Current Problems in Diagnostic Radiology 48 (2019) 348–352

Current Problems in Diagnostic Radiology

journal homepage: www.cpdrjournal.com

Imaging of Intracystic Papillary Carcinoma

Megan E. Speer, MD[a,*], Beatriz E. Adrada, MD[a], Elsa M. Arribas, MD[a], Kenneth R. Hess, PhD[b], Lavinia P. Middleton, MD[c], Gary J. Whitman, MD[a]

[a] The University of Texas MD Anderson Cancer Center, Department of Diagnostic Radiology, Division of Diagnostic Imaging, Houston, TX
[b] The University of Texas MD Anderson Cancer Center, Department of Biostatistics, Division of Science, Houston, TX
[c] The University of Texas MD Anderson Cancer Center, Department of Pathology, Division of Pathology and Laboratory Medicine, Houston, TX

A B S T R A C T

OBJECTIVE: To describe the clinical, imaging, and histopathologic findings of intracystic papillary carcinoma (IPC) of the breast.
MATERIALS AND METHODS: Following institutional review board approval, a database at a single institution was searched to identify cases of patients who received a diagnosis of IPC from 1999-2013 and who had undergone preoperative imaging with mammography, sonography, or MRI. The clinical, mammographic, sonographic, and MRI features of IPC were compared and analyzed using the BI-RADS mammography, ultrasound, and MRI lexicons.
RESULTS: The study sample included 40 patients, 36 females and 4 males. The most common clinical presentation was a palpable mass. Mammographic data was assessed in 31 patients. A tumor was mammographically occult in one patient. The predominant features were oval shape of 17 tumors (57%), obscured margins of 12 (40%), and high density of 20 (67%). Ultrasound data of 37 patients revealed 20 oval masses, 13 irregular masses, and 4 round masses. Fourteen complex solid and cystic masses were identified. One patient underwent MRI that showed a complex, enhancing mass with washout kinetics. Ultrasound guided biopsy was performed on 33 of the 37 masses. Core needle biopsy and fine needle aspiration (FNA) biopsy were most commonly performed on the solid components of the complex solid and cystic masses. IPC was diagnosed by stereotactic biopsy in 1 patient with a suspicious mass on mammography with no correlate on sonography and 6 patients had surgical excision without imaging-guided biopsy.
Pathology showed in situ IPC in 31/40 tumors and 11 were solid and cystic complex masses on ultrasound. Pathology revealed invasive IPC in 9 tumors and five had an irregular mass on ultrasound.
CONCLUSION: Our study reveals no specific imaging features to differentiate in situ vs invasive IPC. The most common ultrasound feature in biopsy proven IPC was an oval mass, however, we identified that a complex solid and cystic mass is more often associated with the diagnosis of in situ IPC and an irregular mass is more often associated with the diagnosis of invasive IPC. Future studies with larger cohorts are needed to further define the clinical and imaging features of this rare malignancy.

Introduction

Intracystic papillary carcinoma (IPC) is a rare variant of papillary ductal carcinoma in situ (DCIS) that accounts for 0.5%-2% of all breast neoplasms.[1] IPC is characterized by thin fibrovascular stalks devoid of a myoepithelial cell layer and a neoplastic cell population with histologic features characteristic of low-grade ductal carcinoma in situ.[2] IPC can be present as an isolated lesion or in association with conventional nonpapillary DCIS and/or invasive ductal carcinoma.[3] The presence of DCIS is associated with an increased risk of local recurrence and the presence of invasive ductal carcinoma is associated with increased risk of metastases.[3] Knowledge of the imaging features of IPC would be useful in alerting breast imagers to this possible diagnosis. We retrospectively evaluated the imaging, clinical, and histopathologic findings of IPC in patients who underwent mammography, sonography, and magnetic resonance imaging (MRI) of the breast.

Materials and Methods

Study Population

A surgical pathology database at a single institution was searched to identify cases of patients who received a diagnosis of IPC from November 1999 to June 2013 and who had undergone preoperative imaging with mammography, sonography, or MRI. Of 52 patients with IPC referred to this institution, 40 had images available for review (31 had mammography images available for review, 37 had ultrasound images available for review and 1 had MRI available for review). A waiver of informed consent was obtained, and the institutional review board approved this HIPAA-compliant study.

Declarations of Interest: None.Funding Support: This publication was supported by the MD Anderson Cancer Center support grant P30CA016672.IRB Statement: An appropriate institutional review board approved this study.

*Reprint requests:, Megan E. Speer, MD, Department of Radiology, The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd, Unit 1350, Houston, TX 77030, USA.
E-mail addresses: mspeer@mdanderson.org, meganespeer@gmail.com (M.E. Speer), Beatriz.Adrada@mdanderson.org (B.E. Adrada), earribas@mdanderson.org (E.M. Arribas), khess@mdanderson.org (K.R. Hess), lpmiddleton@mdanderson.org (L.P. Middleton), gwhitman@mdanderson.org (G.J. Whitman).

https://doi.org/10.1067/j.cpradiol.2018.05.001
0363-0188/

Mammography

Standard 2-view mammography was performed and additional views were acquired as deemed necessary. The mammographically detected lesions were reviewed according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) mammography lexicon.[4]

Sonography

Real-time gray-scale and color Doppler sonography was performed with an Elegra unit (Siemens Healthcare, Erlangen, Germany) with a 13-5 MHz linear array transducer or an ATL Ultramark 9 unit (Phillips Healthcare, Amsterdam, Netherlands) with a 10-5 MHz linear array transducer. The gray-scale parameters assessed included the presence and type of lesion (solid, cystic, complex solid, and cystic, or architectural distortion) and the shape, margin features, posterior acoustic phenomena, echogenicity, and vascularity. Lesions were classified according to the BI-RADS ultrasound lexicon.[5] In addition, the sonographic status of the axillary nodal basins was recorded, according to previously published criteria.[6,7]

MRI

MRI was performed with a 1.5 T whole-body imaging system (Signa Excite, GE Healthcare, Little Chalfront, United Kingdom) and a dedicated 4-channel breast coil. The patient was prone, and images were acquired in the axial and the sagittal planes with the following sequences: unenhanced axial T1-weighted spin echo (TR/TE 500/12); sagittal T2-weighted fat-suppressed fast spin echo (6000/85); dynamic contrast-enhanced sagittal T1-weighted 3D fat-suppressed fast-spoiled gradient echo (18/4; flip angle, 15°; bandwidth, 50 kHz) at 2-minute intervals once before and 3 times after the patient was given an intravenous bolus injection of gadopentetate dimeglumine (0.1 mmol/kg body weight, Magnevist, Mayer Schering Pharma, Berlin, Germany) at 3 mL/s with an injector; and delayed contrast-enhanced axial T1-weighted 3D fat-suppressed fast-spoiled gradient echo images were obtained. The field of view was 160-220 mm, and the matrix size was 256 × 256 pixels. The presence or absence of areas of abnormal enhancement was classified according to the BI-RADS MRI lexicon.[8] Areas of abnormal enhancement were described as masses or as nonmass enhancement. The enhancement kinetics, including initial and delayed phase patterns, were noted.

TABLE 1
Mammographic, sonographic, and MRI findings of intracystic papillary carcinoma

Finding	Number (%)
Mammography (n = 31)	
Mass only	26 (84)
Mass with calcifications	4 (13)
Negative	1 (3)
Sonography (n = 37)	
Mass	37 (100)
Mass characteristics	
Shape	
Oval	20 (54)
Irregular	13 (35)
Round	4 (11)
Margins	
Circumscribed	18 (49)
Spiculated	12 (32)
Microlobulated	6 (16)
Indistinct	1 (3)
Echo pattern	
Hypoechoic	19 (51)
Complex cystic and solid	14 (38)
Heterogeneous	3 (8)
Isoechoic	1 (3)
MRI (n = 1)	
Homogeneous mass enhancement	1 (100)

Note: Values in parentheses are percentages.

Histopathologic Assessment

A text search for "intracystic papillary carcinoma" was performed on the institution's surgical pathology database. The pathologic specimens reviewed included total mastectomy, segmental mastectomy, core biopsy, and fine needle aspiration biopsy specimens. In all cases in the database, at least representative histologic sections of the tumor were reviewed by pathologists at our institution. Information retrieved from the pathology reports, medical records, or both included the presence of associated DCIS and invasive carcinoma, axillary lymph node status, and estrogen receptor, progesterone receptor, and *HER2* status.

Results

Clinical Findings

The study sample included 40 patients: 36 women and 4 men. The median patient age was 59 years (range, 43-98 years). The initial manifestation was a palpable mass in 19 of 40 patients (48%), a screening or diagnostic mammographic abnormality in 17 patients (43%), nipple discharge in 3 patients (8%), and breast pain in 1 patient (3%). The left breast was involved in 17 of 40 patients (43%) and the right breast was involved in 23 of 40 patients (58%).

Imaging Findings

Mammography—Mammography images were available for review in 31 of 40 patients. A mass only was visible in 26 of the 31 tumors (84%) and a mass with microcalcifications was seen in 4 cases (13%). A tumor was mammographically occult in 1 patient (3%). These findings are presented in Table 1. Mammographically, 17 (57%) masses had an oval shape, 8 (27%) masses had an irregular shape, and 5 (17%) had a round shape. The margins of the masses were obscured in 12/30 (40%), circumscribed in 8/30 (27%), indistinct in 7/30 (23%), and spiculated in 3/30 (10%). There were 20/30 (67%) high density masses and 10/30 (33%) equal density masses. Of the 30 masses detected with mammography, 21 (70%) were identified in the upper outer quadrant.

Microcalcifications were present in 4 tumors. The most common morphologic feature was heterogeneous calcifications (2 of 4 tumors, 50%).

Sonography—Sonography was performed on 37 tumors. A mass was visible in all cases. The sonographic features of the masses are presented in Table. Sonography also helped to determine the extent of disease. Of the 37 masses, 6 were multifocal. Thirty of 37 (81%) tumors had vascularity present within the masses and 16 of 37 (43%) tumors showed posterior acoustic enhancement.

Suspicious axillary lymphadenopathy was identified on sonography in four of the 37 tumors (11%). In 2 of the 4 cases with axillary lymphadenopathy, axillary lymph node fine needle aspirations were positive for metastases. No infraclavicular, supraclavicular or internal mammary nodal disease was identified.

Ultrasound-guided biopsy was performed on 33 of the 37 masses. Of the biopsies, 28 (85%) were core needle biopsies, 4 (12%) were fine needle aspiration (FNA) biopsies, and 1 (3%) mass had both core and FNA biopsy. There was also 1 patient with a suspicious mass identified mammographically with no correlate on sonography. Therefore, this mass underwent stereotactic biopsy, revealing evidence of IPC.

Of the 14 solid and cystic complex masses, ultrasound-guided biopsy targeting the solid components was performed in eight cases (57%). The targeted areas of the mass in 1 core biopsy and in 1 FNA

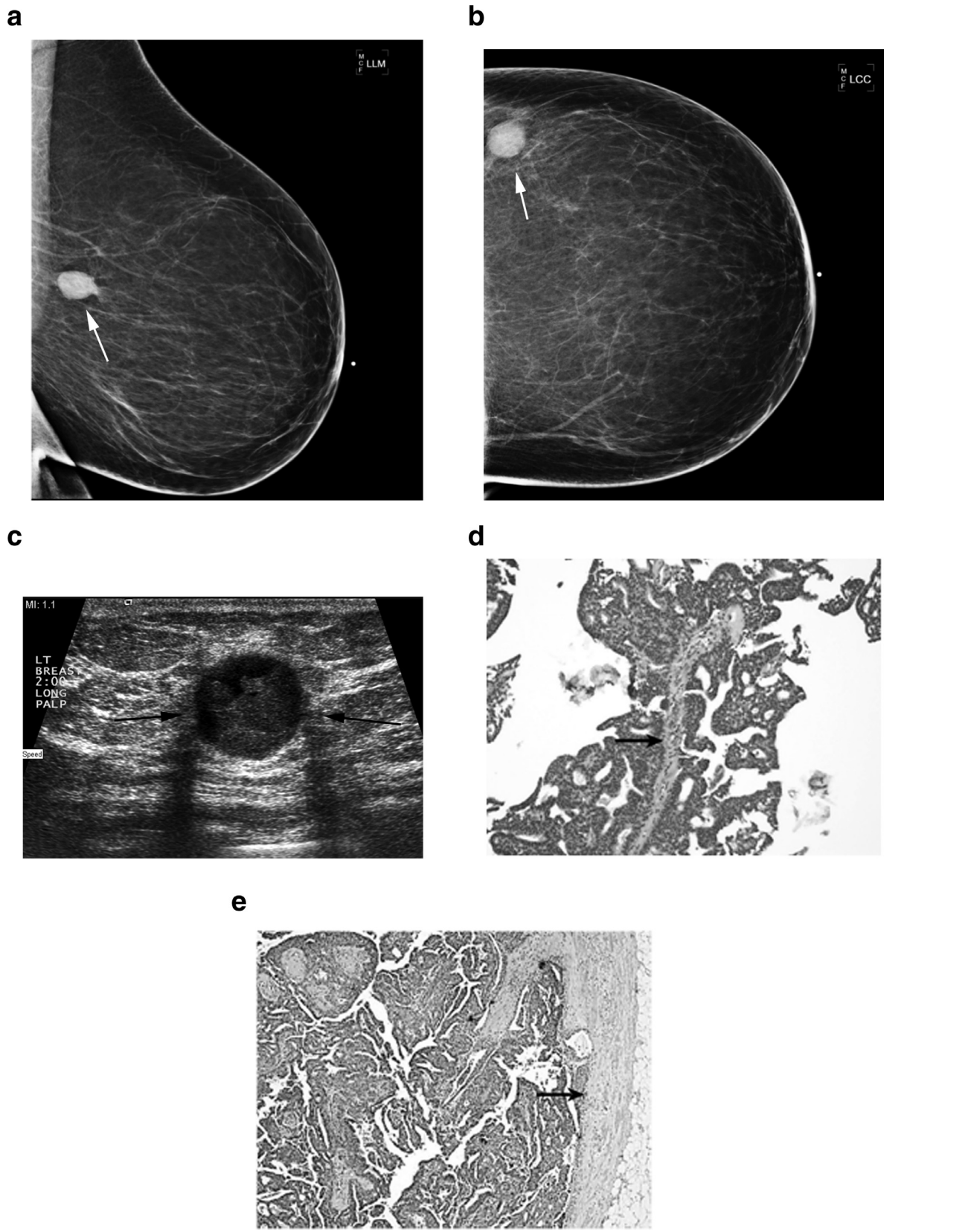

FIG 1. Eighty-year-old woman presented with palpable area in left breast. (A and B). Craniocadual and lateral medial mammograms of the left breast show an oval mass with indistinct margins at 3 o'clock position, posterior depth (arrow). (C). Gray-scale transverse sonogram of left breast shows oval hypoechoic complex mass (arrows). Ultrasound guided biopsy revealed papillary carcinoma. (D). Photomicrograph at 400× of intracystic papillary carcinoma with delicate fibrovascular stalk (arrow). (E). Photomicrograph at 400× of hematoxylin and eosin stained intracystic papillary carcinoma surrounded by dense fibrous capsule (arrow).

biopsy of complex masses were not described. Three complex masses underwent surgical excision without biopsy. Additionally, 1 mass had aspiration of the fluid component of the mass with benign results and the diagnosis of IPC was made at surgery.

A total of 6 patients did not undergo imaging-guided biopsy and the diagnosis of IPC was made at surgical excision. One of these patients had multifocal biopsy-proven DCIS and IDC and IPC was diagnosed at the time of mastectomy.

MRI—MRI was performed on 1 patient. The MRI on this patient revealed a complex, enhancing mass with partially circumscribed and partially irregular margins. The kinetics of this lesion suggested the presence of malignancy with a rapid initial increase and washout on dynamic contrast-enhanced studies.

Treatment and Histologic Findings

Surgery was performed on 39 of 40 patients. One patient did not undergo surgery secondary to a history of concurrent metastatic ovarian cancer. Mastectomy was performed on 14 patients, and 25 patients underwent breast conservation surgery. There were 27 patients who underwent sentinel lymph node biopsy and 4 patients who underwent both sentinel lymph node biopsy and axillary lymph node dissection. Axillary nodal metastases were identified in 4 out of 31 (13%) patients. All 4 patients with axillary nodal metastasis had IPC with invasive carcinoma. One patient had axillary metastasis in the contralateral breast.

There were 31 of 40 (78%) tumors that showed in situ IPC and 9 of 40 (22%) were IPC with invasion. As previously discussed, IPC can present as an isolated lesion or it can be associated with conventional nonpapillary DCIS and/or invasive carcinoma. Our study showed IPC alone in 17 of 40 (43%) tumors, IPC was associated with DCIS in 8 of 40 (20%) tumors, IPC was associated with both DCIS and invasive carcinoma in 8 of 40 (20%) tumors, and IPC was associated with invasive carcinoma in 7 of 40 (18%) tumors.

Estrogen receptor immunohistochemical studies were documented in 31 of 40 tumors (78%) and showed expression in 29 of 31 tumors (94%). Progesterone receptor studies were documented in 30 of 40 tumors (75%) tumors and expression was shown in 25 tumors (83%). *HER2* receptor immunohistochemical studies were documented in 19 of 40 tumors (48%) and showed over-expression in 3 tumors (16%). A total of 20 patients received endocrine therapy and 20 patients received radiation therapy.

Discussion

IPC is an uncommon tumor that has a less aggressive clinical behavior than invasive ductal carcinoma, with a low degree of lymph node involvement.[9-11] IPC presents in both men and women, although the tumor has a predilection for elderly women. The median patient age in our study was 59 years (range, 43-98 years). This is slightly younger than that noted by Akagi et al[9] with a study population of 14 patients and a median age of 72.5 years (range 36-82 years).

Patients with IPC may present with an imaging abnormality, a palpable mass, or bloody nipple discharge. The most common clinical manifestation of intracystic papillary carcinoma in our study was a palpable mass (19 of 40 patients, 48%). However, in a large number of patients (17 of 40, 43%) the masses were detected at screening or diagnostic mammography. The tumor was identified in the upper outer quadrant in 21 of 31 patients (68%). These findings are similar to findings in a study by Solorzano et al,[3] in which a palpable mass (80% of tumors) was the most common clinical finding and the tumor was located in the upper outer quadrant in 60% of patients.

IPC is a variant of papillary ductal carcinoma, confined to a dilated cystic space, and surrounded by a fibrous capsule[3] (Fig 1). IPC can be present as an in situ or invasive lesion and may additionally be associated with ductal carcinoma in situ and/or invasive ductal carcinoma. Thirty-one of 40 (78%) tumors in our study showed in situ IPC and 9 (22%) were invasive.

Previous studies have most often identified IPC on mammography as a round or oval circumscribed mass.[12,13] Our study revealed a round or oval circumscribed mass in only 8 out of 31 (26%) cases. Microcalcifications are not a common mammographic feature and were only present in 4 of 31 cases.

On sonography, prior studies have most often shown a cystic mass with solid papillary masses projecting into the cyst lumen.[12,13] Our study showed a complex solid and cystic mass in 14 of 37 (38%) masses on ultrasound. This finding was more often seen with in situ IPC, present in 11 tumors. Irregular masses on ultrasound were more often associated with invasive IPC. Our study showed that of the 9 lesions with invasive IPC, 5 of them had an irregular mass (56%) on ultrasound.

The MRI findings of intracystic papillary carcinoma have not been well documented. Although MRI was performed on only 1 patient in our study, the mass revealed irregular margins with washout enhancement kinetics, consistent with malignancy.

The prognosis of IPC is excellent for patients regardless of whether the tumor is in situ or invasive.[11,14] There are no clear guidelines on the management of IPC, however the mainstay of treatment is surgical excision. Breast-conserving surgery and mastectomy have been used in the treatment of IPC. In our study, all but 1 patient had surgery. The study by Grabowski et al[11] demonstrated that there is no apparent significant difference in the long-term survival of patients in the in situ and the invasive subgroups of IPC. In most cases, axillary lymph node metastases are not present. In our study, 2 of the 4 patients with axillary lymph node metastases at surgery had abnormal axillary nodes detected on ultrasound.

A limitation of this study was the small sample size, which reflects the rarity of this uncommon tumor. A second limitation was the retrospective nature of the study, in which not all patients underwent imaging of the tumors with mammography, ultrasound, and MRI. Many of the tumors were diagnosed during a period in which MRI was not a widely used preoperative imaging tool.

Conclusion

Our study reveals no specific imaging features to differentiate in situ versus invasive IPC. The most common ultrasound feature in biopsy proven IPC was an oval mass, however, we identified that a complex solid and cystic mass is more often associated with the diagnosis of in situ IPC and an irregular mass is more often associated with the diagnosis of invasive IPC. Future studies with larger cohorts are needed to further define the clinical and imaging features of this rare malignancy.

References

1. Akladios C, Roedlich MN, Bretz-Grenier MF, et al. Intracystic papillary carcinoma of the breast: a diagnostic challenge with major clinical impact. Anticancer Res 2014;34:5017–20.
2. Khoury T, Hu Q, Liu S, et al. Intracystic papillary carcinoma of breast: interrelationship with *in situ* and invasive carcinoma and a proposal of pathogenesis: array comparative genomic hybridization study of 14 cases. Mod Pathol 2014;27:194–203.
3. Solorzano CC, Middleton LP, Hunt KK, et al. Treatment and outcome of patients with intracystic papillary carcinoma of the breast. Am J Surg 2002;184:364–8.
4. American College of Radiology. Mammography. Breast Imaging Reporting and Data System (BI-RADS. 5th ed. Reston, VA: American College of Radiology; 2013.
5. American College of Radiology. Ultrasound. Breast Imaging Reporting and Data System (BI-RADS). 5th ed. Reston, VA: American College of Radiology; 2013.
6. Yang WT, Abuja A, Tang A, et al. High resolution sonographic detection of axillary lymph node metastases in breast cancer. J Ultrasound Med 1996;15:241–6.
7. Vlastos G, Fornage BD, Mirza NQ, et al. The correlation of axillary ultrasonography with histologic breast cancer downstaging after induction chemotherapy. Am J Surg 2000;179:446–52.

8. American College of Radiology. MRI. Breast Imaging Reporting and Data System (BI-RADS). 5th ed. Reston, VA: American College of Radiology; 2013.
9. Akagi T, Kinoshita T, Shien T, et al. Clinical and pathological features of intracystic papillary carcinoma of the breast. Surg Today 2009;27:5–8.
10. Leal C, Costa I, Fonseca D, et al. Intracystic (encysted) papillary carcinoma of the breast: a clinical, pathological, and immunohistochemical study. Hum Pathol 1998;29:1097–104.
11. Grabowski J, Salzstein S, Robins Sadler G, et al. Intracystic papillary carcinoma: a review of 917 cases. Cancer 2008;113:916–20.
12. Knelson MH, El Yousef SJ, Goldberg REA, et al. Intracystic papillary carcinoma of the breast: mammographic, sonographic, and MR appearance with pathologic correlation. J Comput Assist Tomogr 1987;11:1074–6.
13. Dogan BE, Whitman GJ, Middleton LP, et al. Intracystic papillary carcinoma of the breast. AJR Am J Roentgen 2003;181:186.
14. Lefkowitz M, Lefkowitz W, Wargotz ES. Intraductal (intracystic) papillary carcinoma of the breast and its variants: a clinicopathological study of 77 cases. Hum Pathol 1994;25:802–9.