Imaging Approach to Nipple Masses: What a Radiologist Should Know

Toma S. Omofoye, MD, Marion E. Scoggins, MD, and Basak E. Dogan, MD

After participating in this activity, the radiologist should be better able to diagnose lesions of the nipple-areolar complex by imaging and selecting the appropriate biopsy technique.

Category: Breast Imaging
Subcategory: Breast Ultrasound

Key Words: Imaging of Nipple Masses, Nipple Adenoma, Nipple Malignancy, Papilloma

The unique milieu of the nipple can give rise to a spectrum of benign and malignant masses. Nipple masses may present a diagnostic challenge to the radiologist due to their location or symptoms, resulting in difficulties in imaging and biopsy access. The purpose of this article is to examine the imaging appearance, workup, differential diagnosis, and management of lesions of the nipple-areolar complex.

The nipple-areolar complex can be a blind spot for radiologists, due to poor imaging resolution, confluence of multiple structures, and lack of specific guidelines for image targeting this area. It is important to note that approximately 8% of breast cancers arise in the region of the central mammary ducts near the nipple, and subareolar malignancy may be obscured by normal nipple anatomy.

This article examines nipple-areolar anatomy, multimodality imaging techniques used for diagnostic evaluation of nipple lesions, and the differential diagnosis of a nipple mass (Table 1). In addition, because there are unique diagnostic challenges to percutaneous core needle biopsy of a nipple mass, we discuss the range of biopsy techniques available for sampling these lesions.

Anatomy and Physiology

The nipple-areolar complex functions to dispense milk during lactation. It harbors diverse cell types, including squamous epithelium of skin, columnar cells in ducts, and sebaceous and apocrine glands. The nipple represents the terminus for major ducts, and in most nipples, there are 5 to 10 ductal orifices protected by keratin plugs. The individual ducts are surrounded by smooth muscle bundles that aid in nipple contraction. Near the areolar border, raised Morgagni tubercles are formed by openings of large sweat glands (i.e., Montgomery glands). Histopathologic composition of the nipple-areolar complex significantly influences the differential diagnosis of a broad array of disease processes that affect this region, some of which may have similar imaging appearance.

Imaging Techniques

Clinical signs and symptoms associated with nipple masses such as nipple discharge, inversion, retraction, or erythema can help guide appropriate imaging workup and management (Figure 1). The small size and extreme anterior location of the nipple-areolar complex preclude optimal x-ray exposure, presenting a challenge for mammographic evaluation. Optimizing the diagnostic imaging algorithm can help characterize a nipple mass as benign or malignant. For benign nipple lesions, imaging can help tailor therapy or determine the scope of surgical excision.

Mammography. Because the superficial location of the nipple is susceptible to x-ray overpenetration, placement of a...
Table 1. Clinical Presentation and Imaging Findings of Nipple Masses

<table>
<thead>
<tr>
<th>Pathologic Process</th>
<th>Clinical Presentation</th>
<th>Ultrasonography</th>
<th>Mammography</th>
<th>MRI</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma</td>
<td>Nipple enlargement</td>
<td>Isoechoic, hypervascular mass within the nipple</td>
<td>May have calcifications within the enlarged nipple</td>
<td>T2-hyperintense, homogeneous enhancement, plateau enhancement</td>
<td>Skin punch biopsy, fine needle aspiration</td>
</tr>
<tr>
<td>Papilloma</td>
<td>Unilateral nipple discharge</td>
<td>Retroareolar, homogenous hypoechoic mass, which may have a cystic component</td>
<td>Oval, well-circumscribed mass</td>
<td>Homogeneous enhancement with plateau or washout kinetics</td>
<td>Core biopsy</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>Nipple enlargement, skin thickening, pain</td>
<td>Isoechoic mass within the nipple</td>
<td>Enlarged nipple, usually well circumscribed, slow-growing mass, rarely spiculated</td>
<td>Intermediate T1- and T2-signal intensity, peripheral rim enhancement with persistent enhancement</td>
<td>Skin punch biopsy, fine needle aspiration</td>
</tr>
</tbody>
</table>
evaluation for new or asymmetric nipple retraction, and attention to presence of calcifications in the nipple. Magnification views are required if routine mammographic views demonstrate calcifications within or approaching the nipple.

On mammography, a “pseudomass” can result when the nipple is not in profile.

Ultrasound. The nipple can represent a “blind spot” for ultrasound due to its mobility, superficial position introducing an air interface, and inherent acoustic shadowing due to densely arranged connective tissue and dermal elements. In symptomatic patients or patients with mammographic nipple-areolar complex abnormalities, “roll” technique—in which the nipple is rolled over the finger of the sonographer’s nonscanning hand to stabilize it between the finger and transducer—helps visualize ducts that may be parallel to the beam. Using a gel standoff is also beneficial, as it facilitates near-field focusing, transducer-skin coupling, and gives uniformity to the nipple contour (Figure 3).4 A small saline bag placed over the nipple may be used in lieu of a large amount of gel and provides the same benefits. With prolonged scanning and cold, the nipple may contract, which impairs visualization of ducts and nipple detail; therefore, the ultrasound gel and scanning room should be warm to minimize this problem. To help differentiate between true intraductal masses within large retroareolar ducts from proteinaceous fluid, power Doppler with a high-frequency transducer (≥13 MHz) should be used (Figure 4).

MRI. Use of dedicated breast coils and performing breast MRI before and after contrast administration are now standard practice and thus important for nipple-areolar complex evaluation. Most nipples enhance on MRI. This enhancement typically is bilaterally symmetric and two-layered, appearing as superficial linear dermal enhancement with underlying nonenhancement.5

Findings on MRI suspicious for malignancy involving the nipple-areolar complex include thick or nodular enhancement, irregular enhancement posteriorly, or presence of an associated mass.1,6 MRI is helpful in evaluation of breast malignancy, including Paget disease. In Paget disease, there are malignant cells in the epidermis, characterized by an eczematous-type rash that may represent invasive or in situ carcinoma. Although Paget disease frequently does not present with a mass and is mammographically occult in up to 50% of cases, MRI is highly sensitive for detection of Paget disease and may demonstrate additional occult foci of disease, allowing determination of the optimal medical and surgical treatment (Figure 5).1

Most nipples enhance on MRI, and normally the enhancement is bilaterally symmetric.

Ductography. Ductography involves cannulation and introduction of contrast medium into a discharging duct. It

![Figure 2. An 89-year-old woman with urethral cancer presented with mass-like enlargement of the right nipple. Bilateral craniocaudal mammographic views show marked asymmetric enlargement of the right nipple (arrow) compared with the left nipple. In addition, there is right retroareolar asymmetry (dashed arrow). “BB” markers (arrowheads) denote nipple location, facilitating comparison between each side. Image-guided biopsy revealed low-grade, invasive ductal carcinoma.](image)

![Figure 3. A 38-year-old woman presented with a 1-month history of right nipple enlargement and white nipple discharge. Grayscale longitudinal sonographic image with a gel standoff (white box) to even the contour around the nipple (arrow) shows a mass (dashed arrow) within the nipple. At real-time examination, the mass contained mobile echogenic debris and posterior acoustic enhancement, suggesting a cyst with inspissated material. A 21-gauge needle was used for ultrasound-guided fine needle aspiration biopsy. Pathologic analysis indicated a ruptured epidermal inclusion cyst. The remainder of cyst contents was expressed manually after the biopsy.](image)
Figure 4. A 53-year-old woman with slight left nipple retraction. A: Grayscale transverse sonography of the nipple shows a mass (arrow) in the nipple and nipple base. B: Power Doppler transverse sonography shows internal vascularity in the nipple mass. C: Grayscale sonography shows a 16-gauge core biopsy needle (arrow) in prefire position, directed at the nipple mass (box). D: Grayscale sonography shows the biopsy needle (arrow) in postfire position through the mass (box). The biopsy result was intraductal papilloma.

Figure 5. A 57-year-old woman with a 1-year history of right nipple dryness. Punch biopsy of the nipple revealed Paget disease. Mammogram (not shown) demonstrated a few amorphous calcifications within the right nipple. A: Axial, T1-weighted, postcontrast subtraction MR image shows abnormal, asymmetric enhancement of the right nipple (box) compared with minimal, normal enhancement of the left nipple (circle). B: Axial, T1-weighted, postcontrast subtraction MR image shows multiple areas of linear and segmental nonmass enhancement (arrows), suspicious for multifocal ductal carcinoma in situ (DCIS) underlying the known Paget disease of the nipple. Biopsy of a representative area in the medial right breast at 3-o’clock position demonstrated high-grade DCIS. Paget disease and multifocal DCIS were confirmed at mastectomy.
Differential Diagnosis of Nipple Mass

**Epidermal Inclusion Cyst.** This condition presents when there is obstruction of a hair follicle resulting in an epithelial cyst in the dermis. It may be associated with Gardner syndrome. The cyst may be palpable or visible on physical examination. On mammography, an oval mass may be appreciated and a tangential view can demonstrate skin location. On sonography, the cyst presents as an oval mass with variable internal echotexture (ranging from anechoic to hypoechoic) (Figure 3). In addition, the hair follicle may be identified as a linear track extending to the skin. Internal keratin debris may give a hyperechoic “whorled” appearance. When inflamed, an epidermal inclusion cyst may demonstrate vascularity. Biopsy can be deferred when imaging is pathognomonic, because inflammation can result if the cyst is disrupted.

**Sebaceous Cyst.** The pathophysiology of a sebaceous cyst is similar to that of an epidermal inclusion cyst, but a sebaceous cyst results from an obstructed sebaceous gland. Sebaceous cysts may be associated with Cowden syndrome. On physical examination, a sebaceous cyst is often palpable. On mammography, the cyst appears as an oval mass that may have central fat density due to sebum. On sonography, an oval mass is appreciated within the skin, which may be indistinguishable from an epidermal inclusion cyst. Again, biopsy may be deferred, as cyst contents are proinflammatory.

**Papilloma.** A papilloma represents a benign proliferation of ductal epithelium and myoepithelium on a fibrovascular stalk. Papillomas represent the most common cause of bloody nipple discharge. There is a slight associated increase in the risk of breast cancer. Papillomas may be central or peripheral (>70% are central or subareolar). Central papillomas are often solitary, whereas peripheral papillomas are often multiple. Mammography may be nondiagnostic or demonstrate an oval mass with or without accompanying calcifications. On sonography, an intraductal, mixed cystic and solid mass may be identified (Figure 4). On MRI, a papilloma may appear as a mass with variable enhancement. Core needle biopsy is recommended to exclude atypia or papillary neoplasm. Papillomas often are excised, particularly when atypia is diagnosed, as there is a 31% upgrade rate to carcinoma on surgical excision. Malignant lesions are associated with palpability, nipple discharge, and higher Breast Imaging Reporting and Data System (BIRADS) score.

The most common cause of bloody nipple discharge is a papilloma.

**Nipple Adenoma.** Also known as florid papillomatosis, or superficial papillary adenomatosis, nipple adenoma represents a rare benign epithelial tumor. Essentially, it is an intraductal papilloma within the nipple. A nipple adenoma often presents as an erosive or ulcerative nipple lesion with associated nipple discharge and may be confused with Paget disease. On mammography, a nipple adenoma may appear as a circumscribed oval mass within the nipple, or as an asymmetrically enlarged nipple. Nipple adenomas may have associated calcifications. On ultrasound, there is an oval or lobulated mass with homogeneous iso- or hypoechoic echotexture, usually within the nipple or a distal major duct. There is marked vascularity on Doppler ultrasound (Figure 7). On MRI, nipple adenomas are homogeneously enhancing, T2-bright masses with persistent kinetics. Although nipple adenomas may be diagnosed by skin punch biopsy, ultimately, surgical excision is recommended because of growth and pain. Many clinicians and radiologists prefer to refer the patient directly for excision based on imaging findings without percutaneous biopsy.

**Leiomyoma.** Leiomyoma is a rare, benign process arising from smooth muscle. It presents as a slow-growing, painful nipple mass. Pain is often episodic related to smooth muscle contraction from cold exposure or pressure. Leiomyomas may be associated with nipple erosion. Mammography demonstrates nipple enlargement. Ultrasound shows an isoechoic mass. MRI shows a mass with intermediate T1 and T2 intensity, peripheral rim enhancement, with persistent enhancement kinetics. Percutaneous biopsy by fine needle aspiration or skin punch biopsy may be performed.
There is often peripheral vascularity on sonography due to inflammation. Aspiration may be performed for laboratory analysis to guide treatment. It is recommended to obtain short-term clinical follow-up and reimaging after antibiotic therapy to exclude malignancy. Symptoms and imaging findings should improve after 4 weeks of antibiotic treatment.

Following diagnosis of a subareolar abscess, short-term clinical follow-up and re-imaging after antibiotic therapy are recommended to exclude malignancy.

Malignancy. In the nipple, malignancy has a wide range of clinical presentations, including nipple retraction or inversion, enlargement, excoriation, and discharge. Various studies indicate the incidence of unsuspected nipple involvement by breast malignancy, ranging from 8% to 58%. Nipple involvement is more common with central tumor location, large tumor size, metastatic disease to lymph nodes, lymphovascular invasion, and multicentric or multifocal disease. On mammography, an irregular mass with potential retroareolar extension may be seen (Figure 9). Calcifications may indicate in situ disease. On sonography, malignant masses often have irregular borders with increased vascularity. MRI may be helpful in delineating nipple involvement and extent of disease for surgical planning.

Central tumor location, large tumor size, metastatic lymphadenopathy, lymphovascular invasion, and multicentric or multifocal disease are risk factors for nipple involvement by breast cancer.

Biopsy

Percutaneous biopsy of nipple masses is challenging for multiple reasons. The rich vascular and nervous supply of the nipple confers increased risk of pain and bleeding. Some nipple masses may be exophytic, and cosmetic considerations limit biopsy approaches. As a result, skin punch or excisional biopsy is the most direct approach in many cases.
lesions with subareolar extension or components extending immediately posterior to the nipple-areolar complex, needle biopsy is a less invasive and patient-friendly approach (Figure 4). Fine needle aspiration biopsy may help resolve diagnostic questions pertaining to intraductal debris versus solid component within major subareolar ducts. Core biopsy is indicated when mass extension to the sub-nipple-areolar complex location is evident and can be best performed with fully automated cutting needles that allow full-thickness tissue acquisition from all tissue layers in this location (Figure 4).

**Conclusion**

This CME activity emphasizes that nipple masses may be subtle and present a diagnostic challenge. Diagnosis depends on optimization of imaging techniques, familiarity with unusual pathology occurring in this location; and, based on their extent of involvement, use of various biopsy techniques.

**References**

CME QUIZ: VOLUME 38, NUMBER 25

To earn CME credit, you must read the CME article and complete the quiz and evaluation on the enclosed answer form, answering at least seven of the 10 quiz questions correctly. **Select the best answer and use a blue or black pen to completely fill in the corresponding box on the enclosed answer form.** Please indicate any name and address changes directly on the answer form. If your name and address do not appear on the answer form, please print that information in the blank space at the top left of the page. Make a photocopy of the completed answer form for your own files and mail the original answer form in the enclosed postage-paid business reply envelope. Only two entries will be considered for credit. Your answer form must be received by Lippincott CME Institute, Inc., by December 14, 2016. At the end of each quarter, all CME participants will receive individual issue certificates for their CME participation in that quarter. These individual certificates will include your name, the publication title, the volume number, the issue number, the article title, your participation date, the AMA credit awarded, and any subcategory credit earned (if applicable). For more information, call (800) 638-3030.

All CME credit earned via Contemporary Diagnostic Radiology will apply toward continuous certification requirements. ABR continuous certification requires 75 CME credits every 3 years, at least 25 of which must be self-assessment CME (SA-CME) credits. All SAM credits earned via Contemporary Diagnostic Radiology are now equivalent to SA-CME credits (www.theabr.org).

**Online quiz instructions:** To take the quiz online, log on to your account at www.cdrnewsletter.com, and click on the “CME” tab at the top of the page. Then click on “Access the CME activity for this newsletter,” which will take you to the log-in page for http://cme.lww.com. Enter your **username** and **password.** Follow the instructions on the site. You may print your official certificate immediately. Please note: Lippincott CME Institute will not mail certificates to online participants. **Online quizzes expire on the due date.**

1. Which one of the following nipple-areolar complex lesions may contain calcifications on mammograms?
   A. Subareolar abscess
   B. Epidermal inclusion cyst
   C. Nipple adenoma
   D. Sebaceous cyst

2. Which one of the following statements concerning papillomas involving the nipple is false?
   A. They may contain calcifications on mammography.
   B. They may appear cystic on ultrasound.
   C. They often present with bloody discharge.
   D. They are always benign.
   E. The central type is more common than the peripheral type.

3. A 52-year-old woman presented with an enlarged, ulcerated nipple. On mammography, a nipple lesion contained calcifications. On ultrasound, the oval-shaped nipple mass was hypoechoic and abundantly hypervascular on power Doppler. The most likely diagnosis is
   A. sebaceous cyst
   B. nipple adenoma
   C. leiomyoma
   D. subareolar abscess
   E. malignancy

4. All of the following represent the constellation of treatments for a subareolar abscess, except
   A. fluid aspiration
   B. cell culture and cytology
   C. appropriate antibiotic therapy
   D. brachytherapy
   E. follow-up imaging in 4 weeks to exclude malignancy

5. Women with a subareolar abscess generally are
   A. pregnant
   B. lactating
   C. middle-aged, nonlactating
   D. elderly
   E. asymptomatic

6. All of the following are risk factors for involvement of the nipple-areolar complex by breast malignancy, except
   A. recurrent tumor
   B. large tumor burden
   C. metastatic lymphadenopathy
   D. lymphovascular invasion by tumor
   E. multicentric disease

7. Which one of the following statements regarding MRI of the nipple is true?
   A. Contrast-medium administration is unnecessary.
   B. Nipple enhancement is uncommon.
   C. MRI is more sensitive than mammography for diagnosis of nipple tumors.
   D. Normal nipples demonstrate a “three-layered” pattern of enhancement.
   E. MRI is insensitive for the diagnosis of Paget disease of the breast.

8. Which one of the following represents the most worrisome feature of nipple discharge suggesting underlying breast malignancy?
   A. Bilateral and spontaneous
   B. Unilateral and serosanguineous
   C. Unilateral and milky
   D. Involvement of multiple ducts and inducible

9. All of the following represent features of a leiomyoma within the nipple, except
   A. peripheral rim enhancement on MRI
   B. rapid-growing mass
   C. isoechoic mass on ultrasound
   D. nipple erosion
   E. episodic painful mass

10. Which one of the following breast lesions is the most common cause of bloody nipple discharge?
    A. Malignancy
    B. Nipple adenoma
    C. Papilloma
    D. Leiomyoma
    E. Subareolar abscess