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**ORIGINAL ARTICLE**

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## **Mucocele-like Lesions of the Breast: Mammographic, Sonographic, and Pathologic Findings and Upgrade Rate**

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### **ABSTRACT**

**Objectives:** To describe the mammographic, sonographic, and pathologic appearance of mucocele-like lesions (MLLs) of the breast and to determine the upgrade rate following surgical excision.

**Methods:** All patients who attended Queen Elizabeth Hospital, Hong Kong from 1 January 2008 to 31 May 2014 with core needle biopsies (CNB) and MLL as one of the final pathological diagnoses or with mucinous material found within the specimens were identified. All available breast imaging, and pathology slides and reports were reviewed by radiologists and a pathologist specialised in breast imaging, respectively. The upgrade rate of MLL to high-risk lesion or to malignancy was obtained.

**Results:** Twelve patients had either MLL or mucinous material within their CNB specimen. Their mean age was 47 years (range, 31-77 years). The most common mammographic finding was grouped coarse heterogeneous calcifications (56%) and the most observed feature on ultrasound was lesions containing cystic components (71%). Of the 12 patients, six subsequently underwent excisional biopsy of their lesion. One of them had atypia shown on CNB and a final surgical specimen revealing MLL associated with ductal carcinoma in-situ. Of the five patients with CNB showing no atypia, three (60%) were upgraded — upgraded histology included one node-negative papillary carcinoma with foci of mucinous carcinoma and two with high-risk histology of atypical ductal hyperplasia.

**Conclusion:** MLLs of the breast have variable mammographic and sonographic appearances but the common radiological findings include presence of grouped heterogeneous calcifications mammographically and lesions containing cystic components sonographically. A significant proportion of lesions that yielded mucinous material or that were diagnosed as a MLL on percutaneous CNB without atypia were upgraded. Surgical excision is still warranted following a CNB diagnosis of MLL to allow evaluation of the entire area and to exclude the presence of atypia or carcinoma.

**Key Words:** Adenocarcinoma, mucinous; Biopsy, needle; Breast neoplasms; Carcinoma in situ; Mucocele

## **中文摘要**

### **乳腺粘液囊腫樣病變：乳房X光造影、超聲和病理學特徵及分級提高率**

曾凱晴、衛穎莊、趙朗峯、黃安傑

**目的：**描述乳腺粘液樣囊腫病變（MLL）的鈹靶、超聲和病理學特徵，並確定手術切除後的分級提高率。

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**方法：**研究對象為2008年1月1日至2014年5月31日期間到香港伊利沙伯醫院接受粗針穿刺活檢（CNB），最終病理診斷為MLL或標本含粘液性成分的患者。分別由放射科醫生審查所有乳房影像，病理學醫生審查所有病理載片和報告。找出MLL病變升高風險病變或惡性腫瘤的分級提高率。

**結果：**12例患者屬MLL或在其CNB標本中發現有粘液性成分。患者平均年齡47歲（介乎31至77歲）。最常見的乳房X光造影成像特徵為不均勻粗鈣化簇（56%），而超聲成像特徵最常見為包含囊性成分的病變（71%）。12例患者中有6例最終接受病灶切除活檢。其中1例CNB顯示非典型增生，最終手術標本顯示為導管原位癌相關性MLL。5例接受CNB的患者未發現非典型增生，3例（60%）分級提高：包括1例為淋巴結陰性乳頭狀癌伴發粘液癌，另兩例為高危性乳腺導管上皮非典型增生。

**結論：**MLL的乳房X光造影和超聲影像特徵多變，但X光造影可見常見的不均勻的粗鈣化簇，以及超聲上含有囊性成分的病變。產生粘液性成分的病灶或經皮CNB診斷為不伴非典型增生的MLL病灶中，相當部分的分級有見提高。如果經皮CNB診斷有MLL，則需進行手術切除以評估整個區域和排除非典型增生或癌的存在。

## INTRODUCTION

Mucocele-like tumour of the breast is a rare entity analogous to a mucocele of the minor salivary glands. It was first described by Rosen in 1986 as a benign lesion comprising multiple cysts of mucinous material that have ruptured and extravasated into the surrounding stroma.<sup>1</sup> Calcification is frequently present within the cysts, allowing for mammographic detection.<sup>2</sup> Several studies have documented the association between mucocele-like lesions (MLLs) with benign, atypical, and malignant lesions.<sup>3-6</sup> Of note, up to 43% of MLLs diagnosed on core needle biopsy (CNB) are upgraded to atypia or malignancy on excisional biopsy. This contributes to the debate about the need for surgical excision.<sup>7-9</sup> In this study, our aim was to review the mammographic, sonographic, and pathological patterns of MLLs and their upgrade rates in our institution.

## METHODS

### Patient Recruitment

The pathology database at Queen Elizabeth Hospital was searched to identify all breast CNBs performed from 1 January 2008 to 31 May 2014, with either MLL as one of the final pathological diagnoses or with mucinous material found in the specimen. A total of 12 biopsy samples from 12 patients were identified. Of these 12 samples, five were obtained by stereotactic guidance and seven under sonographic guidance using an automated core biopsy device and disposable 14-Gauge core biopsy needle. This retrospective study

was approved by the research ethics committee (Kowloon Central/Kowloon East) with informed consent waived.

### Mammographic Findings

All mammograms of patients with a CNB diagnosis of MLL or mucinous material within the specimen were identified, either from diagnostic mammographic study or as part of their stereotactic-guided core biopsy. All available diagnostic mammograms had been obtained in standard mediolateral oblique, cranial caudal projections, and additional spot compression / magnification views. Images from the stereotactic-guided CNB procedure were also acquired using the same mammographic system with mediolateral projection and multiple spot compression views of the area of concern. Images were reviewed by two radiologists with 15 years and 5 years of breast imaging experience. Any disagreement between the two was resolved through consensus. The mammographic findings were reported according to the lexicons outlined in the 5th edition of American College of Radiology Breast Imaging Reporting and Data System (BI-RADS).<sup>10</sup> When calcifications were present, their morphology (benign, suspicious-amorphous, coarse heterogeneous, fine pleomorphic, fine linear, or fine-linear branching) and distribution (diffuse, regional, grouped, linear, segmental) were assessed. When a mass was present, its shape (oval, round, irregular), margin (circumscribed, obscured, microlobulated, indistinct, spiculated), and density (high-, equal-, low-density, or fat-containing) were analysed.

## Ultrasound Findings

All ultrasound images of the targeted lesions, obtained either as diagnostic workup in our institution or as part of their ultrasound-guided CNB, were reviewed. All diagnostic sonograms or ultrasound-guided CNBs were performed by one of the six radiologists specialised in breast imaging using a GE Logiq 7 unit with a 14-MHz linear transducer. All images were reviewed without reference to the mammographic findings by two breast radiologists. All discrepancies were resolved through consensus. When a mass was present, the following features were evaluated according to the BI-RADS lexicon — its maximum dimension, shape (oval, round, irregular), orientation (parallel, not parallel), margin (circumscribed, not circumscribed), echo pattern (anechoic, hyperechoic, complex cystic and solid, hypoechoic, isoechoic, heterogeneous), posterior features (no posterior features, enhancement, shadowing, combined pattern), calcifications, and associated features.

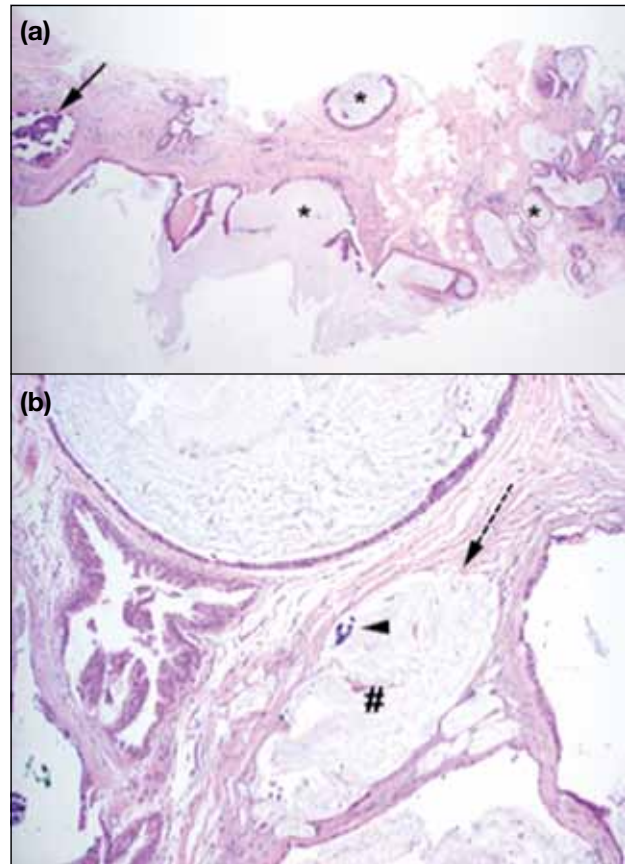
## Histology Findings and Analysis

MLLs are characterised by variably dilated ducts filled with mucin. There is often associated rupture of ducts and extravasation of mucin into the surrounding stroma (Figure 1). The lining epithelium of the ducts may appear attenuated or show a spectrum of proliferative changes from the typical ductal hyperplasia to atypical ductal hyperplasia (ADH) to ductal carcinoma in-situ (DCIS). In some cases, the lining epithelium detaches and floats within the mucin pools. Features that favour a diagnosis of MLL include the presence of associated myoepithelial cells and linear configuration of lining epithelium. One of the most important differential diagnoses is mucinous carcinoma. Differentiation, however, may sometimes be difficult from percutaneous CNB specimens.

All histology slides were retrieved and reviewed independently by a pathologist with 6 years of experience to confirm the diagnosis of MLL or mucinous material within the specimen. All surgical excision specimens were also reviewed to confirm the final diagnosis, presence of atypia, and presence of upgrading to high-risk or malignant pathology.

## Statistical Analysis

All results were analysed with the Statistical Package for the Social Sciences (Windows version 22.0; SPSS Inc, Chicago [IL], US). Statistical significance of age distribution, personal or family history of breast cancer,



**Figure 1.** (a) Low-power histology slide of core biopsy specimen showing variably dilated ducts filled with mucin (\*). Calcifications are also noted within the sample (arrow) [H&E; original magnification, x 40]. (b) High-power histology slide of core biopsy demonstrating extravasation of mucin (#) not contained inside a dilated duct as there is no cell lining (dotted arrow). Associated calcifications (arrowhead) are also present (H&E; original magnification, x 100).

menopausal status, hormone therapy status, presence of mass or calcification on mammography was evaluated by Student's *t*-test and Fisher's exact test.

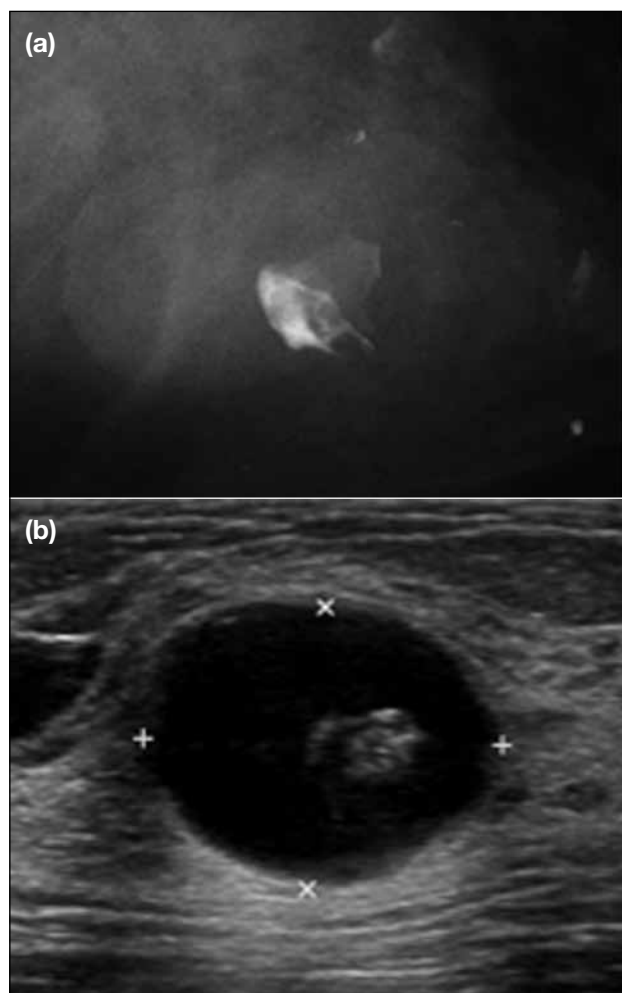
## RESULTS

A total of 12 patients were included in this study. Their age ranged from 31 to 77 years (mean  $\pm$  standard deviation,  $47 \pm 14$  years). Of these 12 patients, only six presented with a clinically palpable mass, two with other breast symptoms and four were screen-detected asymptomatic patients. Six patients underwent subsequent surgical excision of their index lesions. Of the remaining six patients, three had clinical / imaging follow-up period of at least 3 years and showed no development of malignancy. In one patient, the lesion disappeared on follow-up scan after biopsy and two

patients were lost to follow-up. One of the six patients who underwent final surgical excision had atypical cells demonstrated on percutaneous CNB.

Of the 12 patients, five had mammographic findings only, three had sonographic findings only, and four had both mammographic and sonographic findings.

In the nine patients who had mammographic findings, seven had calcifications (Figure 2) and two had a high-density mass (Table 1). The distribution of the microcalcifications was grouped in five and regional in two (Figures 3 to 5). Two of the lesions manifested



**Figure 2.** A 36-year-old woman presented with a 2-month history of palpable right breast mass. (a) Mammogram showing an equal-density mass lesion with well-circumscribed margin associated with internal benign coarse calcification, corresponding to palpable lesion. (b) Ultrasound image showing a complex cystic and solid mass lesion correlating with mammographic finding. Percutaneous core needle biopsy revealing extracellular mucin material and final surgical pathology showing mucocele-like lesion with foci of sclerosing adenosis.

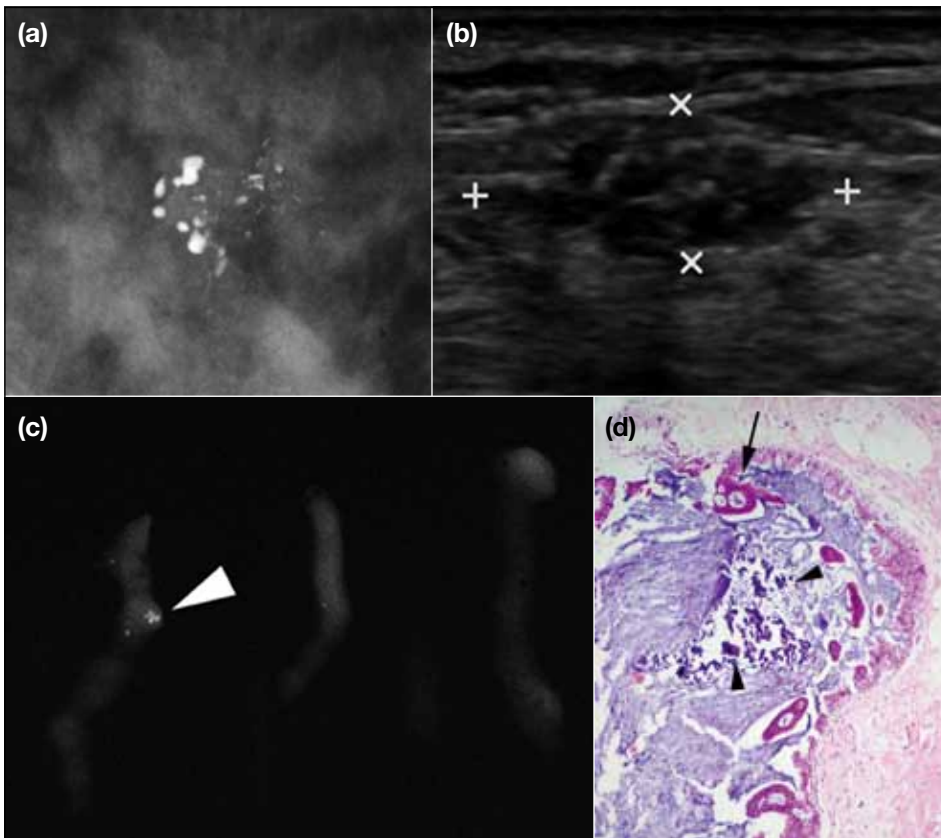
**Table 1.** The mammographic appearances of mucocele-like lesions of breast.

Mammographic appearance	No. (%) of lesions / patients (n = 9)
Calcification	7 (78)
Morphology	
Suspicious	6 (67)
Amorphous	1 (11)
Coarse heterogeneous	5 (56)
Benign	1 (11)
Dystrophic	1 (11)
Distribution	
Regional	2 (22)
Grouped	5 (56)
Mass	
High density	2 (22)

as a high-density mass on mammogram without calcifications. In the two patients with final surgical specimen containing foci of ADH, both showed grouped coarse heterogeneous microcalcifications. One of the high-density masses without calcification was upgraded to papillary carcinoma with foci of mucinous carcinoma (Figure 6).

The sonographic appearance of MLLs varied. Only 10 of 12 cases underwent ultrasound examination of whom seven had positive findings. Four showed complex cystic and solid masses, one as an isoechoic mass, one as a hypoechoic mass, and one as clustered microcysts (Table 2). All lesions had parallel orientation and absent vascularity. All but one showed posterior acoustic enhancement. As outlined in Table 3, there was no statistically significant difference regarding the mammographic and sonographic findings between the benign MLLs and the upgraded / malignant lesions.

From the 12 patients with a CNB that yielded MLL or with mucinous material, two were lost to follow-up (Figure 7). In the remaining 10 patients, only one had rare atypical cells on CNB. Six of these patients subsequently underwent excisional biopsy of their lesions. The final surgical specimen of the lesion with atypia on CNB showed MLL associated with DCIS (Figure 8). Of the five patients with final surgical excisional biopsy and CNB showing no atypia, three (60%) were upgraded. Upgraded histologies included one node-negative papillary carcinoma with foci of mucinous carcinoma and two with high-risk histology of ADH (Figure 3, 4a). The mean age, family or personal history of breast cancer, menopausal or hormonal therapy status had no impact on the upgrade rate (Table



**Figure 3.** An asymptomatic 50-year-old woman presented with abnormality on screening mammogram. (a) Grouped coarse heterogeneous microcalcifications and (b) corresponding oval, parallel, hypoechoic mass lesion with microlobulated margin on ultrasound. (c) Percutaneous core biopsy specimen radiograph showing successful sampling of targeted microcalcifications (arrowhead). (d) Magnified pathology slide of the corresponding calcifications seen in the core specimen (in c), demonstrating the presence of the calcifications (arrowheads) with extracellular mucin. Atypical ductal hyperplasia (arrow) is also shown as characterised by hyperchromatic, monotonous nuclei with punched out lumens. Final surgical specimen confirmed mucocele-like lesion with atypical ductal hyperplasia (H&E; original magnification, x 100).



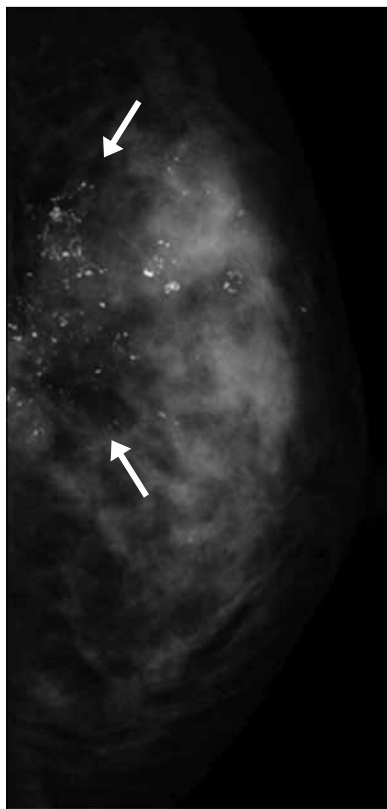
**Figure 4.** (a, b) Grouped coarse heterogeneous microcalcifications in two of the patients with percutaneous core biopsy results yielding mucocele-like lesions. Final surgical excisional histology revealing foci of atypical ductal hyperplasia in (a) and fibrocystic change in (b). (c) Pathology slide of excisional specimen showing mucocele-like lesion with atypical ductal hyperplasia. The atypical cells, characterised by enlarged, hyperchromatic, and monotonous nuclei (dotted circle), are seen adjacent to variably dilated ducts filled with mucin (\*) [H&E; original magnification, x 200].

3). The remaining four patients who did not undergo surgical excision had clinical and / or radiological follow-up and showed no subsequent development of cancer.

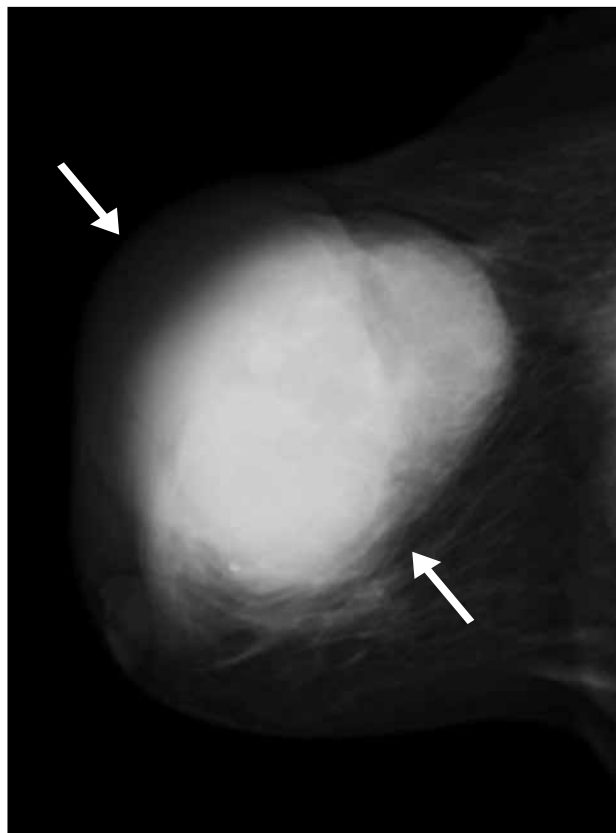
## DISCUSSION

MLL of the breast is a rare benign tumour that has

variable mammographic and sonographic appearances. Rosen<sup>1</sup> was the first to describe the mucocele-like tumour of the breast as a cyst of breast containing mucinous material that has ruptured into the surrounding stroma, analogous to a mucocele of the minor salivary glands. Extravasated mucin can undergo dystrophic calcification and thus be evident on mammogram.



**Figure 5.** A 33-year-old woman presented with lumpiness over the right breast. Mammogram (lateral projection) showing regional coarse heterogeneous microcalcifications in the upper part of right breast (arrows). Stereotactic-guided core biopsy of the microcalcifications revealing features of mucocele-like lesion without atypia. The patient subsequently defaulted from follow-up.



**Figure 6.** A 77-year-old woman presented with an enlarging palpable right breast mass for 1 year. Craniocaudal mammogram showing an oval shaped, high-density mass lesion (arrows) with circumscribed margin occupying almost the whole right breast. Percutaneous core biopsy showing mucocele-like lesion with epitheliosis. Final surgical pathology showed encapsulated papillary carcinoma with several microscopic foci of mucinous carcinoma.

Calcifications in the tumour can have benign to suspicious morphology, with coarse heterogeneous being the most common in our study. Of those with coarse heterogeneous morphology, they usually had either grouped or regional distribution. Nonetheless comparison of the presence of calcifications in the benign MLL group and the group with upgraded lesions showed no statistically significant difference in our study ( $p > 0.05$ ; Table 3). Several studies have reported the appearance of MLL on mammography. D'Orsi et al<sup>10</sup> also reported the most common mammographic appearance of MLL in their study of 44 patients to be grouped coarse heterogeneous calcifications. Glazebrook and Reynolds<sup>12</sup> reported MLL to have a non-specific mammographic appearance, although it could present as indeterminate microcalcifications or as a nodule, often containing calcifications. Hamele-Bena et al<sup>13</sup> determined that malignant MLL had a higher incidence of coarse calcifications than its benign counterparts. Kim et al<sup>14</sup> also revealed that the majority of MLLs (19 of 25) had calcifications on mammography with pleomorphic shapes. Based on these findings, we postulate that one should consider the diagnosis of MLL when a group of coarse heterogeneous calcifications is

encountered on mammography. It should nevertheless be remembered that it is not possible to differentiate benign from malignant based on imaging alone and complete surgical excision will be needed once the diagnosis of MLL is ascertained by percutaneous CNB.

Sonographically, the appearances of MLLs are also diverse but the majority of those in our study appeared to be complex cystic and solid (4 out of 7 with ultrasound-detected lesions). This was also observed by Kim et al<sup>15</sup> where 95.8% (69 of 72) of their study group with MLL had a cystic mass on ultrasound. Most had benign features including a circumscribed border, oval shape, anechoic nature with parallel orientation, thin boundary, and posterior acoustic enhancement.<sup>15</sup> Another study of 18 patients found sonographic findings of MLL to be of cysts with calcified or non-calcified

**Table 2.** The sonographic appearances of mucocele-like lesions of breast.

Sonographic appearance	No. of lesions / patients		
	High-risk / malignant group (n = 3)	Benign group (n = 4)	Total (n = 7)
Shape			
Oval	2	3	5 (71%)
Irregular	1	1	2 (29%)
Echogenicity		†	
Hypoechoic	0	1	1 (14%)
Isoechoic	1	0	1 (14%)
Complex cystic and solid	2	2	4 (57%)
Orientation			
Parallel	3	4	7 (100%)
Margin			
Circumscribed	1	3	4 (57%)
Not circumscribed			
Indistinct	1	1	2 (29%)
Microlobulated	1	0	1 (14%)
Posterior feature			
Enhancement	3	3	6 (86%)
None	0	1	1 (14%)
Vascularity			
Absent	3	4	7 (100%)
Special case			
Clustered microcyst*	0	1	1 (14%)

\* Clustered microcyst denotes lesion consisting of a cluster of anechoic masses, individually <2-3 mm, with thin (<0.5 mm) intervening septation and no discrete solid component. While margins may reflect microlobulation due to individual small cysts, the margin should not be indistinct.<sup>10</sup>

† One had clustered microcyst.

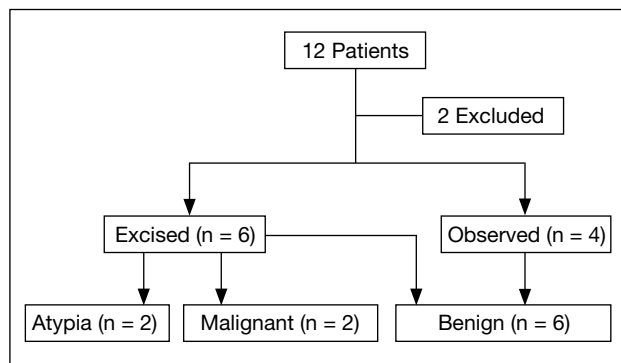
**Table 3.** Summary of statistical comparisons between patients with high-risk / malignant lesion and patients with benign lesion.

	High-risk / malignant group (n=4)	Benign group (n=6)	p Value
Mean (range) age (years)	56.3 (49-77)	43.1 (31-66)	-
Positive family history	0	1	1.00
Positive personal history	0	0	1.00
In menopause	2	2	1.00
Hormonal therapy	0	0	1.00
Palpability	3	3	0.57
Imaging results (mammography)*	(n = 3)	(n = 5)	
Mass	2	1	0.46
Calcifications	1	2	1.00
Imaging results (ultrasound)*	(n = 3)	(n = 4)	
Complex cystic and solid	2	2	1.00
Orientation	3	4	1.00
Margin (circumscribed)	1	2	1.00
Posterior features (enhancement)	3	3	1.00
Vascularity	3	4	1.00

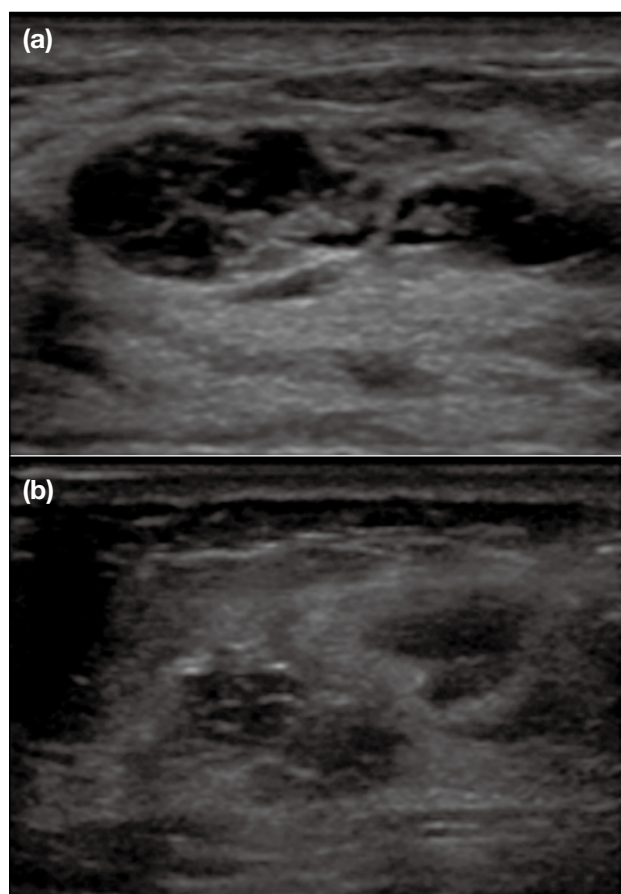
\* Only 8 had mammography and 7 patients had positive findings on ultrasound.

nodules.<sup>14</sup> Based on these studies and ours, we postulate that MLLs of the breasts, when visible on ultrasound, tend to have cystic components. Once again, however, we were unable to demonstrate a statistically significant sonographic feature that can enable differentiation between benign and subsequently upgraded lesions.

It has been observed that the presence of a MLL represents a spectrum of change from a progression of mucin-filled ducts through ADH and DCIS to invasive mucinous carcinoma. The upgrade rates of benign MLL on percutaneous CNB to high-risk / malignant lesion range from 0% to 43% in various studies compared with



**Figure 7.** Summary of pathological outcomes.



**Figure 8.** (a and b) Mucocele-like lesions detected as complex cystic and solid mass on ultrasound. The lesion in (b) was upgraded to ductal carcinoma in-situ on final surgical excision.

60% (3 out of 5) in ours.<sup>7,8,16-18</sup> In particular the upgrade rate to cancer was 20% (1/5) and to high-risk lesion 40% (2/5). Although our study was limited by the small number of cases, it shows a significant upgrade rate such that lesions yielding mucinous material or a MLL diagnosed on percutaneous breast CNB without atypia

should be subject to complete surgical excision. This will allow evaluation of the entire area to exclude the presence of atypia or carcinoma.

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