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Breast Imaging *Pictorial Essay*

Imaging of Noncalcified Ductal Carcinoma *In Situ*

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ABSTRACT

Ductal carcinoma *in situ* (DCIS) is a commonly encountered malignancy, accounting for approximately 20% of new breast cancer diagnoses in the United States. DCIS is characterized by a proliferation of tumor cells within the terminal duct lobular unit with preservation of the basement membrane. Typically nonpalpable and asymptomatic, DCIS is most often detected as calcifications on screening mammography. However, DCIS may also be noncalcified. When compared to calcified DCIS, noncalcified DCIS is more likely to be symptomatic, with patients most often presenting with nipple discharge or a palpable mass. Diagnosing noncalcified DCIS is challenging since it may be occult or subtle on mammography, and ultrasound findings can be nonspecific and may be interpreted as benign fibrocystic changes. In cases with a calcified component of DCIS, the extent of DCIS may be underestimated by mammography because not all involved areas may calcify. Breast magnetic resonance imaging (MRI), although less readily available than mammography and ultrasound, is advantageous in detecting noncalcified DCIS, especially high grade DCIS, which may not develop microcalcifications. MRI relies on abnormal contrast uptake due to tumor vascularity and changes in vessel density and permeability. This pictoral review presents the spectrum of imaging findings of noncalcified DCIS to assist radiologists in accurately detecting and describing its key imaging findings. Utilizing different modalities, we review the differential diagnoses for noncalcified DCIS, show illustrative cases of noncalcified DCIS, and discuss the importance of this entity.

Keywords: Breast cancer, Breast, Ductal carcinoma *in situ*, Magnetic resonance imaging, Mammogram

INTRODUCTION

Ductal carcinoma *in situ* (DCIS) is a non-invasive malignant proliferation of tumor cells with preservation of the basement membrane.[1] It is a neoplasm with variable and nonobligate potential for progression to invasive breast cancer.[1,2] The risk of developing invasive carcinoma is directly proportional to the grade of DCIS. However, the evolution of DCIS to invasive ductal carcinoma is not obligate or linear and may follow multiple pathways.[1,2]

Noncalcified DCIS, which comprises up to 10–20% of all DCIS cases, is more frequently lower grade and has a more favorable prognosis than calcified DCIS. Poor prognostic features associated with DCIS, including high tumor grade, comedo-type necrosis, positive human epidermal growth factor receptor 2 oncogene status, estrogen receptor negativity, and progesterone receptor positivity, are more common in calcified DCIS.[3] These findings suggest that, in general, calcified DCIS has more aggressive histologic features than noncalcified DCIS. However, it is unknown whether noncalcified DCIS progresses to invasive disease less frequently than calcified DCIS.

Because of the inability of DCIS to invade and metastasize, there is ongoing debate regarding whether it should be classified as a cancer. While pure DCIS is considered nonlethal, patients diagnosed with DCIS are 4 times more likely than the general population to subsequently develop invasive disease. Factors associated with a greater risk of development of invasive disease include young age, premenopausal status, Black race, increased body mass index, and detection by palpation.[4]

IMAGING FINDINGS

Mammographic findings

The process that causes some DCIS to calcify is unclear but is likely a combination of passive (degenerative/dystrophic) and active (secretory and activation of bone matrix) processes.[5] On mammography, noncalcified DCIS may present as a mass, an asymmetry, or an area of architectural distortion [Figures 1 and 2].[1] On mammography, DCIS mass lesions most often present with irregular shapes, indistinct margins, and isodensity, mimicking the appearance of invasive carcinomas.[6,7]

DCIS presents without microcalcifications 10–20% of the time and mammographic detection is especially limited in dense breast tissue [Figure 3]. Clinical symptoms are reported in 10–24% of patients with DCIS and are more often seen in patients with noncalcified DCIS when compared to those with calcified DCIS.[1,6] In a cohort of 217 women with DCIS, mammography demonstrated an overall sensitivity of 84%, detecting 51% cases of noncalcified DCIS and 100% cases of calcified DCIS. 49% of the cases of noncalcified DCIS were false negative on mammography, and the remainder were seen as masses (30%), focal asymmetries (15.5%), and architectural distortions (5.5%).[7]

Ultrasound findings

On ultrasound, noncalcified DCIS may present as ductal abnormalities, masses with or without cystic components, or architectural distortions.[1,3] Ductal abnormalities may be seen as an abnormal number of ducts from ductal neogenesis or as abnormal ducts, which may be enlarged or contain intraductal material.[1,8] Ductal ectasia associated with DCIS

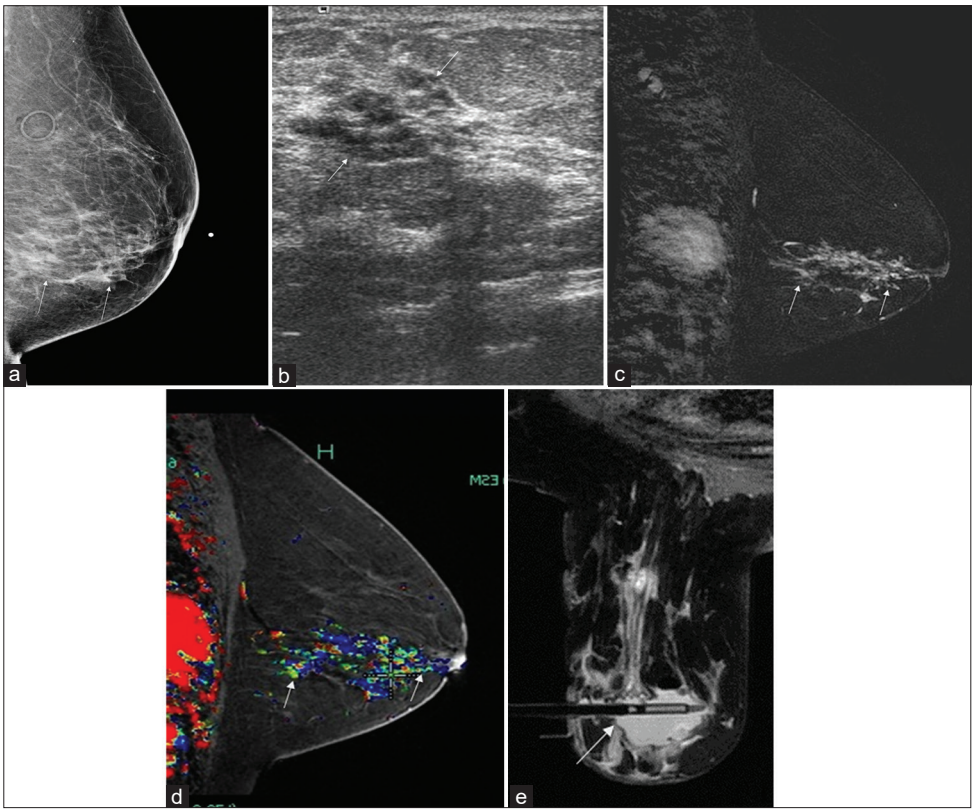

Figure 1: A 63-year-old woman with a remote history of right segmental mastectomy for invasive and *in situ* ductal carcinoma complaining of spontaneous left nipple discharge. (a) Left lateral mammogram reveals a focal asymmetry (arrows) at the 6 o'clock position. (b) Longitudinal ultrasound shows expanded ducts with internal masses and debris at the 6 o'clock position (arrows). Ultrasound-guided biopsy showed markedly atypical cells, suspicious for DCIS. (c) Subtraction and (d) color map images from dynamic contrast-enhanced MRI revealed 9 cm of clumped non-mass enhancement (arrows) in a segmental distribution with extension to the nipple. (e) Two MRI-guided biopsies were performed to define the anterior (arrow) and posterior (not shown) extent of disease; pathology from both biopsies was low-grade DCIS, cribriform and micropapillary forms without necrosis. Mastectomy showed DCIS, spanning 9 cm.

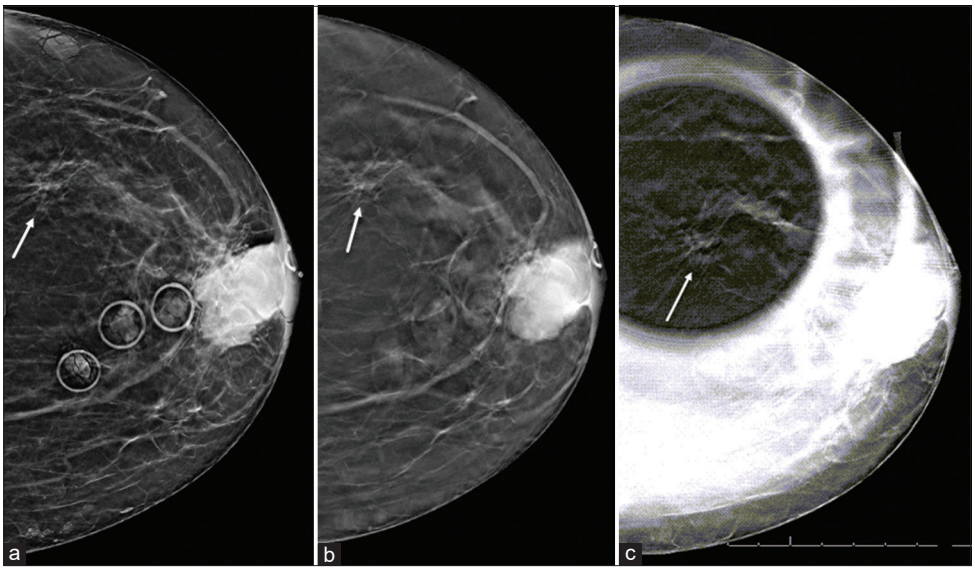

Figure 2: (a) A 67-year-old woman presented with a palpable finding in the retroareolar region of the left breast. Incidentally noted on diagnostic mammogram (a) CC view, (b) CC tomosynthesis view, and (c) CC spot compression tomosynthesis view was an area of architectural distortion (arrow) at 2 o'clock without a sonographic correlate. Stereotactic biopsy and segmentectomy of the area of architectural distortion yielded noncalcified DCIS. Central segmentectomy for the palpable retroareolar mass yielded papillary carcinoma.

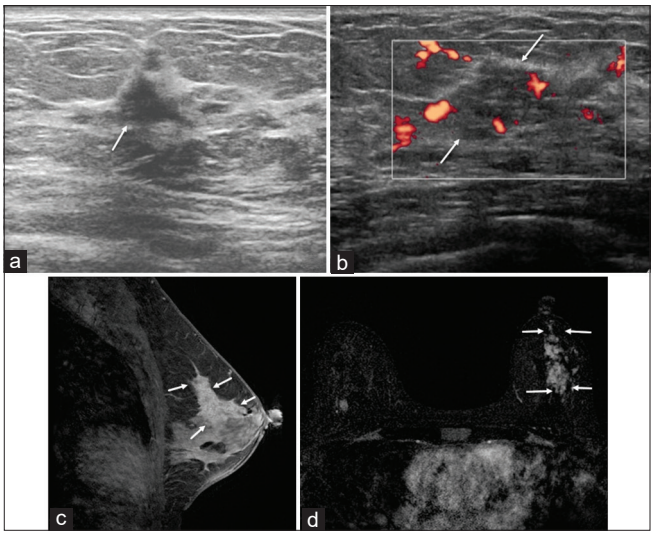

Figure 3: (a) A 40-year-old woman with a palpable mass in the left breast on self-breast examination. Mammography (not shown) was negative. Longitudinal (a) and longitudinal power Doppler (b) ultrasound shows an irregular hypoechoic mass (arrows) with indistinct margins and associated peripheral vascularity. Pathology results from an ultrasound-guided core needle biopsy revealed DCIS, intermediate grade, cribriform type, with focal necrosis. (c) MRI shows extensive clumped non-mass enhancement (arrows) in a segmental distribution, measuring 7 × 3 × 3 cm, best appreciated on the sagittal delayed post-contrast T1-weighted image (c), and the axial subtraction image (d).

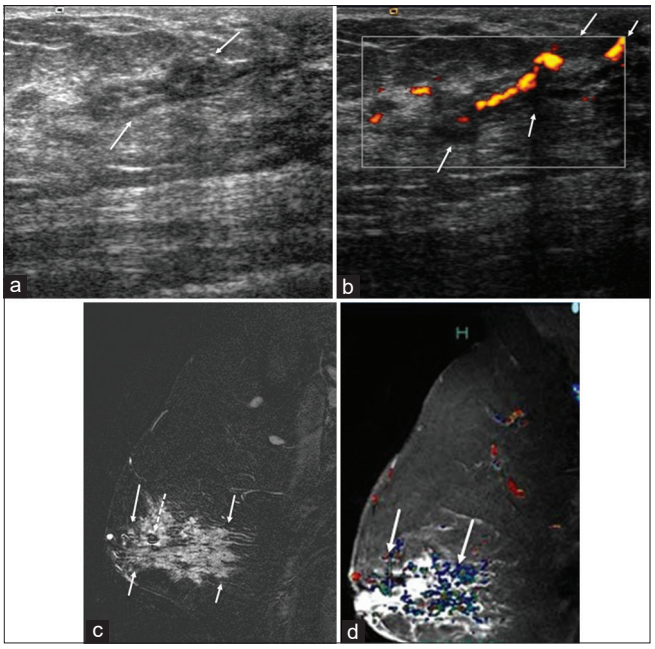

Figure 4: A 67-year-old woman with spontaneous right nipple discharge. Mammography (not shown) revealed no abnormality. Longitudinal (a) and longitudinal power Doppler (b) ultrasound show mild ductal dilatation (arrows) from the 6 to 11 o'clock positions, extending to the nipple base. Ultrasound-guided biopsy with a 14-gauge spring-loaded device yielded atypical ductal hyperplasia. (c) Dynamic contrast-enhanced MRI (c) sagittal subtraction and (d) sagittal color map demonstrate 8 cm of clumped non-mass enhancement in a segmental distribution (arrows) with extension to the nipple. The site of the ultrasound-guided biopsy (dashed arrow) was within this area of abnormal non-mass enhancement. MRI-guided biopsy yielded DCIS, intermediate nuclear grade, predominantly cribriform type, with punctate necrosis.

may be overlooked due to similar findings in benign ductal ectasia [Figure 4].[8] On ultrasound, noncalcified DCIS may appear similar to invasive carcinoma as an area of architectural distortion or as a mass with indistinct, circumscribed or

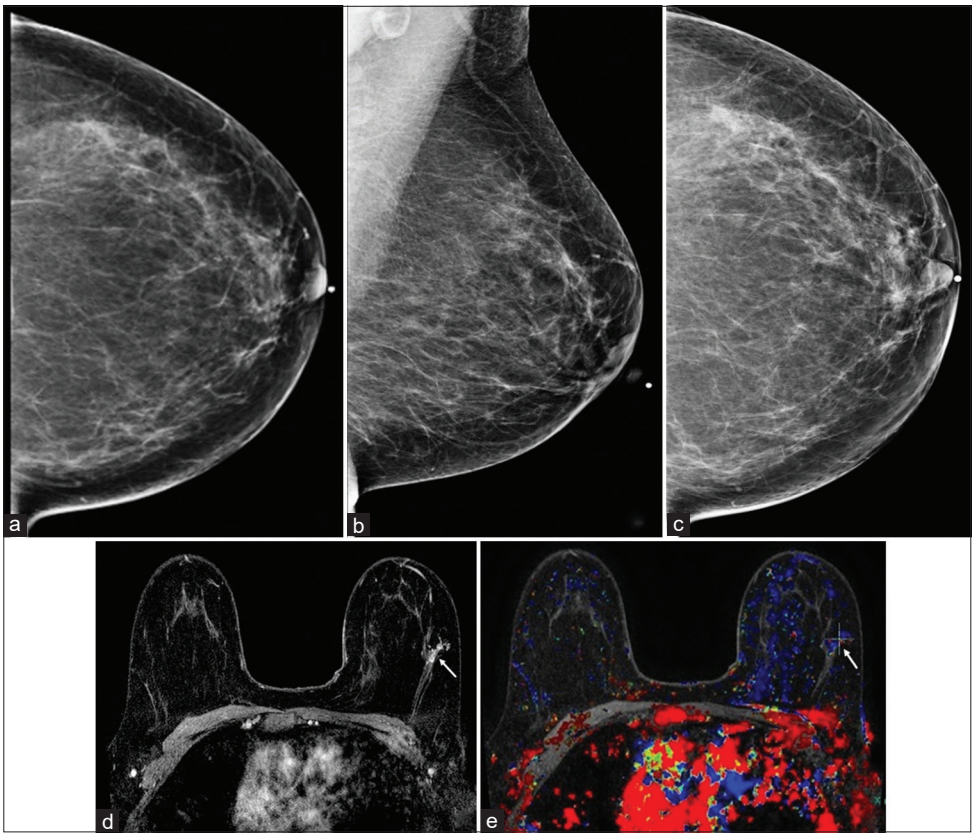

Figure 5: A 47-year-old woman with a BRCA2 mutation. Screening mammography (a, CC). (b MLO) was interpreted as negative with no significant interval change from the prior mammograms (c, CC). (d and e) Dynamic contrast-enhanced screening MRI (d, dynamic axial post-contrast and e, axial color map) shows a 2.1 × 0.8 × 2 cm area of clumped non-mass enhancement (arrow) in the left breast 2 o'clock position. MRI-guided biopsy revealed DCIS, intermediate grade, solid type with punctate necrosis.

irregular margins, with or without intraductal extension. Masses are typically hypoechoic, and they may have mixed solid and cystic components. The orientation is most often parallel.[3]

In a subset of 126 patients with noncalcified DCIS, almost all (95%) lesions were visible on ultrasound. DCIS which is occult on mammography and detected on ultrasound alone is often lower in grade compared to calcified DCIS seen on mammography.[9] There is a superior detection rate of noncalcified DCIS with digital breast tomosynthesis (DBT) and ultrasound compared to digital mammography (DM) alone in all patients, but particularly in those with dense breasts. Su *et al.* reported overall detection rates of DBT, DM, and ultrasound for noncalcified DCIS as 83.7%, 68.4%, and 94.9%, respectively.[6]

Table 1: Calcified versus noncalcified DCIS.

	Calcified DCIS	Noncalcified DCIS
Presentation	More often asymptomatic	More often symptomatic
Visibility by ultrasound	Often not visible	More often visible
Mammography findings	Calcifications with or without associated mass, asymmetry, or architectural distortion	Mass, asymmetry, or architectural distortion
Visibility by mammography	Typically visible	Less often visible, especially in dense breast tissue
MRI findings	NME	Mass or NME

DCIS: Ductal carcinoma *in situ*, NME: Non-mass enhancement, MRI: Magnetic resonance imaging

MRI findings

MRI has a higher sensitivity than mammography in diagnosing DCIS. Classically, DCIS on MRI demonstrates clumped non-mass enhancement (NME) in a linear or a segmental distribution with variable kinetics [Figures 5 and 6].[10] Among enhancement patterns, clumped is most specific for DCIS, representing half of DCIS lesions. Clustered ring enhancement represents gadolinium accumulation in periductal and intraductal spaces, characteristic of DCIS. NME has been reported in 60–72% of DCIS cases, but DCIS may also present as a discrete mass or as a small enhancing focus. These findings may reflect a growth pattern that primarily expands rather than

spreads along the ducts.[10,11] On MRI, no significant differences have been demonstrated between calcified and noncalcified DCIS in terms of morphology, enhancement characteristics, nuclear grade, kinetic appearance, or the presence of necrosis. DCIS presenting as masses and foci is more often lower in grade than DCIS presenting as NME [Tables 1 and 2].[1,2,10,11]

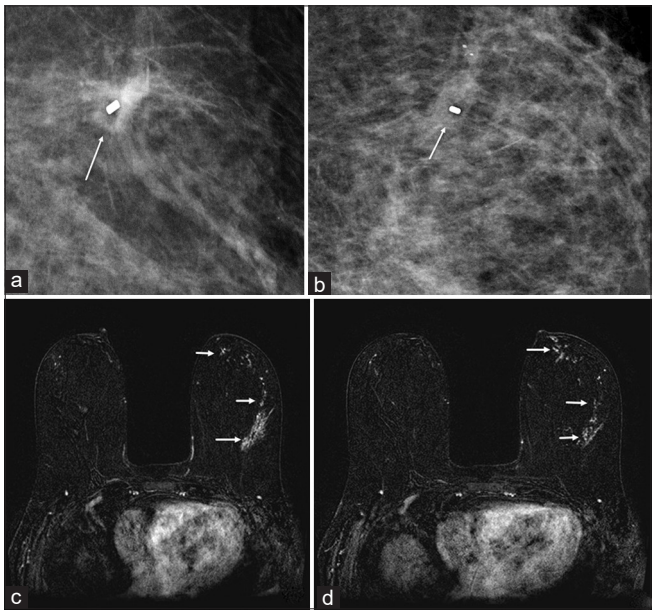

Figure 6: A 61-year-old woman referred to a tertiary center for recently-diagnosed DCIS, high grade, with comedonecrosis, based on stereotactic-guided biopsy of 2.5 cm group of heterogeneous calcifications. Mammograms (a, CC magnification and b, LM magnification images) obtained after the stereotactic-guided biopsy show scattered residual calcifications, post-biopsy changes and a marker clip (arrow). Ultrasound (not shown) showed post-biopsy changes with no additional findings. Dynamic contrast-enhanced MRI shows extensive clumped non-mass enhancement (arrows) in a segmental distribution, measuring 10 × 3.5 × 3.5 cm, on representative axial subtraction images (c and d). The marker clip from the stereotactic biopsy was noted within this non-mass enhancement. MRI-guided biopsy to confirm extent of disease revealed DCIS, high nuclear grade, solid type with punctate necrosis at the anterior edge of the non-mass enhancement.

Table 2: Key imaging features of noncalcified DCIS.

Mammography
Mass
Asymmetry
Architectural distortion
Ultrasound
Mass with or without cystic elements
Ductal abnormalities
Architectural distortion
MRI
Non-mass enhancement
Enhancing mass

CONCLUSION

Noncalcified DCIS is an important entity with a wide array of imaging presentations. It is often subtle or occult on mammography and much more likely than calcified DCIS to present with clinical symptoms.[2,3,6] It is important for radiologists to understand that biopsy of a noncalcified lesion yielding DCIS may represent a concordant result. Because noncalcified DCIS is more difficult to detect mammographically, it is often larger at presentation than its calcified counterpart.[2,3,6] Despite its often larger size at presentation, noncalcified DCIS typically has more favorable prognostic features than calcified DCIS, including lower nuclear grade.[1] Noncalcified DCIS is typically seen on ultrasound and on MRI. There are no specific imaging guidelines for post-operative follow-up of noncalcified DCIS compared to calcified DCIS, but the addition of ultrasound and/or MRI to annual mammography may be appropriate when DCIS is occult or underestimated on mammography.

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Declaration of patient consent

Patient consent not required as the patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest

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