

Digital Galactography and Ultrasound Correlation in Breast Cancer Patients

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Purpose: The purpose of this study was to evaluate of digital galactography correlated with ultrasonographic (US) findings in breast cancer patients with nipple discharge.

Materials and Methods: In 15 patients with breast cancer who underwent both galactography and breast US are included. We retrospectively reviewed galactography and US findings of 15 patients and correlated with pathologic findings.

Results: Abnormal galactographic and US findings were found in all patients. Most common galactographic finding was ductal wall irregularities which were found in 6 patients (40%). Filling defects were found in 3 patients (20%), complete obstruction in 1 patient (6.7%) and combined findings were found in 5 patients (33%). Although galactographic findings had no significant correlation with US findings that had been focused in characterization of intraductal component ($p=0.292$), about 46.7% of these breast cancers which had relatively low level of suspicion to malignancy (one BI-RADS category 3 and six BI-RADS category 4a) on ultrasound US had shown suspicious galactographic findings found as 3 ductal wall irregularities, 2 filling defect and 2 combined findings of ductal wall irregularities and filling defect.

Conclusion: Breast US should be done with galactography as a complementary diagnostic tool to correlate the lesion in patients with pathologic nipple discharge.

Index words: Breast, abnormalities; Breast neoplasm, Ultrasound, Diagnosis;
Breast neoplasm, Galactography, Diagnosis

Introduction

Galactography has been the gold standard for the

evaluation of patients who have pathologic nipple discharge which showed no abnormalities on mammography and diagnostic ultrasound (US). Pathologic nipple discharge is defined as unilateral, single pore, spontaneous discharge. About 8–15% of pathologic nipple discharges are caused by underlying breast cancer (1, 2). However, according to the development of US equipment in recent days that could show not only the nature of a lesion but also its relationship with involved ductal system, some physicians including radiologists

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maintain that galactography is prohibitively time-consuming, and that it can be replaced, at least in part, by US (3–5).

Recent development of digital imaging, galactography can be performed more conveniently. It can be carried out more quickly and accurately while reducing patient discomfort than in conventional film galactography. Digital galactography is a method that uses both digital mammography and injection of contrast material into the milk ducts to obtain an internal picture of the milk ducts in the breast. This information can occasionally be obtained with ultrasound. However, many cases that were diagnosed sonographically without galactography fail to reveal the underlying causes of pathologic nipple discharge, as the lesions are frequently too small, contain no calcifications, or prove to be completely intraductal (2, 5). Digital galactography should be performed precisely, and interpreted well, so as not to miss important signs of breast cancer, and to avoid delayed diagnosis (1, 6–8).

Therefore, if a patient with pathologic nipple discharge is concerned about underlying breast cancer, performing digital galactography and ultrasound at once could detect more suspicious findings without delayed diagnosis and could evaluate the disease extent of the involved duct to the subareolar area.

The purpose of this study was to evaluate the advantage of digital galactography correlated with immediate US findings in breast cancer patients with pathologic nipple discharge.

Materials and Methods

Patients

A computerized search of the electric medical records for one hundred and fourteen consecutive patients presenting nipple discharge from one single duct in one breast underwent galactography during the period from January 2004 to June 2008 performed at our institution. Due to retrospective nature of the study and because the institution's patients sign a general consent form to cover all diagnostic studies, neither institutional review board approval nor informed consent was necessary. Among these patients, 16 patients were shown to have malignant cancer. One patient was excluded be-

cause galactography had failed. Fifteen breast cancer patients were all women, and they were 25–75 years old (mean, 47.2 years). Among these patients, 10 patients had bloody nipple discharge and the remaining 5 patients had non-bloody yellowish discharge. Eight patients were received wide local excision, 2 patients were performed central segmentectomy and 5 patients were received total mastectomy.

Procedure

A light bulb was focused on the nipple for 5–10 minutes, in order to relax the periareolar sphincter muscle. With the patient in a supine position, the nipple and periareolar area were sterilized with the application of a povidone-iodine swab. Cannulation was performed with a 30-gauge Rabinov sialography catheter (Cook Europe, Bjaeverskov, Denmark) attached to a 1 mL tuberculin syringe filled with water soluble contrast material (Telebrex 30; Guerbet, Paris, France). After complete insertion, contrast material was injected slowly until the patient felt discomfort or pressure. All galactography was taken digitally. Digital mammography (Senographe 2000D FFDM; GE Medical Systems, Buc, France) was then obtained in three projections (Craniocaudal, True lateral and Mediolateraloblique). Breast ultrasound was performed immediately after the procedure of galactography in all patients. The beginning of US scan of symptomatic breast was taken within 5 minutes. All breast ultrasounds were performed by high-resolution sonography units equipped with a 10- or 12 MHz linear transducer (Kretz-Medison, Seoul; HDI 5000 or IU 22, Advanced Technology Laboratories, Bothell, WA, USA) with patients in the supine or oblique supine position.

Assessment of Image Findings

Carcinoma involving the ductal system of the breast may manifest as nipple discharge. We analyzed the galactographic findings of breast cancer patients as follows; filling defects, ductal wall irregularities, complete ductal obstructions and combined findings according to the combination of above mentioned three single findings.

In immediate performed breast US, we classified the US findings as follows; dilated duct only, intraductal

mass, mass only without ductal change and mass with ductal dilatation. High resolution US could detect the characteristics of intraductal components of suspicious breast lesion. Therefore we focused the embodiment of duct related breast US findings for schematic correlation with galactography. Lesions were also analyzed according to the BI-RADS (Breast Imaging Reporting And Data System) final assessment category. According to the probability of malignancy, category 4 was subdivided as 3~10% in 4a (low level of malignancy), 11~50% in 4b (intermediate suspicion) and 51~94% in 4c (moderate suspicion). Category 5 (high suspicion) was assessed when the lesion had more than 95% of probability of malignancy.

We reviewed galactography and US findings of these lesions retrospectively.

Data Analysis

Analysis was performed using the χ^2 test, Fisher's exact test, Pearson's correlation and Intraclass correlation in SPSS version 12.0 for Windows (SPSS Inc., Chicago, Ill). P values of less than 0.05 were considered to indicate significant difference.

Results

Of the 15 malignant breast lesions, 5 cases were invasive ductal carcinoma, 7 cases were DCIS (ductal carcinoma in situ) and 3 cases were mucinous carcinoma. Among the five invasive ductal carcinomas, four cases

had DCIS components and all the mucinous carcinoma cases had DCIS components. Only one case of invasive ductal carcinoma had no DCIS component. On mammography, 5(33.3%) breast cancer patients had shown no abnormalities and 4(26.7%) patients had shown as suspicious masses, 2(13.3%) patients as asymmetries and 4(26.7%) patients as suspicious microcalcifications. These findings of mammography had no significant correlation with abnormal galactographic findings ($p = 0.052$) (Table 1).

Abnormal galactographic findings were detected in all (100%) breast cancer patients. Filling defects in galactography were found in three (20%) cases and ductal wall irregularities were found in 6(40%) cases. There was only one (6.7%) case that was shown as complete obstruction in galactography. Combined galactographic findings were found in the remaining 5(33%) cases.

Table 2. Analysis of Galactographic Findings

Galactographic Findings	Number of Cases	Percent (%)
Filling Defect	3	20.0
Ductal Wall Irregularity	6	40.0
Complete Obstruction	1	6.7
Combined		
Filling Defect with Ductal Wall Irregularity	3	20.0
Filling Defect with Complete Obstruction	0	
Ductal Wall Irregularity with Complete Obstruction	2	13.0

Table 1. Correlation of Mammographic and Galactographic Findings

	Mammographic Findings					P
	Negative	Mass	Asymmetry	Microcalcifications	Total	
Galactographic findings						0.052
Filling Defect	3	0	0	0	3 (20.0)	
Ductal Wall Irregularity	0	1	1	4	6 (40.0)	
Complete Obstruction	0	1	0	0	1 (6.7)	
Combined						
Filling Defect with Ductal Wall Irregularity	1	2	0	0	3 (20.0)	
Filling Defect with Complete Obstruction	0	0	0	0	0	
Ductal Wall Irregularity with Complete Obstruction	1	0	1	0	2 (13.3)	
Total	5 (33.3)	4 (26.7)	2 (13.3)	4 (26.7)	15 (100)	

Filling defects with ductal irregularities were found in 3 cases and ductal irregularities with complete obstruction were found in 2 cases (Table 2).

Most common US findings were mass that was accompanied with adjacent ductal dilatations in 7(46.7%) patients. Only mass without ductal change was found in 5(33.3%) cases, two (13.3%) intraductal mass and one

(6.7%) dilated duct without mass (Table 3). Among the 15 breast cancer patients, two cases (13.3%) were category 6 (pathologically proven malignancy) and four cases (26.7%) were category 5, 2 cases (13.3%) were category 4b, 6 cases (40%) were category 4a and one (6.7%) case was category 3(probable benign) (Table 4). There were no significant correlations between galactographic and each US category ($p = 0.341$).

All the abnormal galactographic and US findings were correlated in all breast cancer patients according to the duct correlated US findings (Table 5) and BI-RADS category (Table 4). Three filling defects cases in galactography were demonstrated as two intraductal solid mass (category 4a) and one suspicious (category 4b) mass on

Table 3. Analysis of Sonographic Findings

Sonographic Findings	Number of Cases	Percent (%)
Dilated Duct	1	6.7
Intraductal Mass	2	13.3
Mass Only	5	33.3
Mass with Ductal Dilatation	7	46.7

Table 4. Correlation of Galactographic Findings with Sonographic BI-RADS Assessment Category

	Sonographic BI-RADS Assessment Category						Total	P
	3	4a	4b	4c	5	6		
Galactographic Findings								0.341
Filling Defect	0	2	1	0	0	0	3 (20.0)	
Ductal Wall Irregularity	1	2	0	0	3	0	6 (40.0)	
Complete Obstruction	0	0	0	0	1	0	1 (6.7)	
Combined								
Filling Defect with								
Ductal Wall Irregularity	0	2	0	0	0	1	3 (20.0)	
Filling Defect with								
Complete Obstruction	0	0	0	0	0	0	0	
Ductal Wall Irregularity with								
Complete Obstruction	0	0	1	0	0	1	2(13.3)	
Total	1 (6.7)	6 (40.0)	2 (13.3)	0	4 (26.7)	2 (13.3)	15 (100)	

Table 5. Correlation of Galactographic Findings with Duct Related Sonographic Findings

	Duct Related Sonographic Findings				Total	P
	Dilated Duct	Intraductal Mass	Mass Only	Mass with Ductal Dilatation		
Galactographic Findings						0.292
Filling Defect	0	2	1	0	3 (20.0)	
Ductal Wall Irregularity	1	0	1	4	6 (40.0)	
Complete Obstruction	0	0	1	0	1 (6.7)	
Combined						
Filling Defect with						
Ductal Wall Irregularity	0	0	1	2	3 (20.0)	
Filling Defect with						
Complete Obstruction	0	0	0	0	0	
Ductal Wall Irregularity with						
Complete Obstruction	0	0	1	1	2 (13.3)	
Total	1 (6.7)	2 (13.3)	5 (33.3)	7 (46.7)	15 (100)	

breast US. Six cases of ductal wall irregularity on galactography were shown as four suspicious (two category 4a and two category 5) masses with ductal dilatations (Figs. 1, 2), one suspicious category 5 mass without ductal change (Fig. 3) and one ductal prominence (category 3) only (Fig. 4) on breast US. One complete ductal obstruction finding in galactography was shown as suspicious category 5 mass in US. Combined galactographic findings with filling defects and ductal irregularities were found in three cases, it was shown as two (one category 4a and one category 6) masses with ductal dilatation (Fig. 5) and one category 4a mass on breast US. Combined findings with ductal irregularities and complete obstruction were found in two cases, it was shown

as one suspicious category 4b mass and one suspicious category 6 mass with ductal dilatation on breast US. There were no significant correlations between galactographic and each US findings ($p = 0.292$)

On US, 8 (53.3%) cases were shown as multiple suspicious (more than category 4a) lesions, but only one (6.7%) case was shown as multicentric cancer in galactography. We also compared the disease extent that had measured on each image study with final pathology. Among 15 cases, we excluded three cases because one patient had received central segmentectomy in other hospital, so we could not know the pathologic extent and one patient was shown as complete obstruction on galactography, so we could not evaluate the disease ex-

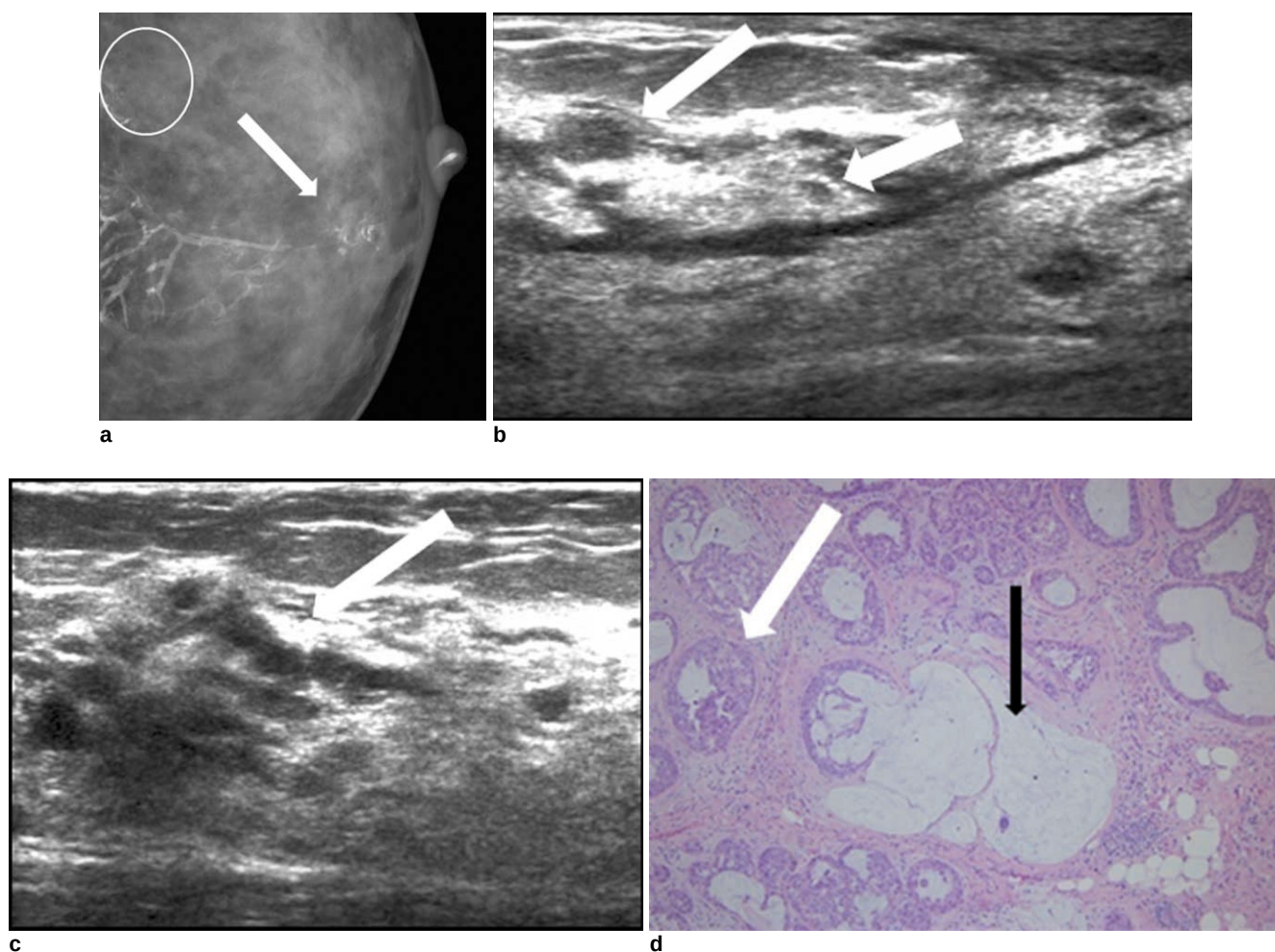


Fig. 1. A 37-year-old patient with left bloody nipple discharge.

a. This patient showed microcalcifications in mammography with architectural distortion and performed galactography for further evaluation of her nipple discharge. Galactography showed ductal wall irregularities (arrows) and microcalcifications (marked round) in deep portion of 12 o'clock area.

b, c. Ultrasound show multiple ill-defined irregular category4a nodules (arrows). Pathology was proved to be ductal carcinoma in situ, mucinous type.

d. Photomicrography show neoplastic cells lining the ducts are seen (white arrow) with spillage mucin in to the adjacent stroma (black arrow).

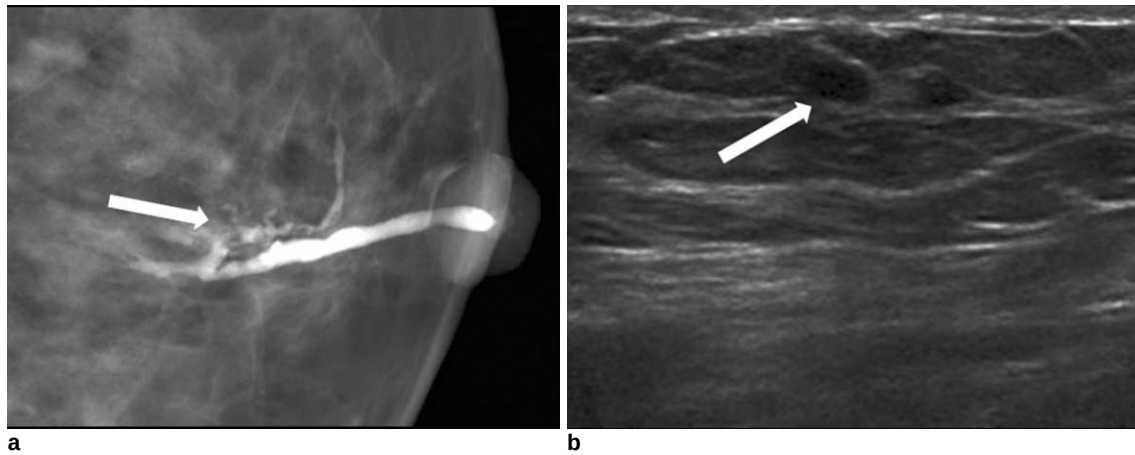


Fig. 2. A 46-year-old patient with left yellowish nipple discharge.

a. The lesion was shown as microcalcifications in mammography in subareolar area performed galactography for further evaluation of her nipple discharge. Galactography showed multifocal ductal wall irregularity in ducts (arrow).

b. This was shown as 0.4 cm sized partially ill-defined hypoechoic nodule, category 4a (arrow) on immediate US. This patient performed core biopsy and the lesion was confirmed as DCIS.

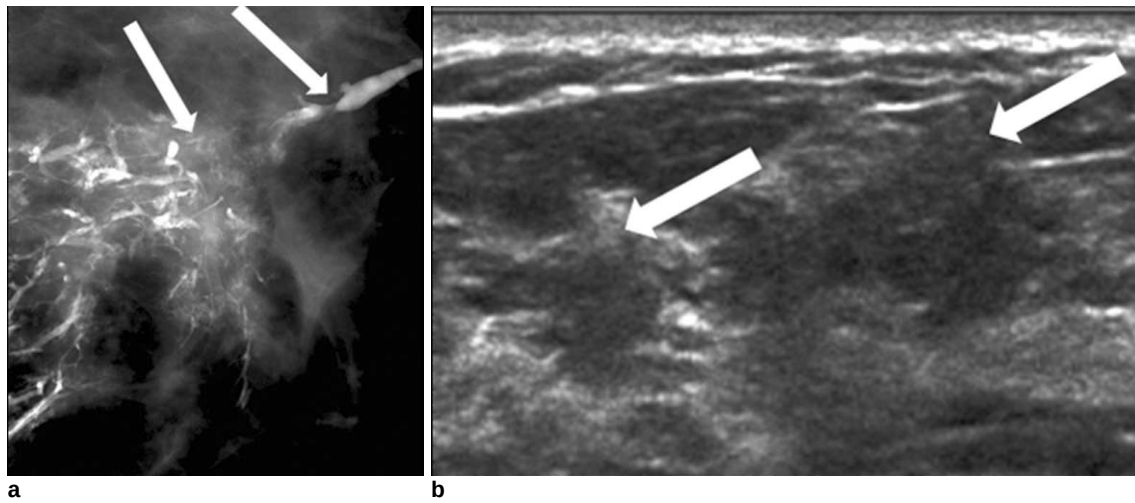
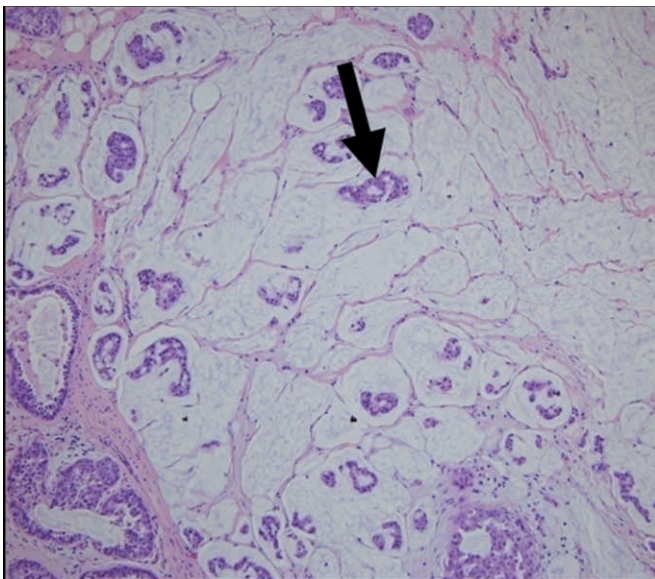


Fig. 3. A 42-year-old patient with left nipple bloody discharge.

a. Galactography showed multiple duct irregularities (arrows) suggestive of malignancy.

b. Ultrasound showed ill defined spiculated nodules (category 5). The patient underwent modified radical mastectomy for left breast and pathology was confirmed as multifocal mucinous carcinomas.

c. Photomicrography shows tumor cell rests in mucinous background (black arrow, H & E stain $\times 40$).



tent and one patient had received preoperative chemotherapy, so there was discrepancy between final pathologic extent and initial image findings. With galactography only, the mean extent of breast cancer was measured about 22.4 mm (5~50 mm). With sonography only, the mean extent of breast cancer was measured about 12.8 mm (4~31 mm). On pathologic reports, the mean extent of breast cancer was 29.1 mm (2~50 mm). Six cases were Tis, two cases T1a, two cases T1b and two cases were T2 stage. Galactographic measurement for evaluation of breast cancer extent had 0.55 Intraclass correlation coefficient (ICC) (Pearson's $r = 0.420$, $p = 0.174$) and US measurement for evaluation

of breast cancer extent had 0.68 intraclass correlation coefficient (Pearson's $r = 0.621$, $p = 0.031$).

We additionally analyzed the US findings that focused the duct correlated schematic feature such as prominent duct only, intraductal mass, mass only without ductal change and mass with ductal dilatation according to the presence of invasiveness on pathology. But there was no significant correlation ($p = 0.218$).

Discussion

Pathologic nipple discharge is an important presenting symptom in patients with breast cancer. Although most

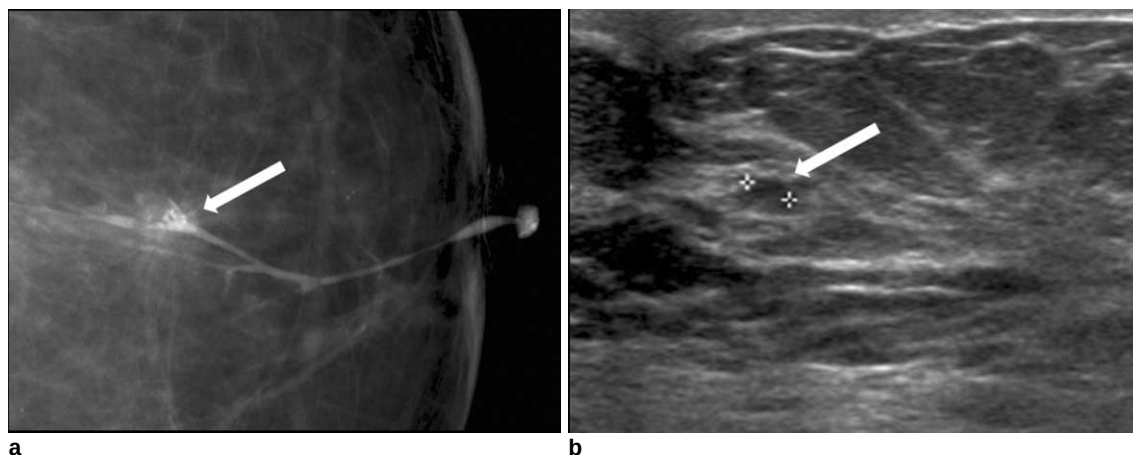


Fig. 4. A 71-year-old patient with left bloody nipple discharge.

a. The lesion was shown as punctate microcalcifications on mammography in subareolar area and performed galactography for further evaluation of her nipple discharge. Galactography showed small intraductal filling defect suspected in subsegmental branch (3rd division) without duct dilatation (arrow).

b. This was shown as only subareolar prominent duct (arrow) and considered as category 3 on immediate US. This patient performed microdochectomy and the lesion was confirmed as DCIS

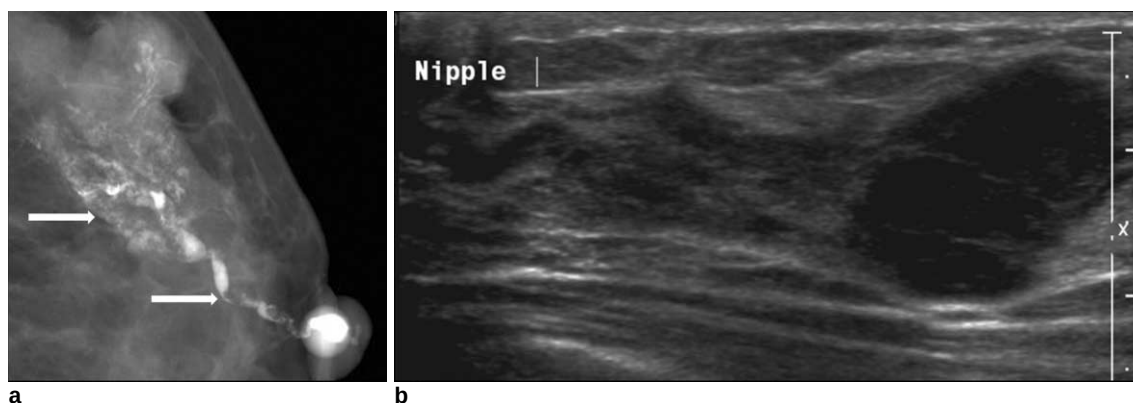


Fig. 5. A 37-year-old patient with left brownish clear nipple discharge.

a. The lesion was shown as asymmetry on mammography and performed galactography for further evaluation of her nipple discharge. Galactography showed, multiple tiny (2 - 3 mm) intraductal filling defects in segmental branch (arrows).

b. This was shown as multiple ill-defined irregular hypoechoic nodules, category 4a with duct dilatations on immediate US. This lesion was confirmed as infiltrating ductal carcinoma with DCIS at core biopsy.

common pathologic causes are benign, 10–15% of patients with nipple discharge are found to have cancer. Moreover nipple discharge may at times be the only sign of breast cancer (1, 2, 9).

Galactographic findings of breast carcinoma present with an irregularly margined, distorted, and displaced duct that shows one or more irregular filling defects thus partially obliterating the normal ductal pattern. Multiple irregular filling defects in non dilated peripheral ducts are highly (70–89%) suggestive of malignancy and ductal wall irregularities represent a non-specific finding but may be detected in 5.7% of DCIS (6, 7, 8, 10–12). Complete ductal obstruction can be observed in both benign (5–47%) and malignant tumors (67–83%) (8, 10). Most of our cases showed as one of the above mentioned suspicious galactographic findings and quite a few cases (35.7%) of breast cancer showed combined suspicious findings.

Among these breast cancers, there was one category 3 lesion that was seen with only ductal prominency on US and five category 4a lesions. With the US findings only, 6(42.8%) cases had low level of suspicion to malignancy that did not warrant surgical excision or even be considered as probable benign lesion that did not need biopsy. However, the category 3 lesion had shown ductal wall irregularities on galactography. Therefore, the patient received microdochectomy and the pathology was proved to be ductal carcinoma in situ (DCIS). In cases of four category 4a lesions, one lesion was shown as filling defect in galactography and proven to be DCIS and two lesions were shown as ductal wall irregularities in galactography and each lesion was proven to be DCIS. The remaining two category 4a cases were shown as combined findings with filling defects and ductal wall irregularities and proven to be DCIS and invasive ductal carcinoma. Additionally, we analyzed duct oriented US findings according to the presence of breast cancer invasiveness on final pathology and that showed no significant correlation ($p = 0.218$). The presence of identifiable US mass or mass with ductal change could not directly mean the basement membrane involvement of breast cancer.

In the evaluation of multifocality or multicentricity of breast cancer, US is obviously superior to the galactography in our study. Most multiple US lesions were

shown as large extent continuous lesion on galactography rather than multifocal cancer. And galactography in itself had limitation for evaluation for the non symptomatic functional unit in the breast. But both imaging study had not showed good correlation with final pathology in the aspect of disease extent. We included not only the invasive focus but also non invasive focus such as DCIS to the final pathology result. In some early cases, there was no systematization for reporting the non invasive focus, so some cases that had size discrepancy were included.

The results of our study suggest that the breast cancer patients who complained of pathologic nipple discharge should undergo breast US with galactography to avoid underestimation of breast cancer findings. Breast US can show more detail of the intraductal lesion of malignancy and it is useful in technically inadequate patients with galactography and in detecting tumor smaller than 0.5 cm. In many cases performing galactography and US together increases practical values and detectability (3). Therefore US should always be carried out with galactography as a complementary diagnostic tool to correlate the lesion in patients with nipple discharge. In these cases, galactography with immediate US findings of malignancy help in detection, diagnostic accuracy can be improved and prompt therapeutic plans can be made.

The limitation of our study was the retrospective assessment of the detectability of both galactographic and US image study on breast cancer. The US images that we had evaluated were not the real time but static captured images. And we had some statistical limitations of small numbers of cases for conducting analysis.

In conclusions, breast US correlation with galactography in symptomatic patients could help the detection and appropriate management for the highly suspicious lesion which may be downgraded as low level of probability for malignancy. Breast US should be carried out with galactography as a complementary diagnostic tool to correlate the lesion in patients with nipple discharge

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유방암 환자에서의 디지털 유관조영술과 유방초음파 소견 비교분석

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목적: 이 연구는 병적 유즙분비 증상이 있는 유방암 환자를 대상으로 디지털 유관조영술과 진단적 초음파영상을 시행하여 그 소견을 비교하고자 한 것이다.

대상 및 방법: 본 연구기관에서 2004년에서 2008년간 유방암으로 진단받은 환자들 중 유관조영술과 유방초음파를 동시에 시행 받은 15명의 환자를 대상으로 하였다. 이들의 유관조영술 및 유방초음파의 영상소견과 병리소견을 후향적으로 비교 분석하였다.

결과: 가장 흔한 유관조영술 소견은 6명(40%)의 환자에서 보인 유관벽의 불규칙성 변화이다. 3명(20%)의 환자에서는 충만 결손이 나타났고 유관의 완전 폐쇄는 1명(6.7%)에게 나타났으며 이들이 복합된 양상의 소견은 5명(33%)에게서 보였다. 유관내 요소를 중심으로 살펴본 유관조영술과 유방초음파소견은 유의한 관계를 보이지 않았다($p=0.292$). 진단적 유방초음파영상소견에서 상대적으로 낮은 의심도를 보인 7례(1례의 BI-RADS category 3와 6례의 BI-RADS category 4a)의 유방암의 경우 유관조영술에서는 악성이 강하게 의심되는 불규칙 유관변화 3례, 충만결손 2례 그리고 이 두소견의 복합양상 2례가 관찰되었다.

결론: 유즙분비 증상이 있는 유방암 환자에게 진단적 유방초음파와 더불어 유관조영술을 부가적으로 시행하는 것은 병변의 정확한 발견과 더불어 악성도가 저평가되는 것을 예방할 수 있다.

Index words: Breast, abnormalities; Breast neoplasm, Ultrasound, Diagnosis; Breast neoplasm, Galactography, Diagnosis