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PICTORIAL ESSAY

Breast Ductography: A Hidden Diagnostic Gem for Patients with Abnormal Nipple Discharge

FFY Wan[1], EPY Fung[2], KM Kwok[2], KM Wong[2], LW Lo[2], WS Mak[2], WP Cheung[2]

[1]Department of Radiology and Imaging, Queen Elizabeth Hospital, Hong Kong SAR, China
[2]Department of Diagnostic and Interventional Radiology, Kwong Wah Hospital, Hong Kong SAR, China

INTRODUCTION

Nipple discharge is one of the commonest breast disease symptoms[1] and it can be physiological or pathological. Physiological nipple discharge typically involves multiple ducts in both breasts. Its common causes include pregnancy, lactation, endocrine disorders, and side-effects from medications.[2] Nipple discharge is considered pathological when it is unilateral single-duct discharge that is spontaneous, bloody, serous, or clear, with or without an associated palpable mass. The commonest aetiology is intraductal papilloma, which is seen in approximately 35% to 48% of patients, followed by ductal ectasia, which is the cause in 17% to 36% of patients.[1] Malignancy, most commonly ductal carcinoma in situ (DCIS), is found in 5% to 15% of patients.[3]

Breast ductography is a valuable investigation for assessment of single-duct nipple discharge. It involves administration of iodinated contrast into the duct, followed by mammographic examination. Ductography can unveil the cause of nipple discharge, including duct ectasia and fibrocystic changes. In the presence of filling defects suggestive of tumour, ductography assists in subsequent surgical planning by localising the abnormalities. The aim of this pictorial review is to illustrate the techniques for a successful examination and classical radiological findings of pathologies detected by ductography.

TECHIQUES FOR PERFORMING DUCTOGRAPHY

Indications and Contraindications

Pathological nipple discharge (PND) from single duct is the indication for ductography. The discharge must be observed during the examination so that the discharging duct can be appropriately identified and cannulated. Ductography is not recommended in lactating women or patients with active mastitis. Allergic reactions to the contrast injected into the ductal system are rarely reported. Nonetheless, patients with a history of mild or moderate allergic reactions to iodinated contrast should still be premedicated with steroids. Patients with a history

Correspondence: *Dr FFY Wan, Department of Radiology and Imaging, Queen Elizabeth Hospital, Hong Kong SAR, China*
Email: wfy471@ha.org.hk

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of severe allergic reactions (e.g., anaphylaxis) should not undergo ductography and alternative investigation such as magnetic resonance imaging (MRI) should be considered.[3]

Patient Preparation Prior to the Examination

Patient preparation is crucial for a successful examination. Patients should be reminded not to squeeze the nipple 1 day prior to the procedure. This ensures that adequate discharge is available on the day of examination for localisation and cannulation of the discharging duct orifice. Similar to mammography, patients should avoid applying deodorant, talcum powder, or lotion in their axillae or on their breasts, since these substances may masquerade as microcalcifications on mammography.

Review of Relevant Imaging

Before the examination, any recent breast imaging, including mammography and ultrasound, should be reviewed for any suspicious findings. If not recently performed, mammography with craniocaudal (CC) and mediolateral (ML) views should be performed for reference prior to duct cannulation.

Discharging Duct Cannulation and Contrast Injection

In our centre, the contrast injection system consists of a 30-gauge Jabczenski cannula (Cook Medical, Bloomington [IN], United States) with right-angled tip connected via small-volume extension tubing to a 1-mL syringe filled with 350 mg/mL non-ionic iodinated contrast material (Figure 1). The use of non-diluted contrast is advised for optimal ductal opacification. The extension tubing and cannula should be properly primed with contrast, and any air bubbles should be expelled from the system to avoid artefacts.

Depending on the location of the duct opening, the patient is placed in the sitting or oblique supine position with the ipsilateral arm resting comfortably on an arm rest (Figure 2). The nipple is cleansed to remove any dried secretions and given a sterile prep. Gentle pressure is applied in the periareolar region to elicit nipple discharge. Identification of the 'trigger point', i.e., the area which repeatedly produces nipple discharge when compressed, is helpful. Once nipple discharge is elicited, it is prudent to confirm that the discharge comes from a single pore since ductography is not the appropriate investigation for multi-pore discharge. In case of difficulty in localising the discharging pore, 'spreading' the nipple with the fingers on the adjacent skin can help visualise the

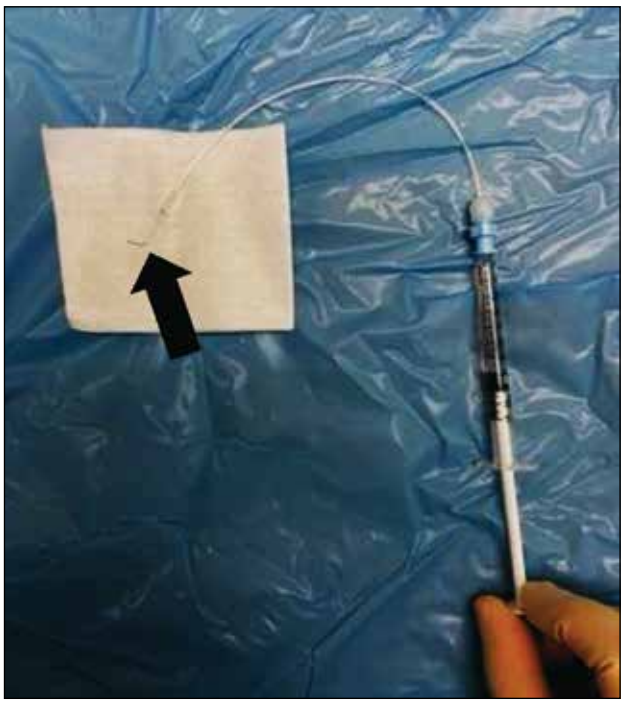

Figure 1. A 30-gauge Jabczenski cannula used for ductography. The right-angled tip (arrow) facilitates easy taping of the device in situ after cannulation.

Figure 2. Patient positioning: sitting or oblique supine position with the ipsilateral arm resting comfortably on an arm rest.

discharging orifice. With careful inspection, the orifice of the discharging duct may appear relatively patulous and slightly erythematous. Once the location of the discharging orifice is confirmed, the nipple is stabilised between the thumb and the index finger with gentle elevation (Figure 3). The tip of the cannula is placed with application of gentle downward guidance (Figure 4). In case of difficulty in cannulating the discharging duct, gentle probing with careful rotation or angulation along the pore may result in successful cannulation. If the most superficial part of the orifice is cannulated but resistance is encountered during further insertion, it is advised to maintain gentle pressure with careful rotation or angulation; forceful cannulation should always be avoided due to risk of ductal perforation.

Figure 3. Stabilising and gently elevating the nipple to facilitate cannulation of the discharging duct.

Figure 4. Placing the tip of the cannula into the orifice of the discharging duct with application of gentle downward guidance.

After successful cannulation, the cannula should be held in position against the nipple. Approximately 0.2 to 0.4 mL of non-ionic contrast is introduced by slow and gentle injection until contrast reflux, high resistance, or pain occurs. Small lesions may be obscured if too much contrast is injected; it is therefore recommended to begin with small amounts. Because the ducts are fragile, pain or a burning sensation may indicate duct perforation or contrast extravasation. Either symptom is an indication to stop further contrast injection. The cannula position is maintained in place by taping it onto the skin (Figure 5), which is facilitated by the right-angled tip of the cannula. This renders further contrast injection feasible and reduces contrast leakage upon subsequent breast compression for mammographic acquisition.

Mammographic Acquisition

The contrast injection system should be held in place and can be secured by taping the syringe and extension tubing onto the patient's chest (Figure 6). Attention should be paid when transferring the patient to the mammography department to prevent the cannula from slipping out.

Mammograms with CC and ML views are subsequently performed. An additional magnification view is useful for detecting faint or subtle microcalcifications associated with the abnormal ductal system. One

Figure 5. Maintaining the cannula in place by taping it onto the skin.

Figure 6. Securing the contrast injection system in place by taping the syringe and extension tubing onto the patient's chest.

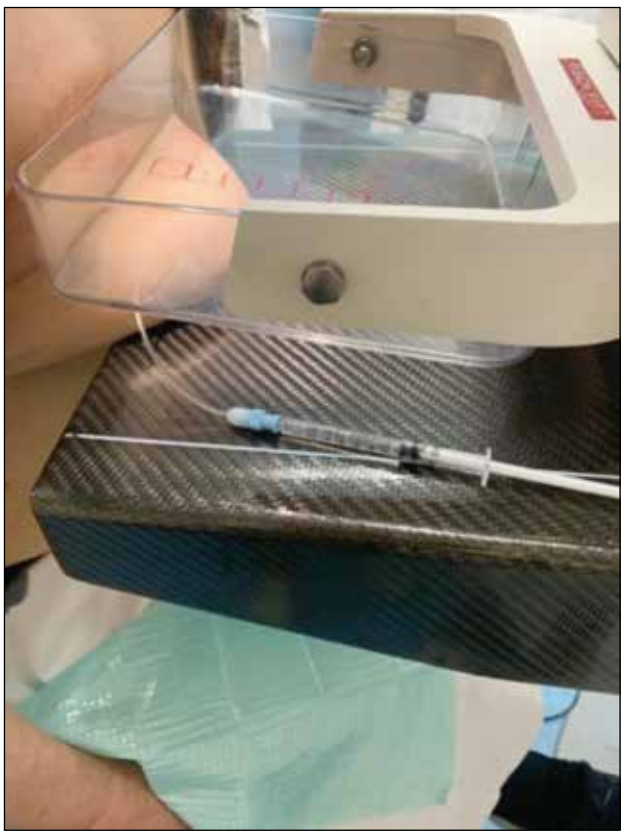

Figure 7. During mammographic acquisition, avoid overlapping of the syringe or extension tubing with the breast parenchyma to avoid abnormalities being obscured.

suggestion when performing mammography is to avoid overlapping of the syringe or extension tubing with breast parenchyma during mammographic acquisition to avoid abnormalities being obscured (Figure 7). If there is significant superimposition of the opacified ducts, a standard ML oblique view or a rolled CC view can be considered. Spot compression views can also be acquired if needed.

Supplementary Ultrasound

After the mammographic examination, supplementary ultrasound is performed with particular attention to any retroareolar or ductal abnormalities and areas with corresponding mammographic abnormalities. It is helpful to perform ultrasound first with the cannula still in situ. The advantage of doing so is that the discharging ductal system may still be distended by the contrast, making any intraductal lesions more conspicuous, and the relationship of the distended ducts and adjacent lesions may be better delineated. Afterwards, the cannula can be removed and the retroareolar region can be scrutinised again.

Because the orifices on the nipple can be closely related and there may be communication between different ducts, this renders the possibility of cannulating the wrong duct, resulting in suboptimal assessment of the ductal system harbouring the pathology. This highlights the importance of careful identification and precise cannulation of the discharging orifice.

Patient Selection

A total of 125 consecutive patients referred to our institution for ductography from January 2016 to July 2022 were reviewed. The procedure was not performed in 20 patients with no nipple discharge during the examination (16.0%) and in five patients with discharge from multiple ducts (4.0%). The examination could not be completed in five patients with failed cannulation (4.0%), two patients with resistance on contrast injection (1.6%), and six patients with contrast extravasation (4.8%). Among patients who completed the procedure, intraductal papilloma (24.1%) was the commonest pathology, followed by duct ectasia (21.8%), DCIS (10.3%), fibrocystic change (4.6%), duct adenoma (1.1%), and invasive carcinoma (1.1%). The rest

(36.8%) had no abnormal findings. Cases with variable normal and pathological ductographic appearances were selected for demonstration.

Imaging Findings

Normal Ductographic Appearances

A normal duct arborises from a single-entry point on the nipple into smaller ducts extending peripherally. Normal ducts are thin and smooth-walled with no filling defects or wall irregularities. Normal ductograms may show variability in ductal calibre, branching patterns, and parenchymal distribution as shown in Figure 8. However, the significance of different branching patterns, extent of ductal distribution, and ductal calibres is unknown.

Lobular blush is caused by contrast filling the lobular portion of the terminal duct lobular unit and is a finding of no clinical significance (Figure 9). It occurs when the ductal system has reached its maximum pressure and there is risk of extravasation with additional contrast administration.

Air bubbles can occasionally be seen within the ducts. Their round morphology and change in position between radiographs are usually sufficient for differentiating them from genuine lesions (Figure 10).

Extravasation

In the event of contrast extravasation (Figure 11), patients usually complain of pain or a burning sensation, but some may be asymptomatic. Common causes include administration of too much contrast material, forceful contrast administration, or too-vigorous manipulation of the cannula causing wall perforation. Infrequently, malignancy causing destruction of ductal wall integrity may lead to extravasation. Since the presence of extravasation may obscure the underlying pathology, the procedure should be rescheduled 7 to 14 days later.

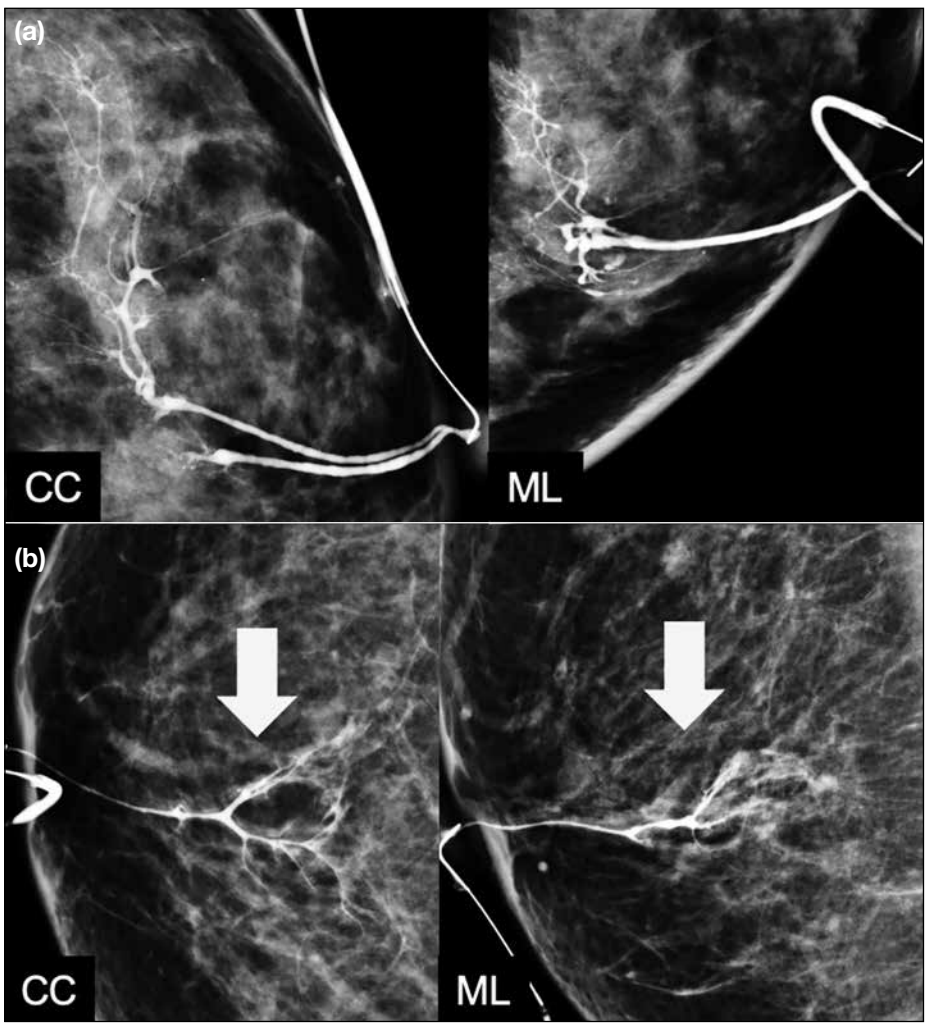

Figure 8. Variable appearances of normal ductograms with craniocaudal (CC) and mediolateral (ML) views. (a) Normal ductal calibre with normal branching and parenchymal distribution. (b) Relatively attenuated ductal calibre with less branching and limited parenchymal distribution.

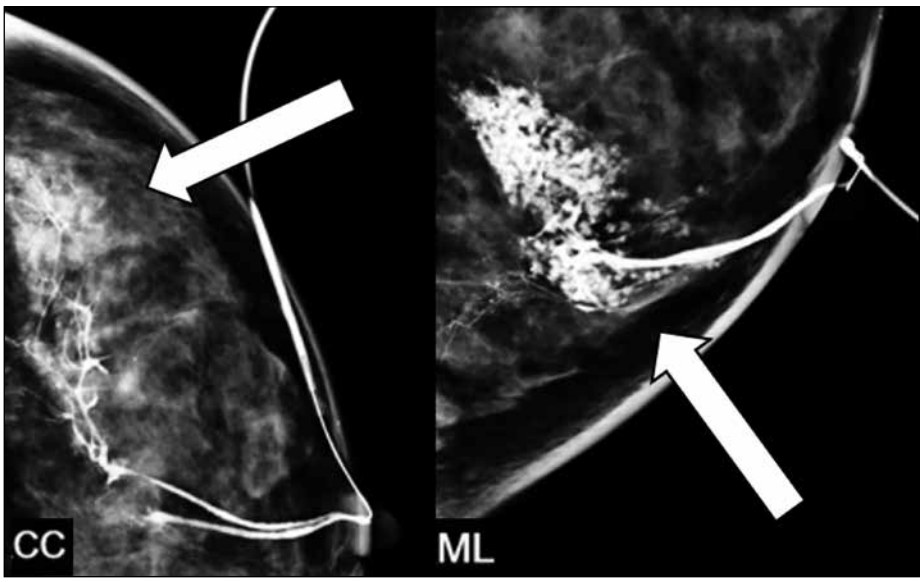

Figure 9. Ductography with craniocaudal (CC) and mediolateral (ML) views. Lobular blush (arrows) due to contrast filled the lobular portion of the terminal duct lobular unit, which is a normal finding.

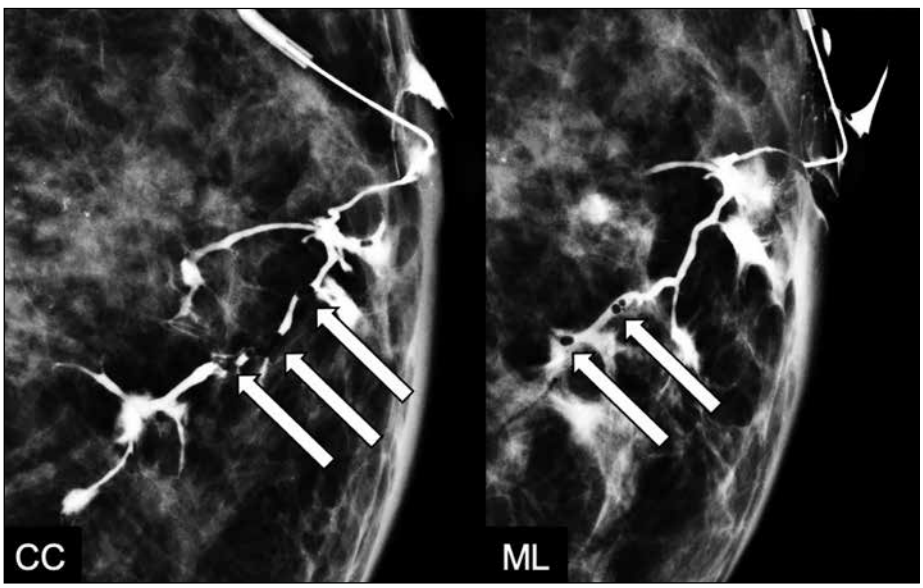

Figure 10. Ductography with craniocaudal (CC) and mediolateral (ML) views. Air bubbles seen as well-defined filling defects within the ducts, characteristically shifting in position between radiographs (arrows).

Duct Ectasia

Duct ectasia refers to non-specific dilatation of mammary ducts and is defined as ductal calibre more than 3 times the width of the cannula.[4] It can cause both physiological and PND. Ductography typically demonstrates a dilated ductal system without intraductal filling defects, ductal wall irregularities, ductal obstruction, or periductal contrast extravasation (Figure 12).

Fibrocystic Change

Fibrocystic change is benign alteration in the terminal ductal lobular unit with or without associated fibrosis. As one of the primary components of fibrocystic change, cysts develop from progressive lobular distension. Cysts communicating with ducts could lead to nipple discharge by decompression of cyst fluid into ducts. Ductography shows normal ducts communicating with cysts (Figure 13).

Intraductal Papilloma

Papillomas are benign masses of breast duct epithelium with a fibrovascular stalk attached to the duct wall. They may be single or multiple and may extend along the ducts. When large, they can appear to be encysted

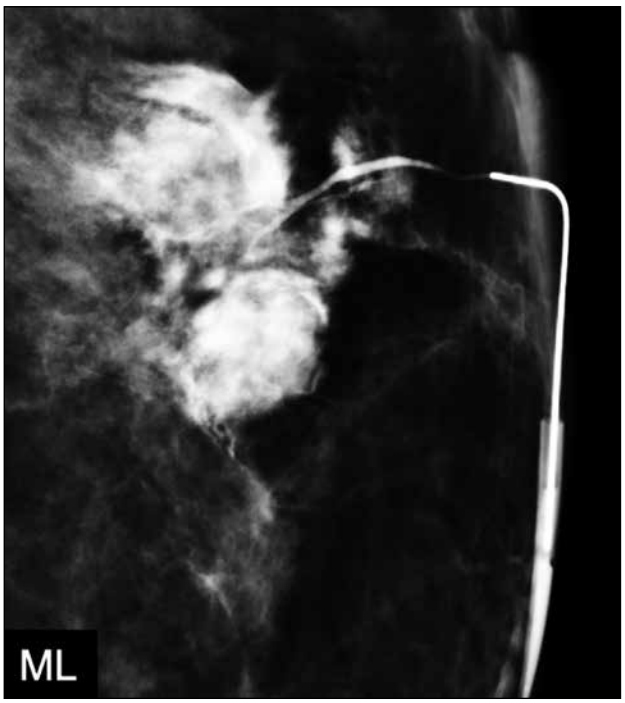

Figure 11. Ductography with mediolateral (ML) view. Contrast extravasation obscured the ductal system, rendering suboptimal assessment.

and multilobulated. This is the commonest cause of spontaneous unilateral single-orifice nipple discharge, accounting for 35% to 48% of cases.[1] The mammogram is frequently negative and ductography could be useful for its detection. Ductographic findings include single intraductal filling defects, multiple intraductal filling defects, ductal wall irregularities, and ductal obstruction (Figure 14a, 14b, 14c, and 14d, respectively). Rarely, contrast may be seen to accumulate within the cystic component of the mass which communicates with the duct (Figure 14e). Although these findings can be non-specific and seen in other entities, malignancy in particular, ductography is still useful in assessing the number, extent and location of the abnormalities. Surgical excision of papillomas with atypia is widely accepted with an upgrade rate to malignancy ranging from 21% to 38%.[2] However, the management of asymptomatic papillomas without atypia is more controversial, with an upgrade rate to malignancy of 2% to 12%.[2] Although some clinicians still recommend surgical excision of all papillary lesions, ultrasound-guided vacuum-assisted excision has been proven to be a safe and effective alternative with high rate of successful lesion removal.[5]

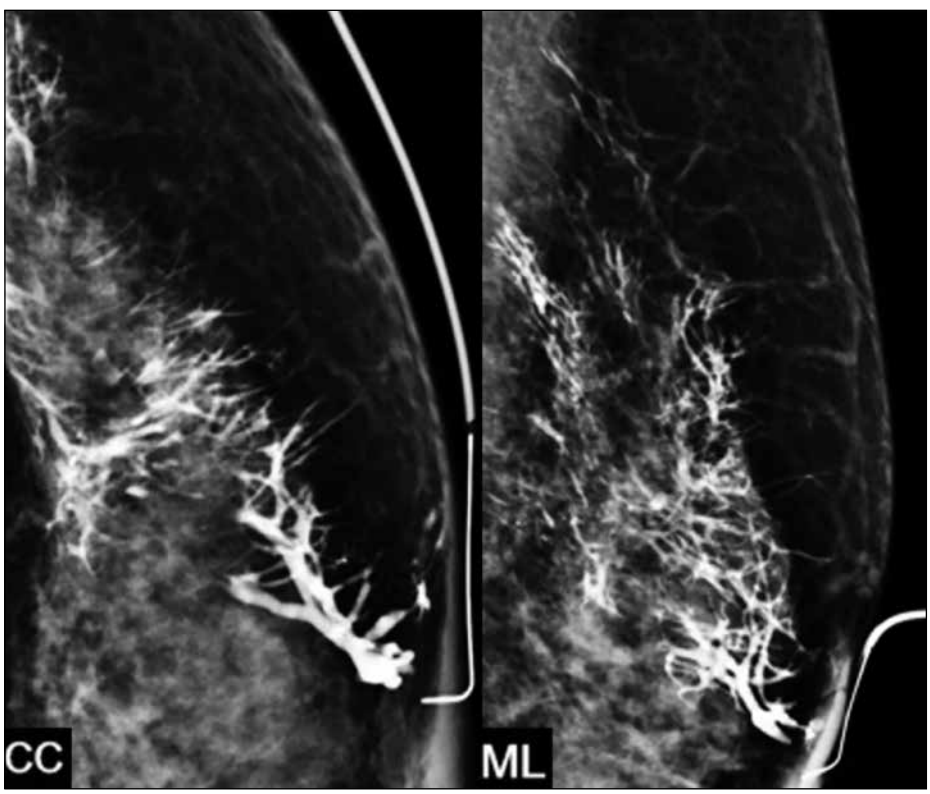

Figure 12. Ductography with craniocaudal (CC) and mediolateral (ML) views showing a dilated ductal system without filling defects, wall irregularities, obstruction or extravasation, suggestive of duct ectasia.

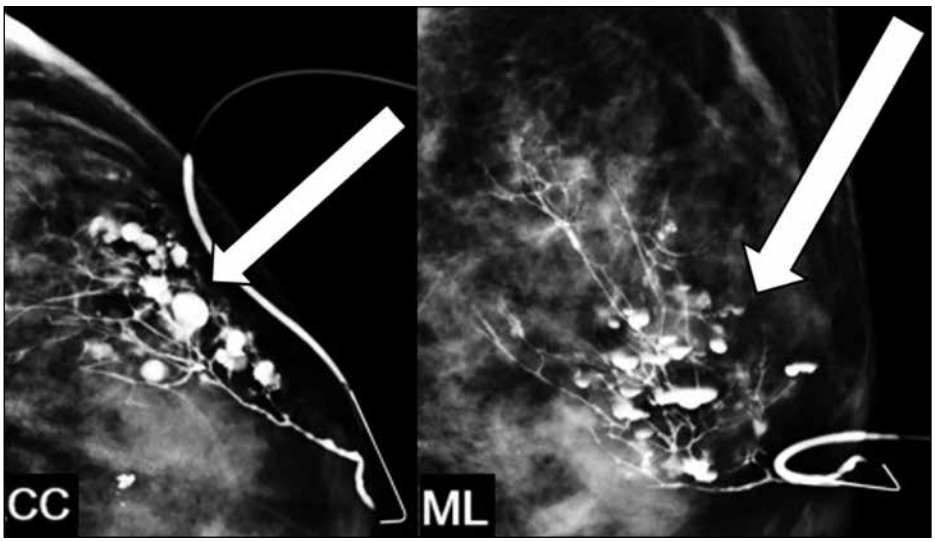

Figure 13. Ductography with craniocaudal (CC) and mediolateral (ML) views showing multiple cysts communicating with the ductal system (arrows) and the ductal system is otherwise normal, compatible with fibrocystic change.

Ductal Carcinoma In Situ

Cancer is found in 5% to 15% of patients with PND, the commonest type being DCIS. Up to 12% of patients with DCIS present with nipple discharge.[6] Ductographic findings of malignancy, most commonly DCIS, may mimic those of intraductal papillomas, including filling defects, abrupt ductal termination, ductal wall irregularities, and periductal contrast extravasation (Figure 15). Histological assessment would be helpful in differentiation of malignancy from other benign entities including papillomas.

Duct Adenoma

Duct adenomas are uncommon benign glandular tumours which usually fill and distend the ductal lumen. They are usually single, occasionally multiple, nodular lesions occupying medium- and large-sized breast ducts but not major subareolar ducts. Because of their location, they more commonly present as palpable lumps, unlike intraductal papillomas which are more likely associated with nipple discharge. Figure 16 illustrates a rare case of duct adenoma presenting with nipple discharge.

DISCUSSION

In patients with PND, mammography and ultrasound are first-line investigations for women who are ≥ 30 years of age.[1] Mammographic abnormalities were found to be positive in 50% to 90% of patients with breast cancer and in < 50% of patients with intraductal papilloma.[7] Mammography often fails to demonstrate lesions that are small, lack calcifications, or are located entirely within the duct.[8] Nevertheless, it is still a crucial initial imaging modality. DCIS is the commonest malignancy associated with PND and it may present as suspicious microcalcifications on mammography. Underlying invasive cancer may also present as mass or architectural distortion. Mammography may be complementary to ultrasound in women < 30 years of age if they are *BRCA*-positive or have other gene mutation predisposing to breast cancer. In particular, it should be considered in women < 30 years of age who present with suspicious masses on ultrasound. This is because mammography can detect any calcifications associated with the mass or the ducts. If present, the extent, pattern, and morphology of the calcifications are best assessed on mammography.[2]

Apart from mammography, ultrasound also plays an important role in the initial evaluation of PND. Ultrasound can identify sub-centimetre ductal abnormalities and associated ductal changes which are occult on mammography, especially in dense breasts. In a study, ultrasound examination in patients with PND but negative mammographic findings led to detection of malignancy in 15% of cases.[9]

If no abnormality explaining the nipple discharge can be detected on both mammography and ultrasound, ductography is usually the next step in imaging examinations in our centre. The value of ductography as a second-line investigation is controversial. It is an invasive examination, although it is actually rather minimally invasive. Despite the possible events of contrast extravasation and ductal perforation, these are minor complications with no reported long-term

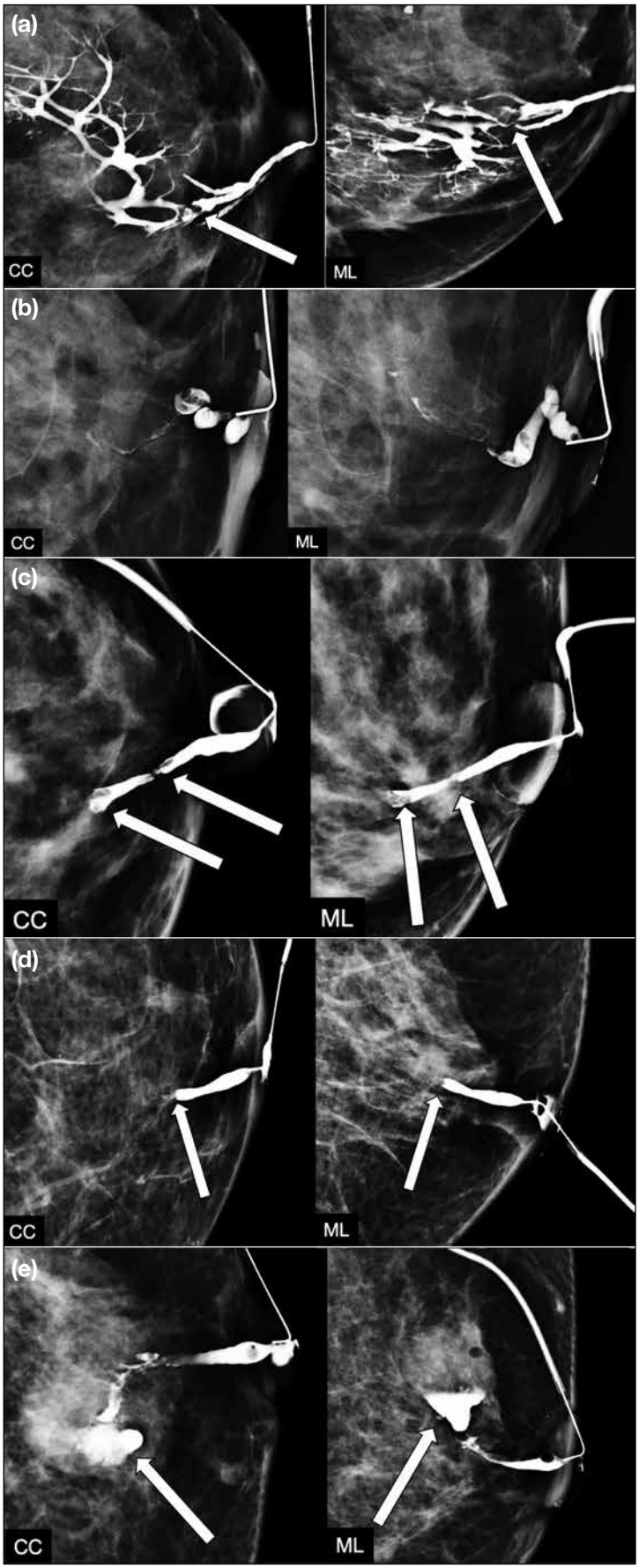

Figure 14. Mammography with craniocaudal (CC) and mediolateral (ML) views showing ductographic appearances of pathologically proven intraductal papillomas: (a) single intraductal filling defect (arrows); (b) multiple intraductal filling defects; (c) ductal wall irregularities (arrows); (d) ductal obstruction (arrows); and (e) contrast accumulation within the cystic component of the mass communicating with the mammary duct (arrows).

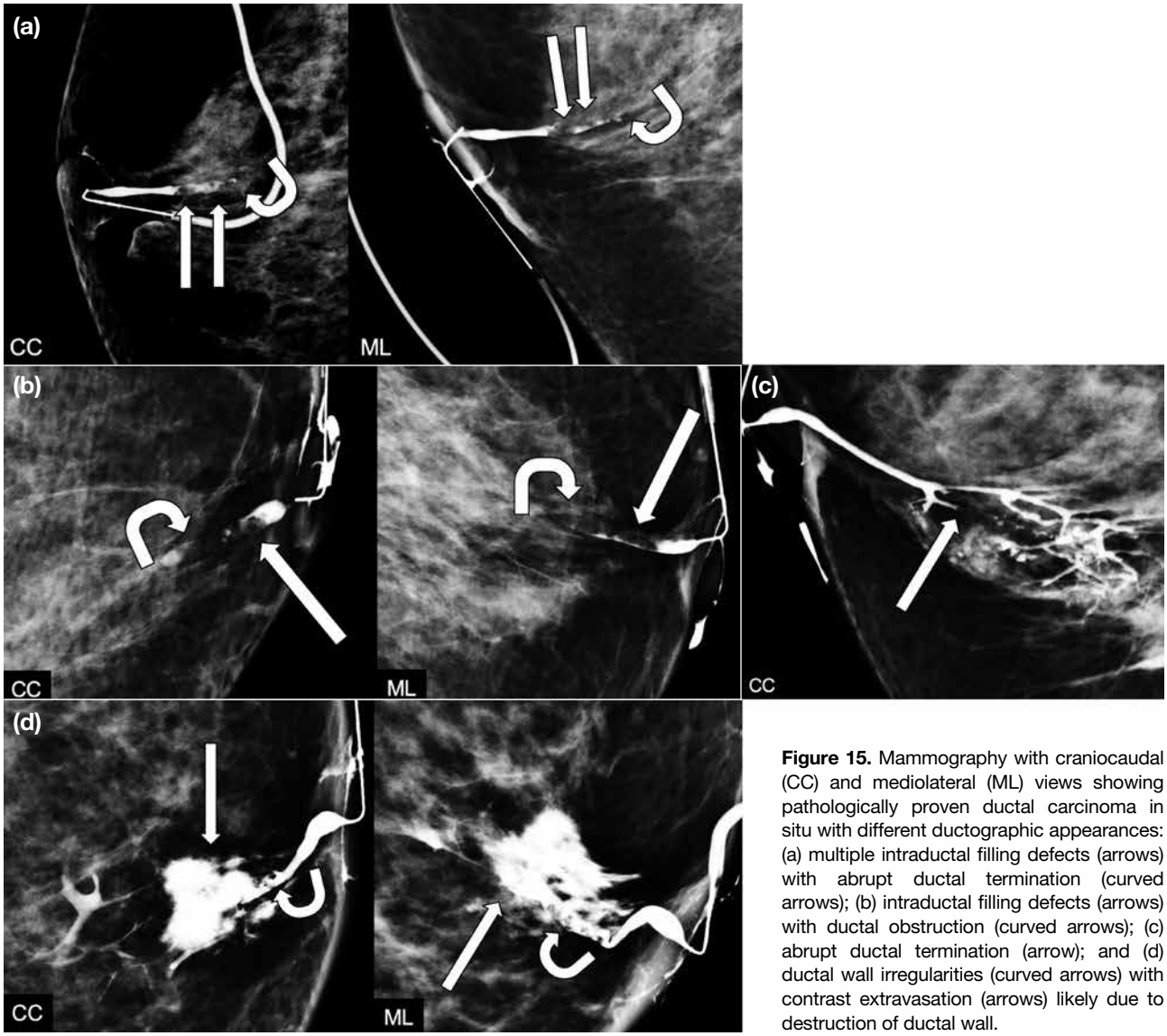

Figure 15. Mammography with craniocaudal (CC) and mediolateral (ML) views showing pathologically proven ductal carcinoma in situ with different ductographic appearances: (a) multiple intraductal filling defects (arrows) with abrupt ductal termination (curved arrows); (b) intraductal filling defects (arrows) with ductal obstruction (curved arrows); (c) abrupt ductal termination (arrow); and (d) ductal wall irregularities (curved arrows) with contrast extravasation (arrows) likely due to destruction of ductal wall.

consequences. The primary goal of ductography is to localise intraductal lesions and assist in surgical planning. Since there is considerable overlap in ductographic findings of papillary lesions and malignancy, histological correlation is usually required to ascertain the benign or malignant nature of an intraductal abnormality.[1]

Ductography is more sensitive than mammography and ultrasound but has lower specificity than those two modalities.[1] In cases of negative findings with conventional imaging, ductography has been shown to localise 76% of otherwise occult high-risk and malignant lesions.[9] However, a negative ductographic examination cannot be used to exclude the possibility of underlying malignancy, with a false negative rate reported to be 20% to 30%.[9]

The management approach for evaluating PND is evolving. Because of its high sensitivity in detecting breast malignancy and its capability for biopsy, breast MRI has emerged as the most sensitive modality in detecting malignancy. Contrast-enhanced breast MRI has been proposed for investigation when conventional imaging modalities have failed to identify the underlying cause of PND. It offers an alternative means when ductography is not performed due to risk of iodinated contrast reaction, failure to cannulate the duct, or patients' preference. MRI can enable detection of

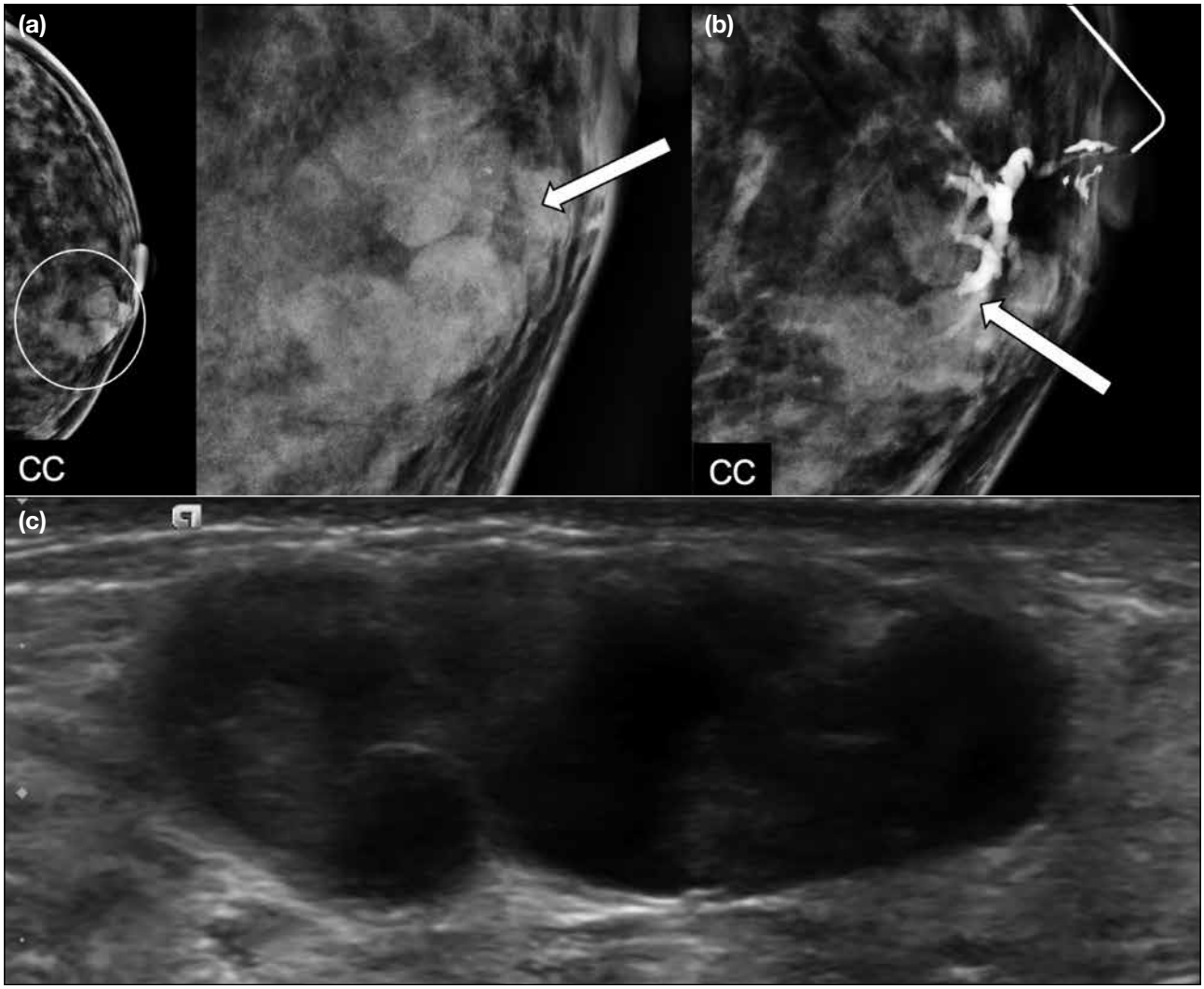

Figure 16. Histologically proven duct adenoma of the breast: (a) preliminary craniocaudal (CC) mammogram with additional spot compression view before ductogram showing an oval isodense mass at the inner part of left breast (circle) with partially obscured margins, associated with amorphous microcalcifications (arrow); (b) CC ductogram showing mildly prominent subareolar ducts and abrupt termination of the ductal system (arrow) near the mass; and (c) subsequent ultrasound demonstrated a mixed solid-cystic mass at 9 to 12 o'clock position of the periareolar region of the left breast.

lesions in peripheral ducts that are beyond the area normally encompassed by ductography or targeted ultrasound. In contrast to ductography, which only detects abnormalities in discharging ducts, MRI allows evaluation of the entire ductal system at the same time and enables identification of additional cancers in both the ipsilateral and contralateral breast. With increasing availability of MRI scanners and growing experience in MRI interpretation, there have been more reports showing the high sensitivity and negative predictive value of MRI for breast cancer. The European Society of Mastology guidelines evaluated 10 papers on the use of MRI in PND and concluded that there is still insufficient evidence to support routine use of MRI for these patients.[10] Its relatively high cost and poor accessibility in less developed countries, as well as patient factors (e.g., claustrophobia, severe obesity, and implantable devices not compatible with MRI examination), could be possible causes of its limited use in many departments. Nonetheless, patients with persistent symptoms after unremarkable or failed ductographic examination may benefit from MRI. Furthermore, it is recommended to perform MRI in *BRCA* mutation carriers and other high-risk patients to minimise radiation exposure.

A new area of research involves MR ductography with use of a three-dimensional heavily T2-weighted fat-suppressed sequence. It is non-invasive and does not require use of contrast. The discharging duct is often dilated with fluid and can be seen on heavily T2-weighted images. The presence of intraluminal filling defects, ductal wall irregularities, or ductal obstruction can be assessed. Compared with conventional ductography, MR ductography can show the distal part of a duct obstructed by an intraductal mass. On the other hand, it cannot reveal a non-dilated duct. According to a feasibility study involving 21 patients,[11] the indirect MR ductography sequence did not show significantly better performance when compared with conventional ductography. More large-scale studies with refinement of the sequence or fusion imaging with contrast-enhanced MRI could potentially be a fruitful area of research.

Apart from MRI, the addition of digital breast tomosynthesis (DBT) to conventional ductography has been investigated as a technique in the evaluation of PND. This three-dimensional reconstruction can provide sectional images from different projection angles, thus reducing overlap of the ductal system and tissue superimposition. Retrospective studies have compared the diagnostic performance of DBT-ductography and digital ductography, revealing higher sensitivity for DBT-ductography without compromise in specificity.[12,13] A recent prospective study by Tao et al[14] evaluated 128 patients with PND and concluded that DBT-ductography increases the sensitivity and specificity of lesion detection by enhancing the image quality without significant increase in the radiation dose. Further studies may be helpful in validating and generalising the findings of DBT-ductography in patients with PND.

Surgical duct excision has been the standard of care to exclude underlying malignancy. There has been increasing trend in adopting surveillance for patients with unremarkable findings on combined assessment using mammogram, ultrasound and ductograpohy.[2] Despite being the reference standard, microdochectomy cannot detect all malignancies, especially those located far from the nipple. Sanders and Daigle[15] examined the role of MRI as an alternative to microdochectomy. Among the 85 patients who underwent MRI prior to duct excision, eight malignant lesions (9.4%) were detected and seven out of these eight malignancies (87.5%) were identified on MRI. The authors proposed that a negative MRI study may obviate the need for microdochectomy in most patients.

CONCLUSION

Ductography is a practical, valuable, and cost-effective procedure in the diagnosis of intraductal lesions. Gaining familiarity with the procedure and including it in the evaluation of patients with PND may facilitate management for these patients. If ductography is technically unfeasible, MRI should be considered as an ancillary tool to investigate for the possible causes.

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