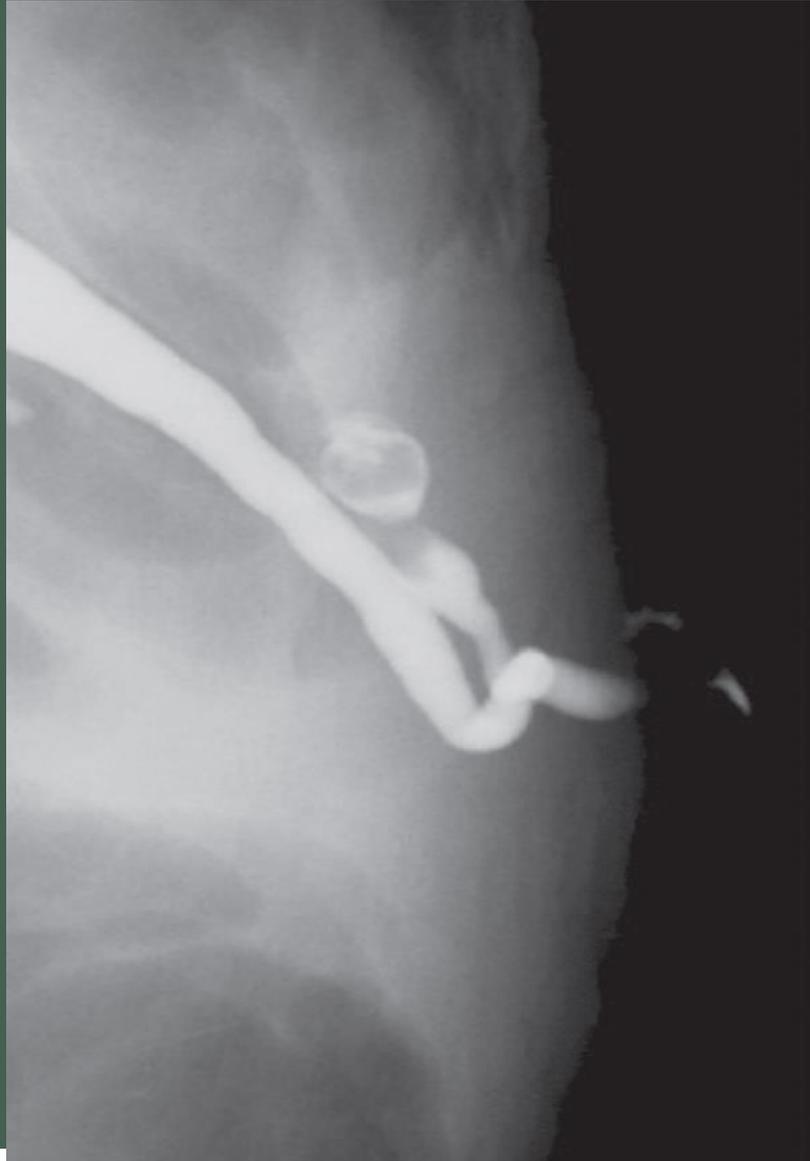
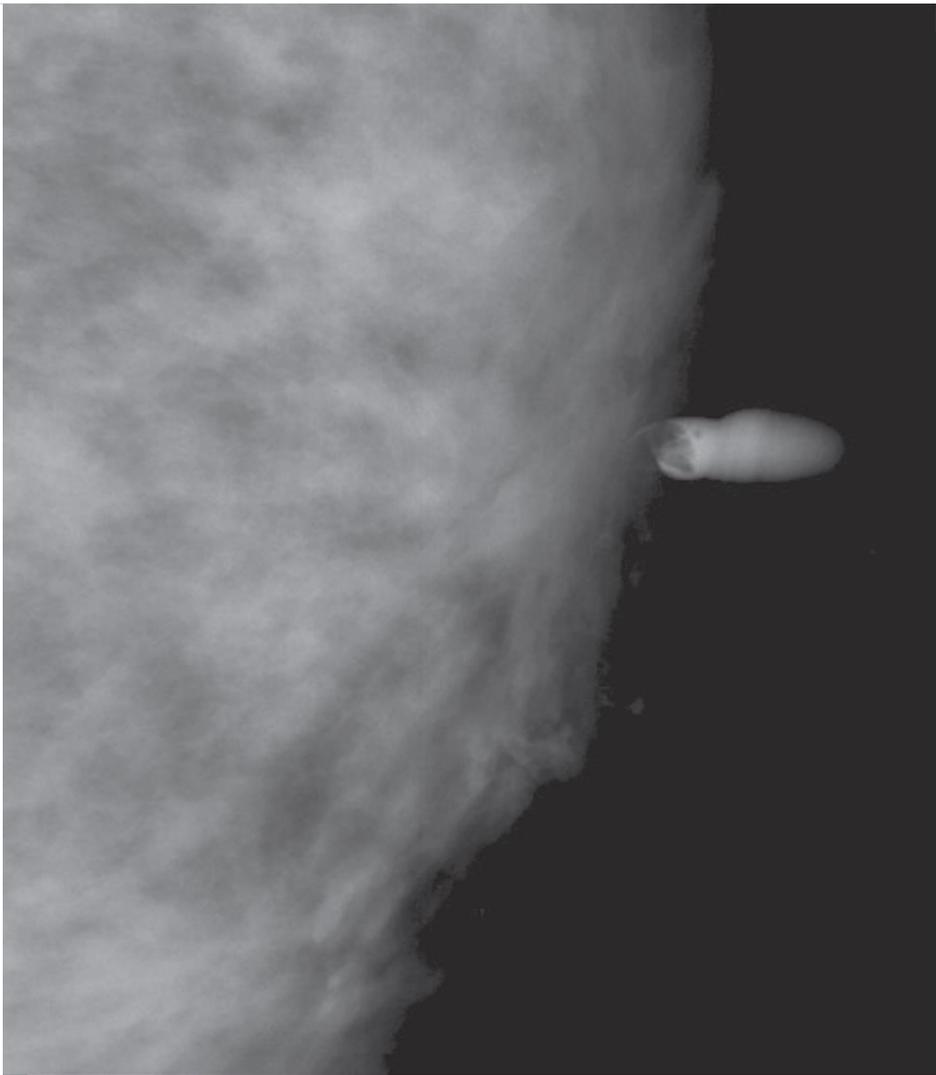


intraductal papilloma.



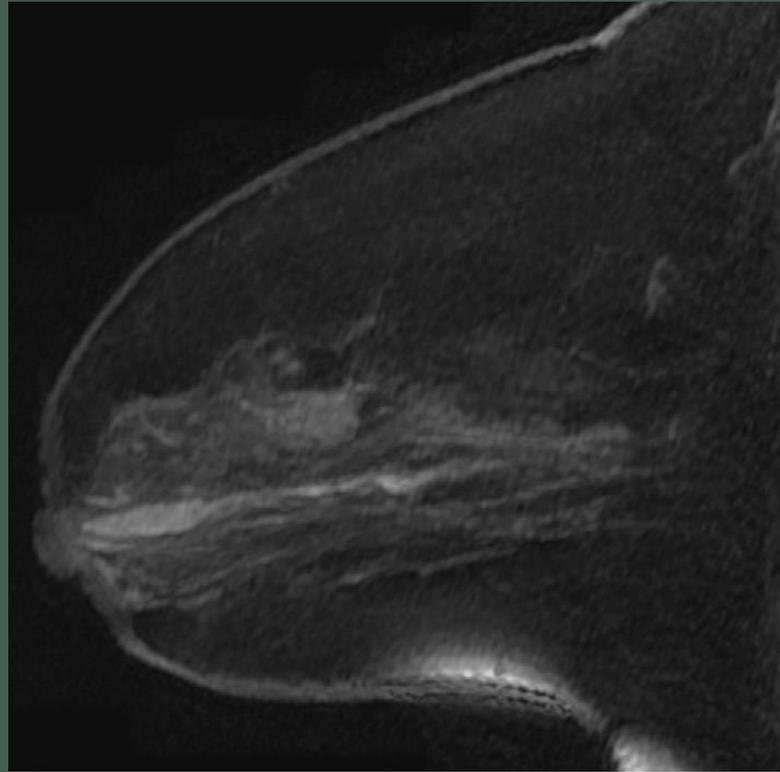
On ultrasound

A papilloma typically presents as a well-circumscribed mass, intracystic mass, or mass with a vascular pedicle within a dilated duct

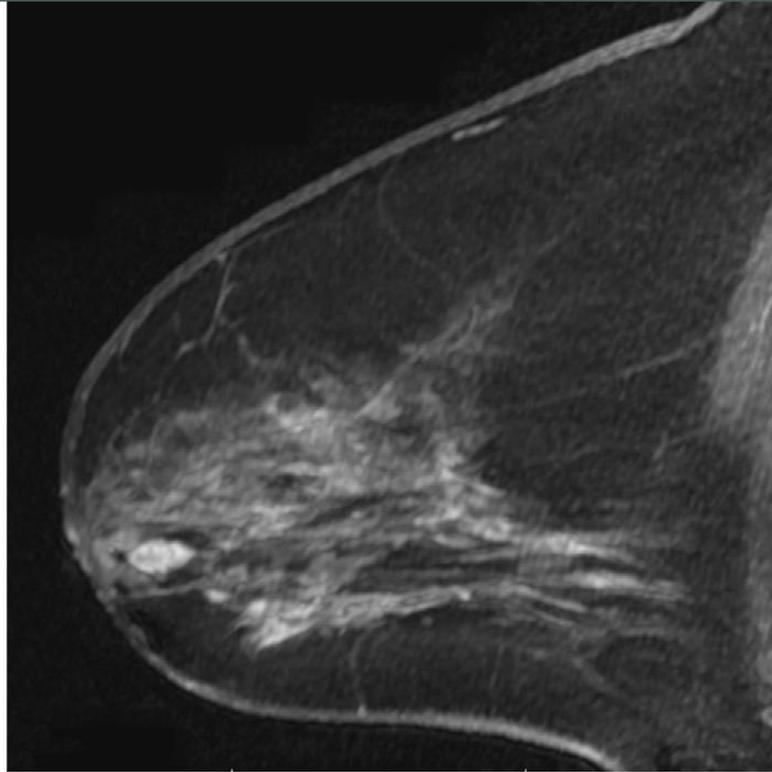


Ductography

although not widely used, may show an intraluminal filling defect or ductal dilatation due to partial or complete ductal obstruction.



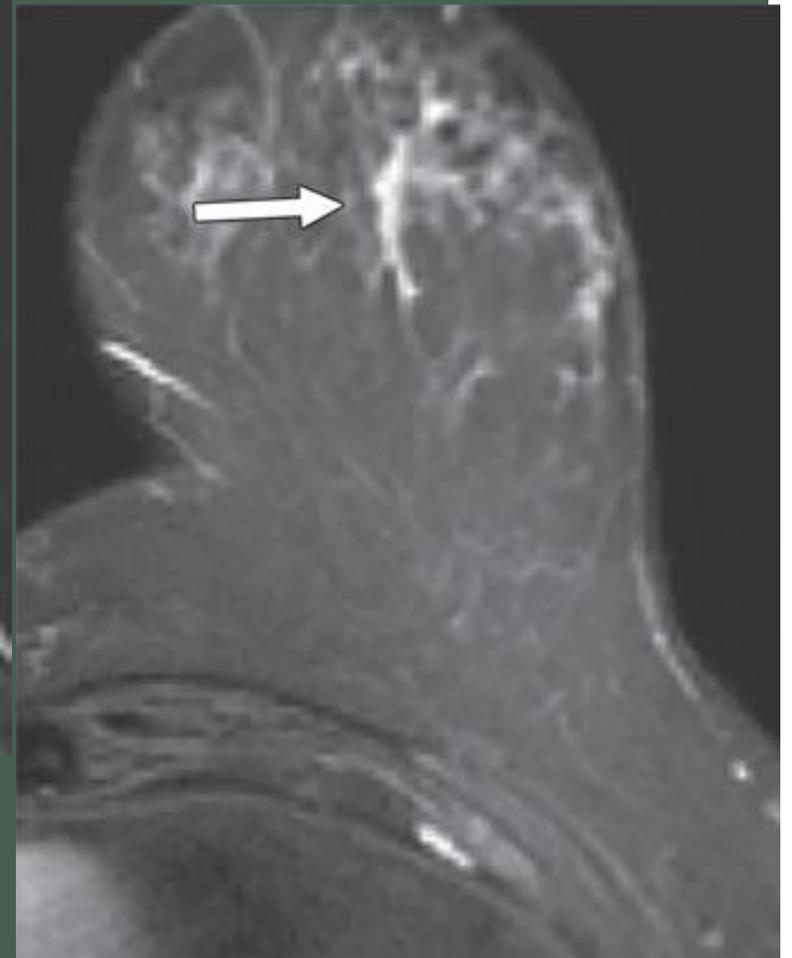
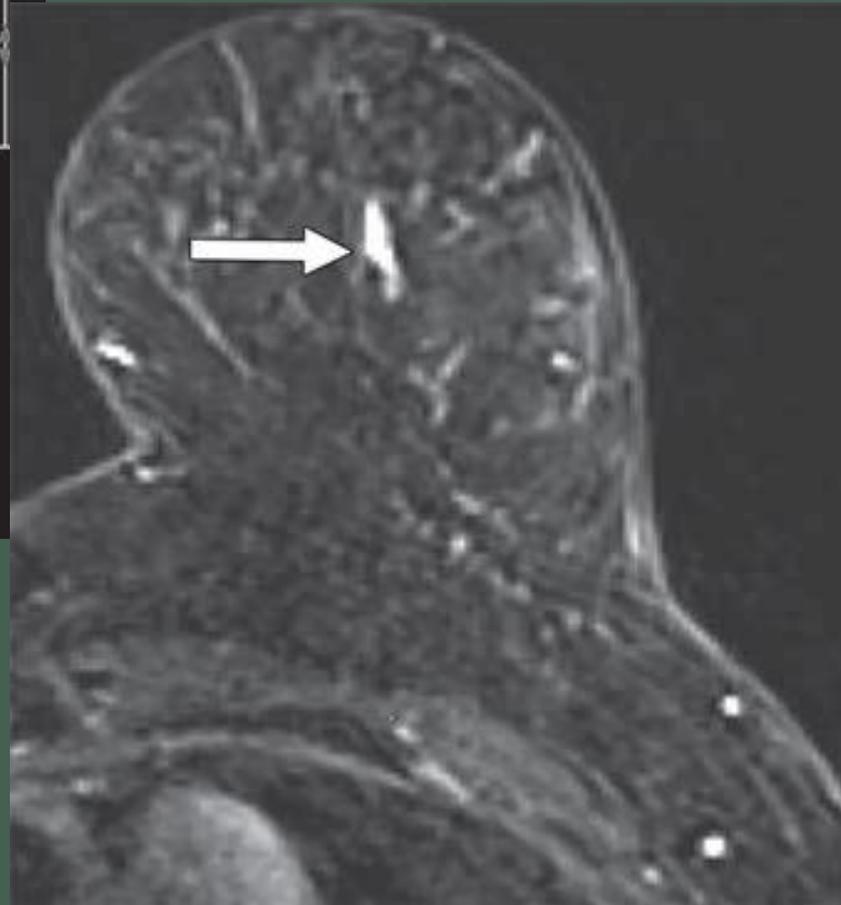
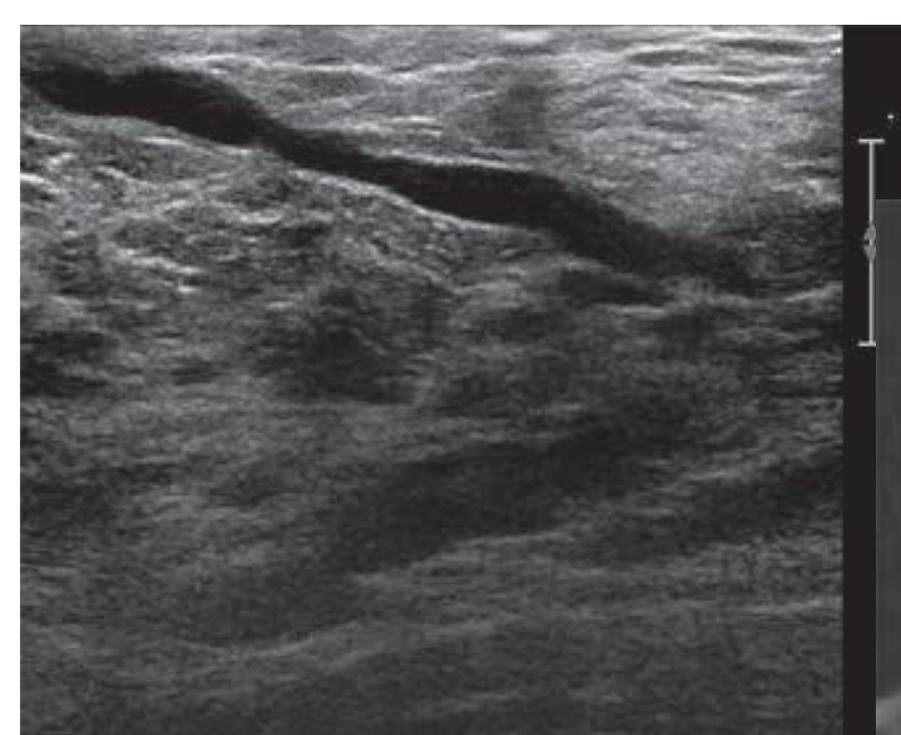
(a)

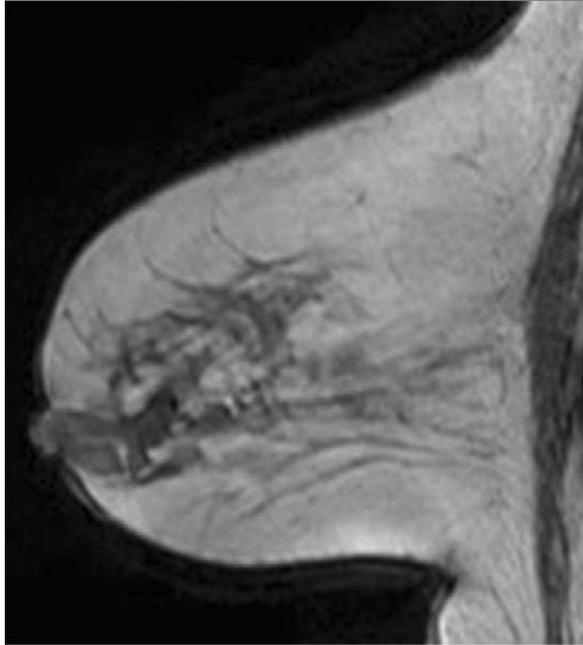


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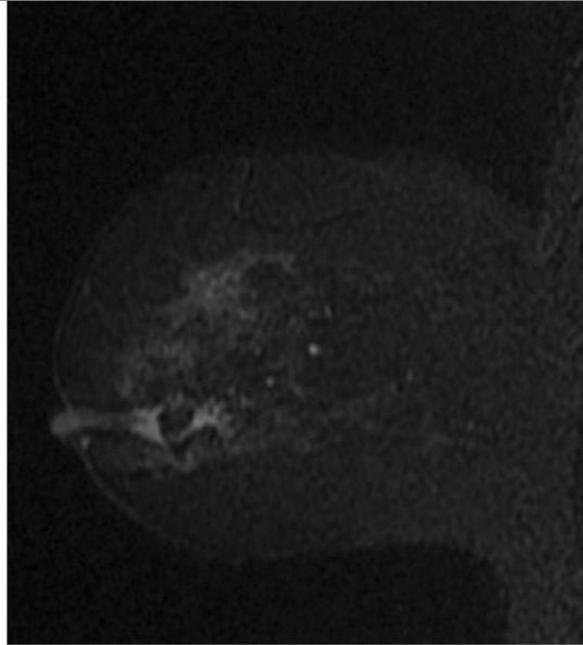
On MRI

Small papillomas can be occult, larger papillomas can present as an enhancing focus or circumscribed mass within a dilated duct

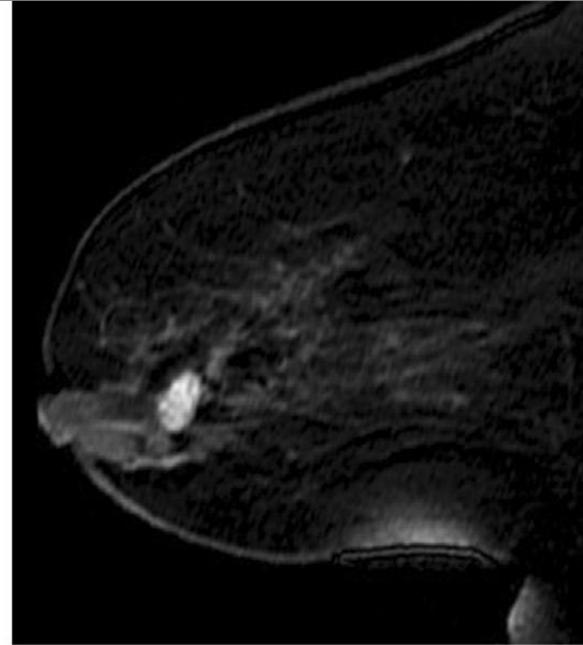




(a)



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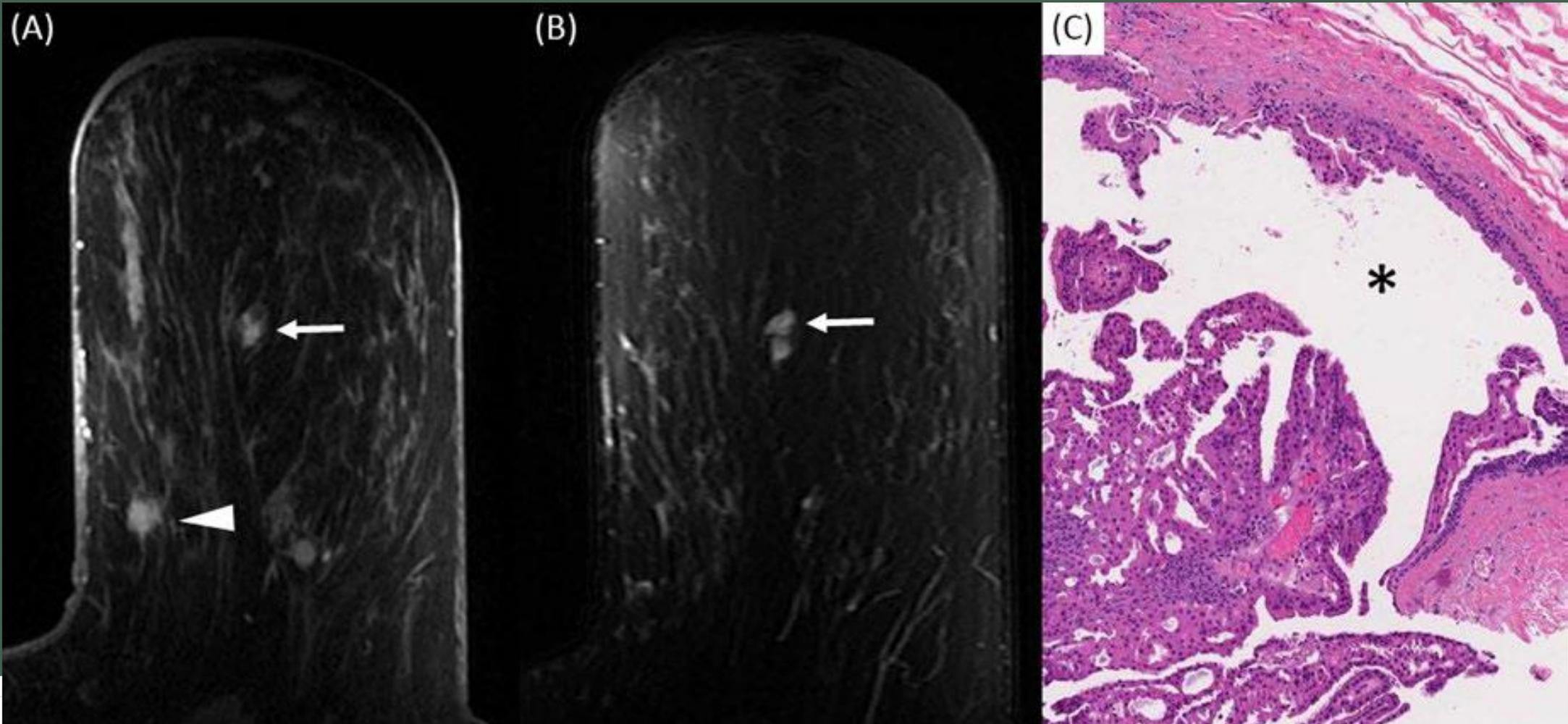


(c)

Atypical papilloma

Atypical papilloma

ipsilateral cancer (arrowhead) and intraductal papilloma (arrow)



Peripheral Papilloma

Arise within the TDLU

Less common

Multiple and bilateral

Younger patients

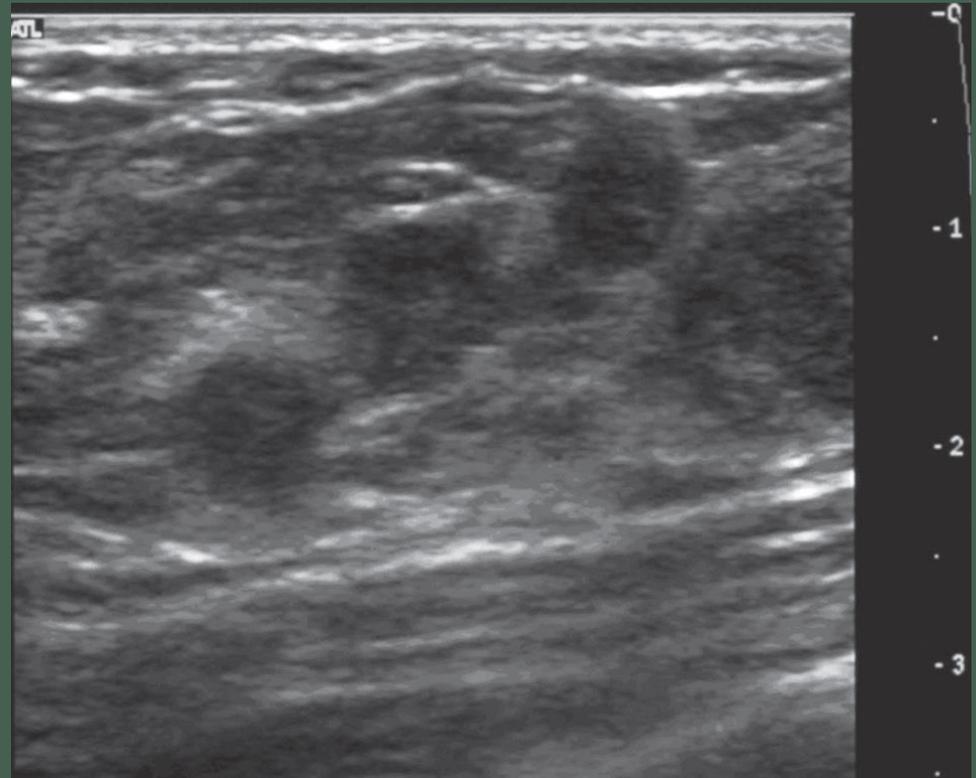
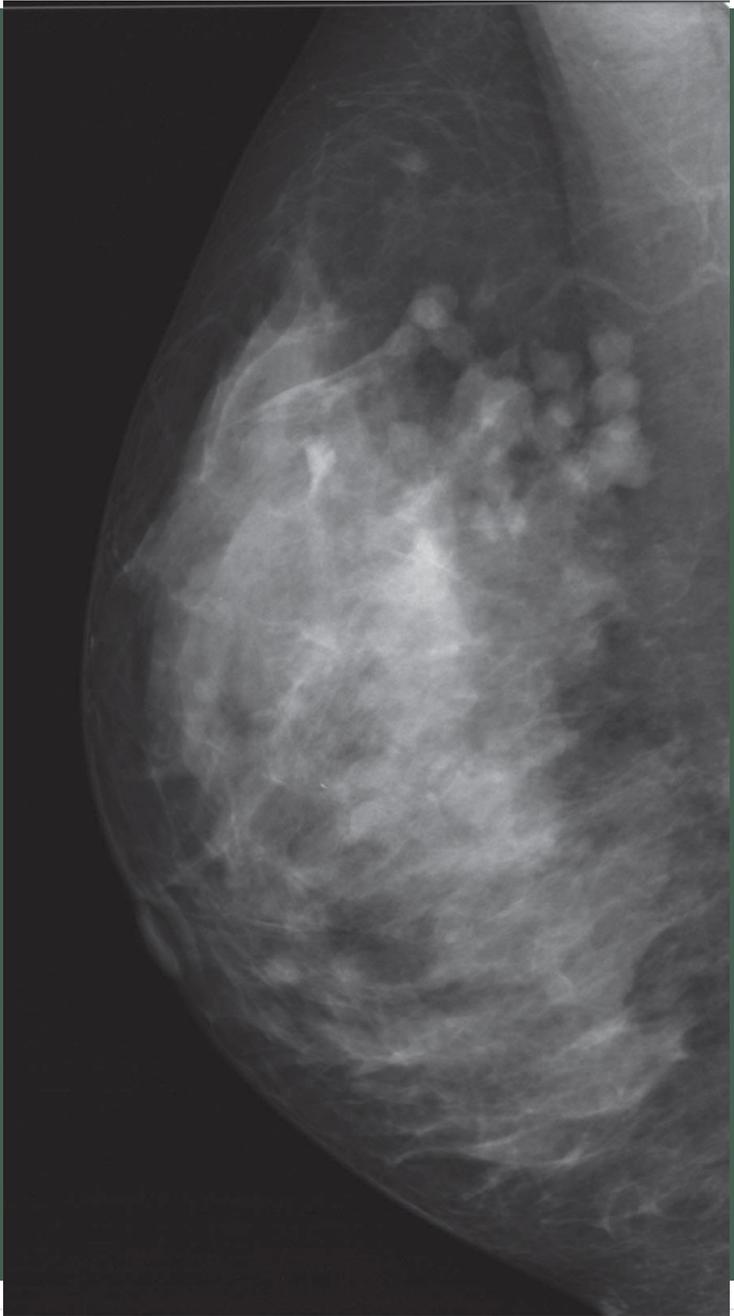
More clinically occult

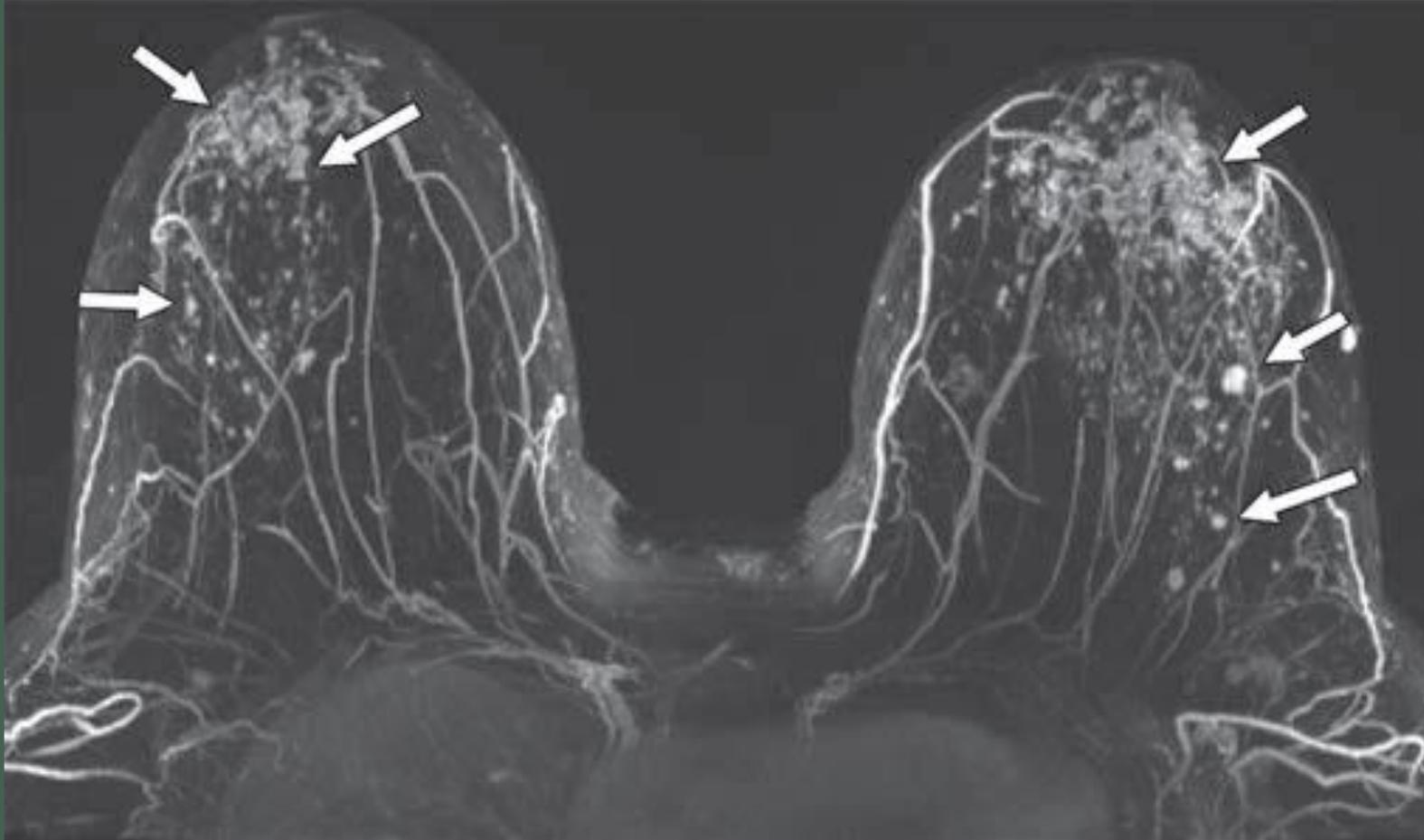
More likely to be associated with high-risk lesions

The imaging features of multiple papillomas are very similar to central papillomas.

No particular imaging characteristic would lead a radiologist to suspect atypia in a central or peripheral papilloma.

- Peripheral papillomas often are discovered as masses on mammograms, less commonly as microcalcifications, and rarely as architectural distortion.
- On US, multiple papillomas can present as round or oval, circumscribed, solid, or complex cystic masses.
- The current role of MRI for evaluation of multiple papillomas is unclear due to their nonspecific imaging appearance. Breast MRI, however, can play a key role in preoperative planning.





Management of Intraductal papilloma

- **Surgical excision**
 - **Atypical papillary lesion**
 - **If nipple discharge is persistent or recurrent after a 2-year monitoring**
 - **patient choice for symptomatic relief**
- **Lower under staging rate in:**
 - **multiple cores**
 - **larger gauge vacuum-assisted biopsy needles**

Solitary benign papilloma without atypia?

- Atypia within a papilloma is defined by the presence of a uniform population of neoplastic cells in an area ≤ 3 mm, whereas DCIS is defined by the presence of such cells in an area >3 mm. Atypical ductal hyperplasia (ADH) within a papilloma may represent a precursor lesion and is regarded as an increased risk factor for the development of breast cancer.

- Papillomas associated with ADH or DCIS may appear identical to benign papillomas on all imaging techniques. Although indeterminate calcifications within a papilloma could suggest the presence of DCIS, similar microcalcifications may also be observed with infarction, haemorrhage, or fibrosis.

Higher post excision upgrade rate of solitary benign papilloma without atypia:

> 50 y/o

Lesion > 1 cm

imaging-pathologic discordance

Concurrent breast cancer

Nipple to lesion distance > 3 cm

bloody nipple discharge

NMEs with segmental or regional distribution on MRI

BRCA 1&2 mutation

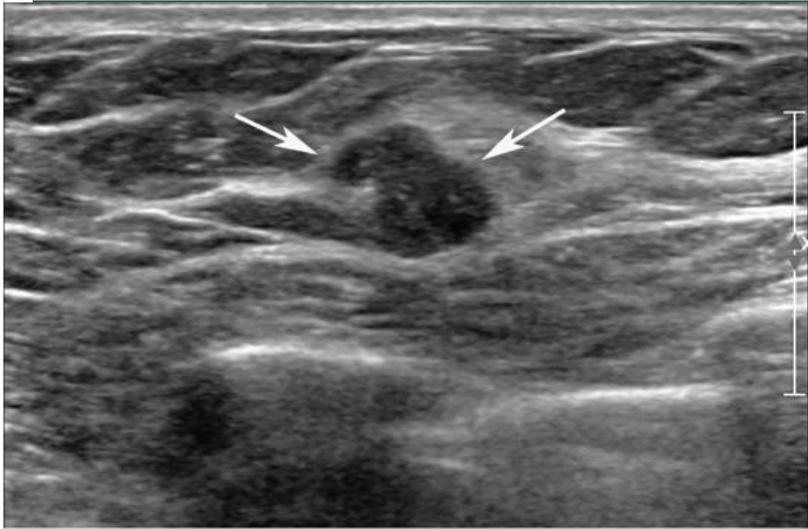
In papillary lesions, the presence of atypia has been shown to be the strongest predictor of an upgrade to malignancy.

Many investigators suggested that areas of atypia or carcinoma may be missed in the limited tissue material gained with needle biopsy, thus requiring excisional biopsy for IDPs. Meanwhile, **Benign breast papilloma without atypia diagnosed with US-guided core needle biopsy (CNB) can be successfully managed with US-guided directional vacuum-assisted removal (DVAR) or US/MRI follow-up without intervention with a low rate of recurrence.**

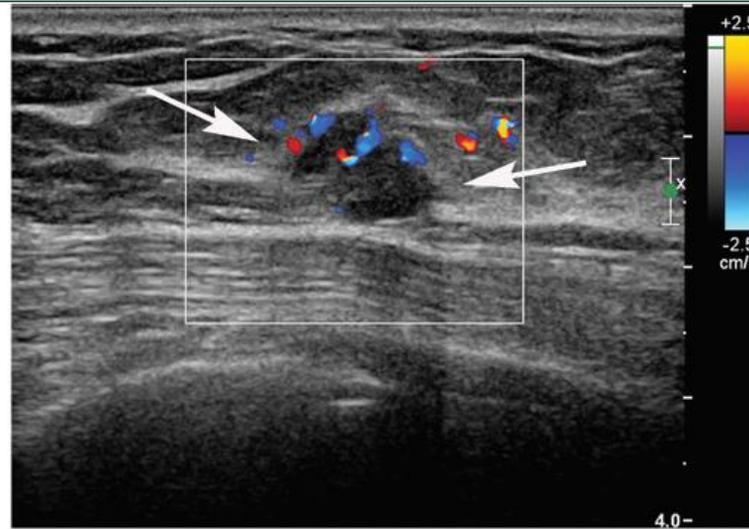
ACR appropriateness criteria 2022:

- The management of papillomas diagnosed on CNB is controversial and varies by institution.
- Because papillomas diagnosed on CNB are often excised, **excisional biopsy instead of CNB may be useful** when a papillary lesion is anticipated based on imaging findings. A recent study suggests that patients with non-bloody pathologic nipple discharge, a benign CNB, or normal imaging (cancer risk <2%) may be considered for nonoperative management if they do not have risk factors such as prior ipsilateral breast cancer, BRCA mutation, or atypia on CNB.
- According to the surgical literature, **major duct excision remains the reference standard to exclude malignancy in patients with unremarkable imaging**, when even a negative ductogram (NPV 63%–82%) or MRI (NPV 87%–100%) does not exclude an underlying cancer or high-risk lesion.

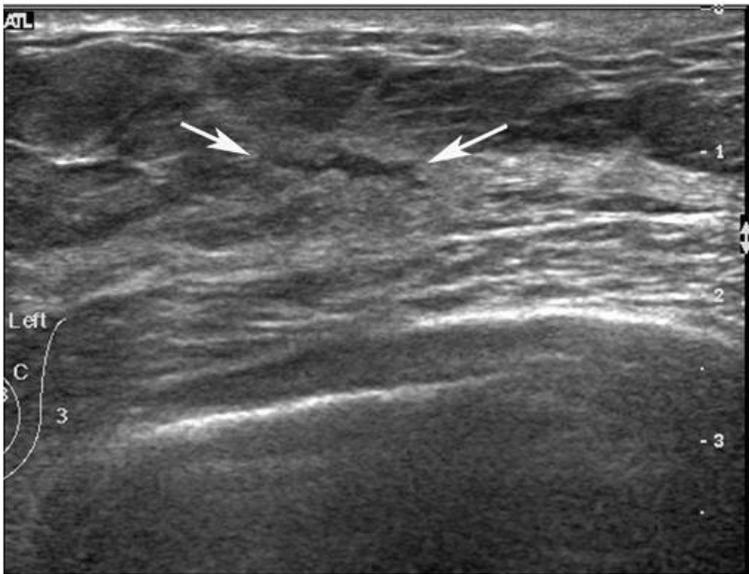
- In addition, US does not reliably distinguish between benign and malignant small intraductal lesions. Therefore, the decision to perform percutaneous biopsy versus major duct excision should involve the patient and their health care provider.
- Image-guided CNB is equally useful in male patients for obtaining tissue diagnosis and assisting in patient management.
- Image-guided CNB is not indicated as the initial examination to evaluate pathologic nipple discharge.



a.

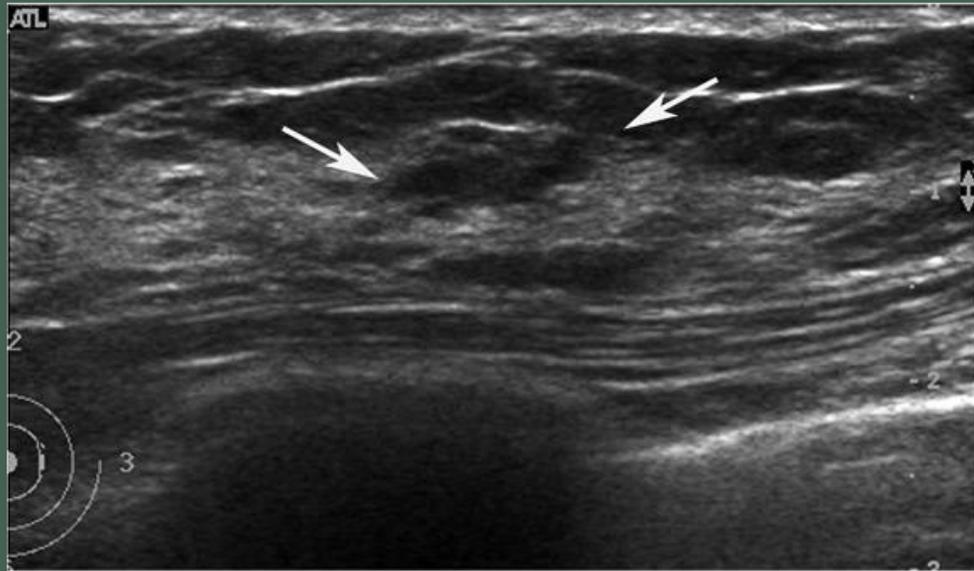


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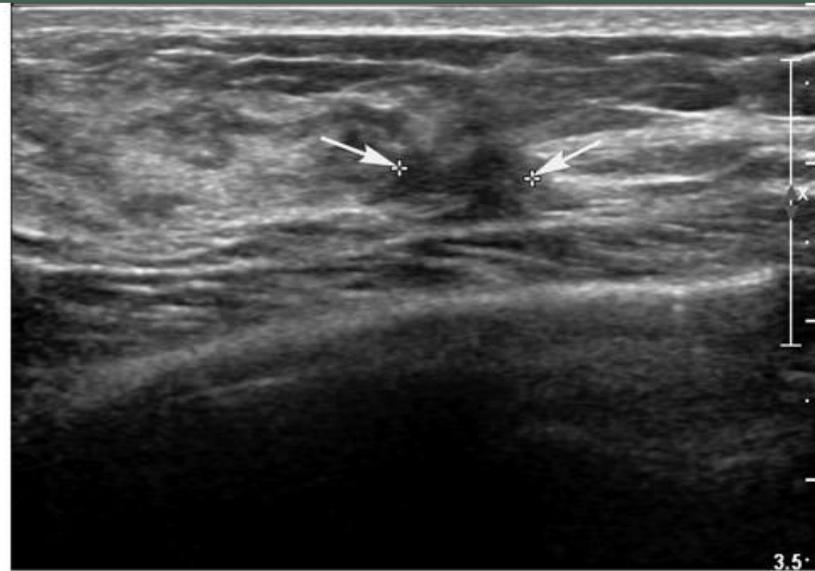


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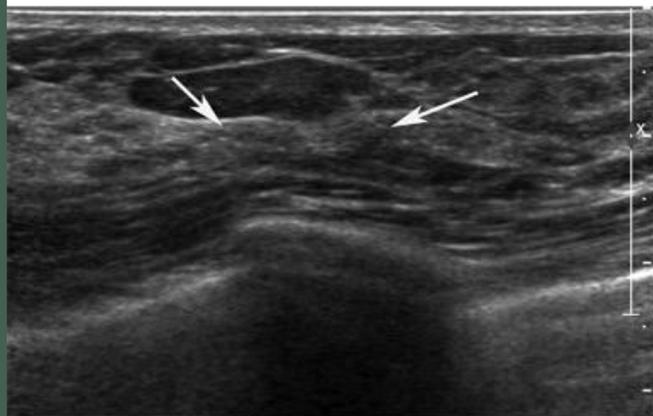
- indistinct irregular hypoechoic solid mass
- This lesion was classified as 4B and diagnosed as a benign papilloma with a 14-gauge needle biopsy.
- DVAR Pathologic examination showed atypical ductal hyperplasia.
- After surgical excision, the lesion was upgraded to ductal carcinoma in situ because a 0.5-cm ductal carcinoma in situ involving nodular adenosis remained at the post-DVAR site.



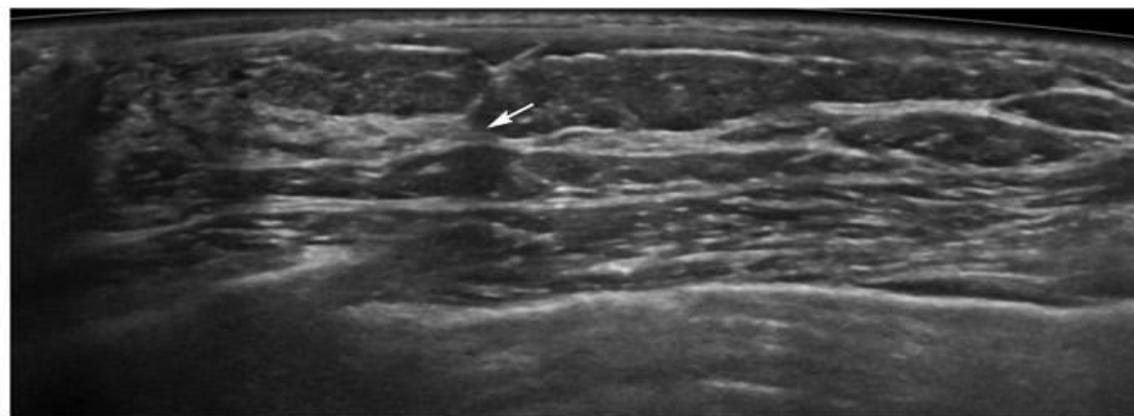
a.



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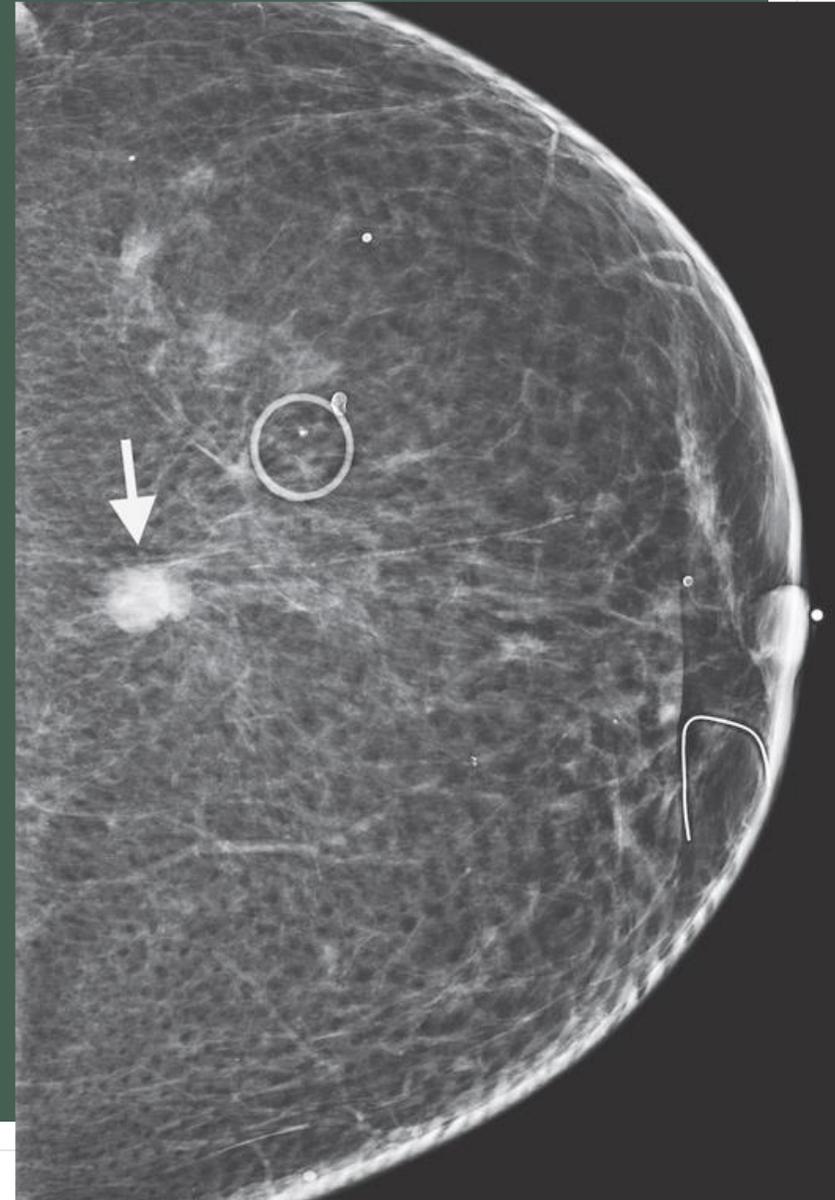
benign papilloma

Malignant Papillary Lesions

- subdivided into
 - **noninvasive** (intracystic papillary carcinoma, solid papillary carcinoma, and micropapillary intraductal carcinoma)
 - **invasive** (invasive micropapillary or papillary carcinoma)

Intraductal Papillary Carcinoma (Papillary DCIS)

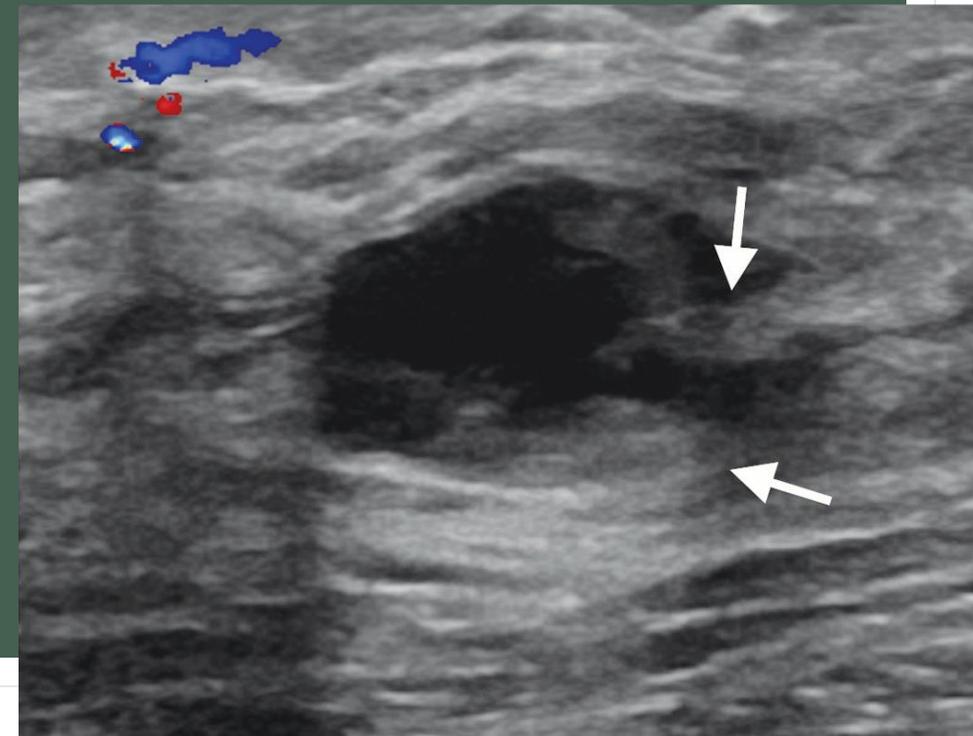
- Noninvasive diffuse form
- Tends to be multifocal
- **Mammographically** presents as single or multiple grouped amorphous or pleomorphic microcalcifications, and less frequently as a circumscribed mass.
- **US** can show ductal distension
- **MRI** may show NME



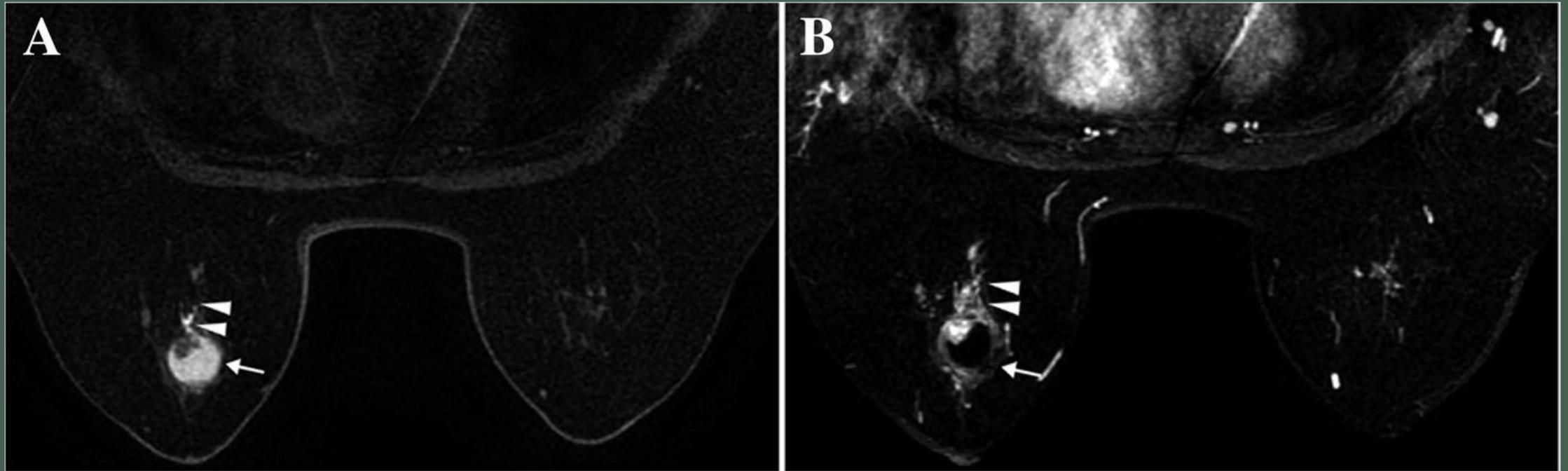
Management of this lesion is similar to that of classic intraductal carcinoma (DCIS), with patients receiving **lumpectomy with or without radiation** therapy. Wider excisions generally are recommended due to the multifocal nature and extensive distribution of papillary DCIS

Intracystic (encapsulated) Papillary Carcinoma

- Noninvasive localized form
- confined within a cystically dilated duct
- **Can present either as a small, centrally located, subareolar mass with nipple discharge or a large, palpable mass anywhere in the breast**

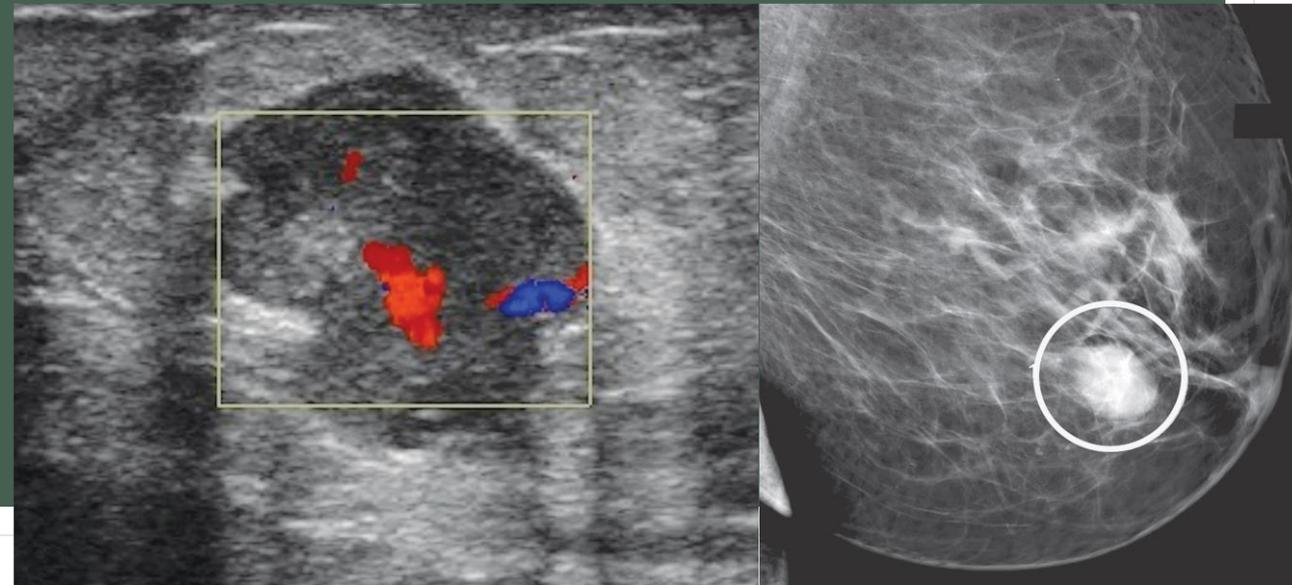


A case of papilloma with DCIS manifesting as a complex cystic mass



Solid Papillary Carcinoma

- Arises within large or dilated ducts.
- most often present as a palpable mass or with bloody nipple discharge
- The mammographic features of SPC most arise in the central part of the breast, appearing as a round or circumscribed mass.
- US may show a complex intracystic mass, a homogeneous solid mass, or a frond-like mass within a dilated duct.



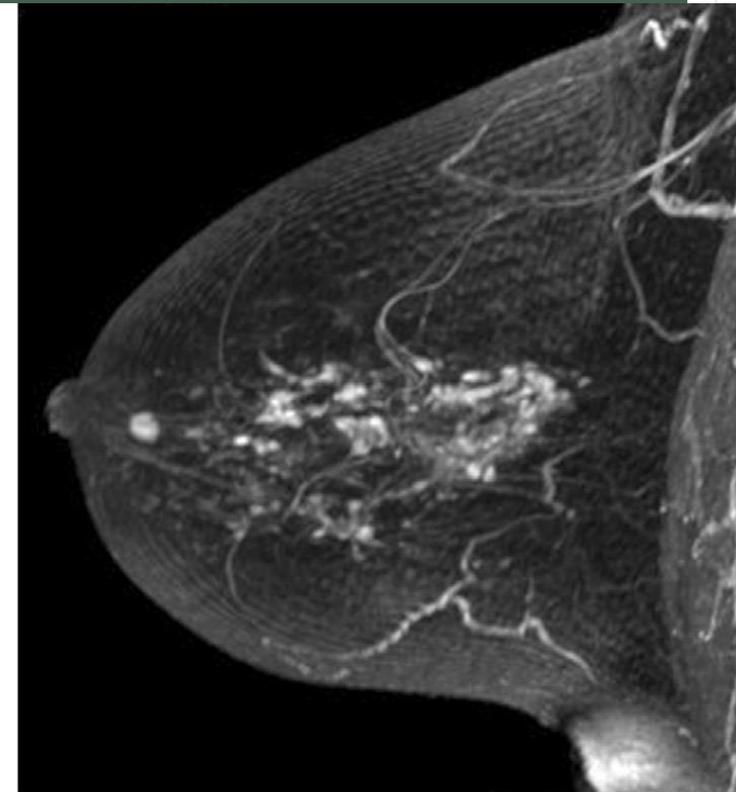
- Therapeutic management IPC and SPC is controversial. The mainstay of treatment is surgical excision, with adjuvant radiation and endocrine therapies when associated with DCIS or invasive carcinoma.
- Have favorable prognosis

Micropapillary DCIS

- Micropapillary DCIS, an uncommon subtype of DCIS, is highly malignant, extensive, and often multifocal and multicentric.



(a)



(b)

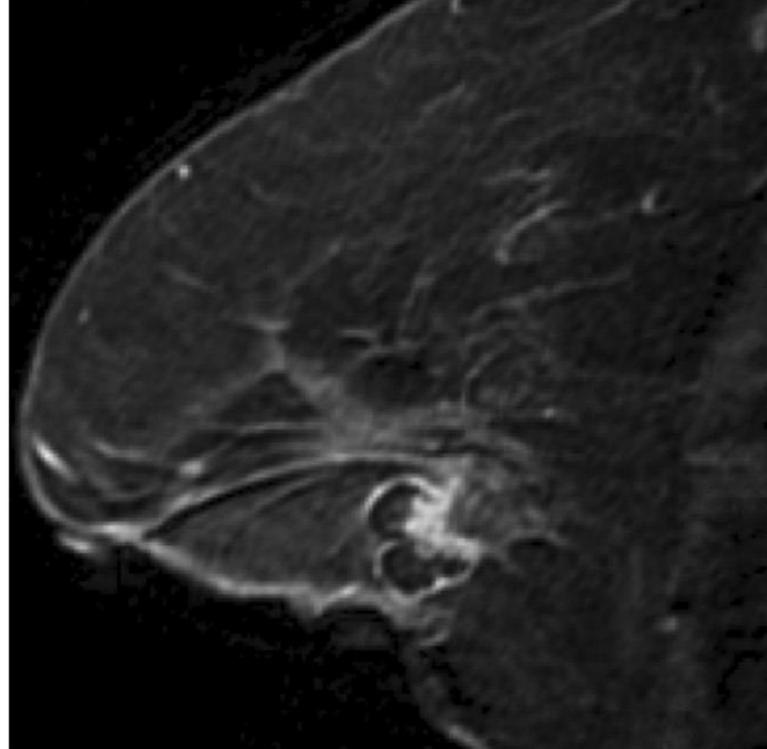
Invasive Micropapillary Carcinoma

- An uncommon, clinically aggressive variant of IDC
- **Mammography** shows a dense irregular or spiculated mass. Calcification is not usually evident on mammography.
- **US** demonstrates a solid, irregular, hypoechoic mass with indistinct margins. **US evaluation of the axilla is crucial for staging.**
- The most common **MR** findings are an irregular mass or diffuse NME, often multifocal.
- Poorest prognosis of all malignant papillary lesions

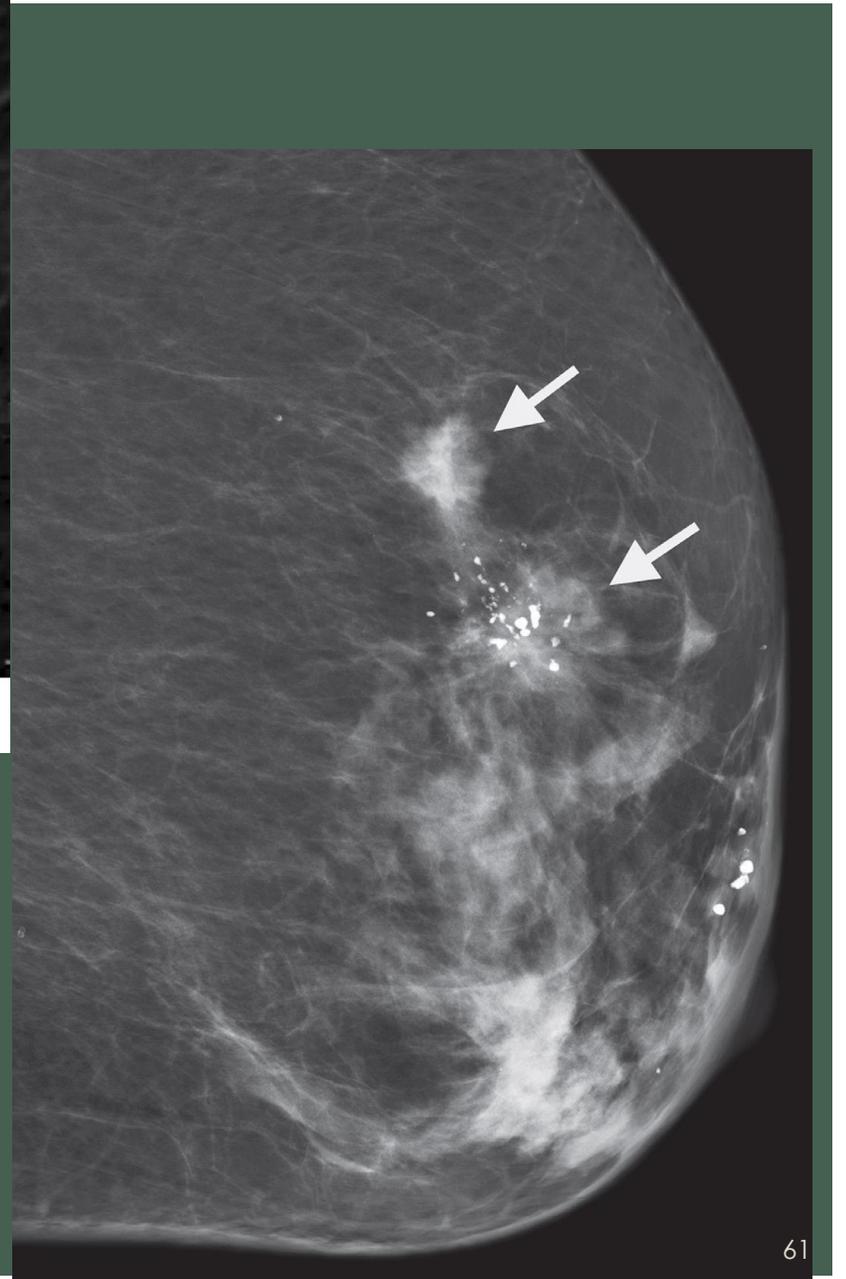
- On **mammography**, invasive papillary carcinoma is usually characterized by **nodular densities, which may be multiple and are frequently lobulate**.
- These lesions are often hypoechoic and irregular on ultrasonography.
- Invasive papillary carcinoma is grossly circumscribed in two-thirds of cases. Other invasive papillary carcinomas are grossly indistinguishable from invasive breast cancers of no particular type.



(a)



(b)



Invasive Papillary Carcinoma

- On **mammography** presenting as a solitary round or oval circumscribed mass or as a cluster of well-defined masses.
- **US** can reveal single or multiple circumscribed or irregular solid masses or complex solid and cystic masses.
- The **MRI** appearance is a circumscribed or irregular-enhancing mass with washout kinetics, which may be T2 hyperintense, or enhancing complex cysts.

- The management is similar to that of other conventional invasive breast cancers and includes local treatment consisting of lumpectomy with radiation therapy or mastectomy and sentinel lymph node biopsy and adjuvant systemic hormonal therapy. Chemotherapy has a limited role.
- **The prognosis of invasive papillary carcinoma generally is better than other forms of ductal carcinoma with less axillary node involvement.**

