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# Macroscopic lymphovascular invasion visualized on mammogram and magnetic resonance imaging: Initially misidentified as ductal carcinoma in situ but properly diagnosed by immunohistochemistry

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**Abstract**

**Objectives:** Lymphovascular invasion (LVI) is a pathologic, microscopic finding associated with invasive cancer, and is a poor prognostic indicator, but has no reported imaging findings. This report presents the first documented case of LVI with seen by imaging. Linear branching microcalcifications were identified on mammography and clumped enhancement was noted on MRI, both imaging findings that are highly predictive of ductal carcinoma in situ (DCIS).

**Methods:** Ultrasound guided core biopsy of the dominant mass was performed, confirming invasive ductal malignancy. Stereotactic biopsy performed on the microcalcifications was initially interpreted by pathology as DCIS.

**Results:** Patient underwent mastectomy. Pathologic evaluation of the surgical specimen confirmed the invasive ductal malignancy. Microcalcifications were re-evaluated with immunohistochemistry (IHC) and re-classified as LVI. Radiology images and IHC stains are shown.

**Conclusion:** This is the first report of LVI identified by imaging with findings that mimicked DCIS and initially mis-identified as DCIS by pathology as well. The implications of this overlap in radiologic appearance are discussed.

**Keywords**

Breast carcinoma, lymphovascular invasion, ductal carcinoma in situ, breast

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## Introduction

Ductal carcinoma in situ (DCIS) represents approximately 20% of newly diagnosed breast cancer. As a pure intraductal malignancy, it demonstrates no invasion through the ductal basement membrane.[1] Its most frequent mammographic finding is microcalcifications, identified in 50%–75% of cases,[2] reflecting the presence of cell necrosis. According to the 5th edition of the ACR BI-RADS Atlas, there are several descriptors of suspicious microcalcifications; however, the most classic appearance of the calcifications is linear (with or without branching), but may be amorphous, coarse-heterogeneous or fine pleomorphic.[3] On magnetic resonance imaging (MRI), DCIS is most often seen as non-mass-like enhancement (NMLE) or less frequently, mass enhancement. Distribution is most commonly segmental, or linear but may be focal, or regional. The internal enhancement characteristics may be clumped, heterogeneous or clustered ring.[4]

Lymphovascular invasion (LVI) represents an important pathologic finding associated with invasive breast cancer, indicating the progression of tumor cells into vascular spaces, either lymphatics or capillaries, and is a necessary first step in the development of metastatic disease. It is associated with a higher risk of lymph node metastases, is a poor prognostic factor in women without lymph node metastases,[5] and increases the risk of tumor recurrence, and overall survival.[6]

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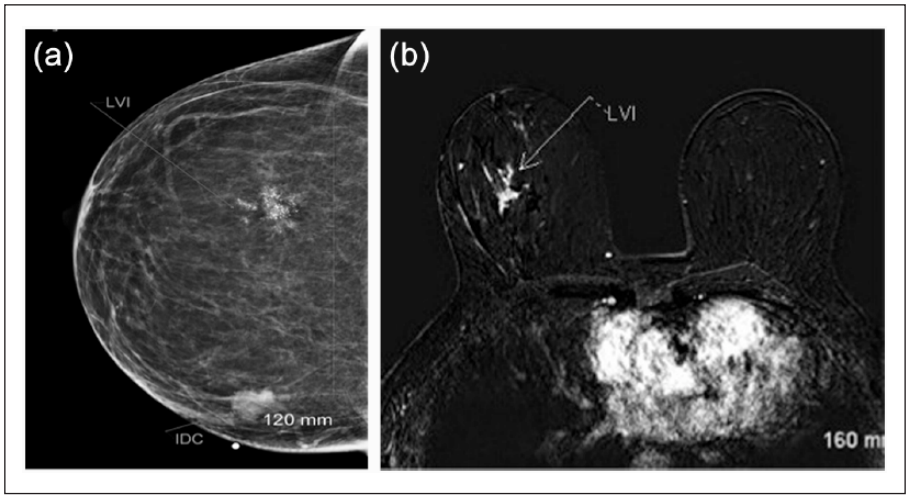


**Figure 1.** (a) Right CC view showing medial invasive cancer and upper outer quadrant microcalcifications suggesting DCIS and (b) contrast-enhanced MRI showing clumped, linear enhancement in the right upper outer quadrant at the site of microcalcifications, suggesting DCIS but shown pathologically to represent LVI.

Since LVI is a histologic finding, it has no reported descriptions in the imaging literature, to the best of our knowledge. The pathology literature, however, cautions that the appearance of LVI may overlap with DCIS on usual hemotoxylin and eosin (H&E) stains, and that immunohistochemical (IHC) stains are useful in differentiating the two entities.

This report describes an unusual case of macroscopic LVI associated with an invasive ductal malignancy in the ipsilateral breast that mimicked DCIS on both mammography and MRI. To our knowledge, the difficulty in properly differentiating DCIS from LVI, while previously reported in the pathology literature, has not been reported in the radiology literature.

## Case report

A 62-year-old woman presented with a palpable concern in her medial right breast. She had no family history of breast cancer, and her lifetime risk of breast cancer was calculated to be 7.7% (using the National Cancer Institute algorithm).

Diagnostic mammogram demonstrated a mass in the right breast at 3:00, measuring 1.7 cm. In addition, an area of branching, pleomorphic casting calcifications was seen in the right upper outer quadrant, 6 cm away, suspicious for synchronous DCIS (Figure 1(a)). Ultrasound-guided core biopsy of the mass revealed invasive ductal cancer (IDC), estrogen and progesterone receptor negative and her2neu receptor negative by fluorescence in situ hybridization (FISH); stereotactic biopsy of the calcifications was interpreted pathologically as DCIS. No IHC stains for endothelial or myoepithelial cells were performed. MRI, performed to evaluate extent of disease, showed an enhancing right medial mass and clumped enhancement in the upper outer quadrant, consistent with biopsy pathology (Figure 1(b)).

Patient underwent total mastectomy with sentinel node procedure. Pathology revealed a 17-mm right 3:00 IDC (Nottingham score 9/Grade 3) with 3/17 positive lymph nodes (T1c, N1a, 7th American Joint Committee on Cancer (AJCC) Staging System). The site originally reported as DCIS appeared unusual in the mastectomy specimen: clusters of malignant cells were detached from the adjacent tissue and the configurations of the neoplastic cells suggested tumor emboli in vascular channels (Figure 1(a) and (b)).

IHC stains were performed to evaluate whether the neoplastic cells represented in situ carcinoma or LVI. Multiple different IHC stains conventionally used to evaluate for myoepithelial cells in breast pathology did not reveal myoepithelial cells: p63 and smooth muscle myosin heavy chain were negative for myoepithelial cells, with the latter decorating muscle in the walls of the spaces. This finding suggested a lymphovascular channel. IHC stain for D2-40, a marker of both myoepithelial cells and lymphatic endothelial cells, was negative in the lining cells of the channels. IHC stain for CD31 was strongly positive in the lining cells of the channels, consistent with vascular endothelial cells. The final pathologic diagnosis of the area in question was tumor emboli in lymphovascular spaces. No DCIS was identified in this site, next to the primary invasive carcinoma, or elsewhere in the breast (Figure 2(a)–(e)).

## Discussion

Invasion of tumoral vessels is thought to be a prerequisite process for the dissemination of metastatic lesions. The presence of vascular invasion is an important pathologic finding which impacts the risk of tumor recurrence and metastases. Lymphatic invasion is the predominant route of vascular invasion in breast cancer, surpassing blood vessel invasion.[7]

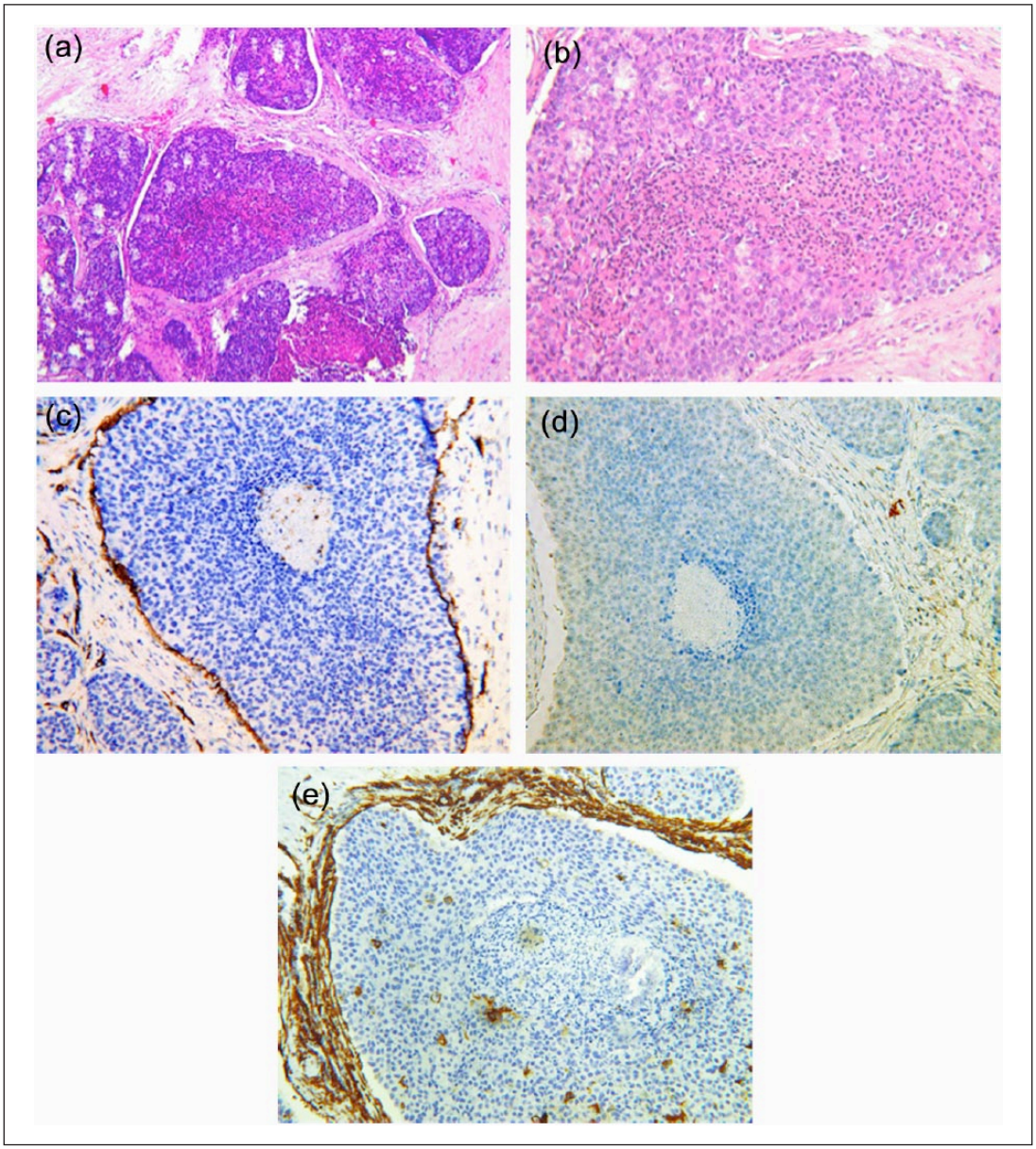


**Figure 2.** (a) Section (H&E, 40×) shows well-defined spaces filled with neoplastic ductal cells and central comedonecrosis, (b) A higher power view (H&E, 100×) of the neoplastic ductal cells with nuclear pleomorphism, hyperchromasia, moderate amount of cytoplasm with central necrosis, (c) Immunohistochemical stain (CD31, 100×) for CD31 highlights the endothelial cells lining the vascular channels, (d) Immunohistochemical stain (D2-40, 100×) for D2-40 is negative in the same lining cells and (e) immunohistochemical stain (SMMHC, 100×) for smooth muscle myosin heavy chain decorates smooth muscle in the wall.

DCIS is surrounded by myoepithelial cells, while LVI sits in vascular channels lined by endothelium. Although myoepithelial cells are often attenuated by light microscopy and endothelial cells are inherently flattened, rendering each of these cell types difficult to appreciate by light microscopy, ancillary studies can highlight these cells and thereby differentiate DCIS and LVI.

IHC stains are color-linked antibodies directed against specific cell antigens. IHC stains are utilized in pathologic analysis to identify cell subtypes, both benign and malignant. D2-40 is a lymphatic marker that preferentially stains the lymphatic endothelium rather than vascular (blood vessel) endothelium[8]; CD31 is a more selective marker of vascular endothelium that does not usually stain lymphatic endothelial cells. Although surprisingly, given the greater predilection for breast cancer to invade lymphatic channels, in this case, the antibody profile is consistent with true vascular invasion.

In this case, the site of LVI, remote from the invasive ductal tumor, mimicked the appearance of DCIS both mammographically and on contrast-enhanced MRI. This radiographic

overlap has not been reported in the imaging literature. IHC demonstrated positive staining for CD31 and negative staining for D2-40 (lymphatic endothelium marker) p63 and smooth muscle myosin (myoepithelial markers), confirming vascular endothelium for tumor emboli rather than breast myoepithelium which would have stained positive in DCIS.

Why is this distinction important? In this particular case, core biopsies proved invasive malignancy in one quadrant and mistakenly diagnosed DCIS rather than LVI in another, necessitating mastectomy. However, if DCIS had been in the same quadrant, lumpectomy would have been a justifiable alternative. LVI is independently associated with a worse prognosis and is an important factor in deciding treatment. LVI raises the risk of recurrence, axillary metastatic disease, and remote metastatic disease. The presence of LVI increases the need for more aggressive surgical therapy including mastectomy as well as possible completion axillary node dissection if the sentinel lymph node is positive and further impacts decisions regarding chemotherapy and radiation therapy.

## Conclusion

This case report describes an imaging presentation of LVI, not previously described in the radiologic literature. Linear, branching mammographic microcalcifications, or clumped NMLE on MRI, associated with a synchronous ipsilateral invasive malignancy, both highly predictive of DCIS on imaging, could represent the unusual possibility of concomitant LVI rather than DCIS. The appearance of macroscopic LVI may mimic the appearance of DCIS on radiologic imaging. It is important to pathologically differentiate between DCIS and LVI with IHC stains. Since IHC stains are not routinely performed, it is possible that macroscopic LVI mimicking DCIS on imaging occurs more frequently than has been heretofore reported.

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### Informed consent

Informed consent for patient information to be published in this article was obtained directly from the patient with a signed consent form. Written consent was obtained from the patient for use of her medical history and images.

### References

1. http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-046202.pdf (accessed 8 September 2016).
2. Yamada T, Mori N, Watanabe M, et al. Radiologic pathologic correlation of ductal carcinoma in situ. *Radiographics* 2010; 30(5): 1183–1198.
3. ACR BI-RADS. *Atlas*. 5th ed., ACR.org.http://www.acr.org/~/media/acr/documents/pdf/qualitysafety/resources/birads/posters/birads%20reference%20card_web_f.pdf (accessed 8 September 2016).
4. Greenwood HI, Heller SL, Kim S, et al. Ductal carcinoma in situ of the breasts: review of MR imaging features. *Radiographics* 2013; 33(6): 1569–1588.
5. Zaorsky NG, Patil N, Freedman GM, et al. Differentiating lymphovascular invasion from retraction artifact on histological specimen of breast carcinoma and their implications on prognosis. *J Breast Cancer* 2012; 15(4): 478–480.
6. Gujam FJ, Going JJ, Edwards J, et al. The role of lymphatic and blood vessel invasion in predicting survival and methods of detection in patients with primary operable breast cancer. *Crit Rev Oncol Hematol* 2014; 89: 231–241.
7. Rabab M, Stewart MG, Gill MS, et al. Improved methods of detection of lymphovascular invasion demonstrate that it is the predominant method of vascular invasion in breast cancer and has important clinical consequences. *Am J Surg Pathol* 2007; 31(12): 1825–1833.
8. Rabban JT and Chen YY. D2-40 expression by breast myoepithelium: potential pitfalls in distinguishing intralymphatic carcinoma from in situ carcinoma. *Human Pathol* 2008; 39(2): 175–183.